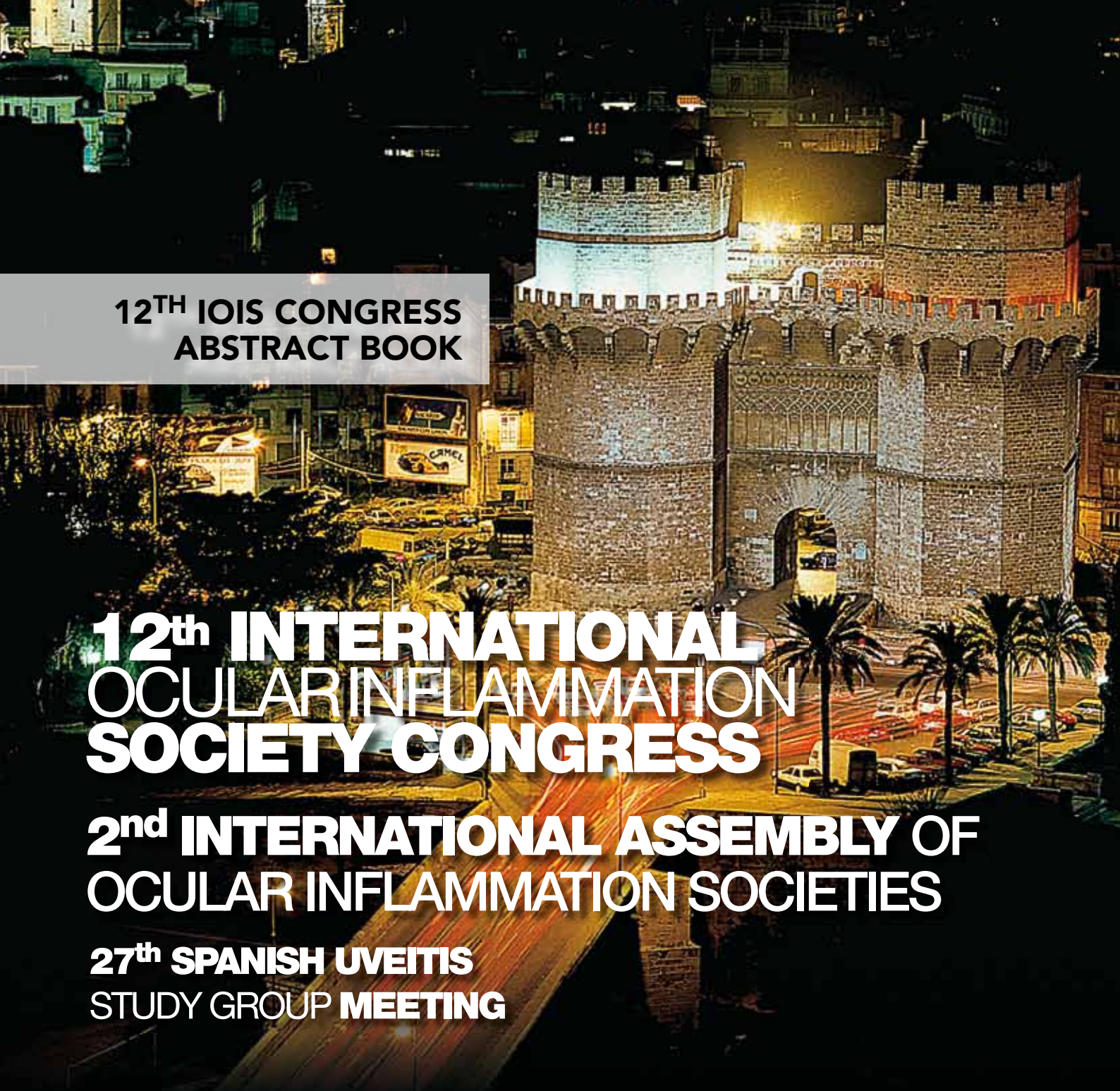

12TH IOIS CONGRESS
ABSTRACT BOOK

12th INTERNATIONAL OCULAR INFLAMMATION SOCIETY CONGRESS

2nd INTERNATIONAL ASSEMBLY OF OCULAR INFLAMMATION SOCIETIES

27th SPANISH UVEITIS STUDY GROUP MEETING

INTERNATIONAL OCULAR INFLAMMATION SOCIETY

IOIS

Sedu Sociedad Española de Uveítis e Inflamación Ocular

Gemu Grupo Español Multicéntrico de Uveítis

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Session 1

American Uveitis Society: *Imaging in Uveitis*

Potential Roles of Autofluorescence and Microperimetry in the Management of Uveitis

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University of Nebraska Medical Center
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To avoid cumulative damage and eventual functional loss, it is important to manage uveitis aggressively and to monitor retinal structure and function closely and objectively. For decades, visual acuity (VA) has been the gold standard in assessing retinal function. However, VA may not be the most objective parameter employed in assessing the health of the retina and response to therapy. Optical coherence tomography (OCT) has been the main tool for assessment of retinal structural integrity. However, the correlation of VA to the conventional methods of assessing retinal structures is inconsistent and hence unpredictable. Given that the functional outcome is the focus of interest and the objective of treatment in uveitis, such disconnect between VA and the status of the retina may limit the use of OCT and the conventional fluorescein angiography as a definitive tool to measure response to therapy. Microperimetry (or fundus-related perimetry) is a relatively new modality that assesses macular sensitivity and provides a near-exact correlation between fundus disease and corresponding functional defects while taking into account the fixation pattern and stability. In recent years, the study of the retinal fundus autofluorescence (FAF) has provided important information regarding the changes in retinal fluorophores with physiological aging and also in pathological conditions such as non-infectious uveitis. With the advent of confocal scanning laser ophthalmoscopy (cSLO), FAF images have left the research laboratories and have become more popular as a tool to assist in the diagnosis, management, and monitoring of retinal pathologies. The exact values of FAF images in the management of patients with uveitis, however, are not yet very well characterized.

Fluorescein Angiography in Uveitis

Albert Vitale, Moran Eye Center/University of Utah

Fluorescein angiography (FA) remains an essential tool in the management of uveitis. It may serve to delineate structural abnormalities that are associated with decreased vision including optic nerve inflammation, macular edema, retinal vasculitis, occlusive vasculopathy, retinal neovascularization, neurosensory retinal detachment, and choroidal neovascularization. The pattern and type of vascular and/or chorioretinal involvement seen on FA may be useful diagnostically in both noninfectious and infectious uveitic entities. Finally, FA is an exquisitely sensitive tool in delineating the degree of activity and extent of intraocular inflammation, and so may influence treatment decisions and is useful in monitoring the response to therapy.

Imaging in Uveitis: Spectral Domain/Enhanced Depth Imaging OCT and Widefield photography

Wendy M Smith, Mayo Clinic, Rochester, MN, USA

Purpose: To discuss the use of Spectral Domain Ocular Coherence Tomography (OCT) and widefield imaging in the diagnosis and management of uveitis.

Materials and Methods: Examples of the utility of these imaging modalities will be reviewed through case examples of different types of uveitis.

Conclusions: OCT can be used to demonstrate structural abnormalities which may not have been suspected on clinical exam, to quantify active inflammatory lesions in the retina and/or choroid, to show resolution and recovery of retinal structures, and to explain vision loss. Widefield photography allows better visualization of the extent of inflammatory activity and/or damage, particularly in cases with peripheral vasculitis or non-perfusion. Both modalities can provide invaluable information to guide uveitis diagnosis and treatment.

Imaging Uveitis With Indocyanine Green Angiography

Janet L. Davis MD
Professor
University of Miami Miller School of Medicine
Bascom Palmer Eye Institute
Miami FL USA

Purpose: Review the principles and capabilities of indocyanine green angiography (ICG) in the diagnosis and management of uveitis.

Methods: Case presentations of birdshot chorioretinopathy, serpiginous choroiditis, granulomatous panuveitis, multiple evanescent white dot syndrome, Vogt-Koyanagi-Harada disease and sympathetic ophthalmia comparing lesion definition achieved with ICG angiography vs. other imaging techniques such as fluorescein angiography, autofluorescence, and choroidal OCT.

Results: ICG angiography is uniquely able to image choroidal inflammatory lesions that are below the retinal pigment epithelium and therefore have normal fluorescein and autofluorescence images. Due to a broader sampling area, it is superior to OCT in detecting poorly visualized choroidal lesions or those that are peripheral to the usual range of OCT scanning. In birdshot chorioretinopathy, VKH and sympathetic ophthalmia ICG provides valuable information regarding disease activity, remission and relapse. Choroidal OCT analysis and autofluorescence can replace some functions of ICG in disease monitoring in VKH and serpiginous choroidopathy. Ability to perform simultaneous fluorescein and indocyanine angiography reduces the cost and inconvenience of the test.

Conclusion: ICG angiography is an old imaging modality that has been improved with high efficiency digital cameras. Despite the ability to perform better and more interpretable ICGs currently, improvements in non-invasive imaging may challenge its role as the most sensitive and specific imaging technique for posterior uveitis.

Session 2

IOIS Session: *Ocular Immunology and Immunopathology*

Role of gamma-delta T cells in experimental autoimmune uveitis (EAU)

Henry J Kaplan, Hui Shao and Deming Sun

γδ T cells are a subset of T cells with regulatory function. We have shown that depending on their activation status mouse γδ T cells can either enhance or inhibit the activity of IL-17(+) autoreactive T cells in EAU. More recently we observed that γδ T cells in naive C57BL/6 (B6) mouse do not express the IL-23R, whereas in immunized mice, it is expressed on >50% of γδ T cells. In vitro studies showed that IL-23R expression on γδ T cells is modulated by their state of activation, as weakly activated γδ T cells expressed the IL-23R, but highly activated γδ T cells did not. Functional studies showed that IL-23R(+) γδ T cells had the strongest suppressive effect on IL-17(+) autoreactive T cells, and that this effect was inhibited when the IL-23R was blocked by anti-IL-23R Ab or in the presence of excessive amounts of exogenous IL-23. We believe that the balance between the enhancing and inhibitory effects of γδ T cells is regulated by their level of IL-23R expression. The expression of variable IL-23R levels allows γδ T cells to have different regulatory effects on adaptive immune responses, conceivably as a result of αβ and γδ T cells competing for IL-23

Iris Involvement in Blau Syndrome

Debra A. Goldstein, MD (Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA)
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Rachida A. Bouhenni, PhD (Department of Ophthalmology, Summa Health System, Akron, Ohio, USA)
Scott Steiner, MD
Jeffrey J. Dunmire, BS (Department of Ophthalmology, Summa Health System, Akron, Ohio, USA)
Deepak P. Edward, MD (Department of Ophthalmology, King Khaled Eye Specialist
Hospital, Riyadh, Saudi Arabia; and Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, USA)

Purpose: To evaluate iris involvement in Blau syndrome using histology and immunohistochemistry.

Methods: Iridectomy specimens of a patient with treated Blau syndrome and a normal control were evaluated by light microscopy and immunohistochemistry using antibodies against CD4+, CD8+, HLA-DR, CD68+, NF-κB and IL-17.

Results: Blau iris tissue demonstrated increased numbers of CD4+ lymphocytes and CD68 negative, HLA-DR positive spindle shaped cells compared to normal iris tissue. Blau iris tissue also demonstrated elevated CD4+/CD8+ ratio and IL-17 and NF-κB immunolabeling. No macrophages, epithelioid cells, or granulomas were noted in the Blau specimen.

Conclusions: The persistent immunolocalization of inflammatory markers in an iris specimen from an aggresively treated patient with Blau syndrome suggests that further pathologic and immunohistochemical investigation of Blau ocular tissue is necessary to better understand the complexities of NOD2 activating mutations in the eye.

Th17 cells in steroid resistant uveitis

Richard Lee, NIHR Moorfields BRC and University of Bristol

This presentation will give an overview of the immune mechanisms by which corticosteroids exert their effects on the immune system and suppress inflammation. It will then focus on their impact on adaptive immunity, and in particular T helper cells, using both human in vitro experimental systems and murine models of intraocular inflammation. This will highlight the differential effect corticosteroids have on individual T cell subsets, and in particular the means by which one of these subsets – Th17 cells – escape corticosteroid suppression. Data generated from gene-expression profiling of human Th17 cells will then demonstrate their potential to be exploited as a predictive biomarker of response to corticosteroid treatment, and as a target for novel, T helper cell subtype-specific, therapies. The talk will conclude by focussing on the principal of patient stratification to tailor immunosuppressive treatment and optimise therapeutic and visual outcomes for patients with sight-threatening uveitis.

HLA-B51 and Behcet's Disease – the possible roles of B51 in the pathogenesis of disease

Yukihiro Horie[1], Akira Meguro[2], Nobuhisa Mizuki[2], Shigeaki Ohno[1]. 1. Department of Ophthalmology, Hokkaido University Graduate School of Medicine, Sapporo, Hokkaido, Japan. 2. Department of Ophthalmology and Visual Science, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan

The etiology of Behcet's disease (BD) is still unclear. However, as in many other inflammatory and/or immune-centered diseases, environmental factors are thought to trigger the symptomatology in individuals that harbor a particular genetic background.

Human leukocyte antigen (HLA) encodes genes involved in antigen processing and the presentation of antigenic peptides to T cells, and is instrumental in many innate and adaptive immune responses. Peptide binding to HLA molecules is the single most selective step in the recognition of pathogens by the adaptive immune system, and depends on specific amino acids in the peptide-binding groove of each HLA allele. The HLA genes are the most polymorphic ones in the human genome, and the alleles of the HLA genes vary widely among individuals. In addition, the distribution of HLA alleles varies widely according to ethnicity and geographic area. Therefore, variability in HLA allele types can lead to differences among individuals/ethnic groups regarding susceptibility to or protection from many diseases.

The strong association between BD and the HLA class I molecule, HLA-B51, has been well established. This association indicates that HLA-B51 is major genetic factor underlying BD. The HLA class I molecules bind peptides derived from endogenous proteins of host or pathogen origin and present them to CD8+ cells. Therefore, it is assumed that the immune response against the specific peptides that bind to HLA-B51-specific amino acids contributes directly to the development of BD. The characteristics of the peptide-binding motifs of HLA-B51 have already been reported; however, HLA-B51-restricted causative antigens for BD remain unclear.

In this presentation, we will show and discuss the HLA-B51 driven immune response in the pathogenesis of BD.

Session 3

Sociedad Panamericana de Enfermedades Inflamatorias Oculares: *Uveitis masquerades*

Primary intraocular lymphoma or intermediate uveitis

H. Nida Sen, National Eye Institute
Monica Dalal, National Eye Institute
Sunir Garg, Wills Eye Hospital
Catherine Morgans, Oregon Health Sciences University

Purpose: To descroibe a case of intermediate uveitis that failed to respond to conventional immunosuppressive treatment

Materials and methods: Interventional case report with a novel diagnostic basic science correlation.

Results: A 60-year-old Caucasian male in good health without systemic complaints was referred for evaluation of chronic bilateral vitritis and slowly progressive vision loss in both eyes over the past year. He had been evaluated by multiple ophthalmologists without a definite diagnosis. His evaluation prior to presentation included a normal neurologic evaluation and magnetic resonance imaging (MRI) of the brain. Vitreous biopsy of the left eye was negative for malignancy. Additionally, he had undergone a trial of oral prednisone followed by mycophenolate mofetil for approximately 4 months without therapeutic response.

His clinical exam at presentation was remarkable for mild intraocular inflammation in both eyes and retinal hemorrhages with apparent choroidal neovascularization (CNV) in the left eye, confirmed by -fluorescein angiogram (FA) and indocyanine green angiography (ICG) testing. Humphrey visual field (HVF) demonstrated diffuse depression in both eyes. Dark-adapted thresholds were markedly elevated. Further diagnostic testing and management will be discussed

Conclusion: Using clinical exam, detailed history and utilizing the application of an innovative approach the patient was diagnosed and treated.

Birdshot Chorioretinopathy?

Careen Y. Lowder, MD, PhD
Katie M. Hallahan, MD, Arun D. Singh, MD

Objective: Extranodal marginal zone B-cell lymphoma may present with complex and variable signs of ocular inflammation. We describe the clinical and histopathologic findings of a patient with extranodal marginal zone B-cell lymphoma who presented with unilateral anterior segment keratic precipitates, posterior inflammation and choroidal lesions mimicking birdshot chorioretinopathy, and a retrobulbar lesion identified on B-scan.

Design: Case report

Participant: Single patient

Intervention: The patient underwent biopsy of the retrobulbar lesion.

Result: Histopathologic examination revealed extranodal marginal zone B-cell lymphoma. The patient subsequently received intensity-modulated radiation therapy of the left orbit.

Conclusion: Extranodal marginal zone B-cell lymphoma should be included in the differential diagnosis of birdshot chorioretinopathy.

Actinomyces Retinochoroiditis ?

Cristobal Couto

A 67 year –old man consulted to our uveitis clinic with sudden loss of vision in the right eye and blurred vision in the left eye. Four months earlier, in a routine examination, it was found a spot on the lung. The patient's son, a chest surgeon, decided not to make a biopsy of the lesion because of the risk of pneumothorax. They performed a bronchoalveolar lavage where an Actinomyces Israelli was isolated and the diagnosis of pneumonia due to Actinomyces was made. Taken into account this medical history and the loss of vision in the right eye and the blurred vision in the left eye, his ophthalmologist made the diagnosis of retinitis due to Actynomyces and referred the patient to our clinic. On examination his BCVA was 20/200 in his right eye and 20/30 in his left eye. Neither anterior inflammation nor posterior inflammation was found. On fundus exmination a deep central, choroidal lesion was observed in both eyes without signs of inflammation. A bibliographic review was performed. We found many cases of endophthalmitis, several cases of corneal ulcers and a few of scleritis due to Actinomyces, however, we didn't find any case of posterior uveitis. Ophthalmoscopic findings resembled more a bilateral choroidal metastasis than a retinitis. A mode B ultrasound was done which confirmed the presence of an occupying mass in the choroid and the diagnosis of choroidal metastasis was made. A lung biopsy was finally performed which revealed the diagnosis of undifferentiated adenocarcinoma. The patient had also brain and liver metastasis and at sixth months follow-up he died.

Behcet's Disease or Not Behcet's Disease?

J. Fernando Arevalo

Introduction: A 33-year-old Arab man presented with a sudden decrease in VA OU. He was diagnosed with bilateral exudative retinal detachments (ERD). He had a history of oral aphthous ulcers.

Case Report: His BCVA was 20/60 OD and 20/200 OS. Slit lamp examination showed no inflammation. Color fundus photographs, fluorescein and SD-OCT will show bilateral ERDs that were thought to be Behcet's disease and treated with immunosuppression (steroids).

Conclusions: The case will be opened for discussion. Later I will demonstrate the correct diagnosis: Bullous Chronic Central Serous Chorioretinopathy exacerbated by steroids managed with discontinuation of steroids, half fluence PDT and IVT bevacizumab.

Acute Retinal Necrosis?

Debra A. Goldstein, MD. Northwestern University, Chicago, Illinois

We present the case of a patient with a clinical diagnosis of acute retinal necrosis. Investigations, including retinal biopsy, ultimately revealed the correct diagnosis.

Session 5

IOIS President'symposium: *Recent Advances in Diagnosis and Treatment of Ocular inflammations and Infections*

Immunosuppression: the evidence base for current practice.

Douglas Jabs, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Over the past 30 years a consensus has emerged that immunosuppression produces superior outcomes for many of the more severe uveitides, particularly posterior and panuveitides. Although much of the data comes from single center case series, more sophisiticated statistical analyses of cohorts (such as longitudinal data analysis) have demonstrated superior outcomes with immunosuppression for birdshot chorioretinitis (BSCR), multifocal choroiditis with panuveitis (MFCPU), Vogt-Koyanagi Harada (VKH) disease in chronic phase, and an inability to control the disease at acceptably low doses of oral corticosteroids (i.e. prednisone 7.5 mg/day or less) without immunosuppression. In juvenile idiopathic arthritis-associated chronic anterior uveitis (JIA CAU), similar statisitcal approaches have demonstrated a decrease in visual impairment and blindness with immunosuppression. Randomized clinical trials have demonstrated efficacy for immunosuppressive agents in Behcet's disease (BD). The Multicenter Uveitis Steroid Treatment (MUST) Trial, a randomized clinical trial, and the Systemic Immunosuppressive Treatemtn for Eye disease (SITE) study, a large retrospective cohort study with long follow-up, have demonstrated the short- and long-term safety of immunosuppression. Collectively these data suggest that patients needing treatment with serpiginous choroiditis, BSCR, MFCPU, BD, and chronic VKH should be treated with immunosuppression, and that patients with JIA CAU requiring more than topical corticosteroids should be treated with immunosuppression. In addition, immunosuppression is needed in the majority of patients with sympathetic ophthalmia for corticosteroid sparing.

VEGF: a pro-inflammatory cytokine

Susumu Ishida Ishida

The discovery of vascular endothelial growth factor (VEGF) in 1989 led to significant breakthrough in elucidation of molecular mechanisms in diabetic retinopathy. VEGF proved to be the identical protein with vascular permeability factor (VPF) originally reported in 1983. Retinal edema and neovascularization, both of which are the major abnormalities directly causing vision loss in diabetic retinopathy, are associated with and dependent on its pathological functions as VPF and VEGF, respectively. Moreover, VEGF was shown to be a pro-inflammatory cytokine that stimulates gene expression of various inflammation-related molecules including leukocyte adhesion molecules and chemoattractants, which led us to regard diabetic retinopathy to be at least in part as a result of inflammation. Nowadays, anti-VEGF treatments as well as corticosteroid therapy are utilized to suppress inflammatory pathogenesis

in diabetic macular edema. In this context, VEGF blockade strategy has recently been expanded to other inflammatory diseases with macular edema. In this presentation, VEGF biology for better understanding of clinical application to macular edema will be discussed.

Peripheral Ulcerative Keratitis (PUK)

C. Stephen Foster, MD, FACS, FACR, FARVO. Harvard Medical School, Massachusetts Eye Research and Surgery Institution (MERSI), Cambridge, MA, USA

Peripheral Ulcerative Keratitis (PUK) may occur as a consequence of trauma, cancer, infection or autoimmunity. Solving a patient's PUK problem obviously demands understanding the underlying cause of the PUK. The matter of such understanding can be a matter of life or death, since some causes of PUK are systemic and potentially lethal. Investigation of the patient with PUK must proceed rapidly but extremely thoroughly, beginning with a meticulous and exhaustive review of the patient's systems, as any good internist would assess the patient's ROS. A questionnaire to assist in this part of the investigation may be found at http://www.uveitis.org/uveitis-questionnaire. Positives on the ROS must be pursued through all manner of investigation, even if that involves biopsy of ocular and/or non-ocular tissue. Case examples of such diagnostic pursuit, as well as treatment of various causes of PUK will be presented.

Diagnosis of intraocular tuberculosis:A multiplex approach

Amod Gupta, Advanced Eye Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, India
Kusum Sharma, Department of Medical Microbiology, Post Graduate Institute of Medical Education and Research, Chandigarh
Reema Bansal, Advanced Eye Centre, Post Graduate Institute of Medical Education and Research, Chandigarh
Aman Sharma, Department of Internal Medicine, Post Graduate Institute of MedicalEducation and Research, Chandigarh
Nikhil Beke, Advanced Eye Centre, Post Graudate Insitute of Medical Education and Research, Chandigarh

The Gene Xpert MTB/RIF (GX) assay is a novel method for diagnosis of tuberculosis and detection of Rifampicin resistance. Multi-targeted PCR (MPCR) is a sensitive method for diagnosis of ocular TB. In this study results of GX are compared with MPCR. Rifampicin resistance results of GX assay were compared with rpoB gene sequencing. Gene Xpert MTB/RIF assay and MPCR were carried out from ocular fluid samples of 74 subjects. 44 were clinically suspected of intraocular tuberculosis (IOTB), 15 were disease controls and 15 were normal controls. All positive cases were also evaluated for Rifampicin resistance by rpoB gene sequencing. Gene Xpert MTB/RIF assay was positive in 15 out of 44 and MPCR was positive in 32 out of 44 patients suspected of IOTB. Both assays were negative in all normal and disease controls. MPCR and Gene Xpert had sensitivity of 72.72 %, and34.04 % respectively. Whereas specificity of both Gene Xpert and MPCR was 100 %. With Gene XpertMTB/RIF assay, true RIF resistance was detected in 1(6.66%) out of 15MTB positive patient and one was detected as false RIF resistance, when results were compared with rpoB gene sequencing. With ropB sequencing 2 out of 32 positive patients were RIF resistant and 30 were Rif sensitive. MPCR is a sensitive method for diagnosis of ocular TB and rpoB gene sequencing is better method for diagnosis of Rif resistance in ocular tuberculosis.

Early ICGA-guided diagnosis and early and sustained treatment modifies the phenotype of birdshot retinochoroiditis.

Carl P, Jr Herbort, University of Lausanne and Centre for Ophthalmic Specialised care
Marina Papadia, Centre for Ophthalmic Specialised care

Background: Diagnostic criteria for birdshot retinochoroiditis (BRC) published as the result of a concensus conference include as a required criterion 3 peripapillary birdshot fundus lesions and as an exclusion criterion keratic precipitates (KPs). These guidelines were established in an ICGA-

refractory environment. The aim of this work was to demonstrate that these criteria are inadequate and even incorrect, not allowing early diagnosis and early management of the disease.

Methods: The impact of early, vigorous, and prolonged therapy on the evolution of indocyanine green angiography (ICGA) signs and fundus appearance of BRC patients. Treatment delay was calculated for each patient, and patients were classified into two groups: treatment delay of less (early group) or more (delayed group) than 10 months. Fundus pictures and ICGA frames from the initial and the last follow-up visit were assessed. Fundus pictures were evaluated for the presence of at least three circumpapillary BRC lesions. ICGA pictures were evaluated for the presence of lesions (hypofluorescent dark dots, fuzziness of vessels). Differences were compared between the two groups and between first and last follow-up visit.

Results: In the "early" group, 5/6 patients had no BRC fundus lesions at presentation, but 7/7 patients in the "delayed" group displayed typical lesions. At last follow-up, 5/6 "early" patients showed no fundus lesions, and 6/7 "delayed" patients retained their fundus lesions. At entry, all 13 patients exhibited lesions on ICGA. At last follow-up, ICGA lesions had disappeared in 4/6 "early" patients and 3/7 "delayed" patients. An adjunct finding was the presence of KPs in 3/13 patients, meaning that in close to 25% of BRC patients would be falsely excluded if those criteria were used.

Conclusion: Early diagnosis using ICGA and early and sufficiently dosed inflammation-suppressive treatment modifies the phenotype of BRC preventing the appearance of typical BRC fundus lesions.

New findings in the ocular treatment of Toxoplasmosisand Prevention of recurrences

Rubens Belfort Jr

Toxoplasmosis infects probably over 1,5 billion of individuals in the world and is the most frequent and important cause of infectious as well as posterior uveitis in many countries. With no probable vaccine in the horizon for the next many years it will continue to be a major problem in normal and immunosuppressed patients. The clinical picture of Ocular Toxoplasmosis is well known and a good ocular exam providesthe diagnosis based also in the presence of specific circulating antibodies or the presence of DNA material on the ocular tissues/fluids or the blood. One of the problems for many patients is the recurrences that threats the remaining vision and bring great morbidity as well as social and economic costs. The treatment for the active cases is still based in the clinical accumulated experience of experts and has never been well addressed with good methodology. The reasons for these attacks comprise the presence of toxoplasma in the retina and extra ocular structures as well as immunologic mechanisms related to the presence of organisms or its DNA even inside circulating mononuclear cells. Also auto immunity related to retinal and choroidal antigens may play a role. The classical treatment (association of pirimethamine with sulfadiazine) presents problems related to side effects and low adherence and has never been proved to be better. Bactrim (sulfamethoxazole and trimethoprim), also available as a generic drug has been used by many.Systemic and intra ocular Clindamycin has also been used including in special cases of contraindications or allergy to the primary treatment. A prospective randomized clinical trial with Bactrim compared to placebo has shown its effect in the prevention of recurrences and our recent data (will be presented) shows a loss of effect years after the drug is suspended and a possible relation to circulating toxoplasmic genetic material.

Neurodegeneration in Optic Neuritis: Can it be fixed

Dr. J. Guy. USA

Targeting the inflammatory response is currently the mainstay of treatments for human optic neuritis (ON) and multiple sclerosis (MS). However, these disease modifying drugs do not alter the

progressive neurodegeneration that leads to irreversible visual loss and disability. Here we focused on the role of the mitochondrion as a potential source of ROS and target of injury. Mitochondria were isolated from the retinas and optic nerves of mice 3 and 6 days after sensitization for experimental autoimmune encephalomyelitis (EAE). At this early stage, none of the animals exhibited clinical signs of EAE. As an initial gauge of ROS activity we used the peroxynitrite-mediated nitration of tyrosine residues. Peroxynitrite formed by the reaction of two other ROS, superoxide and nitric oxide has been implicated in the pathogenesis of EAE, ON and MS. Using mass spectroscopy we identified key mitochondrial proteins HSP70 and NDUFA6 with oxidative damage. Injury to an NDUFA subunit results in misassembly of the 45 subunit complex I. In addition, oxidative damage to mitochondrial heat shock protein 70 (mtHSP70) that acts as a chaperone for transport of nuclear encoded respiratory complexes from the cytoplasm into the inner matrix contributed to a reduction of import of nuclear encoded complex I subunits. Complementation of mtHSP70, NDUFA6 or bypassing the 45 subunit complex I with a single subunit yeast NDI1 complex I restored visual function, improved oxidative phosphorylation and reduced oxidative stress suggesting that targeting mitochondrial injury and dysfunction that primes neurodegeneration may be beneficial in human optic neuritis and MS.

Role of Vitrectomy in Resolution of Medically Non-responsive CME in Uveitis

Henry J Kaplan, MD FACS

The major cause of visual loss in uveitis, regardless of etiology, is cystoid macular edema (CME). In most patients, CME will resolve with control of inflammation through corticosteroid therapy administered topically, periocularly, intravitreally, and/or systemically. In patients who are intolerant or nonresponsive to corticosteroids, the use of corticosteroid-sparing agents (eg, cytotoxic or biologic drugs) may be useful. However, a subset of patients will have decreased vision secondary to CME regardless of the medical regimen employed. The role of an adherent posterior hyaloid over the macula in the persistence of CME in these cases has only recently been appreciated. The importance of OCT imaging in the diagnosis of vitreomacular traction and the therapeutic benefit of surgical removal of the posterior hyaloid in persistent CME associated with uveitis will be discussed.

Session 6

IOIS session: *Diabetes and Age-related Macular degeneration*

Myeloid cell activation can dictate angiogenic potential in retinal and choroid

Andrew Dick, University of Bristol
Dave Copland, University of Bristol
Jian Liu, University of Bristol
Wei-Kang Wu, University of Bristol
Lindsay Nicholson, University of Bristol
Scott Robbie, Institute of Ophthalmology
Robin Ali, Institute of Ophthalmology
James Bainbridge, Institute of Ophthalmology

Myeloid cells are highly adaptable to environmental cues that regulate tissue responses to injury, inflammation or degeneration. The retina and choroid remain healthy as a result of keeping in check the activation status of myeloid cells (microglia and choroidal macrophages) via, for example CD200R and TREM-2. Following inflammation, as observed in Experimental Autoimmune Uveoretinitis (EAU), the tissue myeloid cell number and activation do not return to premorbid state and the result, even in absence of overt clinical inflammation is continued tissue damage and neovascularisation – altered health. Resetting the threshold of activation of myeloid cells is readily observed in the laser induced angiogenesis model (L-CNV), where angiogenic response is precipitated by early influx of CCR2 monocytes as well as microglia to site of laser injury. This can be attenuated and perturbed via augmenting CD200R signaling or via alternative activation of cells via IL-4 or 13 conditioning. The mechanisms will be discussed but the myeloid cell restricted responses affords opportunities to alter the retinal environment, reset myeloid activation responses and return tissue health.

Interleukine-17 as an attractive therapeutic target in age-related macular degeneration

Chi-Chao Chan, National Eye Institute, National Institutes of Health, USA
Daniel Ardeljan, National Eye Institute and Johns Hopkins University Medical School

Age-related macular degeneration (AMD) is the leading cause of central irreversible blindness in elderly. Although the etiology and pathogenesis of AMD remain unclear, AMD pathology illustrates the critical role of the retinal pigment epithelium (RPE). We found aberrant expression of IL-17A (IL17A) and IL17RC in AMD macula. In vitro, IL17A induces RPE cell death characterized by the accumulation of cytoplasmic lipids and autophagosomes with subsequent activation of pro-apoptotic Caspase-3 and Caspase-9, which is blocked by siRNA knockdown of IL17RC. IL17-dependent retinal

degeneration in a genetic mouse model can also be blocked by gene therapy with adeno-associated virus vector encoding soluble IL17 receptor. This intervention rescues RPE and photoreceptors in a MAPK-dependent process. These data suggest that targeting of the IL17 pathways and molecules could hold therapeutic potential in AMD.

Light-induced cellular responses in the RPE-choroid: the barrier disruption and inflammation

Yoko Ozawa

Purpose. To elucidate the influences of light exposure on the retinal pigment epithelium (RPE) in vivo, that may be involved in the pathogenesis of age-related macular degeneration (AMD).

Materials and Methods. BALB/c mice were exposed to light at 2000 lux for 3 hours. Flat-mount RPE samples were immunostained with anti-ZO-1 antibody for evaluating tight junction, anti-N-cadherin and anti-β-catenin antibodies for adherens junction, and stained with phalloidin for actin cytoskeleton. The reactive oxygen species (ROS) level was measured using DCFH-DA, Rho-associated coiled-coil forming kinase (ROCK) activity was by ELISA. Cytokine expression was analyzed by realtime RT-PCR and/or ELISA in the RPE-choroid, and macrophage recruitment was by realtime RT-PCR and immunohistochemistry. Either an antioxidant, N-Acetyl-L-cysteine (NAC), or a ROCK inhibitor, Y-27632, were administered to analyze the roles of ROS and ROCK activation, respectively.

Results. Light exposure disrupted staining patterns of tight junctions, adherens junctions and actin cytoskeleton in the RPE, where ROS was elevated. However, NAC treatment avoided the RPE changes, reducing ROS. ROCK activity increased after light exposure was suppressed by NAC, and the structural disruptions were suppressed by Y-27632. The levels of MCP-1, CCL11, and IL-6 increased after light exposure were suppressed by NAC. Light-induced MCP-1 and IL-6 were suppressed by Y-27632. Macrophage recruitment after light exposure was also suppressed either by NAC or Y-27632.

Conclusions. Light exposure induced ROS and Rho/ROCK activation, which caused disruption of cell-cell junctions (tight junctions and adherens junctions) and actin cytoskeleton, the RPE's barrier structure, and induced AMD-associated pathological changes in the RPE-choroid.

Is diabetic retinopathy an inflammatory disease?

Miho Nozaki, Nagoya City University Graduate School of Medical Sciences
Yuichiro Ogura, Nagoya City University Graduate School of Medical Sciences

Recently, many studies revealed the important role of leukocyte in pathogenesis of diabetic retinopathy. Leukocyte has large cell volume, high cytoplasmic rigidity, natural tendency to stick to the vascular endothelium, and capacity to generate toxic superoxide radicals and proteolytic enzymes. In diabetes, leukocyte has been reported as less deformable and more activated, and may be involved in capillary non-perfusion, endothelial cell damage, and vascular leakage in retinal microcirculation.

We used acridine-orange angiography (AO angiography) technique to label leukocyte, and capture leukocyte in vivo in diabetic rats. These studies showed that leukocyte were trapped associated with areas of downstream non-perfusion in the retinal microcirculation. And in diabetic rats, adhesion molecules were upregulated in the vascular endothelial cells.

And panretinal photocoagulation is a golden standard therapy for proliferative diabetic retinopathy, but sometimes the patients developed macular edema after laser photocoagulation. We studied the effect of laser photocoagulation on mice, and found temporal upregulation of VEGF, ICAM-1, MCP-

1 and IL-6 in the retina. In 2006, semi-automated pattern scan laser technology has been invented, and pattern scan laser is becoming a first-line treatment tool for diabetic retinopathy. We compared the level of inflammatory cytokines with conventional laser and pattern scan laser, and found pattern scan laser induced less upregulation of inflammatory cytokines, which give us supportive data to prevent macular edema after laser photocoagulation.

A novel role for high mobility group box-1 in the pathogenesis of diabetic retinopathy

Ahmed Abu El-Asrar, King Saud University
Ghulam Mohammad, King Saud University
Mohammad Mairaj Siddiquei, King Saud University
Amira Othman, Georagia Health Sciences University
Mohamed Al-Shabrawey, Georgia Health Sciences University

Purpose: Extracellular high-mobility group box-1 (HMGB-1) functions as a proinflammatory cytokine and exhibits angiogenic effects. The pupose of this study was to investigate the expression of HMGB-1 signaling pathway components in the retinas of diabetic rats and to examine the effect of intravitreal adminstartion of HMGB-1 on the retinas of rats.

Methods: The retinas of diabetic and intravitreally injected HMGB-1 rats were studied using immunohistochemistry, Western blotting, co-immunoprecipitation and enzyme-linked immunosorbent assay. The effect of HMGB-1 on retinal endothelial cell barrier function was evaluated using electrical cell-substrate impedance sensing system (ECIS).

Results: Diabetes induced significant upregulation of the expression of HMGB-1, receptor for advanced glycation end products(RAGE), ERK1/2 and nuclear transcription factor Kappa B (NF-κB), whereas the expression of toll-like receptor 2 (TLR2) and occludin was significantly downregulated. Co-immunoprecipitation studies revealed significant increase in interaction between HMGB-1 and RAGE. HMGB-1 reduced transendothelial electrical resistance of bovine retinal endothelial cells. Intravitreal administration of HMGB-1 to normal rats induced significant upregulation of intercellular adhesion molecule-1(ICAM-1), soluble intercellular adhesion molecule-1 (sICAM-1), HMGB-1, RAGE, ERK1/2, and NF-κB, and significantly increased retinal vascular permeabilty, whereas the expression of TLR2 and occludin was downregulated . Oral administration of glycyrrhizin, a specific inhibitor of HMGB1, attenuated diabetes-induced upregulation of HMGB-1 expression, NF-κB activation and downregulation of occludin expression.

Conclusions: Our findings provide evidence that in the diabetic retina, HMGB-1 possibly interacts with RAGE and activates ERK1/2 and NF-κB to generate an inflammatory response and disrupt retinal vascular barrier.

Intraocular inflammation and renin-angiotensin system activation

Susumu Ishida Ishida

The renin-angiotensin system (RAS) plays a potential role in the development of end-organ damage, and tissue RAS activation has been suggested as a risk factor for diabetic retinopathy. We have recently shown the significant involvement of (pro)renin receptor [(P)RR] with retinal inflammation in a rodent model of early diabetes. We herein aim to elucidate (P)RR-associated pathogenesis of fibrovascular proliferation, the late-stage angiogenic complication in human diabetic retinopathy. Vitreous fluids from 23 eyes with proliferative diabetic retinopathy (PDR) and 16 controls with non-diabetic, idiopathic macular diseases (macular hole and epiretinal membrane) were collected and protein levels of soluble (P)RR were measured by ELISA, and immunofluorescence was performed to assess localization of (P)RR and related molecules in

fibrovascular tissues from PDR eyes. (P)RR immunoreactivity was detected in neovascular endothelial cells, co-localized with prorenin, phosphorylated extracellular signal-regulated kinase (ERK) and vascular endothelial growth factor (VEGF). Prorenin application to human retinal microvascular endothelial cells significantly upregulated mRNA expression of VEGF, especially the VEGF165 isoform, which was abolished by (P)RR or ERK signaling blockade. Proteases known for the cleavage of (P)RR including furin were positive in endothelial cells in fibrovascular tissues. Protein levels of soluble (P)RR in the vitreous fluids were higher in PDR eyes than in non-diabetic control eyes, and were significantly correlated with vitreous prorenin and VEGF levels and the vascular density of fibrovascular tissues. Our data using human samples provide the first evidence that (P)RR is associated with pathogenic activity in PDR.

Session 7

IOIS session: *Intermediate, posterior and pan-uveitis*

Intermediate uveitis and retinal vasculitis: clinical findings and imaging

Dr Alfredo Adan (Hospital Clinic,Barcelona University,Spain)
(Definitions. Clinical diagnosis. Prevalence. Outcome measures.)

Retinal vasculitis is a potentially sight-threatening inflammatory eye condition characterized by an abnormal appearance of the retinal vasculature.Intermediate uveitis refers to inflammation localized to the vitreous and peripheral retina.Pars planitis, a specific entity within the anatomical group of intermediate uveitis,is characterized by the presence of white exudates (snowbanks) over the pars plana and ora serrata or by aggregates of inflammatory cells in the vitreous (snowballs). Clinical diagnosis in retinal vasculitis include perivascular sheathing and vitreous cells .Changes in retinal vasculitis and intermediate uveitis can include vascular leakage and occlusion are best appreciated and detected with fluorescein angiography.Wide field retinal Imaging provides 200 degrees of photographic and angiographic views of the fundus In consequence, may be helpful in the clinical management of retinal vasculitis and intermediate uveitis.Areas of neovascularization and non-perfusion were easily identified with wide field fluorescein angiography in those cases . Macular edema is a common structural ocular complication encountered in patients with intermediate uveitis and retinal vasculitis . Optic coherence tomography (OCT) may be the best initial test for evaluation of suspected macular edema in those patients.

Differential diagnosis and systemic work up in retinal Vasculitis

Vishali Gupta

Retinal vasculitis is an inflammatory disease of the blood vessels of the retina that may be associated with primary ocular conditions or with inflammatory or infectious diseases in other parts of the body (systemic diseases). The common primary causes of retinal vasculitis where vessel is the primary target of the inflammatory process and the process is localized to the eye include Idiopathic Intermediate uveitis of the pars planitis type, Frosted branch angiitis, Idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) wheras those involving the eye and other organs (primary systemic associations) include Giant cell arteritis, Takayasu arteritis, Polyarteritis nodosa, Wegener's granulomatosis etc. The causes of secondary vasculitis (where vasculitis is a prominent feature but is secondary to an inflammatory process not primarily directed against the vessel) may be localized to the eye e.g., Ocular sarcoidosis, TB, Toxoplasmic retinochoroiditis etc or may be associated with systemic involvement like Sarcoidosis, Behçet's disease, Multiple sclerosis, Tuberculosis, Syphilis, Lyme disease etc. The laboratory evaluation should be directed by a careful history and physical

examination followed by targeted laboratory and radiological testing. Investigating a case of retinal vasculitis involves a tailored approach. Once a differential diagnosis is derived from a detailed history, ocular examination and a relevant systemic evaluation, only the specific tests are carried out. Random screening with full battery of tests is rarely productive and can be misleading. The presentation aims to discuss the differential diagnosis and systemic work-up in a patient with retinal vasculitis.

Immunopathology of intermediate uveitis and retinal vasculitis

Justine R. Smith, FRANZCO, PhD. Flinders University of South Australia, Adelaide, AUSTRALIA

The immunopathogenesis of human posterior segment intraocular inflammation, including intermediate uveitis and retinal vasculitis, continues to be an active area of research. Genetic studies suggest that susceptibility is linked to specific human leukocyte antigens and polymorphisms of cytokines, including tumor necrosis factor and interleukin-10. Inflammation of the posterior segment of the eye typically involves a mixed leukocytic infiltration with T and B lymphocytes, macrophages and granulocytes. Th1 and Th17 cells are implicated as initiators of disease, although tissue damage has been linked to macrophages, generated from immigrating blood monocytes. Cells enter the posterior eye through a complex molecular interaction with the retinal vascular endothelium that involves adhesion molecules and chemokines. Our efforts to profile the human retinal endothelial cell have demonstrated relatively high expression of multiple proteins involved in leukocyte migration. This suggests that when ocular immune privilege fails and posterior segment intraocular inflammation is initiated, the retinal endothelium is appropriately constituted to facilitate leukocyte ingress. Follow up studies suggest that human Th1 and Th17 cells routinely use intercellular adhesion molecule-1 to cross the retinal endothelium. The molecular signals controlling human monocyte migration are a subject for future study. Adhesion proteins and chemokines may be targets for new biologic therapies in patients with intermediate uveitis and/or retinal vasculitis.

Medical treatment of pars planitis. What has changed

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Purpose. To compare clinical manifestations, frequency of complications and response to treatment of Pars Planitis (PP) in adults and children, and to evaluate indications of treatment

Material and method. A literature review of PP clinical manifestations and outcome was made. The results of a prospective, interventional, longitudinal study of the efficacy and safety of subcutaneous weekly injections of methotrexate (12.5 mg/ m2 corporal surface) in a series of childhood will be presented. Main outcome was decreased in vitreous haze at 3 months of treatment. Secondary outcomes included: change in anterior chamber inflammation, in best-corrected visual acuity (BCVA) and frequency of adverse side effects.

Results. Forty two patients have been recruited, 54.76% are male, mean age 7.5 yrs. (range 3-13 yrs.), 92.86% were bilateral. At admittance BCVA (logMar) was 0.626, vitreous haze (VH) was ≥ 2+ in 45.3% of cases. At 3 mo. (29 patients)BCVA was ≥ 0.48 in 50.1%, VH was ≥ 2+ in 4.8%, 0-0.5+ in 33.3%. No patient reported serious adverse side effects.

Conclusions. In this series of childhood PP cases, subcutaneous injections of metotrexate seems to decrease VH and improve BCVA without serious adverse side effects.

Medical Treatment of Retinal Vasculitis

H. Nida Sen, National Eye Institute Austin Fox, National Eye Institute

Purpose: Retinal vasculitis is a poorly defined and understood ocular inflammatory disease. According to Standardization of Uveitis Nomenclature (SUN) working group definition retinal vasculitis is a descriptive term and is characterized by perivascular sheathing, vascular leakage or occlusion on fluorescein angiogram. Retinal vasculitis can be primary or secondary to systemic inflammatory or infectious diseases. Primary or idiopathic retinal vasculitis occurs as an isolated condition in the absence of any evidence of systemic vasculitis and it is believed to be autoimmune though exact mechanism is unknown. Treatment of retinal vasculitis can range from topical or local treatment to systemic treatment with non-biologic immunosuppressives, biologic disease-modifying antirheumatic drugs, alkylating agents, and depends on the severity and underlying etiology. More recently biologics have been shown to be effective in certain forms of retinal vasculitis. Different treatment options and response to therapy will be discussed.

Methods: Patients with retinal vasculitis with or without associated systemic disease are identified. Retinal vasculitis cases of various etiologies have been reviewed. Systemic disease associations, treatment options and outcomes are discussed.

Results: Majority of patients required more than one immunomodulatory agent with a small minority requiring alkylating agents.

Conclusion: Retinal avsculitis can have a guarded prognosis. Many patients require multiple medications to control inflammation. Biologics and alkylating agents are required in severe cases.

Session 8

International Uveitis Study Group: *Autoinflammation*

Autoinflammation vs Autoimmunity – the basics

Graham Wallace

Autoinflammation has been described by McDermott and McGonigle as self-directed inflammation, whereby local factors at sites predisposed to disease, lead to activation of innate immune cells, with resultant tissue damage. The main parameters for the difference between autoinflammation and autoimmunity are genetic, in that autoimmunity is driven by mutations in genes associated with the adaptive immune response, and autoinflammation in genes associated with the innate system. In particular autoinflammation has been linked to activation of the inflammasome and production of interlukin-1 (IL-1). I will discuss these associations in the context of monogenic diseases, but show that in polygenic conditions both autoinflammation and autoimmunity may play a role.

Systemic autoinflammatory disease

Martin van Hagen, Erasmus University Medical Centre and Eye Hospital Rotterdam, the Netherlands

Autoinflammatory syndromes are characterized by recurrent noninfectious febrile attacks. Activation of the innate immune system, in the absence of autoantibodies or autoreactive T cells, is the immunological basis of these syndromes. Molecular genetics revealed gene defects that are implicated in these syndromes by changing the structure and function of the corresponding proteins. Previously, autoimmune diseases have traditionally been categorized according to the target and the abnormal immune response. Recent studies however suggest that more common immune mediated inflammatory diseases (IMID), including autoimmune diseases, may have an autoinflammatory component. A disease spectrum has been postulated ranging from; monogenetic autoimmune disease-polygenetic autoimmune disease-mixed autoimmune/autoinflammatory-polygenetic autoinflammatory disease-and monogenetic autoinflammatory disease. This spectrum includes various systemic diseases in which the eye can be involved. For example ankylosing spondylitis, psoriasis and Behcet's disease.

In this presentation we discuss the autoimmune/autoinflammatory component in the various systemic IMIDs that are associated with inflammatory eye disease.

Autoinflammation and Uveitis

Manfred Zierhut, Centre of Ophthalmology, University of Tuebingen, Germany

Autoinflammatory disorders are based on a dysfunction of the innate immune system, leading occasionally to ocular inflammation like conjunctivitis and uveitis. The best characterized disorders

of that group of disorders are hereditary diseases belonging to CAP (Cryopyrin-associated periodic)-Syndromes. This group includes the "Muckle-Wells-Syndrome"(MWS), the "Familial Cold autoinflammatory Syndrome"(FCAS) and the "Neonatal-onset Multisystem Inflammatory Disease". CAPS are induced by an overproduction of IL-1ß. We are controlling a Five-Generation-Family with CAPS. Their members show mostly an overlap between MWS und FCAS. Clinical findings of this family will be presented with manifestation in the eyes, skin, joints and ears. In 15 of 29 patients a mutation of the exon 3 of the NLRP3 Genes had been detected.

In 13 members of the family we used an anti-IL1ß (Canakinumab) treatment. Besides a minimal signs of arthritis and a mild conjunctivitis all signs of the CAPS had disappeared. Other types of uveitis may also belong to the group of autoinflammatory disorders, like Behçet's Disease and ankylosing spondylitis.

Autoinflammation in Behcet's Disease

Ahmet Gül, Istanbul, Turkey

Autoinflammatory diseases are first described as a group of inherited disorders that are characterized by seemingly unprovoked episodes of inflammation at certain locations and absence of high-titer autoantibodies or antigen-specific T cells. Its definition has been updated to encompass multifactorial diseases with similar features such as increased inflammatory response, mediated predominantly by the cells and molecules of the innate immune system in patients with a significant genetic predisposition. Behçet's disease is an

inflammatory disorder of unknown etiology, and many of its recurrent manifestations overlap with those of hereditary autoinflammatory conditions. Behçet's disease has a complex genetic etiology, and genetic factors play a role in its peculiar geographic distribution. Association with HLA-B*51 allele is the strongest susceptibility factor described so far. As a Class I HLA molecule, it has both adaptive and innate immune functions, but inflammatory mechanisms related to HLA-B*51 in Behçet's disease are yet to be clarified. Recent genomewide association studies revealed the contribution of relative IL-10 deficiency to the increased inflammatory features of Behçet's disease. Also, certain polymorphisms in the autoinflammatory disease genes such as MEFV and NOD2 as well as in the IL-1 locus were found to be associated with Behçet's disease. Identification of Behçet's disease-related autoinflammatory pathways is expected to help develop more targeted and effective treatments for patients with inadequate response to standard of care.

Therapeutic targets for autoinflammatory disease:

Richard Lee. NIHR Moorfields BRC and University of Bristol

This presentation will focus on the key components of the innate immune response highlighted in the previous talks in this session which have the potential to be manipulated therapeutically. Particular emphasis will be placed on the success of targeted immunomodulation in canonical autoinflammatory diseases. An overview of biologic treatments for autoinflammatory uveitis will then be given, followed by a perspective on future directions in the field.

Session 10

IOIS session: *Drug delivery and emerging treatments of ocular inflammations*

What Is in the Horizon for Uveitic and Ocular Inflammatory Therapy: Should We Have Hope?

IL-1beta Inhibition: How Specific Can We Get?
Ilknur Tugal-Tutkun

IL-1beta is a potent pro-inflammatory cytokine, which is synthesized by cells of the innate immune system in early response to infection and tissue injury It has multiple effects and serves as a link between activation of innate immunity and adaptive immune responses. Blocking IL-1, particularly IL-1β, is now the standard of therapy for a a number of monogenic autoinflammatory diseases. Anti-IL1 treatment may also be beneficial in complex inflammatory disorders such as Behçet's disease where the innate immunity plays a key role in the pathogenesis. There are recent case reports on the successful use of anakinra, a recombinant human IL-1 receptor antagonist, and canakinumab, a human monoclonal antibody that neutralizes IL-1beta, in patients with resistant Behçet disease. In a pilot study in 7 Behçet patients with resistant uveitis, gevokizumab, an IL-1beta regulating antibody, was found to produce a rapid-onset effect for the treatment of intraocular inflammation. Preliminary results of an extension trial showed that continuous use of gevokizumab could provide a sustained efficacy, and no serious adverse event was observed.

IL-6 Inhibition: How Far Have We Gone?

Yasir J. Sepah, MBBS and Jose Maya, MD
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Many forms of uveitis are believed to result from an abnormal immune response characterized by organ or tissue-specific inflammation. The role of cytokines in the pathogeneses of uveitis has been shown to be critical; levels of IL-6 in vitreous specimens collected from patients with active intermediate and posterior uveitis who underwent vitrectomy (for uveitis) were found to be much higher compared to controls. IL-6 is a cytokine that promotes the differentiation of Th17 cells and is produced by T cells, monocytes, macrophages, and synovial fibroblasts and can act through its specific receptor (IL-6R). Tocilizumab (TCZ) and Sarilumab (SR) are both humanized monoclonal antibodies that target IL-6 receptors, thereby blocking the proinflammatory effects of IL-6. The STOP-UVEITIS Study is investigating the safety, efficacy, and bioactivity of TCZ in patients with non-infectious uveitis (NIU). In this phase I-II clinical trial, study patients receive monthly intravenous infusions of TCZ for 6 months. In addition, a phase II study investigating the role of SR in patients with NIU, the SATURN

Study, is also currently underway; patients are being treated with a subcutaneous injection of SR every 14 days up to 50 weeks and compared to a placebo group. Clinical findings from these studies may encourage the development of Phase-III clinical trials evaluating the effect of IL-6 inhibitors in patients with NIU.

TNF alpha inhibition: What are the other biologics in development?

Ariel Schlaen, University of Buenos Aires

Tumor necrosis factor alpha (TNF α) is a pleiotropic cytokine secreted primarily by T lymphocytes and macrophages. Secretion of TNF α is increased in Th1 immune responses, which activates macrophages and stimulates the production of chemokines that lead to polymorphonuclear leukocyte and macrophage chemotaxis. Given the predominant Th1 activity in inflammation related to uveitis, there is a rationale for the use of inhibitors of TNF α in chronic noninfectious intraocular inflammation.

Currently, there are 5 molecules of TNF α blockers commercially available on the market: etanercept (ETP), infliximab (INX), adalimumab (ADA), golimumab (GLB) and certolizumab (CZP). None of these 5 drugs has so far completed a randomized controlled comparative trial to evaluate its efficacy and safety. Notwithstanding, an ongoing phase 3 clinical trial with ADA in patients with noninfectious intermediate, posterior, or diffuse uveitis is being carried out. ETP use in uveitis has shown poor results. Several cases series reporting on the clinical use of INX and ADA, some of them prospective and with long term follow up, have shown that such monoclonal antibodies have a promising efficacy and safety in the control of intraocular inflammation. There are few retrospective series of small number of patients, showing promising outcomes of GLB in the control of chronic uveitis associated with JIA, Behcet disease, and uveitis associated with seronegative spondyloarthropathies cases. Only one case has been reported in which CZP was successfully used in a patient with scleritis associated with rheumatoid arthritis.

Development of more specific TNF alpha inhibitors will allow adequate control of inflammation, while reducing side effects such as susceptibility to infections to a minimum.

mTOR Inhibition - Delivery Route and Potency: Can It Be the Therapy?

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McGaw Memorial Endowed Chair in Ophthalmology
Professor and Chairman
Inaugural Director of the Stanley M. Truhlsen Eye Institute
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Sirolimus (rapamycin) is a macrolide antibiotic produced naturally by Streptomyces hygroscopicus, isolated in soil samples from Easter Island. Although originally developed as an antifungal agent, sirolimus has a potent immunosuppressive and anti-neoplastic activity that depends upon its binding to specific cytosolic proteins (immunophilines) to generate an immunosuppressive complex (RAPA:FKBP). FKBP-12 is the most relevant inmunophiline that inhibits the activation of the mammalian target of rapamycin (mTOR) resulting in the suppression of the cytokine driven T-cell proliferation by blocking and inhibiting several signal transduction pathways (phosphorylation and activation of p70-S6 kinase1 and phosphorylation and inactivating 4E-BP1). The inhibition of the proliferation of B-cell lymphocytes and IL-2, IL-4, IL-5 represents other additional immunomodulatory effects of rapamycin.

Initial studies for uveitis reported that systemic sirolimus was effective in the majority of refractory NIU cases, improving the signs and symptoms of inflammation and reducing the steroid burden. However, the systemic/intravenous route of administration was associated with side effects and/or failure to control uveitis in some patients. The Sirolimus as Therapeutic Approach to UVEitis (SAVE) Study evaluated, for the first time, the safety and efficacy of sirolimus administered as subconjunctival or intravitreal injections in patients with NIU. Other clinical trials, including intravitreal Sirolimus as Therapeutic Approach to UVEitis – Phase 2 (SAVE-2), and The Study Assessing Double-masked Uveitis Treatment (SAKURA) are being conducted to help to establish the long-term safety and efficacy of local ocular formulation of sirolimus. Highlights of the SAVE study and key features of the SAVE-2 and SAKURA studies will be discussed in this presentation.

Session 11

IOIS session: *Pediatric uveitis*

Evaluation and Differential Diagnosis of Pediatric Uveitis

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The incidence of uveitis is lowest in the pediatric group at approximately 7 cases per 100,000.

The most common anatomical category is anterior, making up approximately half of all cases, followed by posterior (25%), intermediate (20%), and panuveitis (8%). The most common uveitic diagnoses ascribed in children are juvenile arthritis, pars planitis, toxoplasmosis, and idiopathic.

Despite advances in uveitis care, children have a high prevalence of ocular morbidity, with almost 8% being legally blind by 10 years of disease duration. The approach to the pediatric patient with uveitis does not differ from that in adults with a thorough history and complete eye examination, complemented by directed physical examination. Laboratory workup should be targeted to the clinical picture, addressing the most likely entities including juvenile arthritis, sarcoid, and infectious causes such as tuberculosis, syphilis, cat scratch, post streptococcal, TINU, toxoplasmosis, and toxocariasis. Patients with underlying autoimmune diseases such as juvenile arthritis and sarcoid should have regular screening eye examinations to detect asymptomatic disease.

Sustained-release dexamethasone intravitreal implant in juvenile idiopathic arthritis-related uveitis

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INTRODUCTION: We present a series of patients with JIA uveitis treated with dexamethasone implant (Ozurdex®).

MATERIALS AND METHODS: Retrospective chart review.

RESULTS: Seventeen eyes of 12 patients (10 girls, mean age 12.5±6.7 years) with JIA uveitis received intravitreal Ozurdex®. Mean duration of: arthritis before starting treatment with Ozurdex was 49±35.6 (12-132) months; uveitis was 31±20.1 (12-72) months; follow-up was 11.6±13.2 (2-24) months. One month after injection, vision improved to 40.2±11 logMAR ($p<0.001$). Seven of 8 eyes that received

Ozurdex for persistent iritis had resolution by clinical exam. Nine of 17 eyes had macular edema prior to injection with central retinal thickness of 437.6±96.2 µm that decreased to 342.4±79.3 µm ($p<0.01$) at one month. Twelve of 17 eyes received a second implant at 7.5±3.1 months after first injection. One month after second implant, iritis resolved in 11 eyes (91.6%), mean BCVA improved to 44.6±8.1 logMAR ($p<0.01$). Five of 12 eyes had macular edema at second injection with central retinal thickness of 399.8±59.8 µm that improved to 250.4±13.7 µm ($p<0.01$) in 4/5 eyes at one month. Five eyes received a third Ozurdex iimplant 7±4.6 months after second injection; of these 5 eyes, 4 had iritis and 1 had macular edema. One eye received a fourth injection 3 months after the third for iritis. Five of 17 eyes were pseudophakic prior to first injection. Of the remaining 12, 8 (66.6%) developed worsening posterior subcapsular cataract at a mean of 7.3±1.2 months after first implant. Three of these 8 eyes required cataract surgery 10.7±4.8 months from initial injection. Prior to Ozurdex injection, none of the 17 eyes was on anti-glaucoma therapy. After the first injection, 1 eye required therapy with maximum IOP of 25 mmHg. Mean IOP prior to first injection was 15 mmHg; at 1 month, 25 and at 3 months, 23. In the 12 eyes that received a second injection, mean IOP was 13.4±1.3 mmHg at the time of injection, 14.6±0.8 at 1 month and 15.3±1.1 at 3 months. None of the eyes receiving 3 or 4 injections developed IOP rises.

Discussion: Our series suggests that Ozurdex can be effective in the treatment of JIA-associated uveitis and macular edema with few side effects.

Quality of Life in Children with Uveitis

Barisani-Asenbauer Talin

Purpose: Aim ofour study was to analyze in children with uveitis QoL and coping mechanisms to get new insights for the management of pediatric uveitis. Further to explore family function, quality of life, and coping mechanisms of affected children and- their mothers.

Material and methods: 40 children, age over 10, and -their mothers were included in this study. -A set of standardized psychological tests including nstruments to analyze familylife & functioning -(Familienbogen for children and parents), quality of life (for children KINDL),- the Youth Self Report (YSR) and the -Child Behavior Checklist CBCL were used.

Results: Children with uveitis were found to have a decreased QoL. Patients of female gender, anterior localization, bilateral disease and the need of immunosuppressive therapy exhibited worse values than others. 72% of the mothers felt a significant disease burden and 55,5% of the mothers considered -the medical management as negatively impacting the family life.

Conclusions: Our findings support the need of psychological counseling and patient support

of children with uveitis and their parents.

Session 12

Brazilian Uveitis Society: *Ocular Toxoplasmosis, State of the Art*

Clinical Pictures of Ocular Toxoplasmosis –

Cristina Muccioli

Ocular toxoplasmosis is characterized by recurrent episodes of necrotizing retinochoroiditis thought to be caused by both proliferation of live organisms that emerge from tissue cysts within the retina and an associated inflammatory reaction triggered by autoimmune mechanisms. Recurrent toxoplasmic retinochoroiditis can be associated with severe morbidity if disease extends to the macula and optic disk or if there is damage to the eye from inflammation. The timing of recurrences varies between individuals and is unpredictable.

The retina is the primary site of T. gondii infection in the eye and the hallmark is a necrotizing retinochoroiditis satellite lesion adjacent to old hyperpigmented scars accompanied by vitreous inflammation and anterior uveitis.

The most common clinical signs of active ocular toxoplasmosis are blurring or loss of vision and floaters. Depending on the location of the lesions and the anterior chamber and vitreous inflammation patients can be more or less symptomatic.

Toxoplasmic retinochoroiditis lesions have the same fundus characteristics, whether they result from congenital or acquired infections. Acute and new lesions are usually intensely white, focal lesions with overlying vitreous inflammatory haze. Active lesions that are accompanied by a severe vitreous inflammatory reaction will have the classic "headlight in the fog" appearance. Anterior uveitis is characterized by inflammatory cells in the aqueous, medium-sized keratic precipitates, and posterior synechiae. Eyes with active toxoplasmic retinochoroiditis will occasionally develop retinal vasculitis with vascular sheathing and hemorrhages in response to reactions between circulating antibodies

Differential Diagnosis

Heloisa Nascimento

Ocular toxoplasmosis is the leading cause of posterior uveitis in Brazil and worldwide. Adjacent retinochoroiditis to an old scar is very suggestive but not pathognomonic of toxoplasmosis. Differential diagnoses include infectious and non-infectious diseases and must be made according to patient's age. Ocular lesions in newborns must be differentiated of other congenital lesions such as rubella, cmv, herpes simplex, tuberculosis and syphilis. Non-infectious diseases include coloboma, persistent hyperplasic primary vitreous, retinopathy of prematurity and retinoblastoma. In adults, syphilis, tuberculosis, herpes, cmv, as well as retinal atrophies and degenerations must be considered.

Adjacent retinochoroiditis can mimic other types of uveitis such as serpiginous choroiditis, acute retinal necrosis, fungal retinitis, endophthalmitis and ocular toxicariasis. Toxoplasmosis can manifest with atypical features as well, such as active bilateral retinochoroiditis and vasculitis. Correct diagnosis is crucial to adequate management.

Laboratory diagnosis

Bahram Bodaghi,

Ocular toxoplasmosis is the main etiology of infectious uveitis. When typical, its clinical presentation is highly suggestive of the disease. However, it remains challenging in immunedeficient hosts and also those presenting with extensive lesions. Atypical phenotypes are identified in nearly 25% of all cases with higher rates in tertiary eye care centers. Laboratory diagnosis becomes a valuable tool in order to exclude similar clinical presentations due to other infectious agents. Both blood and ocular specimens may be collected. Positive IgG serology has no value, especially in endemic regions, unless it confirms a seroconversion with presence of IgM. A negative ELISA serology rules out the infection, therefore becoming highly contributive. Diagnostic confirmation is based on molecular tools such as real-time PCR, local antibody production (Goldmann-Witmer coefficient) and immunoblot, applied to ocular specimens. Aqueous humor is the main source of ocular fluids used for diagnostic tests, followed by the vitreous in some rare situations. The clinician should keep in mind that GWC may be negative during the first 2 to 3 weeks of infection. Unlike viral retinitis, GWC is the most contributive tool in patients with ocular toxoplasmosis. PCR is highly informative in those with immunodeficiency and patients with extensive parasitic replication. Moreover, it may be used to determine the genotype of the parasitic agent with further prognostic implications. Interestingly, parasiteamia could be associated with ocular disease reactivation.

Presentation in immunosuppressed patients

Daniel Vitor Vasconcelos Santos MD PhD
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Toxoplasmosis is the major cause of infectious posterior uveitis worldwide, typically presenting as a unilateral focal necrotizing retinochoroiditis, with variable inflammatory involvement of the vitreous, retinal vasculature and anterior segment of the eye. The disease may be severe and vision threatening, particularly in immunosuppressed individuals. Clinical presentation in these patients frequently include large, multiple and even bilateral retinochoroidal lesions, which may also extend to the sclera, leading to a panophthalmitis. Differential diagnosis in these individuals should include viral retinitis (in the form of acute retinal necrosis / necrotizing herpetic retinopathy), syphilis, tuberculosis intraocular inflammation associated with less usual microrganisms, and even with primary vitreoretinal lymphoma. Despite the ongoing controversy on treatment of immunocompetent patients, Immunosuppressed individuals with active toxoplasmic retinochoroiditis should always be treated, due to its progressive nature in this population, with a high risk of complications and even loss of the eye. Preventive therapy should also be considered in this setting.

Treatment

Áisa H. Lani

The ocular toxoplasmosis therapy includes antimicrobial drugs with or without the presence of corticosteroids. Several drugs have been proposed including pyrimethamine, sulfadiazine, spiramycin, clindamycin and trimethoprim-sulfamethoxazol. The most common drug combination currently used to treat toxoplasmosis is pyrimethamine with folinic acid (to reduce the risk of drug-associated side effects), sulfadiazine and corticosteroids. Another combination is trimethoprim-

sulfamethoxazole (Bactrim®, Septra®). The pyrimethamine and azithromycin drug combination was shown to be similar to the standard treatment with pyrimethamine and sulfadiazine. However, the frequency and severity of adverse effects was significantly lower with the regimen containing pyrimethamine and azithromycin. Intravitreal clindamycin injection and possibly steroids may be indicated for patients that have contraindication of systemic therapy specific for toxoplasmosis.

Complications

Rubens Belfort Jr

Toxoplasmic retinochoroiditis can result in permanent loss of vision because of retinal necrosis, uveitis, and its complications. Central vision will be lost if lesions affect the fovea, maculopapillary bundle, or optic disc. Other reported complications include macular edema, retinal neovascularization, vascular occlusion and vitreoretinal lesions such as vitreous hemorrhage and epiretinal membranes. Subretinal neovascular membranes may be a cause of sudden loss of vision. Rhegmatogenous and tractional retinal detachments may occur as well as secondary glaucoma and cataracts.

The management of its complications requires often a good experience in the uveitis as well as the specific situation since most of them should receive a a tailored individual approach.

The advancement of diagnostic techniques such as OCT and ultrasound have brought important diagnostic and therapeutical information. Also the development of better intraocular lenses for cataract as well as valves for glaucoma have expanded the indications for these surgeries. Phaco-vitrectomy associated to repairment of retinal detachments have become more frequently indicated with good results when indicated at the right time. Another important advance is the incorporation of intra-ocular injections and mainly implants to control the post-surgical inflammation.

Session 14

Uveitis Society of India:
Current diagnostic approaches in Infectious uveitis

Ocular manifestation of TB in India and role of Quantiferon,

Dr.Kalpana Babu

In recent years there is an increasing trend in the diagnosis of ocular tuberculosis due to improved understanding of the disease and availability of better diagnostic techniques. Newer diagnostic techniques include high resolution computed tomography, polymerase chain reaction and Quantiferon TB gold test. In this presentation, we review the role of Quantiferon TB gold test in a south indian patient population.

Leptospirosis and the eye

S. R. Rathinam- India

Leptospirosis is a wide spread water borne zoonotic spirochetal disease of global concern, more common in tropical and sub tropical countries. Leptospirosis is characterized by a broad spectrum of clinical manifestations, ranging from anicteric febrile illness to a severe and potentially fatal illness characterized by acute renal failure and jaundice, popularly known as Weil's disease. Systemic symptoms include acute fever, chills, nausea,vomiting, intense headache, prostration, myalgia and muscle tenderness. Systemic signs include hypotension, meningeal irritation,delirium, anuria or oliguria, cardiac arrhythmia or failure. Physicians may easily miss the diagnosis, as symptoms are extremely variable, and can mimic other infectious disease. Like Syphilis and Lymes disease, leptospirosis result in uveitis as its late complication. Although leptospiral uveitis is common in tropical countries, it remains under diagnosed because of lack of awareness, laboratory tests and specific guidelines for clinical diagnosis. Pathognomonic ocular manifestation in septecemic phase includes conjunctival chemosis and scleral icterus. Most important late ocular complication, uveitis occurs around two to six months following systemic disease. This prolonged symptom-free period in between the systemic and ocular manifestations makes it difficult for the ophthalmologist to correlate the cause of uveitis. The onset and severity of leptospiral uveitis is quite variable and the severity does not correlate with the severity of systemic disease. Leptospiral uveitis commonly presents as unilateral or bilateral acute, non-granulomatous pan uveitis. Hypopyon, optic disc edema, retinal vasculitis and membranous vitreous opacities are the important diagnostic indicators. Micro Agglutination Test is considered as the gold standard serological test. Steroids are the mainstay of treatment for leptospiral uveitis. The preferred mode of delivery depends upon the severity, laterality and anatomical location of inflammation.

Viral infections of posterior segment

Sudha Ganesh, Medical Research Foundation

Aetiology of uveitis varies considerably based on the geographic location around the world. This is attributable to several of factors, genetic, ethnic and geographic and environmental. Infectious uveitis occurs with greater frequency, in the developing world. InIndiainfective uveitis accounts for 11.9% to 30.7% of all uveitis .The most common infectious forms of uveitis seen inIndia, includes herpetic uveitis tuberculosis, leptospirosis and parasitic uveitis.

Herpetic posterior uveitis predominantly has been linked to the ocular syndromes acute retinal necrosis (ARN) and progressive outer retinal necrosis. The latter is mainly found in patients with compromised immune systems, whereas the former typically affects patients with competent immune systems. This syndrome is often caused by varicella zoster virus (VZV) or herpes simplex virus (HSV)–1 and less frequently by HSV-2 and cytomegalovirus. Rapid diagnosis and prompt initiation of treatment are important to control the extent of necrotic lesions,minimize complications such as retinal detachment (RD), and protect vision HSV and VZV can cause a wide spectrum of clinical manifestations ranging from severe acute retinal necrosis to slow-progressing necrotizing and non necrotizing types of inflammation. The non-ARN variants are currently underdiagnosed. Patients with these variants could potentially benefit from earlier recognition and treatment.Reports of non necrotizing herpetic uveitis variants have been published sporadically. Bodaghi et al have patients with positive test results for HSV or VZV in aqueous humor who had nonnecrotizing retinitis consisting mainly of vasculitis, papillitis, or vitritis.

Emergent and resurgent arthropod vector-borne diseases are major causes of systemic morbidity and death and expanding worldwide. Among them, viral and bacterial agents includingWest Nilevirus, Dengue fever, Chikungunya, Rift Valley fever, and rickettsioses have been recently associated with an array of ocular manifestations. These include anterior uveitis, retinitis,chorioretinitis, retinal vasculitis and optic nerve involvement. Proper clinical diagnosis of any of these infectious diseases is based on epidemiological data, history, systemic symptoms and signs, and the pattern of ocular involvement. The diagnosis is usually confirmed by the detection of a specific antibody in serum. Ocular involvement associated with emergent infections usually has a self-limited course, but it can result in persistent visual impairment.

Chikungunya Retinitis

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Introduction : Chikungunya retinitis is one of the sight threatening ocular manifestations for the past few years. Aim: To study the chikungunya retinitis in south Indian population.

Materials and Methods: Prospective, nonrandomized, observational case series of 11 eyes of 7 patients were studied at tertiary eye care centre in south India. Chikungunya was confirmed by demonstration of chikungunya Ig M antibody in the serum. All these patients underwent complete systemic and ophthalmic evaluation. Confocal microscopy of keratic precipitates, OCT, AC tap, PCR from aqueous and serum were done in selected cases. Follow up varied between 6 months to 5 years.

Results: Age group ranged between 27-55 years (median 38 years). Three patients were males. 4 patients had bilateral presentation. Interval between fever and ocular manifestations varied between 4 weeks to 12 Weeks (Median 6 weeks). PCR from the aqueous was positive in one case Visual outcome ranged between CF 1 mtr to 6/6 (median 6/9).

Discussion: Strong clinical association was established based on the temporal association between the systemic manifestations, ocular manifestations &ampamp; positive serology allowing us to make a diagnosis of chikungunya retinitis. Patients with retinitis showed improvement with corticosteroids.

Conclusion: Chikungunya can cause ocular manifestation such as retinitis. Ophthalmologists need to be aware of these features in geographic regions where the chikungunya fever is prevalent.

Role of diagnostic vitreous surgery in infectious uveitis

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Intraocular inflammation essentially manifests as presence of cells and exudation in the various chambers of the eye and may be caused by autoimmune uveitis, infective uveitis or uncommonly by pathologies that masquerade as intraocular inflammation such as B cell lymphoma. While the medical treatment of uveitis is fairly standardized and effective in preventing or even restoring visual loss and maintaining structural integrity of the eye, the diagnosis of the infective uveitis/masquerades often presents a challenge. In the event, a diagnostic tap from the anterior chamber or the vitreous cavity is recommended for subjecting the sample to various laboratory techniques such as cytology, polymerase chain reaction studies for various organisms, antibody titers or cytokine profiling. However, the results may be compromised by inadequate sample from the various taps especially if there are only few inflammatory cells in the anterior chamber or the vitreous cavity. Aspirates from the vitreous may be dry due to the gel consistency of the vitreous. We have been prospectively subjecting challenging cases of uveitis to diagnostic small gauge vitreous surgery and have found the procedure to be well tolerated. Indications include unusual presentations of uveitis that have either negative or equivocal results form non invasive tests, or those who do not respond or show a very aggressive sight threatening course to the conventional treatment. Short case presentations would illustrate include cases of aggressive necrotizing retinits due to toxoplasmosis in immunocompetent, mixed infection with VZV and toxoplasmosis in immunocompromised, persistent inflammation due to B cell lymphoma, persistent inflammation due to non necrotizing viral posterior uveitis, paradoxical worsening of serpiginous like choroiditis, and detection of drug resistant Mycobacterium tuberculosis from the eye. While the procedure is by and large well tolerated, complications have included hypotony, choroidal detachment, and negative laboratory results.

Real time polymerase chain reaction in the diagnosis of tubercular uveitis

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Purpose: To find out the role of real time PCR for Mycobacterium tuberculosis (MTB) in suspected tubercular uveitis. Material methods: Aqueous aspirate of suspected tubercular uveitis was collected and sent for real time PCR testing for MTB genome. The results were analyzed with respect to their clinical features and outcome. Period of study – Jan 2012 to Dec 2012

Results: Total 10 patients were included in the study. Clinical diagnoses included intermediate uveitis- 4 eyes, sub retinal abscess-2 eyes, and 1 each of- retinal vasculitis, serpiginous like choroiditis, granulomatous uveitis and tuberculoma of choroid. Of these, 4 were positive for RT-PCR for MTB which included retinal vasculitis, serpiginous like choroiditis, tuberculoma of choroid and one eye

with intermediate uveitis. The copy numbers ranged from 14 to 2204. Quantiferon TB Gold (QFT-G) test was positive in 3 patients. Of these 3 patients with QFT-G positivity, only one was positive for RT-PCT for TB while of the 4 patients who were positive for RT-PCR, 3 patients underwent QFT and only one was positive. Mantoux test was done in 4 patients and was positive in 2 of them. Of the 4 patients who were positive for RT-PCR, 2 patients underwent PPD out of which only one was positive. Among the 4 RT-PCR positive patients, 3 patients underwent HRCT and 2 showed suggestive features of tuberculosis. One patient with HRCT features suggestive of TB, RT-PCR was negative.

Conclusion: RT-PCR is a very helpful tool in the diagnosis of tubercular uveitis

Session 15

Behçet's disease and Uveitis group from Turkey: *An update on Behçet's disease uveitis*

Ocular- lesions and differential diagnosis

Merih Soylu, Adana World Eye Center

Behçet's disease is a multisystem inflammatory disorder, and diagnosis is based on the presence of characteristic ocular and systemic manifestations. Eye is the most commonly involved vital organ in these patients, so it is important to diagnose and start treatment as early as possible, in order to prevent complications that can lead to blindness. The current diagnostic or classification criteria sets do not allow diagnosis of Behçet's uveitis based on ocular findings alone. it is important to recognize Behçet's uveitis as a distinct entity that can be diagnosed in the absence of systemic manifestations. The typical ocular finding is relapsing panuveitis and retinal vasculitis in Behçet's disease. Nongranulomatous anterior uveitis, diffuse vitritis, retinal infiltrates, sheathing of retinal vessels (mainly veins), and occlusive retinal vasculitis are the typical manifestations of ocular involvement. There is a sudden onset of acute inflammatory signs, which has a relapsing course with spontaneous resolution and recurrences. It is important to know the clinical characteristics of this disease and make differential diagnosis especially with infectious and noninfectious diseases causing nongranulomatous anterior, intermediate, and posterior uveitis, occlusive retinal vasculitis, and retinitis.

Posterior Segment Imaging In Monitoring Disease Activity

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Fundus photography, fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) are the main imaging techniques employed in the evaluation and monitorization of a Behcet patient with posterior uveitis. FFA demonstrates diffuse fluorescein leakage from retinal vessels including the capillaries and the optic disc during acute inflammation. It can reveal fundus changes even in Behçet patients with normal findings on clinical examination. With FFA macular edema, capillary leakage, retinal vascular leakage and staining, optic disc staining,macular ischemia, areas of nonperfusion due to vascular occlusions resulting from vasculitis, pinpoint leakage, and retinal and optic disc neovascularization can be better identified.-

OCT is a relatively new technique for high-resolution cross-sectional imaging of retinal thickness. It is non-invasive, therefore is ideally suited for the measurement of retinal thickness in the diagnosis and follow-up of patients with cystoid macular edema in Behçet's patients. Spectral domain OCT is indispensable in the evaluation of outer retinal layers especially the inner segment/ outer segment (IS/OS) line, integrity of which is important in visual functions. With EDI OCT it became possible to evaluate the choroid, shown to be thickened in active phase of Behcet uveitis.

In conclusion, the activity of the disease and the response to treatment is commonly monitored by adjunctive use of these three posterior imaging modalities.

Laser flare photometry in monitoring disease activity

Nilüfer Yalçındağ, Ankara University Faculty of Medicine

Intraocular inflammation causes disruption of the blood-ocular barriers and entry of proteins and inflammatory cells into the aqueous humor. Effective management of uveitis requires a reproducible and quantitative method to determine and monitor intraocular inflammation. Laser flare photometry is the only noninvasive, objective and quantitative method to reliably measure intraocular inflammation. Laser flare photometry studies have shown that Behçet patients have persistent subclinical flare in between acute episodes and exacerbations can be predicted by an elevation of flare levels. Also, a positive correlation has been found between flare values and fluorescein angiographic leakage in Behçet uveitis. Laser flare photometry might reduce the need for fluorescein angiography in monitoring subclinical retinal vascular inflammation during clinically quiescent periods and may be an indicator of posterior segment activity when fluorescein angiography can not be performed.

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Conflict of interest: None

The outcome of Interferon α 2b in a large cohort of Behçet's syndrome with severe ocular involvement: a single centre experience

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Purpose: Interferon α 2b (IFN) is effective in treating uveitis associated with Behcet's syndrome (BS). We surveyed IFN use in a large cohort of BS patients with severe ocular involvement refractory to the combination of azathioprine (AZA) and cyclosporine (CSA).

Methods: In a dedicated multidisciplinary Behcet outpatient clinic we have been using IFN in severe ocular involvement with sight threatining posterior uveitis since 2000. Up to now more than 200 patients (mostly males) who used IFN for such involvement were identified. These patients had a) serious side effects due to CSA and AZA such as hypertension or elevation of serum creatinine level, b) had been steroid dependant c) or had solely posterior uveitis refractory to the combination of AZA and CSA. When IFN was started AZA and CSA were stopped. Only corticosteroid use if necessary, was allowed. Patients were evaluated retrospectively with regards to change in both actual and baseline visual acuities (either before or after an acute attack starts or subsides), and ocular damage. Duration of corticosteroid use and the cumulative dose was calculated. Side effects during IFN treatment were also studied.

Results: The mean age and mean disease duration were 33 ± 8 and 8 ± 4 years, respectively. All patients had used AZA and CSA before starting IFN for a mean of 3 years. The beginning of IFN dose was 5 MU/day in the majority (80 %) of the patients. After IFN treatment the mean actual VA seemed to be improved. Corticosteroids had to be used in fewer patients once IFN was started. About 30 % of the patients had to stop IFN due to side effects such as depression, cytopenia, flu-like syndrome or autoimmune diseases.

Conclusions: In Behcet patients with severe refractory ocular involvement, IFN seems to be effective. As this is an ongoing study the recent figures are subject to change.

Long-term results of anti-TNF therapy

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The uveitis associated with Behcet's disease, if vision-threatening, requires an aggressive therapeutic approach. Recent use of biologic agents for this disease has greatly improved visual outcomes over that achieved with standard immunosuppressive therapy. In particular, infliximab, approved in Japan for the specific indication of refractory uveoretinitis in Behcet's disease, was shown in an 8-center study evaluating post-marketing data for the first year of treatment to have good safety and marked efficacy. However, this same study also revealed a small but statistically significant increase in number of attacks in months 7-12 when compared to the same in months 1-6. Factors that may relate to this increase in attacks include lack of concomitant immunosuppressive drug use in some patients and/or development of anti-drug antibodies. In order to overcome an increase in attacks, increasing infliximab doses, decreasing infliximab infusion intervals, adding/increasing concomitant immunosuppressive drugs, or changing to a different biologic agent may be considered. Furthermore, the question of if and when infliximab can be discontinued in patients with good suppression of disease activity remains. This talk will review the record on the safety and efficacy of infliximab for ocular Behcet's disease, and present more recent 4-year data showing stable disease control with this treatment.

Session 16

Uveitis Society of China: *The study of uveitis in China*

Studies on the association of gene polymorphism with Behcet's disease and VKH syndrome in Chinese population

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Behcet's disease (BD) and Vogt-Koyanagi-Harada (VKH) syndrome are two common seen uveitis entities in China. BD is a chronic systemic autoinflammatory disease affecting the eye, skin, oral mucosa, gastrointestinal tract and central nervous system. VKH syndrome is an autoimmune disease characterized by a bilateral granulomatous panuveitis and systemic disorders including poliosis, vitiligo, alopecia, and central nervous system and auditory signs. Accumulative evidences show strong genetic basis for BD and VKH syndrome confirmed by familial aggregation, geographical ethnic distribution, and strong association with especially Human leukocyte antigen (*HLA*) antigens. To explore the genetic factors for BD and VKH syndrome, our group investigated the association of these two diseases with multiple immune response genes and has identified multiple BD or VKH syndrome-related immunoregulatory pathways in the Chinese Han population. A large number of gene polymorphisms were studied including mir-146a, mir-196a, JAK1, STAT4, IL23R, CD40, CCR1/CCR3, STAT3, OPN, IL17, JAK2, MCP-1, CTLA4, PD-1, PD-L1, PD-L2, TGRBR3, CCR6, PTPN22, FCRL3, IRF5, SUMO4 and UBAC2 for BD. Significant associations were found between BD and mir-146a, mir-196a, JAK1, STAT4, IL23R, CD40, CCR1/CCR3, STAT3, MCP-1, TGFBR3, FCRL3, SUMO4, UBAC2. We also identified multiple associated genes with VKH syndrome in Chinese Han population including CTLA4, PDCD1, IL17F, TNFAIP3, JAK1, MIF and FGFR1OP. These findings are helpful in elucidating the pathogenesis of Behçet's disease, Vogt-Koyanagi-Harada syndrome and will hopefully allow the development of novel treatment regimes.

Outcomes of Treatment of Fungal Keratitis: A 10-Year Retrospective Analysis

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PURPOSE:To evaluate the outcomes of medical and surgical management of fungal keratitis.

METHODS: A retrospective review was performed of 49 patients with a diagnosis of microbiologically or histopathologically confirmed fungal keratitis at Qilu Hospital, Shandong University during 2004 to 2012. The main outcome measure was a microbiological cure with either medical therapy alone or medical therapy combined with therapeutic keratoplasty (TKP).

RESULTS: Forty-nine eyes met the inclusion criteria. A microbiological cure was achieved in 49 eyes (100%). Eight eyes (16.33%) were treated with medical therapy alone, and 41 (83.67%) eyes required 1 TKP (38 eyes) or 2 TKPs (3 eyes). Among the 41 eyes treated with TKP, 27 eyes maintained a clear graft. Among 14 eyes with opaque grafts, 11 eyes ultimately achieved clear grafts after anti-rejection therapy while 3 eyes with failed grafts remained clear after 2 TKPs. The final median best-corrected visual acuity was 20/40.

CONCLUSIONS: Early diagnosis and appropriate treatment are essential to avoid blindness. A high microbiological cure can be achieved in eyes with fungal keratitis; however, TKP is often needed to achieve this objective. A good final visual outcome can be achieved in most cases.

KRY WORDS: Keratitis, fungal, keratoplasty

Role of Rheum Polysaccharide in the Cytokines produced by peripheral blood monocytes in TLR4 Mediated HLA-B27 Associated AAU

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Purpose: To evaluated the effect of a traditional Chinese medicine, Rheum Polysaccharide(RP), on the in vitro production of tumor necrosis factor alpha (TNF-a) and interleukin-10(IL-10) by lipopolysaccharide (LPS)-stimulated human monocytes from HLA-B27 associated acute anterior uveitis patients of convalescence stage.

Method: PBMC samples were isolated from 10 HLA-B27 associated acute anterior uveitis, incubated respectively, and divided into 4 groups as following: 1)controls, PBS was added in final concentration of 1mg·L-1, 2) stimulated by LPS, LPS was added in final concentration of 1mg·L-1, 3) stimulated by LPS+HTA125, 30 minutes before the adding of LPS in final concentration 1mg·L-1, the final concentration 5mg·L-1 of the HTA125 was added. 4) stimulated by LPS+RP, 30 minutes before the adding of LPS in final concentration 1mg·L-1, the final concentration 100mg·L-1 of the RP was added. Supernatants were used to quantify the amounts of TNF-a, and IL-10 released in time course using enzyme-linked immunosorbent assay (ELISA).

Result: After stimulated by lps, the concentrations of TNF-a and IL-10 in culture supernatants of patients are significantly higher than control group at all time points ($p<0.01$). Blockage of TLR-4 by HTA125 can decrease the production of TNF-a and IL-10 compared with lps group ($p<0.01$, except at 4h group of IL-10). Concentration of TNF-a and IL-10 also decrease in the LPS+RP group ($p<0.01$), but not so significantly as in the LPS+HTA125 group.

Conclusion: As Anti-TLR4 monoclonal antibodies, Rheum Polysaccharide can also inhibit the secretion of cytokines produced by monocytes from HLA-B27 positive AAU patients of convalescence stage.

Cytokine expression profiles in aqueous humor and sera of patients with acute anterior uveitis

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Aims To evaluate cytokine expression profile in aqueous humor and sera in patients with HLA-B27 positive acute anterior uveitis (AAU) and HLA-B27 negative idiopathic AAU.

Methods Twenty patients with AAU and 17 controls were recruited from August 2012 to March 2013 . Study subjects with uveitis were divided into two groups: 9 patients with HLA-B27 negative idiopathic AAU (group I) and 11 patients with HLA-B27 positive AAU (group II). Complete ophthalmological examinations were performed and clinical features of each group were clearly documented. Aqueous humor and sera were collected and the concentration of 15 immune mediators (IL-1β, IL-4, IL-6, IL-10, IL-17A, IL-17F, IL-21, IL-22, IL-23, IL-25, IL-31, IL-33, TNF-α, IFN-γ, sCD40L) were measured in both aqueous humor and sera simultaneously by multiplex immunoassay.

Results There were significant higher levels of multiple cytokines in aqueous humor in patients with uveitis compared to controls, including IL-1β, IL-4, IL-10, IL-17A, IL-17F, IL-25, IL-31, IL-33, TNF-α, sCD40L. The levels of IL-17A and IL-17F in aqueous humor correlated significantly with disease activity in patients with HLA-B27 negative idiopathic AAU ($r=0.756$ and 0.702, respectively, $P<0.05$), while the level of IFN-γ in aqueous humor correlated significantly with disease activity in patients with HLA-B27 positive AAU($r=0.668$, $P=0.025$). There was no significant difference in serum cytokine expression between uveitis patients and controls.

Conclusions Cytokine expression pattern in aqueous humor other than serum may reflect intraocular immune reactions during active inflammation in patients with AAU. A predominant Th17-driven immune response may play an important role in the immunopathogenesis of idiopathic AAU, while Th1 dominant immune response may be responsible for the inflammation in HLA-B27 positive AAU.

Expression of CD4 CD25high regulatory T cells in peripheral blood of Chinese uveitis patients

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Purpose: To study the expression of CD4 CD25high regulatory T cells in peripheral blood of uveitis patients in China and to investigate it's role in the clinical development of uveitis.

Methods: Peripheral blood lymphocytes were collected from 30 Chinese patients with active uveitis which included 9 cases of panuveitis, 8 cases of anterior uveitis, 5 cases of intermediate uveitis and 8 cases of posterior uveitis. 11 healthy subjects were used as controls. The frequencies of CD4 CD25high T cells and the expression of CTLA-4 on CD4 CD25high T cells were studied by immunofluorescence method and analyzed by flow cytometry (FCM).

Results: The percentage of CD4 CD25high T cells in peripheral blood of uveitis patients was higher than that of the healthy controls (8.56% ±4. 22% vs 5.72% ±3.11%, $P = 0.022$) and correlated very well with the disease severity of uveitis. However, there was no statistic difference in the expression of the CD4 CD25high T cells in the different sites of uveitis. Otherwise, the percentage of CD4 CD25high

CTLA-4 T cells in uveitis was also higher than that of the healthy controls (4.97% ±3. 06% vs 3.05% ±1. 90%, P = 0.012).

Conclusion: The higher expression of CD4 CD25high T cells in peripheral blood of Chinese uveitis patients suggests that CD4 CD25 regulatory T cells may play an important role in the development and immunoregulation of uveitis disease.

Iris and Choroid Thickness in Remission Stage of Uveitis

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Purpose: To investigate the iris and choroid thickness in uveitis patients that affected posterior segment.

Methods: Forty-seven eyes of 24 patients with posterior or pan uveitis and 42 eyes in 22 healthy age-matched controls from the department of ophthalmology, Peking University First Hospital were collected. All the patients were at the remission stage of uveitis. Heidelberg optical coherence tomography was used to measure the iris and choroid thickness.

Result: There were 8 patients (16 eyes) of Vogt-Harada disease, 8 patients (15 eyes) of Behcet's disease, 6 patients (12 eyes) of intermediate uveitis, 2 patients (4 eyes) of sarcoidosis included in this study. The mean age of the patients was 42.6 years (20 ~ 66 years), 10 were males and 14 were females. The mean age of the uveitis onset was 33.8 years (from 9 to 61 years). The duration of the disease was 9.7 years (ranged 2 to 24 years). Visual acuity varied from 0.1 to 1.2. No inflammation cell was seen in both anterior and posterior segment of the eye. The mean age of the normal control was 48 (24 ~ 57 years). 14 were females and 8 were males. The mean macular choroid thickness in 42 eyes of the normal was 276.1μm. In the uveitis patients, the choroid thickness was 215.2μm, much thinner than control. The iris thickness in uveitis group was thinner than control (data is under collected). The result showed that more times of uveitis recurrence or the longer of uveitis history, the thinner of the iris and choroid thickness.

Conclusion: The iris and choroid thickness was obvious thinner in remission stage of uveitis patient.

Session 17

IOIS session: *Inflammatory ocular surface disorders, keratitis*

Corneal nerves and sensitivity

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Functional roles of corneal nerves include transmission of sensory information of the ocular surface, afferent arm for regulation of tear secretion and blinking and trophic maintenance of the ocular surface. The study of corneal innervation is changing the scope of diseases like dry eye or keratoconus with clinical implications in diagnosis and treatment. We present experimental research regarding cold receptors and clinical research in ocular surface disorders were the early changes are detected in ocular sensitivity.

Inflammation in dry eye: toward new strategies

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Ocular surface disorders (OSD) constitute a series of complex diseases involving the lacrimal gland and the tear film, meibomian glands and eyelids, and all cellular components of the cornea and the conjunctiva. Whatever the mechanisms initially involved causing dry eye, i.e., allergic, infectious, toxic or environmental aggressions, blepharitis, autoimmunity or steroid hormone imbalance, they stimulate a series of pathological pathways, the main two being inflammation and apoptosis. Tear film instability or hyposecretion can be considered as the central key point of DED. They will cause local or diffuse hyperosmolarity of the tear film and therefore of superficial epithelial cells of cornea and/or conjunctiva, stimulating epithelial cells and resident inflammatory cells. Cell damage that will result at levels of cornea and conjunctiva, by mean of apoptosis, direct mechanical and/or osmotic stress, will stimulate the reflex neurosensory arc, stimulating lacrimal gland and neurogenic inflammation, with inflammatory cytokine release, MMP activation and inflammatory involvement of the conjunctival epithelium. Goblet cell loss is thus directly related to chronic inflammation and surface cell apoptosis subsequent to cell hyperosmolarity and chronic damage, resulting in further tear film instability/imbalance and actually leading to a vicious circle, characteristic of severe dry eye disease. Either primary, and directly cause of tear film impairment, or secondary to corneoconjunctival damage, inflammation has therefore become a major therapeutic target. Various anti-inflammatory strategies based on steroids, topical cyclosporin A, oral doxycycline or other immunomodulating agents have been developed or are under investigations.

Inflammation in ocular allergy

Alvise La Gloria Valerio, University of Padua
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Allergic conjunctivitis are often considered an easy-to treat and self limiting allergic inflammation of the conjunctiva without long term complications and potential damage for the visual function. However, the ocular allergic syndromes include a variety of inflammatory diseases of the ocular surface affecting lids, cornea, lachrymal gland and tear film, at different levels of severity. The inflammatory mechanism of seasonal (SAC) or occasional allergic conjunctivitis is typically type I hypersensitivity IgE-mediated, whereas in chronic allergic disorders, such as vernal keratoconjunctivitis (VKC) or atopic keratoconjunctivitis (AKC), the mechanisms are more complex and probably involve both IgE and T cell-mediated responses. Nevertheless, acute and chronic diseases have in common: 1) the possible sensitization to environmental allergens; 2) the IgE-mast cell activation with subsequent mediator cascade; 3) the conjunctival inflammation with a prevalence of eosinophils; 4) the presence of lymphocytes with a Th2 profile of cytokine production; 5) a mucosal hyperreactivity. Corneal inflammatory involvement is common in VKC and AKC associated with tissue remodelling and fibrosis, resulting in potential scarring and corneal opacities. Understanding inflammation in ocular allergy may provide indication for a rational treatment of these diseases and future potential therapeutic approaches.

Autoimmune keratitis: current understanding and therapeutic options

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Corneal melting due to autoimmune disorders remains a serious clinical condition. As with the underlying disease, autoimmune reactions based on a patient's genetic predisposition are assumed to be of significance in disease pathogenesis. Emerging evidence also points to additional morphological and physiological ocular characteristics in the pathogenesis of corneal ulceration. This presentation provides an overview of clinical aspects, pathogenetic background as well as new therapeutic options for corneal involvement in autoimmune keratitis.

Reconstruction of the ocular surface in inflammatory ocular disorders

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Surface damage in inflammatory disease, severe enough to require surface reconstruction, is uncommon, and usually in patients with Stevens Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), mucous membrane pemphigoid (MMP), and ectrodactyly-ectodermal dysplasia-cleft (EEC) syndrome. The surface may be lost in acute SJS/TEN and slow to heal. The severity of the acute disease in SJS/TEN is the principal risk factor for late complications causing both corneal epithelial stem cell failure, and loss of the conjunctival fornices. Case series support the use of oral and topical steroids and amniotic membrane (AM), either sutured over the surface or applied at the bedside on a symblepharon ring. For severe fornix shortening in late SJS/TEN and MMP fornix reconstruction may be needed to reduce corneal exposure due to lagophthalmos, particularly when combined with entropion surgery, which may exacerbate exposure. AM gives poor results as a conjunctival substrate but oral mucosa is effective and usually safe in MMP if combined with adequate immunosuppressive therapy. Cultured sheets of mucosa may soon come into clinical use. Corneal epithelial reconstruction for vision is only needed in advanced disease, and may use donor or cultured allografts or autologous cultures mucosal transplants. Most of this subset of patients have dry eyes and chronic uncontrollable surface inflammation leading to low success rates (1/8 in one of the authors series). In the event of failure to epithelialize conjunctival flaps or free buccal mucosal grafts will save the eye for a later osteo-odonto-keratoprosthesis.

Session 18

Foster Ocular Immunology Society: *Genetics and Biomarkers in Ocular Diseases: Past, Present and Future*

Genetics of Diabetic Retinopathy

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Purpose: To describe the current understanding of the genetic susceptibility underlying the development of diabetic retinopathy.

Materials and Methods: A review of heritability, candidate gene and genome-wide association studies performed to date was executed. In addition, the status of ongoing studies in the genetics of diabetic retinopathy was summarized including an admixture genetic association study for proliferative diabetic retinopathy in African Americans and a multi-ethnic genome-wide association study using liability threshold modeling of diabetes duration and glycemic control.

Results: Diabetic retinopathy is a complex genetic disease with a strong influence of diabetes duration and systemic glycemic control. The heritability of overall diabetic retinopathy and proliferative diabetic retinopathy are as high as 27% and 52%, respectively. Results from most candidate gene studies have not been reliably reproduced. The strongest, but not entirely consistent, evidence for association exists for proliferative diabetic retinopathy and polymorphisms in the erythropoietin (EPO) promoter and TCF7L2, a consistent risk locus for type 2 diabetes. Genome-wide association studies to date have also not produced any consistent risk loci. Ongoing studies, particularly additional genome-wide association studies and admixture studies, have larger sample sizes, focus on the extremes of the diabetic retinopathy phenotype and utilize methods to increase power that incorporate mean duration of diabetes and degree of glycemic control.

Conclusions: The underlying genetic risk factors for diabetic retinopathy are incompletely understood. Studies that focus on collecting larger sample sizes and extremes of the phenotype are currently underway to try to fill this gap in our knowledge.

Genetic Testing in Age-Related Macular Degeneration: Pro or Con?

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Age-related macular degeneration (AMD) is a multifactorial disease in which genetic variants and environmental factors contribute to disease risk. Several genetic variants have been consistently associated with AMD. Variants in the complement factor H (CFH) gene, complement component 3 (C3), HTRA1/ARMS2 locus on chromosome 10, and other genetic variants have been associated with AMD. Commercial genetic testing is available for some AMD risk variants; however, there is no consensus yet on how genetic testing should be integrated into clinical practice.

Genetics and Response to Therapy in Patients with Birdshot Retinochoroidopathy

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Birdshot retinochoroidopathy (BSRC) is an autoimmune ocular inflammatory disease which, untreated or with corticosteroid monotherapy, produces progressive retinal dysfunction and eventual profound visual handicap. The disease has by far the strongest association with a particular HLA genotype, with 96% or greater patients with BSRC having the HLA-A29 gene. Conversely, although the HLA-A29 gene is present in 7% of the Caucasian population, only a very small proportion of such individuals develop BSRC. One might logically conclude that there are other genetic and non-genetic factors involved in the development of BSRC. Indeed, one such other genetic factor may be the genes encoding for killer cell immunoglobulin-like receptors (KIR). Certain KIR-HLA-A 29 combinations in some patients may make them more susceptible to developing BSRC. Thus, those HLA-A29 positive individuals who have the KIR2DS2, 2DS3, and 2DS4 along with KIR genes associated with weak inhibition of autoimmune responses (KIR2DL2/3pHLA-C1 and KIR3DL1pHLA-Bw4 may have a greater risk of developing BSRC than do other gene combinations. Once triggered, BSRC may develop and may exhibit varying responses to therapy, depending upon various gene patterns. We have shown that BSRC is curable in a large proportion of patients with the disease, yet some show great resistance to induction of remission, and yet others even go on to develop a second autoimmune ocular disease, with production of antibody directed against retinal and optic nerve elements.

The many faces of HLA-B27

Erik Letko, MD

The HLA-B27 gene is one of the most fascinating in medicine. While the close relationship between ankylosing spondylitis (AS) and HLAB-27 was established only forty years ago, DNA analysis of a mediaeval skeleton with AS suggests that the two travel together through ages. The prevalence of HLA-B27 varies from 50% in Haida Indians to 25% in Eskimos to 8% in UK population to none in Australian Aborigines. Although the association between HLA-B27 and AS is most prominent, a spectrum of other autoimmune diseases have been linked to this gene. Additionally, HLA-B27 was shown to have protective effect against certain infections, while increasing susceptibility to others. Recent studies suggest that subtypes of alleles and gene combinations might be responsible for penetration and phenotypic expression of HLA-B27, explaining why only a subset of people with HLA-B27 develops one or more of the associated diseases. Approximately 1% of HLA-B27 carriers experience acute anterior uveitis (AAU). On the other hand, about half cases of AAU are HLA-B27

positive, but those who experience a recurrent episode of AAU have 70% chance to carry the gene. The presence of HLA-B27 also plays a significant role in patients with Behcet's disease, Herpes simplex eye disease, and the level of TNF-a in the aqueous humor. Although major insights into pathogenesis of HLA-B27 associated conditions have been made in the past decades, the gene continues to possess many secrets that will keep on intriguing medical community for decades to come.

Update on Genetics of Fuchs' Dystrophy

Dr. B. Tannen USA

Fuchs Endothelial Corneal Dystrophy (FECD) is a blinding disease characterized by slowly progressive endothelial cell loss, concommitant formation of guttae, and eventual corneal edema and clouding requiring corneal transplant. Genetically, the disease can be divided into a rare, but well-characterized early-onset form, and into the much more common but less well-defined late-onset forms. Early-onset FECD starts in the first decade and leads to corneal decompensation over the next two to three decades.

Multi-generational family studies demonstrate an autosomal dominant (AD) pattern of inheritance in early-onset FECD. Two mutations in the Col8A2 gene located on chromosome 1p34.3-p32 have been described. Both affect the triple helical domain of collagen VIII potentially altering the collagen lattice in Descemet's membrane. Late-onset forms of FECD typically first manifest in the 5th decade and progress over the next two to three decades. The genetics of late-onset FECD is complex and heterogeneous, demonstrating variable expressivity and incomplete penetrance. An AD pattern with incomplete penetrance has been shown in several large pedigrees, though generally only half of the cases of late-onset FECD demonstrate family clustering. Four genetic loci (FCD1-4) have been identified on chromosomes 13, 18, 5, and 9. The FCD2 locus on chromosome 18 (18q21.2-q21.3) covers at least 28 known genes and is the most common locus to date. Three causal genes ZEB1, SLC4A11, and LOXHD1, representing a small proportion of the total genetic load of FECD have been identified. Further understanding of the genetics of FECD may help to clarify the pathogenesis of the disease and lead to potential non-surgical treatments.

Session 19

Società Italiana Uveiti e Malattie Infiammatorie Oculari: *Herpetic Eye Disease*

Diagnostic tools in ocular herpetic disease

Andrea Leonardi

Although cutaneous lid or corneal lesions are typical, an attempt should always be made to isolate or identify herpes virus (HV). This is important not only because certain other conditions can mimic HV ocular disease, but also to allow potential strain characterization and information regarding mutations and superinfection by other strains. Moreover, it is often difficult to determine whether a vascular or avascular corneal scar is herpetic in origin. Laboratory tests are aimed at—cell cytology, viral antigen detection (immunoassays), viral DNA detection (polymerase chain reaction - PCR) and virus isolation (tissue culture).

Different techniques of PCR carries a sensitivity of up to 100% and are very useful for detecting evidence of virus DNA in the tear film, conjunctival, cornea and aqueous but do not always differentiate between latent and infectious virus. Only RT-PCR can provide indirect evidence for virus replication by the number of DNA copies produced and hence can also be used for evaluating the efficacy of antiviral medications. As PCR and immunohistochemistry detect different components of HV, used in combination may improve the diagnostic specificity.

Corneal sensitivity and confocal microscopy may improve the diagnosis of herpetic corneal infection. In addition, the detection of biomarkers in ocular fluids may help to evaluate the inflammatory cascade associated to the HV infection and reaction.

HSV and VZV Uveitis

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Herpetic ocular disease is an important cause of ocular morbidity and a major health problem with remarkable impact on visual outcome and quality of life. Two major factors are responsible for ocular morbidity: the recurrent nature of the disease and the lack of a treatment able to clear latent virus, although acyclovir has been extensively used to reduce severity and number of recurrences in infected patients resulting in a better visual outcome. HSV and VZV share a similar pathogenetic mechanism characterized by intermittent period of latency in the nervous system and clinically recurrent ocular manifestations. Uveitis secondary to HSV and VZV may occur in association with keratitis or without corneal involvement. Active herpetic keratitis and uveitis can occur concurrently, but more frequently the patient has a history of recurrent HSV keratitis or characteristic VZV skin eruption. Iris atrophy may be present in about 35-40% of cases of herpetic uveitis. Glaucoma and cataract secondary to both chronic inflammation and to chronic use of topical corticosteroids are the most frequent

complications of this type of uveitis. The pathogenesis of herpetic uveitis is complex and includes various mechanisms such as active viral replication and immune reactions against viral antigens.

Cytomegalovirus uveitis

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Purpose: cytomegalovirus (CMV) infection has been recently recognized as an important aetiology for anterior uveitis in immunocompetent patients. The aim of this study was to report on the long-term prognosis of CMV anterior uveitis

Methods: retrospective chart review of patients with CMV anterior uveitis (positive PCR in aqueous humor) with a minimum follow-up of 24 months

Results: 15 patients, 9 males and 6 females, were included. Mean age at uveitis onset was 35.7 + 14 years (range: 17-59 years). Uveitis was unilateral and hypertensive in all the cases, acute relapsing in 8 (53.3%) and chronic in 7 (46.6%). Corneal involvement was found in 2 cases (13.3%), cataract developed in 9 patients (60%) and 2 presented the first episode of uveitis after cataract extraction (13.3%). Chronic raised IOP/glaucoma was found in 14 patients (93.3%), 9 requiring surgery (60%). Two patients received oral valganciclovir, which was stopped 5 months after because of leukopenia.

At the end of follow-up (mean: 62.7 + 27.7 months) all the patients have a quiescent uveitis, 11 of them under topical low dose steroid therapy (73.3%), in 4 cases combined with systemic acyclovir. Eleven (78.6%) patients are on antiglaucomatous therapy (mean final IOP: 16.3 + 5.1 mmHg; range 10-32 mmHg) and the mean visual acuity at last examination is 0.85 + 0.23.

Conclusions: CMV-associated anterior uveitis has a fairly good long-term visual prognosis, although cataract and raised IOP/glaucoma are frequent complications. A multicentre study on the most useful therapeutic approach is warranted

Viral Retinitis

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Viral Retinitis is the most frequent etiology of Acute Retinal Necrosis, in particular due to Herpes Virus Group; but also immune pathogenesis like in Behcet disease or in Malignant disease, and especially in Intra Ocular B Cell Lymphoma, must be considered. Samples in aqueous or vitreous are mandatory to perform Polymerase Chain Reaction or molecular analysis; these analysis are important to do a rapid and correct differential diagnosis, necessary to properly start treatment in these dramatic ocular diseases. Viral Retinitis is generally necrotizing retinitis but less frequently can evolve with intraocular inflammation without necrotising lesions. Viral Retinitis is possible in both immunocompetent and immunodepressed patients.

We considered a new clinical evidence due to Citomegalovirus retinitis in systemically immunocompetent but intraocular immunodepressed patients, frequently related to intravitreal steroid injection.

Session 20

IOIS session: *Advances in Imaging have made of uveitis a precise clinical science or "The use of SD-OCT in inflammatory ocular diseases"*

Anterior Segment OCT in Uveitis

Dr Alastair Denniston PhD MRCP FRCOphth, University Hospitals Birmingham NHSFT, UK

As we look to make uveitis a more precise clinical science, we ask whether OCT will revolutionise the assessment of the anterior segment and does it have the potential to provide objective measures of disease activity and damage in anterior segment uveitis? Advances in OCT technology from Time-Domain through to Spectral-Domain and Swept-Source, and the advent of improved eye-tracking systems have greatly improved the resolution of images obtained. First applications of anterior segment OCT were primarily as an alternative method of imaging major structures, but higher resolution systems are enabling identification and even quantification of anterior chamber cells, keratic precipitates, iris granulomata, peripheral anterior synechiae and other angle pathology. The current status of anterior segment OCT in uveitis will be reviewed, and the potential impact for uveitis specialists will be discussed.

Optical coherence tomography (OCT) imaging in uveitis

Ilknur Tugal-Tutkun

OCT imaging is routinely used for the diagnosis and monitoring of posterior pole pathologies in patients with uveitis. Spectral-domain OCT has become a standard technique for the evaluation of uveitic macular edema as well as other macular pathologies such as epiretinal membrane formation, vitreomacular traction, and macular holes. High-resolution OCT imaging of morphological changes in the retina, vitreoretinal interface, and choroid have led to a better understanding of disease processes and distinctive features of uveitic entities. With the introduction of enhanced depth imaging, visualization of the choroid and choriocapillaries has allowed early detection and monitoring of choroidal inflammation. Thus, OCT imaging has become an indispensable tool both for the differential diagnosis and for the follow-up of inflammatory diseases of the retina and choroid.

EDI-OCT: new insights into pathogenesis of posterior uveitis or just another tool to play with

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By providing high-resolution, cross-sectional images of the neurosensory retina, optical coherence tomography (OCT) imaging has transformed the diagnosis and management of retinal diseases. Until recently however, visualization of the choroid was not possible with OCT systems - a significant shortcoming given the

central role of choroidal inflammation in many uveitic diseases. Choroidal imaging with OCT has now become possible with current, commercially-available OCT systems, through the use of specialized protocols for image acquisition.

This is referred to as "enhanced depth imaging" (EDI)-OCT. The next generation of commercially-available OCT technology (e.g., DRI-1 "Atlantis", Topcon) employ "long-wavelength" (~1050 nm) light sources to allow further enhancements in choroidal visualization. With these advances, choroidal imaging with OCT may improve the diagnosis and phenotyping of uveitic disorders, as well as allowing improved monitoring of disease activity. In this presentation, our current experience with choroidal OCT imaging in uveitis will be discussed, along with potential future applications in this area.

What is the practical contribution of Fundus Autofluorescence (FAF) to the appraisal of uveitis?

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Carl P. Herbort J.R., Inflammatory Eye Diseases, Centre for Ophthalmic Specialised Care (COS), Lausanne, Switzerland

Purpose: to determine the practical contribution of blu light fundus autofluorescence (BL-FAF) and near infrared fundus autofluorescence (NIR-FAF) to the appraisal of uveitis with particular cure to the inflammatory diseases of the choriocapillaris.

Methods: BL-FAF signal depends on both the amount of bisretinoids in the RPE and the absorbion of light by photoreceptor pigments, macular pigment and RPE melanin. During the photobleaching process (absorbion of photons by photopigment in the outer photoreceptor segments), there is a reduction of the photopigment density and so an increase of the visualization of the autofluorescent signal coming from the RPE. NIR-FAF measures the autofluorescence of melanin in the RPE and choroid; it's related to amount of melanin and/or compounds closely related to melanin (oxidized melanin, melanolipofuscin) in the RPE.

Results: the visualization of different FAF patterns may reflect disease activity in the setting of uveitis. In MEWDS and MFC, the more striking BL-FAF alteration is an increase of the autofluorescent signal and SD-OCT shows a disruption of ellipsoid and interdigitation zones, probably sign of dismanting outer photoreceptor segments; there is not an increase of NIR-FAF and after the photobleaching process, the areas of increased BL-FAF become isofluorescent. This could mean that the areas of hyperautofluorescence are due to a better visualization of the autofluorescent signal because there is a reduction of the visual pigments and not to an increase of the fluorophores. In the APMPPE group, during the convalescent stage, increased BL-FAF and NIR-FAF are often seen in the center of chorioretinal scars, corresponding to accumulation of fuorophores debris and to hypertrophy/hyperplasia of RPE cells.

Conclusions: In uveits, BL-FAF and NIR-FAF analysis can contribute additional information to other imaging methods for studying the lesion process but this imaging technique is especially useful for

the of PICCPs, including MEWDS and MFC. Photobleaching process, NIR-FAF and spectral-domain OCT findings may explain the increased BL-FAF, present in the acute phase of these diseases, as a loss of the photopigments and not to an increase of fluorophores, because there is a limited pertubation of choriocapillaris circulation with a slight ischaemic insult to outer retina.

Multimodal imaging has made uveitis an exact clinical science

Carl P, Jr Herbort, University of Lausanne and Centre for Ophthalmic Specialised care

Background: In the last two decades several investigative techniques and imaging modalities have allowed to precisely evaluate intraocular inflammation in all its compartments leading to improved diagnosis and monitoring capabilities. In parallel new therapeutic modalities became available that can be precisely evaluated thanks to these new technologies.

Objective: Using multiple imaging methods including fundus photography (FP), fluorescein angiography (FA), indocyanine green angiography (ICGA), Optical coherence tomography (OCT), fundus autofluorescence (FAF) and ultrasound biomicroscopy (UBM) as well as functional tests such as automated visual field testing and microperimetry together with laser flare photometry (LFP), it will be shown how a global picture of complex inflammatory cases can be obtained.

Conclusion: Considering the degree of precision obtained by multimodal imaging and other recently developed investigative modalities, it is difficult to understand why some of these procedures are still not routinely used in many centres taking care of inflammatory conditions of the eye.

Session 21

Taiwan Uveitis Study Group: *Infectious Uveitis*

Topical ganciclovir for cytomegalovirus corneal endotheliitis

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Purpose: To evaluate the efficacy of topical ganciclovir treatment in cytomegalovirus (CMV)-associated anterior segment infections.

Methods: Seventy-four eyes (67 patients) with positive results of the CMV polymerase chain reaction from aqueous humor tapping were enrolled. All eyes were treated with continuous topical 2% ganciclovir eye drops after positive results of the CMV PCR. The therapeutic assessments were analyzed in three aspects of trabeculitis, iritis, and endotheliitis, measured by intraocular pressure (IOP) control, anterior chamber reaction, and corneal endothelial cell density (ECD) preservation, respectively.

Results: All eyes showed undetectable level of CMV DNA at repeated taps. The follow-up time was 31.76 ± 13.15 months. Under topical ganciclovir treatment, 28 eyes (37.8%) experienced IOP crisis (IOP ≥ 30mmHg) and 10 eyes (13.6%) needed further glaucoma surgery. The occurrence of iritis was detected in 19 eyes (25.7%). Among them, none presented with corneal edema or keratic precipitates and most episodes of iritis were not accompanied by IOP elevation. The initial and last ECD measurements were 1553 ± 727 cells/mm2 and 1479 ± 681 cells/mm2, respectively. The mean percentage of individual endothelium change was -0.78%.

Conclusion: Topical 2% ganciclovir had the capacity to clear viral load in anterior chamber, prevent iritis recurrence, assist intraocular pressure control, and preservation of corneal endothelium. Under uninterrupted topical application of 2% ganciclovir, CMV-associated endotheliitis had the most favorable remission rate followed by iritis and trabeculitis.

Acute retinal necrosis in Taiwan

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Purpose: to report the clinical characteristics of acute retinal necrosis (ARN) in Taiwan

Methods: multicenter, retrospective study

Results: There are 50 eyes in 47 patients (22 females and 25 males) including in this study. The average age is 49.41 years of age (range: 15-76 Y/O). Initial visual acuity (VA) ranged from 20/20

to light perception. 4 patients had both eyes involved. RD developed in 24 eyes. Final VA (range from 20/20 to NLP) improved in 12 eyes, deteriorate in 23 eyes and stationary in 7 eyes. Initial VA is closely related to final VA ($p<0.05$). In eyes with retinal detachment undergoing surgical repair, only 4/23 eyes had final VA equal or greater than 20/200, and 4 eyes had final VA of no light perception. Aqueous PCR was performed in 27 eyes, in which herpes zoster virus was detected in 77.78% eyes (21/27 eyes), herpes simplex virus 18.52% (5/27) and cytomegalovirus in 3.7% (1/27) eye.

Conclusion: Herpes zoster is the leading cause of ARN in Taiwan. Early detection and management often lead to better visual outcome. In spite of the improved surgical technique, final VA is still guarded in cases with retinal detachment.

Infectious intraocular inflammatory disease with uncommon pathogen in Taiwan

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Ming-Ling Tsai, Tri-Service General Hospital, Taipei, Taiwan

Purpose: To report the clinical presentations and results of infectious intraocular diseases with uncommon pathogen in Taiwan. Case reports: Infectious intraocular inflammations with uncommon pathogen: Burkholderia pseudomallei, Roseomonas, Acinetobacter baumannii, Enterococcus, Enterobacter gergoviae, Penicillium, and Stenotrophomonas are reported. Conclusions: Uncommon pathogens have specific risk factors. The visual prognosis is variable and depends on the virulence of the pathogens.

Ocular syphilis and the trend of syphilis in Taiwan Chinese

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Purpose: To analyze ocular syphilis and the trend of syphilis in Taiwan Chinese.

Materials and Methods: Retrospective review medical charts with ocular syphilis in a tertiary referral center (TSGH). The number of reported syphilis cases to Taiwan Center for Disease Control and Prevention (CDC) was analyzed as well.

Results: The reported case numbers with syphilis to Taiwan CDC increased from 4158 at 2001, peak 6668 at 2009, to 6373 cases at 2011. Besides, eleven cases were diagnosed in TSGH as ocular involvement by active inflammation, serologic treponemal tests, and a reduction of the inflammation after antibiotic. Co-infection with human immunodeficiency virus was reported in eight patients. The ocular lesions included: chorioretinitis (one case), retinitis (two cases), panuveitis (two cases), uveoscleritis (one case), neuroretinitis(one case), anterior optic neuritis (one case), and retrobulbar optic neuropathy (one case). Ocular inflammation resolved in all patients after treatment. However, two cases revealed poor visual outcome (LP, NLP) in the patients with optic nerve involvement.

Conclusions: Syphilis has re-emerged and remained an issue in Taiwan public health. In Taiwan Chinese, ocular syphilis demonstrated highly correlated with HIV infection. Ocular syphilis in HIV-positive patients should be treated as neurosyphilis. Moreover, HIV may acceleration syphilis progression. Careful diagnosis and prompt are necessary.

Endogenous Fungal Endophthalmitis – Taiwan Experience

De-Kuang Hwang, Taipei Veterans General Hospital
Shih-Jen Chen, Taipei Veterans General Hostpial

Endogenous Fungal Endophthalmitis is relatively rare in Taiwan. The infections usually occur in immunocompromised people or patients under immunosuppressing drugs. However, sometimes it may happen in immunocompetent subjects such as in healthy pregnant women. Symptoms and presentations of this disease are different with other infectious endophthalmitis (e.g. less reaction in anterior chambers, less pain or slower onset), lead to a great diagnostic challenge for clinical ophthalmologists.

Candida species are the most common cause of endogenous fungal endophthalmitis and developed in 9% to 45% of patients who had systemic candidemia. Not only hospital-based but also nationwide studies have shown that the incidence of candidemia has increased over the past few decades in Europe and the United States. The increasing of incidence was contributed by the greater use of broad-spectrum antibotics or immunosuppressive agents, more invasive procedures, advanced life support in patients with severe diseases and the improvement of diagnostic methods. It deserves us; the ophthalmologists to raise our awareness and pay more attention on ocular involvement of this infection.

In the presentation, we will report the clinical manifestations and managements of cases with endogenous fungal endophthalmitis as well as the nationwide population-based epidemiologic studies in endophthalmitis comorbid with fungemia in Taiwan.

Endogenous KP endophthalmitis

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Endogenous bacterial endophthalmitis (EBE) is a potentially blinding form of intraocular endophthalmitis resulting from hematogenous spread of bacterial from a focus of infection into the eye. *Klebsiella pneumoniae* (*KP*) has been recognized as a major cause of EBE in Asian populations. It is also an emerging infectious disease in the United States and the rest of the world. The visual outcome of *K. pneumoniae* EBE is generally poor, ranging from finger counting to evisceration or enucleation of the eyes.

Risk factors reported in the literature include diabetes, disseminated intravascular coagulation and delayed diagnosis and treatment. Of these, underlying diabetes is the most consistently reported. Based on a large series of retrospective study, we confirmed the important role of diabetes as a significant risk for developing endophthalmitis in patients with KP liver abscess. Poor initial vision is a significant risk for poor visual outcome. Besides, diabetes is an important factor in preserving eyes with endogenous *Klebsiella pneumoniae* endophthalmitis from undertreatment. Ophthalmologist should consider endogenous *KP* endophthalmitis an emergency condition, especially in diabetic patients.

Session 22

Hellenic Society for the study of Intraocular Inflammations and Infections: *Controversies in Uveitis*

Vitrectomy is the cure for uveitis

Periklis Brazitikos,Department of Ophthalmology, Aristotle University, Thessaloniki, Greece

Pars-plana vitrectomy (PPV) has been a natural accompaniment to pharmacotherapy in the treatment of ocular inflammatory diseases as it offers a surgical means to clear vitreous opacities and repair structural complications. For PPV itself, technology and technique have been important lines of development, but for ocular inflammatory diseases, the evolution of vitrectomy has mainly involved a search for clear indications for surgery and an assessment of outcomes. As already had reported in literature PPV led to a decrease in the activity of uveitis and a reduction in both recurrences and dependence on immunosuppressive or anti-inflammatory medication.

Our results demonstrate with respect to the safety and efficacy of transconjunctival sutureless 25-gauge PPV system on 14 patients (15 eyes) with uveitis who underwent PPV for posterior segment involvement secondary to uveitis that sutureless 25-gauge surgical technique is a safe and efficacious approach in selected uveitis cases. BCVA improved in almost all cases (14/15). Only one eye resulted in phthisis due to retinal detachment secondary to toxocara granuloma. PPV in an important confounding factor in observational series clearing the ocular media that report good results from surgical therapy, because vitreous haze is one of the signs used to grade intraocular inflammation.

It is not clear whether vitreous inflammation is an epiphenomenon to the real events of intraocular inflammation or a self-perpetuating depot of immunologically active cells with an ill-defined antigenic load that is indeed part of the disease process. Intraocular antibody production and detection of infectious organisms in uveitic eyes without overt active infection support the concept of the vitreous as an active reservoir of disease. Analysis of vitreous specimens from uveitic eyes might help create hypotheses regarding its biologic activity.

Although the final role of vitrectomy in the management of patients with uveitis remains to be determined, our experience reveals that the 25 g surgical technique is a safe and efficacious approach in selected uveitis cases. Remissions and exacerbations can occur anytime in the postoperative period therefore careful attention to postoperative control of inflammation is still necessary.

Pars plana vitrectomy has a disease-modifying therapeutic role in uveitis – Pro

Alexander Charonis, Athens Vision Eye Institute

Objective: To highlight the disease-modifying therapeutic role of PPV in specific uveitic entities.

Methods: Literature review / analysis.

Results: There is a substantial body of evidence supporting the disease-modifying therapeutic role of PPV in specific uveitic entities, both in terms of functional and anatomic outcomes, as well as systemic immunomodulatory burden needed to control inflammation. This evidence will be critically analyzed emphasizing on the shortcomings of assessing postoperative inflammatory markers which often guide treatment decisions.

Conclusions: PPV, apart from addressing clinically significant structural sequelae of uveitis, appears to have a "direct" disease-modifying role on an individualized basis that merits further investigation.

"I treat based on BCVA"

Sofia Androudi, MD, Assistant Professor of Ophthalmology, University of Thessaly

"I treat based on OCT"

Chris Kalogeropoulos, Associate Professor of Ophthalmology, University of Ioannina

THE GOAL OF THERAPY IN PATIENTS WITH UVEITIS:

- Eliminate ocular inflammation
- Reduce ocular and systemic morbidity

We suggest a stepladder algorithmic approach for the treatment of non-infectious uveitis. The process in deciding which medication to choose for treating uveitis is based upon a multitude of factors. Some of these factors include age, sex, social and past medical history, compliance factors, and most importantly, their specific ocular inflammatory disease. The administration of these medications and the monitoring of these patients becomes a joint effort between the ophthalmologist and multiple sub-specialists (rheumatology, oncology and hematology).

The first step for many patients with ocular inflammation begins with the initiation of corticosteroid treatment; this may dispensed topically, through local injection or systemically. Corticosteroids are often started because they usually are able to control inflammation quickly. Although excellent at quelling inflammation initially, oftentimes these agents are not curative for the problem, as many times patients are unable to completely wean off corticosteroid therapy without having a recurrence of their uveitis.

In this session we are going to highlight (through a debate) the decision to treat uveitis based on BCVA decrease (Dr. Sofia Androudi) or OCT changes (Prof. Chris Kalogeropoulos)

Orbital Inflammatory disease: steroids or biologics?

George Kalantzis, St. James's University Hospital, Leeds, UK
Nikolaos Chalvatzis, 2nd Ophthalmology University Department, Thessaloniki, Greece

Orbital inflammatory diseases can be classified as either specific or non-specific. Aetiology of specific orbital inflammation include thyroid orbitopathy, infection, granulomatous disorders (sarcoidosis,

xanthogranulomatous diseases) and vasculitis (polyarteritis nodosa, Wegener's granulomatosis, giant cell arteritis). The definition of non-specific orbital inflammation (idiopathic orbital inflammatory disease, orbital myositis, dacryoadenitis) remains clinical and consists of processes that have specific anatomical localizations within the orbit . Corticosteroids remain the mainstay of treatment, with pulsed intravenous methyl prednisolone being more effective, and with fewer side effects, than the oral route in orbital inflammatory diseases. Neither route is without risk, although those associated with intravenous methyl prednisolone tend almost exclusively occur with consecutive or alternate doses >500mg. In some occasions adjunctive treatment with non-steroidal anti-inflammatory drugs, cyclophosphamide and / or azathioprine is useful and efficacious. Newer biologics offer hope of more targeted therapeutic modalities, but can potentially cause severe adverse effects including significant haematologic cytopenias, exacerbation of demyelinating disease and induction of systemic lupus erythematosis. However, it should be stressed that an orbital biopsy must be performed in the majority of orbital inflammatory diseases especially if there is evidence of persistent, progressive, recurrent orbital disease or those unresponsive to therapy.

Orbital Inflammatory disease: steroids or biologics?

George Kalantzis, St. James University Hospital, Leeds, UK
Nikolaos Chalvatzis, 2nd Ophthalmology University Department, Thessaloniki, Greece

Idiopathic orbital inflammation (IOI) represents a continuum of disease with a constellation of clinical presentations. The diagnosis of IOI requires exhaustive radiologic and histopathologic investigation while its management is often challenging. Furthermore, relapses are frequent and sometimes may become devastating for both, the patient and the clinician. The notion that IOI universally and swiftly responds to steroids has recently been abandoned and replaced by modern concepts focusing on targeted therapeutic options. Biologic immuno-modulators open a new, exciting avenue in selective management of IOI. Rituximab, Infliximab, Adalimunab and Etanercept are arguably effective in a number of systematic inflammatory diseases as well as in certain malignancies. Use of these agents in IOI is supported by investigations of the molecular biology of the disease. However, only a few studies have proven the clinical efficacy of the above modulators. Certainly, further research should aim to evaluate these treatments and their safety in IOI.

Session 23

IOIS session: *Orbital and optic nerve inflammations*

Differential diagnosis of orbital infections

Valerie TOUITOU, DHU Vision and Handicaps, Pitie-Salpetriere Hospital, Paris, France

Orbital infections remain an emergency to rule out in the face of periorbital complaints with a painful red eye, proptosis and decreased ocular motility. Systemic symptoms are important to consider, as well as CNS symptoms if case of cavernous sinus involvement. The type of microbial agent is important to consider as treatment modalities, outcome and final prognosis may differ.

The conditions that can mimic orbital infections need to be carefully ruled out. Orbital imaging is very helpful to establish the etiologic diagnosis, and an appropriate systemic work-up will allow prompt and specific therapy. Orbital biopsy can be necessary in challenging cases. Diffuse idiopathic orbital inflammation may have a similar presentation at its onset. Several neoplasia may mimic orbital infections, such as MALT lymphoma, Burkitt lymphoma, leukemia, metastatic carcinoma, retinoblastoma, rhabdomyosarcoma. Specific inflammatory conditions such as sarcoidosis, histiocytosis X (Letterer-Siwe), and ANCA-associated vasculitis are important diagnosis to rule out. IgG4-associated disease is also a differential diagnosis to consider. Finally, acute thyroid eye disease is another important trap to detect.

With prompt recognition and aggressive medical and surgical treatment the prognosis can be excellent.

Mucormycosis: old disease with new strains effecting the healthy

Daniel Briscoe MD, Ori Scheyer MD, Raoul Colodner PhD, Judit Krausz MD, Raoul Raz MD. Emek Medical Center Afula, Technion Faculty of Medicine, Israel.

Background: Orbital Mucormycosis is commonly known as a disease of immunocompromised patients and develops through extension from the ethmoidal and maxillary sinuses into the orbit. Immunocompetent hosts are generally not considered to suffer from this disease although in recent years infection with a rare strain of Mucor has changed this. Apophysomyces elegans Mucormycosis is an aggressive disease which results in amputation or death in the immunocompetent patient and death in the immunocompromised patient.

Methods: We present a case of Apophysomyces elegans Mucormycosis causing endophthalmitis in a young healthy adult. A review of similar cases in the literature, and management is discussed.

Results: Diagnosis was made using biopsy and PCR tests. Treatment was with local and systemic antifungals in addition to treatment with hyperbaric oxygen.

Conclusion: Apophysomyces elegans mucormycosis effects healthy patients in warm tropical climats and can be fatal. Early diagnosis is essential and adjuvant treatment with hyperbaric oxygen may be helpful.

Idiopathic orbital inflammation and IgG4 related disease: a rapidly emerging disease

Alvaro Bengoa González, Hospital Universitario 12 de Octubre. Madrid

IgG4 related disease is considered a systemic disease. It is an inflammatory condition of unknown etiology that involve the pancreas, liver, lung, breast, kidney, biliary tract, salivary gland, ocular adnexal (orbit and lacrimal gland) and other organs. The number of organs and diseases associated with IgG4 related disease continues to grow. This disease is clinically characterized by tumor like presentation, frequent recurrence, with or without high serum IgG4 levels and steroids responsiveness. Numerous lymphoplasma cell infiltrations with abundant IgG4 –positive plasma cells, reactive lymphoid follicles and sclerosing fibrosis are common histological characteristics. Emerging evidence is now showing that idiopathic sclerosing orbital inflammation is linked to IgG4 related disease especially if the presentation is bilateral. An orbital biopsy must be done for accurate diagnosis and to guide appropriate treatment. Long term observation is also warranted in these patients because a few case reports suggest there may be an increased incidence of orbital lymphoma arising from a background of IgG4 positive inflammation. There is a growing understanding of how the disease manifests itself and this is critical to develop a clinical strategy for the diagnosis and effective treatment.

Orbital Myositis

Mehrad HAMEDANI

Orbital myositis is a common presentation of nonspecific inflammatory syndromes. The main clinical signs are diplopia, proptosis and conjunctival injection over muscle insertions. Myositis may involve one or several muscle(s), in one orbit, or bilaterally. Often, there is no association with systemic diseases. Differential diagnoses are mainly thyroid associated orbitopathy, lymphoma and metastases. Treatment is based on steroids. Biopsy should be considered in case of recurrence or atypia, to rule out differential diagnoses and to permit the change of treatment to immunosuppressive drugs.

Session 24

Canadian Uveitis Society: *Complications in uveitis*

Canadian experience of Dexamethasone Intravitreal Implant (0.7 mg) in patients with macular edema associated with uveitis

Wai Ching Lam, University of Toronto
Darryl Baptiste, Allergan Inc

Purpose: To evaluate the real-world use, efficacy and safety of Ozurdex® (dexamethasone intravitreal implant [DEX implant], Allergan Inc., Irvine, CA, USA) 0.7 mg in patients with non-infectious uveitis affecting the posterior segment. Study design: Retrospective observational cohort study.

Methods: Patients receiving ≥1 intravitreal injection(s) of DEX implant for treatment of macular edema (ME) secondary to retinal disease, having ≥3 months of follow-up after the first DEX implant, were identified from medical records (December 2010-December 2012) from 10 Canadian retinal practices. Mean changes from baseline in visual acuity and central retinal thickness (CRT) along with safety data were collected.

Results: 101 patient charts yielded data on 120 eyes diagnosed with DME (n=34), uveitis (n=23), BRVO (n=19), CRVO (n=11), post-surgery (n=13), or other indications (n=20). Uveitis patients had a mean age of 49.8 years and were predominantly Caucasian (85%). At baseline, 52.2% of the uveitis eyes were pseudophakic and 56.5% had disease ≥12 months. Baseline mean(±SE) visual acuity and CRT was 0.69(±0.7) LogMAR and 511.4(±39.3) µm, respectively. The mean(±SE) DEX implant injections for uveitis group was 1.7(±0.2). The mean(±SE) changes in vision and CRT following DEX implant(s) ranged from 1.0(±0.6) to 2.5(±0.6) lines and -56(±76) to -260(±62) µm, respectively. IOP-lowering medication was required in 34.8% of uveitis eyes with only one eye requiring glaucoma surgery. Cataract surgery was required in 45.5% of phakic uveitis eyes.

Conclusions: DEX implant(s) alone or in combination with other treatments and/or procedures resulted in anatomical and functional improvements in long-standing non-infectious uveitis affecting the posterior segment.

Retinal and choroidal neovascularization in uveitis

Nupura Bakshi, University of Toronto

Retinal and choroidal neovascularization are uncommon but serious complications of uveitis. Risk factors for neovascularization include posterior uveitis and uveitis affecting the RPE-choroid interface, as well as uncontrolled inflammation. Careful fundus examination and ancillary imaging modalities are helpful in confirming the diagnosis. The treatment strategy is two-fold, targeting both

the underlying inflammatory disease, and the neovascular process. Current evidence for treatment paradigms and outcomes will be reviewed.

Glaucoma and Ocular Hypertension Associated with Uveitis

Chloe Gottlieb, University of Ottawa Eye Institute

Glaucoma associated with steroids was recognized and studied in the early 1960's with 30% of eyes exposed having elevated IOP. Of eyes with uveitis treated with intravitreal triamcinolone, 60% required IOP-lowering medications, 24% of eyes treated with the dexamethasone implant after 6 months and 70% of eyes with the fluocinolone implant at 3 years. Only 5% of the general population are steroid responders, but this proportion rises to 60% in patients with ocular inflammation. Attempts have been made to predict steroid response with topical steroid challenge. The positive predictive value approached 100%, however, the negative predictive value was 60. A US study confirmed that 20% of patients with uveitis develop glaucoma. The mechanisms are variable, and include open angle (trabecular meshwork resistance) and closed angle (pupil block with posterior synechiae, peripheral anterior synechiae and rotation of ciliary body.) Medical treatment, laser and surgery are used to control intraocular pressure in uveitis. We compared trabeculectomy with mitomycin-C and aqueous tube shunts for glaucoma or ocular hypertension associated with uveitis. We found that 91% of patients with trabeculectomy and 80% of patients with tube shunt met target pressure and the difference was not statistically significant. At 6 months follow-up, there was so statistically significant difference in the BCVA, number of glaucoma medications or uveitis flares between the two groups. 39% of eyes required needling within 6 months and 17% had bleb leaks, which is similar to previously published data. Trabeculectomy and tube shunts appear to be equally effective in patients with uveitis.

Complications of immunosuppressive therapy for uveitis in children

Kinda Najem, University of Montreal
Marwan Elfakhfakh, University on Montreal
Eric Fortin, University of Montreal

To evaluate the complications related to immunosuppressive drugs in the treatment of uveitis in a pediatric population.

Materials and methods: This is a retrospective study of pediatric patients suffering from uveitis followed between 2002 and 2012 in the uveitis subspecialty clinics of Maisonneuve-Rosemont Hospital and Sainte-Justine Hospital in Montreal, Canada. For inclusion, patients were required to have initiated systemic immunosuppressive treatment for uveitis before their 18th birthday. Charts were reviewed for complications related to the immunosuppression including: reported side effects, significant infections, signs of toxicity on laboratory tests, secondary neoplasia, hospitalizations and mortality. Agents used, duration of therapy and cause for cessation of therapy were also recorded. Secondary data such as visual acuity and ocular complications of the uveitis were also analyzed.

Results: 410 patient charts identified as within pediatric age group and followed between 2002 and 2012 were reviewed. Over 50% of these patients had received systemic immunosuppressive treatment during their period of follow-up. The most commonly used agents included prednisolone, methotrexate and adalimumab. Less commonly used agents included cyclosporin, tacrolimus, azathioprine, mycophenolate mofetil, infliximab and abatacept. Tolerance and side-effects/toxicity of each of these agents will be discussed. There were no cases of secondary neoplasia or mortality in this patient cohort over the ten year study period.

Conclusion: Complications of immunosuppressive drugs in a pediatric uveitis population have not been extensively studied in previous literature. Our study aims to report the most common

complications encountered in this population with standard therapy presently used. Overall, the treatment was well tolerated by patients with only rare significant toxicity reported.

Outcome of cataract surgery with intraocular lens implantation in patients with pre-existing uveitis

Larissa Derzko-Dzulynsky, University of Toronto, Department of Ophthalmology and Vision SciencesHarry Dang, University of Ottawa
Crystal Cheung, University of Toronto, Department of Ophthalmology and Vision Sciences
Hannah Chiu, University of Toronto, Department of Ophthalmology and Vision Sciences
Parnian Arjmand, McMaster University
Theodore Rabinovitch, University of Toronto, Department of Ophthalmology and Vision Sciences
Deepak Khosla, University of Toronto, Department of Ophthalmology and Vision Sciences

Purpose: To describe current approach and outcomes of cataract surgery in patients with uveitis.

Methods: Retrospective cohort study and literature review.

Results: Cataracts occur in up to 50% of patients with uveitis. Outcomes of cataract surgery have improved significantly due to advanced surgical techniques, biocompatible intraocular lenses and intensive control of uveitis for several months prior to cataract surgery and postoperatively. Preoperative and postoperative steroid treatment regimens can vary. A retrospective review of 246 eyes (216 adult patients) with phacoemulsification and acrylic posterior chamber intraocular lens implantation was performed. Best-corrected visual acuity (BCVA) and uveitis grade (SUN criteria) were measured at 1 month preop, 1 week postop and at 1, 6, 12 months postoperatively. 84.6% of eyes had rare or 0.5 anterior chamber cells at 1 week postop and maintained uveitis control (77% no uveitis and 18.9% 0.5 anterior uveitis) at 1 year postoperatively. No patients had active intermediate or posterior uveitis at any time point. Mean BCVA improved from 0.76 ± 0.37 logMAR preoperatively to 0.37 ± 0.36 at six months ($p<0.01$) and to 0.30 ± 0.25 at 12 months ($p=0.01$) postoperatively. Postoperative complications included posterior capsule opacification (18%), epiretinal membrane (9%) and cystoid macular edema (5%). 4% of patients required an Nd:Yag capsulotomy.

Conclusions: Cataract surgery with acrylic PCIOL implantation is effective at improving visual acuity in patients with uveitis. Posterior capsule opacification is the most frequent postoperative complication. Postoperative visual outcome can be limited by pre-existing and postoperative macular complications of uveitis.

Session 25

Australian and New Zealand Uveitis SIG: Uveitis down under

Prevalence of Uveitis in Australia and New Zealand

Sam Lertsumitkul, Liverpool Hospital, Sydney, Australia

Little is known about prevalence of inflammatory eye diseases in Australia (since 1986) or New Zealand. There are to date only one epidemiologic study in Sydney1 and one in an Aboriginal community2. With recent increased migration from both Europe and Asia, Australia is likely to have similar prevalence data as the rest of the world. We examined data extracted from 3 different databases, namely a public hospital eye outpatient, a private ophthalmic practice and New Zealand.

1. Australian public tertiary hospital outpatient in a highly concentrated migrant community
Database (2000-present) prevalence is 425 cases out of 17192 or **2.47%**

1. Australian private ophthalmic practice with subspecialty in uveitis (GP referral 50%, optometrists 18.75%, Specialist 31.82%)
Database (2005-present)prevalence is 176 cases out of 8229 or **2.14%**
Anterior – 64.20% Compared to pre 1986 - 75%
Intermediate – 14.20%---------- - 2%
Posterior – 9.66%---------- - 21%
Panuveitis – 12.50%---------- - 4%
Idiopathic – 42.60%---------- - 52%

1. Australian Aboriginal community (2005-2008)
Anterior – 0.21%
Intermediate – 0%
Posterior – 0.59%
Panuveitis – 0%

2. New Zealand[3]
Demographics overall:
510 caucasian (53%)
78 maori (8.1%)
112 pacific Islander (11.7%)
259 "other" (indian next biggest group) 27%
Tot: 959

Overall anatomical location by all ethnicities:
671 Anterior- 74.7%
50 Intermediate 5.6%
71 Posterior 7.9%
106 Panuveitis 11.8%
Total: 898

Pacific islanders:---------- Maori:
Anterior- 72%---------- 66%
-Intermediate- 6%---------- 9.9%
Posterior- 1%---------- 5.6%
Panuveitis- 21%---------- 18.3%
total: 100---------- total: 71

Scleritis in Australia

Peter McCluskey,
Co-authors: Julie Morrison, Ethan Nguyen, Jess Brennan, Lyndell Lim, Richard Stawell

This talk will present the results of a retrospective case series of 90 patients with scleritis managed at tertiary referral centres in Sydney and Melbourne. The aetiology, clinical features, treatment and outcomes will be detailed

Translational Studies of Ocular Toxoplasmosis

Justine R. Smith, FRANZCO, PhD. Flinders University of South Australia, Adelaide, AUSTRALIA

Toxoplasma gondii is a ubiquitous apicomplexan parasite that infects approximately 2 billion persons worldwide, including an estimated 1 in 5 Australians. Human infection with T. gondii manifests most often as an inflammation of the retina, which is frequently recurrent. Damage to the retina occurs both because of lysis of retinal cells by the parasite and from the local immune response to the parasite. The retinal pigment epithelium (RPE) is an essential component of the blood-retinal barrier, and it contributes to ocular immune privilege. Our laboratory is investigating the ability of human RPE to regulate the immune response to T. gondii within the eye. Our results indicate that infection of the RPE with T. gondii induces alterations in gene expression of immunomodulatory molecules, and that this effect is dependent on parasite strain. Such alterations are expected to impair the ability of the RPE to regulate the immune response within the eye during infection. Thus infection with different T. gondii strains may influence the visual outcome of ocular toxoplasmosis.

Adalimumab in refractory uveitis

Stawell, Richard J; Lim, Lyndell
Centre for Eye Research Australia, University of Melbourne, East Melbourne, Australia.
Royal Victorian Eye and Ear Hospital, East Melbourne, Australia.

Purpose: To present the Royal Victorian Eye & Ear Hospital, Ocular Immunology Clinic's experience in using Adalimumab for severe refractory uveitis.

Method: A retrospective case history review of all seven patients in the clinic on Adalimumab was conducted to demonstrate the response to this drug where there had been resistance to treatment with conventional immune suppression regimes. The previous details of drug therapy, flare-ups, treatments and the inflammatory scores whilst on Adalimumab were collected.

Results: Of the seven patients, 4 had Behcet's related retinal vasculitis, 2 to had multifocal choroiditis and one patient had intermediate uveitis. All patients were commenced on Adalimumab 40mg every 2 weeks. Currently, four patients are also taking mycophenolate moffetil, three are on methotrexate, and two patients are also slowly tapering oral prednisolone. Uveitis is controlled in all patients.

Conclusion: This small cohort of patients has shown a marked improvement in the control of their uveitis since commencing Adalimumab, where traditional regimes of immunosuppression have failed.

Session 26

Society for Ophthalmo-immunoinfectiology in Europe: *Diagnostic delays, challenges and mistakes in uveitis*

The hit-parade of diagnostic delays in uveitis

Carl P, Jr Herbort, University of Lausanne and Centre for Ophthalmic Specialised care

Early diagnosis is crucial in order to apply an appropriate therapy as early as possible. This retrospective single centre study concerned the period from 1990 to 2000 in a centre where mostly referred patients were seen and reflects a period when new investigational modalities such as multimodal imaging, IGRA testing and others were either not available or not practiced routinely. Seven uveitis entities with straightforward diagnostic criteria were chosen and classified into frequent (HLA-B27 uveitis, Toxoplasmic retinochoroiditis), intermediate (Fuchs' uveitis) and more rare occurrence (Behçet's uveitis, ocular tuberculosis, Vogt-Koyanagi-Harada disease, birdshot retinochoroiditis). Among commonly seen patients in our setting (>10% of uveitis cases), diagnostic delay was 7.9±15.8 months (0.65 years) for HLA-B27 uveitis and 9.0±16.5 months (0.75 years) for toxoplasmic retinochoroiditis. Fuchs' uveitis, representing 5.7% of uveitis cases in our setting, was diagnosed with a delay of 3.67±4.34 years. Among rare conditions in our setting (1.2-2.4% of uveitis cases), diagnostic delays were 1.9±3.7 years for VKH disease, 2.1±3.3 years for Behçet's uveitis, 2.87±1.5 years for birdshot retinochoroiditis and 5.7±4.1 years for presumed ocular tuberculoisis. The reasons for such diagnostic delays will be analysed and this retrospective group will be compared to a more recent collective of patients seen between 2008 and 2013.

The top big fails in diagnosing and managing uveitis

Vishali Gupta

The diagnosis and management of uveitis is full of challenges including mistaking non-uveitic entities for uveitis and vice versa; mistaking infectious for non-infectious uveitis and vice versa; ignoring the subtle clinical clues that may indicate towards a specific etiology; failing to diagnose masquerade syndromes; failure to make specific diagnosis and instituting specific therapy; injudicious use of corticosteroids/ immunosuppressive agents/biologics and most importantly failure to revise the diagnosis over a period of time in cases where the course of disease is varied. This presentation aims to highlight the big fails in diagnosing and managing cases by simulating real life situations with the help of illustrative cases.

Challenges and pifalls in the diagnosis of inflammatory optic disc edema

Khairallah Moncef, Fattouma Bourguiba University Hospital, Monastir, Tunisia
Kahloun Rim, Fattouma Bourguiba University Hospital, Monastir, Tunisia
Abroug Nesrine, Fattouma Bourguiba University Hospital, Monastir, Tunisia

Optic disc edema (ODE) can occur in the setting of any ocular inflammatory condition. Clinician should be aware of mistakes in the diagnosis and management of ODE and their potential subsequent visual morbidity. Inflammatory ODE may be clinically overlooked or confused with non-inflammatory ODE or inflammatory or non-inflammatory macular disease. Misinterpretation of ocular symptoms, clinical characteristics of inflammatory ODE, and associated findings may lead to mistakes in establishing a differential diagnosis, initiating work-up, and planning a management strategy. Early, proper diagnostic approach to inflammatory ODE is of utmost importance for prompt initiation of appropriate therapy to prevent permanent visual loss related to ODE and associated ocular changes. It relies on a careful analysis of clinical features and laboratory and imaging findings.

Misdiagnosis of Behcet uveitis based on the use of current clinical criteria

Ilknur Tugal-Tutkun

The diagnosis of Behçet disease is based on a combination of clinical findings. Ocular lesions defined in the current sets of diagnostic or classification criteria are nonspecific. It is important to recognize characteristic features of Behçet uveitis because there are patients with Behçet disease but other forms of uveitis by coincidence, and patients with typical ocular involvement but without systemic manifestations of the disease. The course of ocular Behçet disease is characterized by recurrent nongranulomatous uveitis attacks of variable severity. Transient nature of the acute inflammatory signs is the most important diagnostic clue. Transient retinal infiltrates and inferior peripheral pearl-like precipitates are the pathognomonic findings that help differentiating Behçet uveitis from other causes of panuveitis and retinal vasculitis.

Diagnostic Challenges in retinal vasculitis

Bahram Bodaghi, MD, PhD, FEBO ; Phuc LeHoang MD, PhD, FEBO, DHU Vision and Disabilities, UPMC, APHP, Paris, France

Retinal vasculitis remains a common condition in patients with uveitis. The anatomic classification of the disease, recently revised by the SUN group, validates this important finding in intermediate, posterior or panuveitis. Excluding a masquerade syndrome or a vasculopathy is a major preliminary step. Analysis of vitreous haze, type of affected vessels and association to other retinal lesions must be considered before any work-up planning. Severity factors are also important to consider for the best therapeutic management. In the face of retinal arteritis without vitreous haze, systemic vasculitis must be excluded with more rarely SUSAC or IRVAN syndromes. Retinal vein involvement with vitreous haze is frequently associated with Behçet's disease, sarcoidosis, sympathetic ophthalmia, multiple sclerosis and birdshot retinochoroidopathy. Molecular tools, serologies and IGRAs are highly valuable tools to confirm viral retinitis, atypical toxoplasmosis, tuberculosis, syphilis and different emerging entities.

Treatment strategies are adapted to the clinical presentation and the etiological work-up. The main severity factors are extension of vasculitis and presence of retinal ischemia. Corticosteroids are proposed in most of the cases if an infection has been ruled-out or in association with specific antibacterial, antiviral or antiparasitic regimens. Immunomodulatory agents, aspirin and laser photocoagulation may become mandatory in order to maintain a good visual prognosis. The new

generation of biologic agents has improved the management of severe forms of retinal vasculitis in order to protect the visual function as long as possible.

The good, the bad and the ugly of posterior uveitis

Piergiorgio Neri, The Eye Clinic, Polytechnic University of Marche, Ancona-Italy
Ilir Arapi, The Eye Clinic, Polytechnic University of Marche, Ancona-Italy
Vittorio Pirani, The Eye Clinic, Polytechnic University of Marche, Ancona-Italy
Michele Nicolai, The Eye Clinic, Polytechnic University of Marche, Ancona-Italy
Andrea Saitta, The Eye Clinic, Polytechnic University of Marche, Ancona-Italy

The clinical spectrum of posterior pole ocular inflammatory diseases has increased during the years: the expanding number of clinical tests and the increasing number of treatment options have contributed to drive the ocular immunology towards pioneeristic horizons of both diagnosis and treatments never explored before. Both the new diagnostic techniques, and the advances in therapeutic approaches have greatly changed the perspectives of many severe ocular diseases. The combination of steroids and new immunosuppressive agents represents an important aspect of the management of posterior uveitis. This ensures suitable control of inflammation, as well as the reduction of concomitant steroids dose. Neverthless there are cases which do not show a fully satisfactory response. Recently, the role of biologics has represented a breakthrough in the treatment of uveitis. Beside the enthusiasm that these new treatments have created, the high costs and the use off-label of such therapies represent still unsolved issues. In addition, severe sight threatening sequela, such as cystoid macular oedema and inflammatory choroidal neovascular membranes, are still challenging topics for the ocular immunologists. Although no guideline is provided, the current medical literature can give the basis for a successful treatment strategy. This presentation will describe the current hot topics in posterior uveitis, by analyzing the medical literature as well as by presenting original data of a tertiary referral centre.

Session 27

Japanese Ocular Inflammation Society: *Evaluation of ocular fluids to reveal disease mechanisms*

Molecular diagnosis in Ocular Infections

Soon-Phaik Chee, Singapore National Eye Centre;Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore; Singapore Eye Research Institute;Duke-NUS Graduate Medical School.

Precise diagnosis of ocular infections has been made possible with the application of molecular diagnostic techniques to ocular samples. In the past, samples were drawn from mainly from the posterior segment but in recent years, this has evolved to include aqueous sampling for uveitis not diagnosed by conventional means. Polymerase chain reaction (PCR) is able to analyse small quantities of ocular fluids rapidly and is useful for acute or chronic infections and infections especially in immunocompromised eyes. Applying this technology, idiopathic entities such as Posner Schlossman Syndrome have become diagnosed with a viral etiology. Paucibacillary disease such as tuberculosis and fastidious bacteria such as Propionebacterium acnes, where the slow growing pathogens result in a false negative culture result can now be more readily diagnosed using PCR. Obtaining a specific diagnosis is of paramount importance to its management, since therapy can be directed at the infection rather than using steroids alone, which may escalate the infection. False negatives may occur especially in chronic uveitis such as Fuchs Uveitis Syndrome, or infections in immunocompetent eyes. These may be better diagnosed using the Goldmann-Witmer coefficient.

Cell Population Analysis in Vitreous Specimens as a New Diagnostic Tool for the Classification of Uveitis

Kazuichi Maruyama

Uveitis can be caused by several idiopathic diseases, such as sarcoidosis, Behcet's disease and in Japan, Vogt-Koyanagi-Harada disease, as well as by infectious diseases caused by viruses, funguses, and bacteria. To identify the causes of uveitis clinically, it is important to obtain a detailed medical history and perform a through physical examination. Observing the course of the disease is also considered one of the best ways to diagnose uveitis. However, if clinical examination and laboratory analysis of patient specimens are omitted, many cases of uveitis will not be correctly diagnosed. These omissions may be responsible for the high rate of idiopathic uveitis in the Japanese population, which has reached 30%. Previously, we reported that flow cytometric analysis of vitreous samples from uveitis patients was a useful diagnostic tool for ocular sarcoidosis. It has been reported that an increased CD4 helper T cell type 1 (TH1) lymphocyte subset (lymphocytosis) in the vitreous fluid and a CD4/CD8 ratio greater than 3.5 are helpful in diagnosing ocular sarcoidosis. More precisely, we found that for the diagnosis of ocular sarcoidosis, the sensitivity and specificity of the vitreal CD4/CD8 ratio, with a cut-off point of 3.5, were 100% and 96.3%, respectively. We believe that this

study has shown that the CD4/CD8 ratio of lymphocytes, 4 and 8 measured in vitreous specimens are promising diagnostic indicators of uveitis. We also demonstrated that a high CD4/CD8 ratio is highly specific to sarcoidosis, and is an efficient indicator of the disease for differential diagnosis. Additionally, we found that a high vitreal 8 had a very good diagnostic value for viral infections.

Significance of Intraocular Drug Levels

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In the management of uveitis, pharmacologic agents are often being administered without clear appreciation of the subsequent intraocular drug concentration. Such information may help to determine the appropriate approach to control the disease. It is important to investigate and evaluate the presence and concentration of the drug in the anterior chamber and/or the vitreous, which may help to elucidate the mechanism(s) of the pharmacologic agents. Certainly, retinal and choroidal presence is also very important; however, it is often very challenging, in clinical reality, to detect presence of the drug in the retina or choroid.

The presentation will discuss the role and significance of evaluation of levels of drug and various biomarkers in the anterior chamber fluid of patients with non-infectious uveitis who are participating in a clinical trial. Correlation of drug and biomarker levels with degree of disease activities will also be made.

Session 29: IOIS Session

Controversies in diagnosis and management of Uveitis: *Etiologic diagnosis of Fuchs Heterochromic Iridocyclitis*

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Fuchs heterochromic iridocyclitis (FHI) is a disease of unknown etiology characterized by low grade intraocular inflammation, iris heterochromia or atrophy or both, characteristic keratic precipitates(KPs) distributed all over the endothelium, absence of synechiae, development of cataract and less frequently, of glaucoma. Associations with toxoplasmosis, toxocariasis, sarcoidosis, rubella vaccination, cytomegalovirus, herpes simplex virus, chikungunya virus infections, retinitis pigmentosa, Horners syndrome, Ushers syndrome and previous trauma have been described in the literature. In this presentation, we get an insight into the possible etiologies in fuchs hetrochromic iridocyclitis described in the literature and our experience

Controversies in treatment of Ocular Tuberculosis

Shishir Narain, Shroff Eye Centre

In recent years, ocular involvement due to tuberculosis (TB) has re-emerged. It is important to have high index of suspicion for ocular TB in patients with chronic uveitis. Lack of uniform diagnostic criteria for intraocular TB has led to confusion regarding diagnosis. Absence of clinical evidence of pulmonary tuberculosis does not rule out the possibility of ocular TB as up-to 60% cases with extra-pulmonary TB may have no evidence of pulmonary disease. In the absence of microbiologically and molecular biologically proven TB, diagnosis may be presumed ocular tuberculosis in these cases. Multi-drug Anti-Tubercular Treatment (ATT) regimen with 4 drugs is necessary due to prevalence of multi-drug resistance. Even therapeutic trial test now necessitates 4-drug ATT instead of INH alone over 4-6 weeks for positive response. ATT needs to be given from at-least 9 months upto 15 months & prolonged therapy is recommended in ocular tuberculosis. ATT may cause paradoxical reaction in ocular TB requiring high doses of systemic corticosteroids with / without immunosuppression. Concomitant corticosteroids limits ocular tissue damage from delayed hypersensitivity but may rarely flare-up systemic disease. Rifampicin acting as ligand for glucocorticosteroid receptors may decrease bio-availability of steroids. Various factors contribute to multi-drug resistance requiring revised regimens with additional agents like rifabutin, fluoroquinolones, interferon-γ and linezolid. Serious side effects including hepatotoxicity, optic neuritis from ethambutol and rifabutin induced anterior uveitis therefore necessitates definitive diagnosis, judicious administration and close monitoring in ocular tuberculosis.

Management of Acute VKH with Immunomodulatory Agents

J. Fernando Arevalo

Purpose: To describe ocular clinical characteristics, complications, surgical outcomes and treatment among patients with Vogt-Koyanagi-Harada (VKH) disease.

Methods: We retrospectively analyzed 194 patients (382) eyes diagnosed with VKH disease in a tertiary center from January 1986 through December 2011.

Results: Mean baseline best-corrected visual acuity (BCVA) was 20/125 (logMAR 0.8 ± 0.72) in both eyes. The most common form of presentation was panuveitis in 151 (77.8%) eyes. Retinal detachment (RD) was present in 163 (42.7%) eyes, an exudative retinal detachment (ERD) was diagnosed in 161 (98.7%) eyes, and rhegmatogenous retinal detachment (RRD) in 2 (1.3%) cases. Oral prednisone was the first line of treatment in 168 (86.6%) patients. Immunosuppressive treatment with cyclosporine was employed in 87 (44.8%) patients, azathioprine in 58 (29.9%), intravenous steroid in 50 (25.8%), mycophenolate mofetil in 18 (9.3%), and methotrexate in 12 (6.2%) patients. Visual acuity was better than 20/50 in 240 (62.8%) affected eyes and 20/200 or worse in 72 (18.8 %) affected eyes at the last visit. More common complications at the last visit were glaucoma in 135 (35.3%) eyes, followed by posterior synechia 96 (25.1%), cataract in 25 (6.5%), and choroidal neovascularization (CNV) in 21 (5.5%) eyes.

Conclusions: In Saudi Arabia, VKH uveitis affects predominantly young women. Bilateral panuveitis is the most common ocular manifestation. At presentation, exudative retinal detachment is present in 161 (42.1%) eyes. Oral prednisone is the first line of treatment in these patients. More than 60% of eyes maintain a visual acuity of 20/50 or better.

Paradigm shift in the treatment of ocular Behçet's disease

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Behcet's disease is one of the light threatening disease. It occurs in young adulthood, and repeated ocular inflammatory attacks destroy ocular tissues and lead to loss of visual function. Of course, it is important to rescue ocular tissues from destructive inflammation when acute ocular attacks occur. However, it is also important to prevent forthcoming ocular attacks.

So far, we have used various immunomodulatory drugs to prevent ocular attacks including azathioprine, colchicine, and cyclosporine. Although these drugs showed a certain level of efficacy to suppress ocular attacks, they could not induce complete remissions, and patients still showed some ocular attacks. Even more, some patients could not keep taking them due to side effects. Therefore, we have required new therapies with more efficacies and less side effects.

Recently, we have had biological drugs including infliximab and Interferon alpha-2a for the treatment of Behçet's disease. Infliximab is an anti-TNF-alpha chimeric monoclonal antibody, and most of patients can keep remission with infusion every 8 weeks. Most notable side effect is infectious disease including tuberculosis which is mostly preventable by careful systemic screening and regular examinations. Interferon alpha-2a is also an effective drug to suppress ocular attacks. Furthermore, it can induce durable remissions even after cessation of the therapy. However, various side effects are sometimes seen.

Now, other new biological drugs are going to be developed and they may also be used for Behçet's disease in the near future. Although they have still problems about the high cost and the limitation of the available region in the world, their high efficacy will achieve good visual prognosis in Behçet's disease patients. We surely feel the progress of the paradigm shift from immunomodulatory drugs to biological drugs in the treatment of Behçet's disease.

Prevention of recurrent toxoplasmic retinochoroiditis: is there a validated treatment?

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Toxoplasmosis is the leading etiology of infectious posterior uveitis. The disease may be recurrent and vision threatening, so that preventive therapy may be considered for selected cases. This presentation will briefly discuss the current indications and regimens for secondary prophylaxis of toxoplasmic retinochoroiditis, weighing the risks and benefits in an evidence-based approach.

Controversies in the diagnosis and treatment of primary vitreoretinal Lymphoma

DR. J. PULIDO

Introduction: Recent studies have changed our understanding of primary vitreoretinal lymphoma (PVRL). We wish to describe questions that still need to be answered.

Results:

In terms of diagnosis, we know that the presence of vitreous cells, retinal or subretinal infiltrates in the absence of Cystoid macular edema should raise the possibility of PVRL. In addition, biopsy is a critical aspect of the diagnosis. The use of PCR for monoclonality or FACS requires extensive cells. In the presence of a good pathologist, histology and immunohistochemistry requires less cells and can make the diagnosis. With improvement of PCR, this might be a better option in the future. Aqueous levels of IL10 are helpful in the following treatment responses but not in making the diagnosis. Whether earlier diagnosis changes the ultimate prognosis is not known. Local recurrences are common so intravitreal therapy is better than ocular radiation since treatment with intravitreal therapy can easily be repeated. Whether systemic therapy should be used with bilateral disease is unknown. In the presence of recurrent CNS lymphoma (CNSL) stem cell therapy has some efficacy, Finally, the nidus from which the the PVRL develops is unknown as well.

Conclusion: Many question still remain in the diagnosis and treatment of PVRL and CNSL

Session 30

IOIS Session: *Surgical interventions and endophthalmitis*

Bacterial Endophthalmitis: Current approach to treatment

Odette Houghton, University of North Carolina - Chapel Hill

Purpose: To review the current approach to the treatment of bacterial endophthalmitis.

Methods: Medline database search and review of pertinent literature regarding the treatment of bacterial endophthalmitis.

Results: Bacterial endophthalmitis is a complex condition with potentially devastating consequences.- While prevention and early recognition of endophthalmitis is uniformly recognized as mainstay to minimize morbidity, there is no consensus regarding a definitive approach to the treatment of bacterial endophthalmitis.

The Endophthalmitis Vitrectomy Study (EVS) was a landmark study which forms the basis of many ophthalmologists' treatment strategies for endophthalmitis. While this study provides valuable information, many questions remain unanswered and several categories of endophthalmitis fall outside EVS protocol. Recent advances in vitrectomy techniques, as well as the introduction of oral and topical antibiotics that reach adequate intraocular concentrations, have led to a re-evaluation of the current relevance of EVS.

Intraocular antibiotics remain the primary treatment for bacterial endophthalmitis, but the role of vitrectomy remains controversial. There is evidence supporting better functional and anatomical outcomes following post-surgical endophthalmitis with vitrectomy, compared to intraocular antibiotics alone. The supplemental use of systemic antibiotics remains standard of care for traumatic and endogenous bacterial endophthalmitis. Most authors continue to recommend vitrectomy for endophthalmitis associated with *Propionibacterium acnes* and trauma.

Conclusions: Current approaches to the treatment of bacterial endophthalmitis revolve around the use of broad spectrum antibiotics and vitrectomy. Recent technological advances have focused attention on the benefits of early surgical intervention. Future surgical and pharmacological innovations will continue to reshape our treatment strategies for bacterial endophthalmitis.

Surgical Management of Intraocular Parasitic Infestations

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Purpose: To describe the surgical management of intraocular parasites in the anterior and posterior segment

Materials and Methods: The clinical presentation, preoperative picture, investigations, medical supportive treatment, surgical video and postoperative picture of 3 cases of intraocular parasitic infestations: 1. Anterior chamber Dirofilaria, 2. Submacular live Cysticercus Cyst and 3. Posterior pole Toxocara granuloma are described.

Results: 1. The patient made excellent recovery of vision and intraocular inflammation after surgical removal of the Dirofilaria worm. 2. Six weeks post-silicone oil removal, the patient with submacular Cysticercus cyst had BCVA of 6/18 with attached retina. 3. Post-operatively successful anatomical outcome was achieved with poor visual recovery due to extensive scarring involving the disc and macula due to Toxocara.

Conclusions: 1. Intraocular infection with Dirofilaria is a rare presentation. Successful surgical removal resulted in complete recovery of uveitis and visual status in affected eye. 2. Large sub macular cysticercus can be managed successfully with patient delivery and silicone oil tamponade. 3. Toxocara granuloma can be managed with Avastin followed by vitrectomy involving difficult membrane peeling but visual recovery is poor due to scarring.

Chorioretinal biopsy in masquerade syndromes

Lucia Sobrin, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, USA

Purpose: To review the indications, surgical techniques and appropriate sample handling and testing for chorioretinal biopsy in the diagnosis of posterior retinitis and/or choroiditis.

Methods and Materials: Charts and surgical videos of patients undergoing chorioretinal biopsy at the Massachusetts Eye and Ear Infirmary from 2006 to present were reviewed. A search of the medical literature for articles pertaining to chorioretinal biopsy was performed.

Results: The main indications for chorioretinal biopsy are retinitis of unclear etiology and atypical uveitis with primary retinal or choroidal pathology. Ideal biopsy specimens are peripheral, sufficiently large, and include the junction of involved and uninvolved retina. Important components of successful surgical technique include careful vitrectomy around the sclerotomy site and gentle handling and extraction of the specimen. Videos demonstrating the surgical steps will be shown. Conferring with a pathologist prior to the procedure is key to obtaining a diagnosis. This will allow for appropriate specimen allocation and media selection for histopathology, immunohistochemistry, electron microscopy, microbiology and polymerase chain reaction testing.

Conclusions: Chorioretinal biopsy is an important diagnostic tool in cases of retinitis or choroiditis of unclear etiology. Preoperative planning for correct specimen handling is key to successful diagnosis from this procedure.

Anterior chamber biopsy in recalcitrant uveitis and simulating entities

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Purpose: To provide an overview of the utility of anterior chamber biopsy in the diagnosis and management of recalcitrant uveitis and masquerade syndromes.

Methods: Representative cases and a review of the literature on ocular fluid sampling and molecular diagnostic testing for the diagnosis of refractory or atypical uveitis will be presented.

Results and Conclusions: Anterior chamber biopsy is a minimally invasive technique that can be performed in cases of atypical or recalcitrant uveitis. Molecular diagnostic testing from small samples of ocular fluid can further elucidate possible infectious etiologies of anterior and posterior uveitis, including well-defined clinical entities such as Fuchs heterochromic iridocyclitis and Posner Schlossman syndrome. Cytokine testing and immunogenetics can also be performed on aqueous fluid samples in suspected masquerade syndromes. Anterior chamber biopsy provides valuable information in cases of diagnostic uncertainty in anterior and posterior uveitis.

The Fluocinolone Acetonide Intraocular Implant for the Surgical Management of Uveitis

George Papaliodis, Massachusetts Eye and Ear Infirmary

Purpose: The use of the fluocinolone acetonide intraocular steroid implant has provided a valuable surgical tool for the management of ocular inflammatory diseases. This presentation will review the major published results since the release of the implant and the Massachusetts Eye and Ear Infirmary experience.

Materials and Methods: There have been many case series assessing the efficacy and safety of the fluocinolone acetonide steroid implant. This presentation will review the published data and report a retrospective case series on the Massachusetts Eye and Ear Infirmary experience.

Results: 18 fluocinolone acetonide implants were performed at the Massachusetts Eye and Ear Infirmary from 2009 through 2012. The most common diagnosis at our institution requiring the implant was ocular sarcoidosis. Mean logMAR visual acuity improved from 1.31 pre-operatively to 0.84 ($p=0.008$) and 0.82 ($p=0.009$) at 6 and 12 months, respectively. 12 eyes were pseudophakic at the time of implantation; 6 had combined steroid implant/cataract surgery. 44.4% required no glaucoma treatment prior to fluocinolone implant and continued to require no therapy subsequently. 11%had surgical interventions to control intraocular pressure prior to implantation; 33% required surgical management of glaucoma after steroid implantation.

Conclusion: The fluocinolone acetonide intraocular implant is a valuable surgical option for the control of intraocular inflammation. Efficacy has been demonstrated via improvement in visual acuity and reduction of immunosuppressive medications. The implant has a high rate of complications including glaucoma and cataracts.

Session 31

Netherlands UveitisSociety: *Systemic disease and uveitis*

Update on uveitis treatment with biologicals in the Netherlands

Robert Kuijpers, ErasmusMC, Rotterdam
P Martin Van Hagen, ErasmusMC, Rotterdam

Purpose: To report the experience of the use of biological agents for treatment of uveitis in the Netherlands.

Material and Methods: We have sat up an observational register that aims to include all Dutch patients with uveitis treated with biological agents. In the register patient characteristics, activity of uveitis and treatment are documented. In the Netherlands we have experience treating uveitis patients with biological agents since 1998. The use of the agents is off-label and in the first years financed by the hospitals. Because of a national directive by the Dutch uveitis working group, endorsed by the Dutch ophthalmological society, treatment with biological is reimbursed by the assurance companies .

Results: Mostly, anti-TNF alpha has been prescribed i.e. Adalumimab and Remicade. Because the costs of biological agents is a factor 10 higher than other treatments, the efficacy of the treatment is an important factor for continuing reimbursement. Using the registry we hope to substantiate the use of these agents and to preserve financing in the future. Presented on behalf of the Dutch uveitis working group, The registry was sponsored by Abbot.

"All" you wanted to know about systemic sarcoidosis

Martin van Hagen (on behalf of the Dutch uveitis working party) Erasmus University Medical Centre and Eye Hospital Rotterdam, the Netherlands

Purpose: to report on sarcoidosis, a multisystem disorder of unknown etiology which is considered to be T cell driven. The hallmark of sarcoidosis is the occurrence of non-caseating granulomas characterized by epithelioid- and CD4+ T cells surrounded by fibroblasts, CD8+ T cells and B lymphocytes. In advanced stages, a restricted repertoire of T cell receptors and oligoclonal T cell expansions suggest selective immunological activation.

Methods; review of literature and our cohort of 450 patients.

Results: sarcoidosis may affect every organ but has a predilection for hilar lymph nodes, lungs, skin and the eye. Ocular involvement may be the presenting symptom and occurred in up to 30 % in our cohort. There are no definite criteria sets available for the diagnosis of sarcoidosis. The clinical diagnosis requires three elements; typical clinical and radiographic manifestations, exclusion of other granulomatous diseases (such as tuberculosis) and histopathologic confirmation of noncaseating granulomas. The extend of disease can be determined with various imaging techniques including

FDG-PET-scan and OctreoScan. There are no validated marker sets available for disease activity at this moment. The mainstay of drug therapy in systemic sarcoidosis remains glucocorticosteroids. However, the development and availability of new targeted therapies (including anti-TNF therapy) boosted important evolutions in the treatment of systemic inflammatory diseases.

Conclusions: novel diagnostic and therapeutic possibilities changed profoundly our management of patients with systemic sarcoidosis.

Successful treatment with Adalimumab in sarcoidosis patients with chronic non-infectious uveitis

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Purpose: To report the effect of adalimumab on refractory uveitis in sarcoidosis patients.

Design: Prospective interventional series.

Methods: In this prospective, institutional study patients with refractory posterior uveitis (n=56,) were followed after initiation of adalimumab for at least nine months. Inclusion criteria were non-responsiveness or intolerance to prednisone or other immunosuppressive drugs (mainly methotrexate). Main outcome measures were visual acuity, vasculitis, papillitis, and/or macular edema improvement, stabilization or no recurrence of the uveitis. Furthermore, other clinical manifestations of sarcoidosis were followed.

Results: Adalimumab appeared successful by having a favourable outcome on the visual acuity in 47 (85%) of the 56 studied patients. The vasculitis, papillitis and macular edema improved. During follow-up no recurrences were reported in those successfully treated. Fatigue improved in 28 out of 42 of those suffering from fatigue. Moreover, the inflammatory parameters improved as well. Only 2 patients needed to stop the adalimumab because of side effect of nausea early in the treatment. No severe side effects were recorded during the follow up. A minor side effect reported was stinging during the injection.

Conclusion: Adalimumab appeared to be a successful treatment for chronic non-infectious uveitis in sarcoidosis patients, demonstrating a favourable outcome on visual acuity and disease progression. Further studies are needed to evaluate the effect of adalimumab on sarcoidosis manifestations beside uveitis and to determine the most appropriate dose and duration.

Update on uveitis associated with juvenile idiopathic arthritis

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Juvenile idiopathic arthritis (JIA) is the most common childhood rheumatic disease and the most prevalent systemic disorder in children with uveitis. Clinical features of JIA-uveitis (JIAU) are anterior in location, insidious at onset, chronic course, and frequently asymptomatic. JIAU is a serious blinding disease and early diagnosis is warranted to prevent structural ocular damage.- In a recent retrospective study with 364 patients with juvenile idiopathic arthritis (JIA), elevated erythrocyte sedimentation rate (ESR) appeared to be predictive for the occurrence of uveitis. In multivariate analysis ESR appeared to be predictive for development of uveitis with an odds ratio of 1.015 (p=0.003) after adjusting for gender, JIA subtype, age of onset of JIA and presence of antinuclear antibodies. Since ESR is already routinely tested in patients with recently diagnosed JIA, it can easily be implemented in ophthalmologic screening protocols for uveitis in patients with JIA in the future. Since uveitis might

be in about 20% of patients the first presentation of JIA, before the onset of arthritis, there is a strong rationale for efforts to identify specific biomarkers. Moreover, we detected a specific protein in aqueous humor of patients with JIAU compared to other uveitis entities and non-inflammatory controls, which was identified as transthyretin by mass spectrometry analysis. Transthyretin could be a potential intraocular biomarker of JIA-uveitis but its exact role in the pathogenesis of JIA-uveitis needs further investigation.

Myfortic or cyclosporine in steroid refractory uveitis? A single blinded, randomized head to head clinical trial

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Purpose: to study new generation immunosuppressive therapy with Myfortic for second-line systemic therapy of uveitis.

Materials and Methods: randomization of 18 patients with steroid refractory chronic non-infectious uveitis, receiving either Myfortic bid 720mg or cyclosporine bid 5mg/kg/d for 4 months both combined to 1 mg/kg (max 60m) prednisone tapered swiftly within 3 months if possible. Ocular and physical parameters and adverse effects (AE's) were analyzed.

Results: Duration of response were similar for both groups (289 vs 261 days). Study exit caused by flares were seen in 3 and 2 patients for Myfortic and cyclosporine, respectively, all occurring after 16 weeks of treatment. No significant differences were seen during treatment and 8 months thereafter concerning vitreous cells, haze, flare, CME, visual acuity, or total amount of steroids. AE's were mild, but more often and higher graded in cyclosporine (19 vs 28, 5 vs 1, respectively). AE's were drug specific; 12.5% abdominal pain and diarrhea in Myfortic, for cyclosporine; impairment of renal function and hypertension (up to 33% and 17% as compared to initial values). Two patients had to decrease the dose of cyclosporine due to AE's, but this not interfere with ophthalmic parameters.

Conclusions: Myfortic is equally effective as compared to cyclosporine in patients with steroid refractory chronic non-infectious uveitis. Significantly more and severe AE's were seen after cyclosporine. Therefore it seems reasonable to consider Myfortic preferable over cyclosporine in the second line treatment of steroid refractory uveitis patients

Syphilitic uveitis

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Background: Since long ocular syphilis has been known as "the Great Imitator" as the clinical picture varies from patient to patient. The association between specific ocular symptoms and the visual prognosis is unclear. In this multicenter study we investigated relationships between various clinical features and the visual outcome after treatment.

Methods: We analyzed retrospectivelly the clinical data of patients with positive serologic tests for syphilis and ocular signs from 4 academic hospitals and the Rotterdam Eye Hospital.

Results: The data of 85 patients (70 men, 15 women, 139 eyes) were suitable for analysis. 14 Patients suffered from anterior uveitis, 2 from intermediate uveitis, 27 from posterior uveitis and 39 from panuveitis. All patients were treated with antibiotics, some patients in combination with oral or local steroids. Mean logMAR visual acuity raised from 0.55 (SD 0.66) (139 eyes) before appropriate treatment to 0.27 (SD 0.51) (117 eyes) six months after the initiation of treatment. Six patients (10 eyes) suffered from visual loss due to several different mechanisms: ischaemic optic neuropathie (4 eyes), subretinal fibrosis (3 eyes), retinal detachment, glaucoma and hypopyon (each one eye). A lower visual acuity at presentation and a longer delay in treatment were associated with a lower visual outcome six months after treatment. HIV status of the patient, administration route of antibiotics and the addition of steroids didn't influence the visual outcome.

Conclusions: Proper therapy of syphilitic uveitis leads to visual improvement in the majority of cases. In this study visual outcome is dependent on visual acuity at onset and treatment delay.

Session 32

Bangladesh Uvea Society:
Uveitis - Bangladesh experience

Pattern of Uveitis at National Institute of Ophthalmology and Hospital, Bangladesh

Arif Prof.Md. Arif Mian, NIO

Purpose: To evaluate the clinical patterns, causes, and systemic associations among patients presented with uveitis in National Institute of Ophthalmology and Hospital, Bangladesh.

Methods: This prospective randomized study was done at National Institute of Ophthalmology and Hospital on patients presented at outpatient department form June, 2011 to December, 2012. Results: The study subjects consisted of 80 among which 68 (85%) males and 12 (15%) females.Mean age was32± 12.5 years, range was 19-48years. Unilateral cases were 75% (60) and bilateral were 25% (20).The most common anatomic diagnosis was Anterior Uveitis 72 (90%).Panuveitis uveitis was diagnosed in 8 (10%) cases. 65% (52) uveitis patients were idiopathic. 25% (20) patients were Mantoux positive. 20% (16) patients strongly positive (indurations >15mm) . 5% (4) Sputum for AFB positive. 2.5% (2) CXR suggestive of TB. Out of 5patients, 2 ALS-Assay suggestive, 1highly suggestive. Out of 3patients, 2 were QFT positive.5% (4) diagnosed as TB at the time of presentation. 2.5% (2) patients diagnosed as cervical spondylo-arthopathies. 1diagnosed as toxoplasmosis and 1diagnosed as JCA.

Conclusions: Uveitis is a vision threatening conditionusually affect the young adults.Tuberculosis has emerged as an important cause of uveitis even when the classical picture is not manifest.We would recommend more details research on this issue in different ophthalmic facilities in Bangladesh.

Ocular Tuberculosis: Bangladesh experience

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Purpose: Primary purpose is to present the diversity of clinical features in four cases of ocular tuberculosis with ocular as well as extraocular manifestations. Secondary purpose is to discuss the diagnostic approach with treatment and outcome.

Methods: An observational case series of four cases of periocular and ocular tubeculosis with or without systemic involvement. Detail history, thorough clinical examination, best corrected visual acuity, slit lamp bio-microscopy, indirect ophthalmoscopy, Fundus fluorescein angiography, B-scan

untrasonography ; Optical Coherence tomography scan, Erythrocyte Sedimentation Rate, Skin test for tubercle protein, histopathological examination of biopsy from lesion were performed according to the cases. Diagnosis was made by clinical history, ocular findings, appropriate ancillary tests and laboratory investigations according to the merit of the diseases. Response to anti tuberculous (TB) therapy were observed which gave an anchor to the diagnosis. An internet search (medline search) and review of current literature on ocular tuberculosis were done and information relevant to our objectives were obtained.

Results: Four cases of ocular tuberculosis with variable menifestations were presented. Our First three cases were female only last case was male and all of them were young at or under the age of forty. Two patients had extra ocular manifestation; one was Tuberculous Dacryoadenitis & other was Tuberculous Dacryocystitis. Two patients had eyeball involvement; one was Tuberculous Necrotizing Scleritis, another one had tubercular vasculitis retinae. Out of four three had bilateral involvement. All four patients were diagnosed as a case of tuberculosis after ophthalmic evaluation. Three of them respond well to anti TB & anti inflammatory therapies; one respond to anti TB therapy only.

Conclusions: Tuberculosis can affect any structure of eye and adnexae. Ocular tuberculosis is difficult to diagnosis because of diversity of presentation and most of the time there is absent of concurrent systemic infection. Early diagnosis and treatment of ocular tuberculosis can prevent blindness or severe ocular morbidity. In cases of non healing lesion and atypical inflammatory presentation, we stress the need for a high index of suspicion regarding tuberculosis.

Clinical features and visual outcome in Vogt Koyanagi Harada Syndrome (VKH) in a tertiary eye care centre in Bangladesh

Tariq Reza Ali

Purpose: To report the presentation, initial findings,investigations, treatment modalities, results and complications in a small series of patients at a tertiary eye care hospital in Bangladesh.

Type of study: Retrospective data analysis

Materials and Methods: 25 consecutive patients from January 2009 to October 2009 of VKH disease diagnosed at the retina center of Islamia Ispahani Eye Institute and Hospital, Dhaka, Bangladesh were evaluated. The medical records were reviewed for demographic data, clinical features, investigations, treatment and follow up. Initial and final visual acuity was measured with Snellen's Chart.

Results: There were 18 female (72%) patients with 37 years of mean age (SD±14.23). The median follow up was 11 months (6 to 16 months). 13 (52%) came within 1 month of symptoms. Anterior uveitis was present in 14 (56%), vitritis in 12 (48%), disc oedema in 17 (68%), focal subretinal fluid in 13 (52%), bullous serous retinal detachment I 14 (56%) and choroidal detachment in 4 (16%) patients.B-scan ultrasonogram was done in 20(80%) and fundus fluorescein angiography was done in 13 (52%) patients. Oral systemic steroid was given in 24 (96%) and intra venous methyl prednisolone for 3 days was prescribed in 11 (44%) patients on initial presentation. Additional immunomodulator (azathioprine) was given in 12 (48%) patients. Presenting visual acuity was 20/400 in 33 eyes, 20/100 to 20/200 in 9 eyes, 20/50 to 20/80 in 6 eyes and 20/40 in 2 eyes. On final follow up visual acuity was 20/40 in 12 eyes, 20/50 to 20/80 in 16 eyes, 20/100 to 20/200 in 13 eyes and 20/400 in 9 eyes. Notable complications were cataract in 12 eyes, glaucoma in 4 eyes, macular scar in 4 eyes, retinal detachment and phthisis bulbi in 1 eye.

Conclusion: The demography, presenting symptoms, treatment modalities and complications of VKH disease in Bangladesh is comparable to other countries. We need a study comprising more sample size for better understanding of the disease.

Ocular Toxoplasmosis in Bangladesh

Zahedur Rahman Zahedur, Bangladesh Eye Hospital
Niaz Abdur Rahman Niaz, Bangladesh Eye Hospital
Md. Saleh Uddin Saleh, OSB Eye Hospital

Objective: To determine the pattern of toxoplasma retinochoroiditis presenting to a uveitis clinic in a tertiary eye hospital in Bangladesh. Materials and method: Retrospective analysis of Hospital records of uveitis patients attending Bangladesh Eye Hospital from December 2008 to January 2013.

Result : A total of 570 patients of uveitis reported to Bangladesh Eye Hospital from December 2008 to January 2013. 40.88% (n-233) were diagnosed as anterior uveitis, 22. 10% (n-126) had posterior uveitis, 21.40% (n-122) intermediate uveitis and 15.61% (n-89) panuveitis. Of all the uveitic patients 5.50% (n-34) were diagnosed to have toxoplasma retinochoroiditis, which were 27 % of all posterior uveitis patients and most common cause of posterior uveitis. It was calculated that toxoplasma retinochoroiditis is the 2nd most common cause of intraocular infection, next to tuberculosis.

Conclusions : The toxoplasma retinochoroiditis contribute to a major part of uveitis in Bangladesh.

Local treatment for VKH: an option in developing countries

Shah Md. Bulbul Islam Bulbul, Dhaka National Medical College
Zahedur Rahman Zahedur, OSB Eye Hospital
Shah Md. Rajibul Islam Rajibul, National Institute of Ophthalmology

Objective: To observe and evaluate the outcomes of VKH treatment with Steroids. Materials & Method: Prospective analysis of 45 VKH patients from 2009 to June 2013 attending the hospital. Out of 45, 14 were male and 31 were female with age ranging from 22 to 65 years (43.5 years on avg). The diagnosis was made on clinical presentation of 1. sudden bilateral panuveitis, 2. blurring vision, 3. disc hyperemia, 4. No history of ocular trauma and 5. absence of systemic disease. All the patients started with intravenous methyl prednisolone, 1 gram bolus dose for 5 days followed by oral prednisolone (1 mg/Kg body wt) daily. Topical and periocular steroids were also simultaneously started with cycloplegics. Systemic steroids were tapered to 5 mg per day within 6 weeks and maintained for at least 6 months. Topical steroids were continued as well. Patients visual acuity, IOP, fundus examination were noted every 3 weeks. Glycemic status, liver function and blood pressure were checked regularly.

Result: Vision was saved in both eyes of 44 patients. After 06 months, visual acuity was 6/9 and better in 13 (28.88%) patients, 6/12 to 6/24 in 07 (15.55%), 6/36 to 6/60 in 24 (53%) and HM in 01 (2.02%) patient. Poor visual outcome was attributed to cataract (11.11%), glaucoma (13.33%), corneal decompensation (2.02%), post segment change (11.11%). 01 (2.02%) patient needed Azathioprine as steroid sparing due to cushing syndrome. Acne formed in 05 patients (11.11%), GI upset in 16 patients (35.56%). Interestingly significant weight gain was not noticed in any case.

Conclusion: Steroid still remains the mainstay of management of VKH in countries where meticulous investigation and follow up facilities fail short. At the same time so far steroid treatment is economically viable and can be afforded even at the remotest areas.

Session 33

IOIS session: *Scleritis*

Clinical presentation and classification of scleritis.

Carlos Pavesio, Moorfields Eye Hospital

Inflammation of the sclera may be a very serious condition, not only because it can produce structural damage to the globe and eventually result in blindness, but also because it may be a manifestation of a life-threatening systemic disease.- It is predominantly a disease of the middle aged and elderly, probably reflecting the age group of the commonly associated systemic diseases. Females are more likely to be affected, and no geographical or racial differences have been detected, either in incidence or prevalence. There is also no evidence of any genetic predisposition. The disease may start in one eye only but becomes bilateral in one third of the patients, the second eye becoming involved from three months to six years after the first. It is typically a very painful condition, but painless scleritis can occur. It is classified in anterior and posterior scleritis, with anterior scleritis further subdivided in diffuse, nodular and necrotizing scleritis. Clinical features of anterior and posterior scleritis and relevant aspects of classification will be discussed.

Immunopathology of scleritis

Daniel Vitor Vasconcelos Santos MD PhD, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

The immunopathology of scleral inflammatory disorders vary upon the underlying insult, with most cases being regarded as noninfectious and associated with a local immune-mediated response. This presentation will briefly dissect the most relevant immunopathologic aspects of scleritis. Major distinctive features of each type of scleral inflammation will be revisited, emphasizing recent insights into the fascinating pathogenesis of these disorders, illustrated with cases of clinicopathologic correlation.

Emerging Therapies for Non-infectious Scleritis

C. Stephen Foster, MD, FACS, FACR, FARVO.Harvard Medical School . Massachusetts Eye Research and Surgery Institution (MERSI).Cambridge, MA, USA

Non-infectious scleritis may occur as a consequence of trauma, cancer, degeneration or autoimmunity. Traditional therapy for autoimmune scleritis revolved around systemic corticosteroids for 50 years in most centers. And even after Lopez-Garcia of Madrid, Spain, demonstrated the superiority of systemic immunomodulatory therapy in patients with rheumatoid arthritis associated necrotizing scleritis, in 1950, it took the rest of the world another 30 years to embrace the idea of non-steroidal therapy for this ocularly destructive and potentially lethal problem. Today, happily, not only have large numbers of physicians world-wide adopted such therapy with anti-metabolites and calcineurin inhibitors and

alkylating agents, but a steadily increasing array of biologic response modifers, approved for the care of patients with systemic autoimmune disease¸is finding its way into ophthalmology centers for the care of scleritis associated with systemic autoimmune disease and even in the care of patients with idiopathic non-infectious scleritis. Such BRM's will be the subject of this presentation, with case examples and case series demonstrating the safety and the efficacy of this practice.

Session 34

International workshops on VKH, Sympathetic Ophthalmia, Ocular Sarcoidosis, Ocular Tuberculosis and Ocular Behçet's disease: *Recent advances in Granulomatous Uveitis and Behçet Uveitis*

Past, Present and Future of International Workshop on Ocular Sarcoidosis

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Miyata Eye Hospital, Miyakonojo, Japan2)

Past: Ocular sarcoidosis is one of the major causes of uveitis in the world. The disease typically presents granulomatous uveitis associated with systemic sarcoidosis. Yet, diagnostic criteria internationally accepted by ophthalmologists had not been available until the International Workshop on Ocular Sarcoidosis (IWOS) meeting proposed international criteria for the diagnosis of ocular sarcoidosis. The meeting was held in Tokyo in October, 2006. The criteria consist of 7 ocular signs and 4 non-invasive laboratory tests. The 2nd IWOS meeting was held in Singapore in March, 2009, and an international validation study for the diagnostic criteria was proposed. The 3rd IWOS meeting was held in Goa in November 2011 and an interim report of the international validation study was reported. The 4th IWOS meeting was held in Taiwan in April 2013 asking whether ocular sarcoidosis is prevalent or not in Asia and Pacific.

Present:The international validation study headed by Dr. Nisha Acharya is ongoing to clarify if the criteria are really applicable to many different countries and various ethnic groups.

Future: Revised diagnostic criteria should be considered based on the results of the international validation study for IWOS criteria. This will be the major topic in the 5th IWOS meeting during 2014 IOIS congress in Valencia.

Challenges in diagnosis of ocular tuberculosis

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Diagnosis of intraocular tuberculosis has remained a major challenge as the usual diagnostic techniques either by the smear examination for the AFB or culture of the intraocular fluids fail to demonstrate Mycobacterium tuberculosis (Mtb). Moreover, more than 60% of the cases of extrapulmonary tuberculosis (TB) do not show evidence of pulmonary TB. Thus by the time patient presents with intraocular tuberculosis, there may not be any evidence of systemic disease. For want of any diagnostic criteria, the intraocular tuberculosis is either under diagnosed or over diagnosed especially in the TB endemic countries. For making a presumptive diagnosis of intraocular tuberculosis in patients who show ocular signs that are suggestive of TB such as broad posterior synechiae, retinal vasculitis with choroiditis, choroidal granuloma or multifocal serpiginous choroiditis we often depend upon corroborative evidence such as positive tuberculin skin test, interferon gamma release essay or X-ray/CT chest/PET-CT scans, besides efforts are made to demonstrate by histopathology at any extraocular sites. In recent years polymerase chain reaction to detect the genome of Mtb from the intraocular fluids has been used to diagnose these cases .However all these tests lack sensitivity and do not confirm the disease and merely indicate the presence of the DNA of the organisms.

Treatment of Behçet uveitis: New horizons for an “old” disease

Ilknur Tugal-Tutkun, Moncef Khairallah

Behçet disease is a multisystem inflammatory disorder that is an important cause of morbidity worldwide. Recent genetic studies have confirmed the role of shared genetic factors in populations with a high disease prevalence. The disease mechanisms seem to be similar to polygenic autoinflammatory diseases. While fluorescein angiography remains an essential tool in evaluation of retinal vasculitis in Behcet disease, a novel clinical scoring system has been developed to monitor intraocular inflammatory activity and was used to compare disease activity before and after infliximab therapy. Amulticenter study in Japan has shown good safety and marked efficacy of infliximab. However, an increase in number of ocular attacks was noted in moths 7-12 compared to the first 6 months of infliximab therapy. IL-1 blocking agents have been successfully used in patients with autoinflammatory disorders refractory to anti-TNF-alfa therapy. There are recent case reports on the successful use of anakinra, a recombinant human IL-1 receptor antagonist, and canakinumab, a human monoclonal antibody that neutralizes IL-1beta, in patients with resistant Behçet disease. In a pilot study, gevokizumab, a recombinant humanized monoclonal antibody regulating IL-1beta activity, was found to produce a rapid-onset effect for the treatment of intraocular inflammation. Preliminary results of an extension trial showed that continuous use of gevokizumab could provide a sustained efficacy, and no serious adverse event was observed. Studies are underway to prove safety and efficacy of anti-IL-1 therapy in Behçet patients with refractory uveitis.

Session 35

Asia Pacific Intraocular Inflammation Study Group: *Infectious uveitis*

Ocular toxocariasis

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Ocular toxocariasis is caused by infection due to the parasite *Toxocara canis* in dogs or *Toxocara cati* in cats. The parasite is widespread, and domestic animals as dogs and cats are its natural hosts. Infection levels may reach 90% in tropical/sub-tropical countries, whereas 2.5-35% in developed countries. *Toxocara* as a cause of panuveitis accounted for 2% of patients with uveitis in Japan.

As clinical investigations, serum IgE, specific serological titer, and ultrasonography have been applied. Currently polymerase chain reaction (PCR) analysis can detect *Toxocara* genes directly in ocular fluid, and enzyme-linked immunosorbent assay (ELISA) shows high sensitivity and specificity.

Immunochromatography was recently developed for rapid screening for toxacariasis as simple, quick, and inexpensive investigation by Japanese parasitologist. Both ocular fluids and serum samples are available for this immunochromatograhy-screening test. Though serum sample is easier and less invasive to collect from the patients than intraocular fluid, the latter is clear to evidence the pathogen in the eye. We then show a 63-years old female case diagnosed as ocular toxocariasis certainly by identifying anti-*toxocara* antibody in the vitreous fluid collected during the operation for epiretinal membrane by using immunochromatography and ELISA, who had been once suspected it by positive blood test.

Endogenous endophthalmitis

Shwu-Jiuan Sheu

Endogenous or metastatic endophthalmitis is typically the result of hematogenous spread of organisms from a primary site of infection to internal ocular spaces. Gram-positive bacteria, gram-negative bacteria and fungi are most common causative organisms, although even protozoa had been reported. There are considerable regional variations in incidence and causes. In general, gram-negative organisms (especially Klebsiella pneumoniae) are responsible for most cases of endogenous endophthalmitis in east Asia, whereas, gram-positive organisms and fungi are more frequent

causative agents in North America and Europe. Most of the patients have underlying risk factors for systemic infections, such as diabetes, HIV, malignancy, intravenous drug use, transplantation, immunosuppressive therapy, and/or catheterization. Although it's metastatic origin, most patients presented unilaterally. The associated systemic symptoms are usually non-specific, the diagnosis and treatment is sometimes delayed and cause profound visual impairment. Treatment includes systemic antibiotic, and intravitreal antibiotics. Surgical intervention helps in diagnosis, persistent inflammation and complication. High awareness of the possible diagnosis and early treatment is the key to say the eyes.

Factors Associated with Anatomic and Visual Outcomes in Acute Retinal Necrosis

Nobuyuki Oguro, Osaka Koseinennkinn Hospital
Chiharu Iwahashi-Shima, Osaka University Graduate School of Medicine

Purpose: To examine the factors associated with anatomic and visual outcomes in Japanese patients with acute retinal necrosis (ARN).

Methods: One-hundred-and-four patients with ARN were followed for more than 1 year at nine referral centers were reviewed. Retinal involvement at initial presentation was classified into four groups: zone 1 (posterior pole, n=22), zone 2 (midperiphery, n=54), zone 3 (periphery, n=25), and unknown (n=3). Forty-eight eyes underwent prophylactic vitrectomy before development of retinal detachment (vitrectomy group); 56 eyes were treated conventionally without prophylactic vitrectomy (observation group).

Results: The retina was attached in 28 (58.3%) of 48 eyes in the vitrectomy group and 42 (75.0%) of 56 eyes in the observation group at final visit (P=0.071). At 1 year, 56 eyes (53.8%) had a best-corrected visual acuity (BCVA) of 20/200 or worse. Multivariate logistic regression analyses identified that zone 1 disease (odds ratio=4.983) and optic nerve involvement (odds ratio=5.084) were significantly associated with BCVA of 20/200 or worse. Among zone 3 eyes, significantly (P=0.012) more eyes in the observation group than the vitrectomy group had an attached retina.

Conclusions: Prophylactic vitrectomy did not improve the final BCVA in any eyes. Zone 3 eyes had better outcomes without prophylactic vitrectomy.

HLA B27 uveitis: Is there a bacterial association?

Peter McCluskey,
Co-authors: John Chang, Shahriar Amjadi, Denis Wakefield

This talk will review the evidence implicating bacterial triggers in HLA B27 associated acute anterior uveitis

Ocular Tuberculosis

Dr. Jessica Marie Abaño

Tuberculosis (TB) is one of the most widespread infectious diseases in the Asia-Pacific region. In 2010, the World Heath Organization reported at least 5 million new cases and more than half a million death from TB. In the Philippines, it is the 6th major cause of morbidity and mortality. Tuberculosis can affect any part of the eye either as an infection or a hypersensitivity reaction. Ocular involvement is estimated to range from 2-20%. Clinically, its presentation is varied from a simple interstitial keratitis to a sight threatening retinitis. Other forms include scleritis, choroiditis,

and choroidal or optic disc nodules. Generally, definitive diagnosis of ocular tuberculosis remains a challenge, as it is often difficult to obtain microbiologic evidence of the disease form intra-ocular tissue. However, introduction of diagnostic tools including PCR and interferon gamma release assay (IGRA) has helped clinicians in identifying the disease. This case-based talk focuses on the diverse presentations of ocular TB as well as its diagnosis and management.

Nematode infestation of the eye

S.R. Rathinam.

Ocular endoparasites belong to either simple unicellular protozoans or complex multicellular metazoans. Metazoa parasites includes helminths such as nematodes, (round worms) cestodes (tape worms) and trematodes (flatworms). Nematodes are elongated, with long cylindrical bodies that contain an intestinal system and a large body cavity. Parasitic nematodes vary in length from several millimetres to approximately 2 metres and have larval stages and adult worms of both sexes. Approximately 60 species of roundworms can infect humans. Nematodes in humans can be found in the intestines, muscles and other tissues including ocular tissues. Common nematode species of ocular importance are T. canis, T. catis, Loa loa, Dirofilaria repens. Gnathostoma spinigerum and O. volvulus. However other rare nematodes cause diffuse unilateral subacute neuroretinitis. People can get infected with various nematodes through several ways: ingestion of the eggs, skin penetration by the larva or through the bite of an infected vector. Prior to making a final diagnosis, ophthalmologists have to get dietary history, as most parasitic transmission is through food and water contamination. Travel history to endemic areas is important to determine the source of infection. When the humans are not the definitive hosts, but play the role of an accidental or intermediate host, the parasites do not mature into adult worms. Eggs or cysts are seldom found on stool examination. It is important for the ophthalmologists to understand the life cycle of the worm to select proper diagnostic tests. The clinical picture depends on various factors including the presence of live or dead worm in the eye, structural damage and immunological reaction by the patient. Because of protean manifestations and lack of clinical suspicion the diagnosis is often missed. This presentation talks on several patients with ocular nematode infections and the way they were managed.

Session 37

IOIS session: *Systemic Associations & systemic therapy in Anterior uveitis*

HLA B27 uveitis 40 years on

Presenter: Peter McCluskey,
Co-authors: John Chang, Tanya Karaconji, Shahriar Amjadi, Denis Wakefield

This talk will review our progress in understanding HLA B27 associated acute anterior uveitis

Syphilis, TB, sarcoid

Susan Lightman, UCL/Institute of Ophthalmology and Moorfields Eye Hospital, London, UK

Patients presenting for the first time with AU may or may not have an underlying disease process. AU can only be the diagnosis when the eye has been examined in detail and intermediate and posterior/ panuveitis excluded. The common feature is of AC cells but other ocular signs may give further clues as to an underlying systemic infection/inflammatory disorder. In some patients the systemic disease is already known but in many the eye disease can be the first presentation to medical care. Patients need to be questioned for the symptoms of underlying disorders. For syphilis this includes at risk behaviour, previous gumma formation which has settled, skin rash, in TB symptoms such as night sweats, cough, weight loss and in sarcoidosis the symptoms can be varied, overlap with TB but can also include parotid gland swelling, breathlessness, VII nerve palsy. Many patients may not have or admit to any symptoms apart from those related to the eye. In the eye very careful examination from front to back may be rewarding in terms of signs pointing to a particular diagnosis. In the anterior segment type and distribution of KP, iris nodules an others may be found. Blood investigations include on all patients' serum ACE and VDRL with a CXR if respiratory symptoms. Quantiferon gold testing is useful when patients have been at risk of TB and/or have had previous BCG vaccination making interpretation of Mantoux tests more difficult. Further investigations by the relevant physicians may then be required and appropriate treatment given.

Systemic Therapy in Anterior Uveitis

Maite Sainz de la Maza, MD, PhD

Initial therapy in noninfectious anterior uveitis typically includes topical corticosteroids and short-acting cycloplegic agents. Sometimes this approach is not sufficient and systemic therapy becomes necessary. This is most frequent in anterior uveitis associated with juvenile idiopathic arthritis (JIA) and entities related to human leukocyte antigen B27 (HLA-B27) including ankylosing spondylitis (AS), reactive arthritis, psoriatic arthritis, and inflammatory bowel disease. Also included in this group are

sarcoidosis, which may present with a nongranulomatous anterior uveitis, and acute tubulointerstitial nephritis and uveitis (TINU). In many patients with JIA-related uveitis, systemic corticosteroids alone are not sufficient to control the inflammation, and immunomodulatory therapy will be necessary. Long-term oral methotrexate (MTX) is often an effective steroid-sparing therapy. Children treated with MTX for at least 3 years prior to discontinuation may have a longer relapse-free interval. Cyclosporine, azathioprine, and mycophenolate mofetil (MMF) have also been useful steroid-sparing therapies. Biologic response modifiers (BRM) including infliximab and adalimumab may be useful for children with persistent inflammation despite standard immunomodulatory therapy. Patients with spondyloarthropathies with chronic or recurrent uveitis who are unresponsive to short courses of systemic corticosteroids or develop adverse effects from corticosteroid therapy may need immunomodulatory therapy including MTX or MMF or BMR including infliximab, etanercept, and adalimumab. These agents may be useful in reducing the number of flares of anterior uveitis in patients with AS. Adalimumab has been shown to reduce the rate of anterior uveitis flares by at least 50% in a large open-label study. Severe refractory cases of anterior uveitis associated with sarcoidosis or TINU may also require systemic immunomodulatory therapy.

Session 38

IOIS session: *Epidemiology and Clinical trials in uveitis*

The Standardization of Uveitis Nomenclature (SUN) Project: Current Status

Douglas A. Jabs, MD, MBA for the SUN Working Group

Classification criteria are a type of diagnostic criteria used for identifying diseases for clinical research. Although they seek to optimize sensitivity and specificity, when a trade-off is needed, they favor specificity. Successful examples of classification criteria include those developed in the field of Rheumatology for identification of the rheumatic diseases. The goal of the SUN Classification Criteria Project is the development of classification criteria for 28 of the major uveitic diseases. The SUN Working Group consists of 75 investigators from 59 centers in 19 countries. The SUN Classification Criteria Project has four phases: 1) informatics; 2) case collection to establish a preliminary database of 250 cases of each disease; 3) case selection, using consensus techniques, to establish a final database of ~200 cases of each disease; and 4) analysis, using techniques such as classification and regression trees and polytomous discrimination, to develop a parsimonious set of criteria for each disease that optimizes sensitivity and specificity. The informatics phase is complete; the case collection phase 77% complete; and the case selection phase begun.

Factors predictive of remission of new-onset anterior uveitis and of intermediate uveitis.

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Departments of Epidemiology[11], and Ophthalmology[12], The Johns Hopkins University, Baltimore, Maryland; the Laboratory of Immunology[13], National Eye Institute, Bethesda, Maryland; Department of Ophthalmology[14], Department of Medicine[15], Oregon Health and Science University, Portland, Oregon; Portland Veteran's Affairs Medical Center[16], Portland, Oregon.

Purpose: To identify factors predictive of remission of inflammation in new-onset anterior uveitis and in intermediate (only) cases presenting for tertiary uveitis care.

Design: Retrospective cohort study.

Participants: Patients presenting to participating academic uveitis clinics within 90 days of initial diagnosis of anterior uveitis; all cases of intermediate uveitis which had sufficient follow-up time to be "at risk" of meeting the outcome definition.

Methods: Retrospective cohort study based on standardized chart review.

Results: Nine hundred ninety eyes (687 patients) had a first-ever diagnosis of anterior uveitis within 90 days prior to initial presentation and had at least 90 days' follow-up thereafter. The median follow-up time was 160 days. Presenting characteristics predicting a lower incidence of remission of new onset anterior uveitis were juvenile idiopathic arthritis, Behçet Disease, bilateral uveitis, prior cataract surgery, ≥1+ vitreous cells, and a visual acuity of 20/200 or worse. Among 434 non-infectious intermediate uveitis cases (773 eyes) followed over 925 person-years (1650 eye-years), remission occurred at a rate of 8.9/100 eye-years. Prior pars plana vitrectomy and diagnosis of intermediate uveitis within the last year were favorable prognostic factors.

Conclusions: Factors predictive of a lower incidence of anterior uveitis remission should be managed taking into account the higher probability of a chronic inflammatory course. All cases of intermediate uveitis had a low remission rate, with newer cases less unlikely to remit. While pars plana vitrectomy was associated with more remission, the majority of treated eyes did not experience remission.

Clinical Epidemiology of Uveitic Macular Edema (7 min/250 words)

Jennifer E. Thorne, MD, PhD, Division of Ocular Immunology, Wilmer Eye Institute, Johns Hopkins University School of Medicine

Macular edema is the most common ocular structural complication and an important cause of vision loss among patients with uveitis. In the Multicenter Uveitis Steroid Treatment (MUST) Trial, macular edema was present in ~40% of eyes with uveitis at enrollment with a similar frequency for patients with intermediate, posterior, and panuveitis, and was the leading cause of treatable visual loss in this study. A retrospective study from two uveitis referral centers in the Netherlands reported a similar proportion with uveitic macular edema (40%) and that macular edema accounted for 41% of visual impairment. In patients with intermediate uveitis, the presence of macular edema is the most common indication for treatment and in these patients, control of macular edema and preservation of visual acuity can be accomplished with regional corticosteroid injections in 30-50% of patients who need treatment. For patients treated with systemic agents, approximately 50% of eyes with uveitic macular edema will have incomplete resolution of the edema despite control of intraocular inflammation (defined as no inflammatory cells present in the anterior chamber or vitreous and control of the chorioretinal inflammatory lesions), and these patients will require further supplemental therapy for the macular edema. Therefore, uveitic macular edema represents a significant problem in the management of uveitis. The purpose of this talk is to describe the epidemiology of macular edema complicating uveitis and its impact on vision by reviewing the available data in the published literature.

Validating International Working Group on Ocular Sarcoidosis (IWOS) Diagnostic Criteria

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n/a International Workshop on Ocular Sarcoidosis Working Group, n/a

Purpose: To evaluate the usefulness of guidelines for diagnosing ocular sarcoidosis proposed by the International Workshop on Ocular Sarcoidosis (IWOS) in 2009 and to compare the clinical features of uveitis patients with and without a suspected diagnosis of sarcoidosis.

Methods: This is a multi-center international study based on medical record review. Eighteen centers in 12 countries have been collecting data from patients with uveitis. Data collected includes clinical findings and suspected cause of uveitis at presentation, as well as subsequent laboratory investigations and any changes in suspected diagnosis. Logistic regression will be used to determine which of the variables collected are associated with a diagnosis of suspected ocular sarcoidosis. IWOS guidelines will be evaluated using latent class analysis and by comparing classifications for sarcoid and non-sarcoid patients.

Results: As of November 2013, clinical and laboratory results have been collected from 626 patients with uveitis. One hundred seventy-five patients (28%) have sarcoidosis as the suspected cause of their uveitis. At presentation, 145 patients (23%) showed at least 3 of the 7 clinical signs proposed by the IWOS group as suggestive of ocular sarcoidosis. In total, 73 patients (12%) had biopsies, with 50 (68%) positive for sarcoid. Following the IWOS criteria, 50 patients met the definition for "definite ocular sarcoidosis," 60 for "presumed," 15 for "probable," and 1 for "possible." Of the patients who had a suspected clinical diagnosis of sarcoidosis, 78 (45%) did not meet any of IWOS diagnostic criteria levels for ocular sarcoidosis.

Conclusions: Data collection is still ongoing. Results will be presented at the IOIS meeting in Valencia.

Visual Outcome of Inflammatory Eye Disease Patients Undergoing Cataract Surgery and Effect of Preoperative Inflammatory Control on Postoperative Vision.

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Institutional Review Board Approval

The project was conducted in accordance with the principles of the Declaration of Helsinki, with the approval of the governing Institutional Review Boards of each institution, each of which has granted waiver of consent, allowing all living and deceased patients to be included.

Purpose: To evaluate the visual outcome of cataract surgery in inflammatory eye disease cases and to assess prognostic factors, including the effect of controlling inflammation for 3 months prior to surgery.

Design: Retrospective cohort study.

Participants: A total of 498 noninfectious inflammatory eye disease patients (656 eyes) undergoing cataract surgery treated at five subspecialty uveitis clinics were included.

Methods: Retrospective cohort study based on standardized chart review.

Results: By one year following cataract surgery, the median change in VA was an improvement of 5 ETDRS-equivalent lines (interquartile range (IQR) 1-10 lines). Postoperative VA was significantly better than preoperative VA for phacoemulsification, extracapsular, and pars plana surgery (each $P < 0.001$) and marginally better for intracapsular cataract extraction ($P=0.052$). Sixty-two percent of eyes gained ≥3 lines of vision after surgery, whereas only 4.6% lost ≥3 lines. Eyes with anterior uveitis and scleritis were more likely to have postoperative VA ≥20/50 when compared to eyes with other types of inflammatory eye disease ($P = 0.005$, $P = 0.001$, respectively). The proportions of eyes with visual improvement were highest in eyes with panuveitis (0.71, $P = 0.016$) and anterior uveitis (0.67, $P = 0.036$) and lowest in eyes with posterior uveitis (0.44, $P = 0.016$). Eyes with 3 months of controlled inflammation preoperatively had less moderate (20/50 or worse) and severe (20/200 or worse) impaired postoperative VA ($P = <0.001$, $P = 0.028$, respectively) compared to eyes that had slightly active or active inflammatory disease in the preoperative period. But after controlling for other factors, there was not a significant difference in the odds of gaining 3 lines of vision or in the odds of having a postoperative VA of 20/50 or worse whether an eye had active inflammation or was quiet prior to surgery. Macular scar was the most commonly identified factor limiting visual outcome.

Conclusions: Our results suggest that after cataract surgery, visual improvement in eyes with inflammatory eye disease is common and vision loss is rare. Visual outcomes are poorer when the underlying uveitis primarily involves the posterior segment, although substantial improvement still may occur in these cases, especially in panuveitis cases. Uveitic quiescence for three months preceding surgery is preferable, though not an absolute, as eyes with active disease despite preoperative treatment, may still benefit from cataract extraction.

Session 40

Singapore Uveitis Study Group: *CMV anterior uveitis*

Clinical Manifestations of Cytomegalovirus Related Anterior Uveitis in Immunocompetent Patients

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Purpose: This study aims to describe clinical features of Cytomegalovirus (CMV)-related anterior uveitis in immunocompetent patients and to compare clinical manifestations of CMV DNA positive cases with CMV DNA negative cases. Furthermore, this study aims to correlate these clinical features with CMV viral load.

Method: Records of all patients with hypertensive anterior uveitis seen at the Singapore National Eye Centre from January 2012 to April 2013 were reviewed. Percentage of endothelial cell loss was calculated using the formula: [(ECC fellow eye – ECC affected eye)/ ECC fellow eye] x 100. Patients with previous unilateral intraocular surgery were excluded. Patients with bilateral surgery were included if both eyes underwent the same procedure.

Results: Fifty-five CMV DNA positive and thirty-six CMV DNA negative cases were identified by tetraplex PCR. No difference was seen in mean age and gender. CMV positive cases presented with keratic precipitates (KPs) in the inferior 2/3 of the cornea. Color, size and shape of KPs were not associated with tetraplex result. Average intraocular pressure (IOP) in affected eyes was significantly higher in CMV positive cases. There was no difference in percentage of endothelial cell loss between the two groups. No correlation was found between IOP, percentage of endothelial cell loss and CMV viral load in CMV positive cases.

Conclusion: Clinical features of CMV positive and CMV negative cases are comparable except for IOP of the affected eye and distribution of KPs on the cornea. CMV positive patients had significantly higher IOPs and KPs tended to be located in the inferior 2/3 of the cornea.

Cytomegalovirus positive corneal stromal edema with keratic precipitates Post Penetrating Keratoplasty: A case control study

Aliza Jap, Singapore National Eye Centre

Purpose: To identify differences between cytomegalovirus (CMV) positive and negative eyes presenting as suspected endothelial graft rejection post penetrating keratoplasty (PK).

Design: Retrospective consecutive case-control series.

Methods: Aqueous humour samples of all eyes with corneal stromal edema and keratic precipitates (KPs) post PK seen at the Singapore National Eye Centre from 2007 to 2010 were analyzed for CMV DNA by polymerase chain reaction. Their charts were reviewed for demographic data, medical and ocular history, best corrected visual acuity (BCVA), intraocular pressure (IOP), anterior segment clinical findings and therapy.

Results: Of eleven eligible eyes (11 patients) 7 were CMV positive . All were negative for herpes simplex and varicella zoster virus. The 2 groups were similar in age, gender and previous ocular surgery. The main differences were the presence of extensive, heavily pigmented KPs, descemet's membrane (DM) folds and the absence of vascularization of the donor in CMV positive eyes (100% versus 0%, P= 0.003, Fisher's Exact test). All the CMV positive eyes were treated with ganciclovir (5 systemic, 2 topical) and the control eyes received immunosuppression. However all the grafts failed. BCVA at the last visit was worse than 20/400 in all except one control eye that had follow-up of 30 months.

Conclusions: There is a high prevalence of CMV infection in eyes that develop corneal stromal edema with KPs post PK. Heavy endothelial pigmentation, DM folds and the absence of donor vascularization may aid in the diagnosis of CMV in the event that aqueous analysis is not possible.

Keratic Precipitate Confocal Microscopy in Infectious Uveitis

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Purpose: To describe the morphologic patterns of keratic precipitates (KPs) in uveitis using in-vivo confocal microscopy (IVCM) in relation to the underlying etiologies.

Materials and Method: Prospective case-series. New cases with uveitis from various etiologies seen at the Singapore National Eye Centre were recruited with informed consent. All patients underwent detailed ophthalmic evaluation including slit-lamp biomicroscopy and dilated fundal examination. Clinical diagnoses were made using standard clinical criteria with the aid of investigations performed at the discretion of the uveitis consultant. KPs IVCM was performed using a digital corneal confocal Laser Scanning Microscope (Heidelberg Retina Tomograph III with Rostock Cornea Module, Heidelberg Engineering GmbH, Dosssenheim, Germany) with a water immersion lens (Zeiss, 63x/N.A. 0.95W) under local anaesthesia by a trained technician. The images of patients with definitive clinical diagnoses are presented.

Results: Owl eye morphologic features were seen in the corneal endothelial cells in CMV anterior uveitis (AU) and endotheliitis. Dendritiform KPs were observed in CMV AU, and presumed Fuch's uveitis syndrome. Large globular KPs were observed in chronic CMV AU. Dendritiform KPs were seen in syphilis and varicella-zoster AU. Non-infectious uveitis such as HLA-B27 associated AU have stippled and globular KPs and do not have dendritic KPs.

Conclusions: Confocal microscopy of KPs in our series of uveitis patients agreed with the few published studies on KP IVCM that the observation of dendritiform KPs can direct the relevant investigation for infectious etiologies.

Histopathology of CMV keratouveitis and other investigations

Anita Chan,Singapore National Eye Center, Singapore general hospital, Singapore Eye Research Institute, Duke-NUS, NUS-YLL School of Medicine

Purpose : To describe the histopathology of CMV keratouveitis.

Materials and Methods : Prospective review of all corneal tissue removed for graft failures and rejection over 2011 to 2013 in the SGH-SNEC Ophthalmic pathology service.

Results: From 2011 to 2013, 3 cases of CMV related graft failure were seen SNEC. We present the histopathological, electron microscope and immunohistochemistry features of these 3 cases.

Conclusions: CMV keratouveitis may present as graft rejection and in advanced cases result in graft failure in the apparently immunocompentent individual. The histological features of this newly recognized entity has not been well documented. Although intraocular analysis of aqueous is a useful clinical method for detection of CMV related graft rejection, analysis of the corneal button for specific viral cytopathic features are also important as they may not be clinically apparent at the time of surgery to prevent postsurgical recurrence.

Posterior segment manifestation of CMV anterior segment in the immunocompetent.

Gemmy Cheung, Singapore National Eye Centre
Melissa Wong, Singapore National Eye Centre
Soon Phaik Chee, Singapore National Eye Centre

Objective: Cytomegalovirus (CMV) ocular infection in immunocompetent patients is commonly known to involve the anterior segment. The aim of this study was to investigate and describe the clinical spectrum of posterior segment findings if any, in immunocompetent patients presenting with CMV associated anterior uveitis. Design: This was a prospective study conducted at the Singapore National Eye Centre, a tertiary referral centre from August 2010 to June 2011.

Participants: Eleven eyes of eleven patients with CMV anterior uveitis and confirmed by polymerase chain reaction on aqueous sampling were recruited based on the study criteria.

Methods: Patients underwent aqueous sampling, fundal and indocyanine green angiography as well as optical coherence tomography. They were also further evaluated by the Infectious Disease physician for immunocompetence. Main outcome measures: posterior segment manifestations on both clinical examination as well as on imaging in immunocompetent CMV anterior uveitis patients. Secondary aims were to describe any correlation between posterior segment and anterior segment findings in this group of patients.

Results: None of the eyes had evidence of retinitis or hemorrhage. Posterior segment findings included cystoid macular edema detected both clinically and on imaging, disc swelling and vasculitis. A significant finding on fundal angiography was a prolonged arm to retina time in 81.8% eyes. (p=0.03) Mean arm to retina time was 24.8 ±10.6 seconds. Indocyanine green angiography was unremarkable.

Conclusion: Posterior segment manifestations can be seen in a proportion of immunocompetent patients with CMV anterior uveitis.

Session 41

IOIS session: *Management of Uveitis complications*

Cataract surgery in the adult patient with uveitic cataract

Dr. Jorge Alio

Cataract surgery in the adult patient with uveitic cataract is cumbersome and sometimes has important hazards. The main complications associated to the cataract are the posterior synechia, glaucoma, and the advanced condition of the cataract, many times intumescent level or hard due to the longstanding delay of the surgery. I classify these patient into two groups, those that need associated cataract and glaucoma surgery and those who do not. In this presentation I shall present my approach to both types of cases, and how I approach glaucoma surgery at the moment of cataract using microshunts such as the Express Valve associated to antifibrotic agents such as mitomycin C. For those patients without the need for glaucoma surgery, the cataract surgery should be adequately planned to overcome the associated anatomical distortions of the anterior chamber, pupil stretching or hooks are necessary to enlarge the pupil and the use of capsular staining is mandatory in most of the cases. Most of the times, hydrodissection is difficult because of cortex adherence to the capsule and I have frequently unstable condition of the zonular which leads to further complicated surgery. Phacoemulsification is better performed with oscilatory energy associated to a small amount of ultrasound. The goal is to minimize the amount of ultrasound energy to base the surgery more on fluidics. Following these recommendations, my outcomes in this type of surgeries have been uniformly acceptable even with the limitations in the visual outcomes that happens in these cases.

Cataract: surgery in pediatric patients

Soon-Phaik Chee, Singapore National Eye Centre;Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore; Singapore Eye Research Institute;Duke-NUS Graduate Medical School.

Management of chronic uveitis in childhood with aggressive immunosuppression is key in preventing cataract formation. Appropriate timing of surgery striking a balance between achieving disease quiescence for 3 months prior to surgery and preventing amblyopia is often challenging. Whether an intraocular lens should be implanted or not, the IOL material and power, and posterior capsule/anterior vitreous management are other important factors to consider. Surgical techniques which minimize surgical trauma in releasing the iris bound by membranes and synechiae and complete removal of lens material are important to prevent postoperative fibrin and subsequent membrane formation. This talk will highlight surgical pearls which minimize surgical trauma.

Cystoid Macular Edema: Anti-Vegf Agents

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Cystoid macular edema (CME) is one of the most frequent sight-threatening complications in patients with uveitis. It may appear throughout the evolution of the inflammatory disease or following intraocular surgery. The aim of this paper will be to provide a rationale and an extensive summary of the reported evidence about the use of vascular endothelial growth factor inhibitors administered intravitreally for cases of CME.

Session 43

Uveitis Society of Thailand combined with Indo-China Ocular Inflammation Study Group: *Common infectious uveitis*

Human immunodeficiency virus (HIV)-induced uveitis

Kessara Pathanapitoon, Chiang Mai University

The eye can form a sanctuary where human immunodeficiency virus (HIV) might replicate and cause an inflammatory reaction. Intraocular HIV-1 RNA was detected in 32% (13/40) of HIV-positive patients with uveitis. Intraocular HIV-1 RNA loads were associated with high HIV-1 RNA plasma loads ($P<0.001$) and not being on HAART ($P= 0.005$). In addition, detectable intraocular HIV-1 RNA levels were higher in patients with the absence of retinal lesions ($P= 0.008$).1

HIV uveitis was diagnosed in six patients (8 eyes) who had an extremely high intraocular: plasma HIV-1 RNA ratio. None of the patients were receiving HAART or had clinical or laboratory evidence, or both, of opportunistic infections. The mean plasma load was 218,688 copies/ml (median, 137 500 copies/ml; range, 24,900–540,000 copies/ml), and the mean intraocular HIV load was 20,937,755 copies/ml (median, 7,499,000 copies/ml; range, 2,460,000–89,800,000 copies/ml). The average CD4 cell count was 192 cells/ul (median, 248 cells/ul; range, 5–342 cells/ul). The anatomic location of uveitis was anterior in all patients, and associated vitritis was present in 4 patients; none exhibited retinal lesions or scars. After the administration of HAART, the intraocular inflammation disappeared entirely within several weeks in all of the patients and the intraocular and plasma HIV loads decreased.2

HIV-induced uveitis should be suspected in HAART-naïve, HIV positive patients or in those in whom this treatment fails and who have anterior uveitis without any retinal lesions and exhibit no response to topical corticosteroids.1.2

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Viral necrotizing retinitis: The ARN and PORN

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Necrotizing retinitis is one of the devastating inflammatory eye diseases which leads to permanent visual impairment in large number of patients. The disease is caused by viruses in Herpes family.

Although the disease has been described for many decades, little has been changed regarding the treatment modality and prognosis. Previous studies show that final visual outcome and complication are associated with the amount of affected area and prognosis is better in cases with good presenting VA. However, variation of eye findings in different stage of the disease may occur which leads to diagnostic dilemma in cases with dense vitritis precluding retinal lesions. Diagnostic aqueous or vitreous aspiration for polymerase chain reaction is essential in such equivocal cases. Some cases have been treated with systemic steroid before referral. This topic will describe cases of viral necrotizing retinitis including ARN and PORN in Thailand. The most common causative virus is varicella zoster. Unlike previous reports, several cases have 2 viruses identified by PCR. Correlation between clinical factors and treatment outcome are analyzed and vitreous haze of grade 3 or more is associated with poor treatment outcome. Systemic steroid given before antiviral therapy and prophylaxis laser retinoplexy do not have significant effect on final outcome. The rate of retinal detachment and final VA are comparable with other reports.

ViralOrelated anterior uveitis in Thailand

Pitipol Choopong.

Viral-related anterior uveitis is one of the most common infectious anterior segment inflammations. The common clinical features are medium-sized mutton fat keratic precipitates, endotheliitis, iris atrophy, and ocular hypertension in the unilateral eye. Previously, it was differently classified as Fuchs heterochromic iridocyclitis or Posner-Schlossman syndrome. Fuchs heterochromic iridocyclitis is asymptomatic, mild, chronic iritis with diffuse stellate keratic precipitates. Chronic inflammation causes cataract and depigmentation of the iris in the involved eye leaded to different color of the eyes. Posner-Schlossman syndrome presents with acute intermittent mild iritis associated with high intraocular pressure. Decreased vision due to corneal edema is common during the uveitis attack. Later, the aqueous humor of the patients was evaluated and it revealed suspicious viral etiology of the diseases. The common viruses identified by polymerase chain reaction or Goldmann-Witmer coefficient were herpesviridae and rubellavirus. We here demonstrate the epidemiologic picture of viral-associated anterior uveitis in Thailand.

CMV retinitis versus IRU

Supinda Leeamornsiri, Department of Ophthalmology, Thammasat University Hospital, Pathumthani, Thailand

Cytomegalovirus (CMV) retinitis remains the most common intraocular infection in patients with acquired immunodeficiency syndrome (AIDS) and typically occurs in individuals with CD4 T cell counts below 50 cells/µl. Three distinct features have been described including a classic retinitis or fulminant retinitis with retinal hemorrhage in the posterior pole, a granular or indolent form found often in the peripheral retina and a perivascular infiltration form often described as frosted branch angiitis. CMV and HIV trans-activate each other. CMV retinitis is associated with increased mortality. Anti-CMV medication demonstrates the efficacy of CMV retinitis therapy and systemic anti-CMV treatment decreases AIDS mortality. Immune recovery is the most important factor for long term control. In some patients, recovery of the immune system following highly active antiretroviral therapy (HAART) initiation can be sufficient to suppress CMV retinitis without concomitant anti-CMV therapy. Ocular complication related to HAART induced immune reconstitution, so called immune recovery uveitis (IRU) may occur. It is characterized by paradoxical worsening of treated CMV lesions or the unmasking of previously subclinical CMV retinitis. It is also associated with vision-impairment complications including macular edema, epiretinal membrane, vitritis and neovascularization. Patients without immune reconstitution require life-long therapy. Viral resistance to anti-CMV medication has been described with prolong treatment and associated with the worse clinical outcome including mortality.

Bacterial Endogenous Endophthalmitis In VietNam

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Nhu Hon Do, Viet Nam National Institute of Ophthalmology

Background/AIMS: To compare vitrectomy with silicone oil temponade with conventional vitrectomy for patients with severe bacterial endogenous endophthalmitis (BEE).

Methods: In this randomized controlled trial, 108 patients with severe BEE (defined by the absence of pupil red reflex at presentation and/or dense vitreous opacity on ultrasound and no improvement after 24-36 hours of medical treatment) were randomly assigned to 2 groups: Group 1: early vitrectomy and Group 2: early vitrectomy with silicone temponade. Overall success: was defined as of visual acuity ≥ Count fingers at 1metre and and flat retina without oil in the eye.

Results: There were 53 patients in Group 1 and 55 patients in Group 2. The mean age of study subjects was 32 years and baseline clinical characteristics were similar in both groups. At the final follow-up visit at 9 months, the overall success rate of Group 2 (67.3%) was significantly better than Group 1 (43.4%, p=0.01). There were also fewer devastating complications (such as inoperable retinal detachment, phthisis bulbi) in Group 2 compared with Group 1(21.8% versus 43.4% with p=0.01).

Conclusions: The outcome at 9 months of patients with BEE treated by vitrectomy with silicone oil was better than those treated by vitrectomy alone.

Session 44

Middle East Africa Council of Ophthalmology: *New insights in VKH disease*

Etiopathogenesis of Vogt-Koyanagi-Harada Disease

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Vogt-Koyanagi-Harada (VKH) disease is an autoimmune disease characterized by inflammation in melanocytes-containing tissues, such as the eye, meninges, ear, and skin. The disease is more in pigmented ethnic groups such as Japanese than in Caucasian people. The pathogenesis of VKH disease has been investigated for many years to seek the pathogenic antigens. Histo-pathology revealed lymphocyte infiltration targeting melanocyte in the eye and CD4+ T cell infiltration in the choroid. However, the pathogenic antigen for the disease had not been clarified until Yamaki and his colleagues established an animal model for VKH disease. They found that a melanocyte-associated antigen, tyrosinase, induced autoimmune inflammation in the eye and the skin resembling VKH disease in experimental animals. Furthermore, peripheral lymphocytes of VKH patients, but not other uveitis, responded to tyrosinase. Not only peripheral lymphocytes, but also ocular CD4+ T cells from VKH patients, responded to tyrosinase peptides, but not to control antigen, in a dose respond manner. Thus, melanocyte associated antigen, tyrosinase, is the pathogenic auto-antigen for VKH disease. However, it is still unclear how the auto-antigen can cause immune reaction and inflammatory response in VKH patients. A hypothesis if an exogenous antigen might have structural homology with tyrosinase and the molecular mimicry might cause immune response and inflammatory reaction in melanocyte-containing tissues. A data- base survey found an exogenous antigen, CMV envelope antigen, which as a structural homology with thrysinase. In fact, peripheral lymphocytes as well as T cells from the eye of VKH patients, but not from other uveitis, responded to both tyrosinase and CMV antigens, but not to control antigen.

These findings indicate that etiopathogenesis of VKH disease is an autoimmune response to a melanocyte-associated antigen, tyrosinase, and molecular mimicry with CMV-associated antigen plays a role to establish the autoimmune responses.

Clinical Findings of Vogt-Koyanagi-Harada disease

Vishali Gupta, KKESH

The classical clinical features of VKH include bilateral panuveitis associated with exudative retinal detachment, meningism, tinnitus hearing loss, and cutaneous changes, such as vitiligo, alopecia and poliosis. The clinical features depend upon the stage of the disease and vary with the time of presentation and the treatment received. Presence of ocular and two or more extra-ocular features

is considered as complete form of VKH disease wheras incomplete VKH disease includes bilateral typical ocular involvement plus either neurologic/auditory or cutaneous changes. Patients with only ocular features are categorized as probable VKH disease. The presentation aims to describe the clinical signs in correlation to the etiopathology of the disease.

Vogt-Koyanagi-Harada disease: Multimodal imaging

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Attia Sonia, Fattouma Bourguiba University Hospital, Monastir, Tunisia
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Early diagnosis of acute Vogt-Koyanagi-Harada (VKH) disease is of utmost importance for prompt initiation of corticosteroid therapy to prevent chronicity, recurrences, complications, and subsequent permanent visual loss. The diagnosis of acute VKH can be made or highly suspected on the basis of specific clinical findings in most cases. Multimodal imaging is helpful in establishing the definitive diagnosis, particularly in the absence of extraocular manifestations or when there is no clinically evident exudative retinal detachment (ERD). Fluorescein angiography (FA) typically reveals multifocal delayed choroidal perfusion, pinpoint leakage, optic disc hyperfluorescence, late pooling and staining of the dye, and choroidal striations, in a subset of patients. Indocyanine green angiography (ICGA) findings include choroidal filling delay, choroidal vascular hyperpermeability, hypofluorescent dark dots that are most noticeable at the intermediate phase, pinpoints, and optic disc hyperfluorescence. Optical coherence tomography (OCT) is very useful in the evaluation of ERD, and may detect subclinical retinal fluid. It also typically shows subretinal septa, hyperreflective subretinal dots, and multifocal folds of the retinal pigment epithelium. Enhanced-depth Spectral domain OCT shows markedly thickened choroid. B-scan ultrasonography may also be useful, especially when visualization of the fundus is poor. It reveals a characteristic low to medium reflective choroidal thickening most prominent in the posterior fundus. Furthermore, fundus autofluorescence (FAF) demonstrates hyperautofluorescence in the macula associated with hypoautofluorescence in the areas of ERD. In conclusion, multimodal imaging including FA, OCT, ICGA, and ultrasonography provides useful diagnostic clues in acute VKH disease.

Physiopathology, monitoring and significance of choroidal involvement in Vogt-koyanagi-Harada disease

Carl P Jr Herbort, University of Lausanne and Centre for Ophthalmic Specialised care

Choroiditis has recently been divided into choriocapillaritis when the impact is at the level of the choriocapillaris and into stromal choroiditis when the inflammation is situated in the choroidal stroma. The choroidal stroma can be the chance location of an infectious or non-infectious systemic disease such as tuberculosis or sarcoidosis and is then termed secondary stromal choroiditis. The situation is different in Vogt-Koyanagi-Harada (VKH) disease, as well as sympathetic ophthalmia, where the exclusive origin of inflammation comes from the choroidal stroma, the site of an auto-immune mechanism directed against a stromal melanocyte associated protein. As the primary and only inflammatory reaction is selectively situated in the choroidal stroma and nowhere else, these entities are called primary stromal choroiditis. The choroidal inflammation develops first silently while it is still confined to the stroma. Probably this phase corresponds to the prodromal stage of the disease. It is only when the inflammation spills over, usually in an explosive fashion, to neighbouring compartments such as the retina, optic disc and vitreous, that the disease becomes clinically apparent The fact that the choroidal stroma is the "primum movens" means that the follow-up of choroidal inflammation by ICGA is crucial and that therapy has a good impact because the choroid is easily accessible to systemic therapy. However therapy has to be sustained and ICGA-assisted, as subclinical choroidal recurrence of inflammation has to be immediately dealt with.

Prognostic Factors and Management

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Purpose: To determine prognostic factors in patients with Vogt-Koyanagi-Harada disease who were treated with high-dose corticosteroids.

Methods: Retrospective analysis of 87 patients (174 eyes).

Results: At presentation, there were 53 patients with initial-onset acute VKH disease and 34 patients with chronic recurrent VKH disease. Chronic recurrent presentation was significantly associated with more severe anterior segment inflammation at presentation as indicated by presence of mutton-fat keratic precipitates, anterior chamber reaction >/=2, iris nodules and posterior synechiae (p20/200 (odds ratio = 4.25; 95% Confidence interval (CI) = 1.53 – 11.89) and age older than 16 years was significantly associated with the development of complications (odds ratio = 3.15; 95% CI = 1.04 – 9.48).

Conclusions: Chronic recurrent VKH disease is significantly associated with more severe anterior segment inflammation and less exudative retinal detachment at presentation, more ocular complications and a worse visual outcome than initial-onset acute VKH disease. Use of immunomodulatory therapy significantly improved the clinical outcomes.

Session 45

Centro Mexicano de Enfermedades Inflamatorias Oculares: *Utility of new imaging studies in ocular inflammatory diseases*

Fundus autofluorescence-in recurring phase of Vogt Koyanagi Harada Disease

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Purpose. fundus autofluorescence (FAF), is a new non-invasive method using the fluorescent properties of lipofuscin to study the health and viability of the retinal pigment epithelium (RPE), This method has been applied on various disorders involving RPE, such as age-related macular degeneration and central serous chorioretinopathy, as well as inflammatory disorders, its usefulness in ocular inflammatory diseases has not been well established .

Materials and Methods. In this study, the FAF and indocyanine green (ICG) angiography images of patients with recurrent VKH disease seen at Asociación para evitar la ceguera en Mexico hospital were prospectively reviewed. All of the angiography and FAF photography were performed with a confocal scanning laser ophthalmoscope (Heidelberg Retina Angiograph 2, HRA2; Heidelberg Engineering, Heidelberg, Germany). Bluelight FAF (BL-FAF) photography was performed using a 30 grades field of view and 512 x 512 pixel resolution centred on the macula. The modality uses blue light at 488 nm for excitation and a barrier filter at 500 nm.

Results. The FAF demostrated hyperautofluorescence spots accompanied hypoautofluorescence spots corresponding to the areas of fibrosis, atrophy or pigment migration characteristics of the convalescent phase Found. The hyperautofluorescence seen in the FAF corresponded to multifocal hypofluorescence on ICG angiographym. Such hypofluorescence on ICG angiography is thought to represent the sub clinical choroidal inflammatory foci.

Conclusions. According with this results, we propose that the study of autofluorescence fundus is a noninvasive method that can highlight areas of subclinical choroiditis which may be present even then the apparent control of inflammation, and these findings should guide the clinician to continue aggressive treatment until the hyperautofluorescence disappears.

OCT. Variation of choroidal thickness in different phases of VKH

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Asociacion Para Evitar La Cuguera En Mexico

Purpose. Analyze subfoveal choroidal thickness by Optical coherence tomography (OCT) using enhanced depth imaging (EDI) (EDI-OCT) in all stages of Vogt-Koyanagi-Harada disease (VKH).

Material and Methods:

A prospective study of all patients seen at our Clinic from 2012 through 2013 at Asociación Para Evitar la Ceguera en México. All with diagnosis of VKH at any stage were examined by the Heidelberg Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) with eye tracking and image averaging systems. The vertical and horizontal scans were obtained at each measurement to evaluate the center of fovea precisely. Each image was the product of 100 scans. With the software (version 1.5.12.0) with Heidelberg Spectralis OCT, the choroid was measured from the outer border of the hyperreflective line corresponding to the RPE to the inner scleral border. The subfoveal choroidal thickness was measured and also four measures 1000µ from fovea to temporal, nasal, inferior and superiorly. The reported measurements from OCT images represented the average of the measurements made by three co-authors.

Results: Preliminary results include 16 patients, 32 eyes. 15 women. Uveitic stage in 48.5%, convalescent in 42.4% and in recurrence in 6.1%. At first visit central choroidal thickness in uveitic stage with mean 267.62µ ± 130.92, in convalescent stage central choroidal thickness 237.28µ ± 119 and in recurrent stage central choroidal thickness 413µ ± 76.36.

Conclusion: EDI-OCT allows a noninvasive evaluation of choroidal thickness and plays a vital role in the pathophysiology of VKH disease. Rebound of choroidal thickening was observed in recurrent phase eyes. -Eyes in patients with VKH and long-standing disease had thinner choroids.

UBM findings as factors for visual prognosis in patients with Pars Planitis after cataract surgery

Jose Antonio Unzueta, Luz Elena Concha-del-Río, Brenda Juárez,Lourdes Arellanes-García

Introduction

Pars planitis (PP) is a subtype of intermediate uveitis, frequently seen in children. It represents 7.78% of all the referred cases to the Inflammatory Eye Disease Clinic of the Asociación Para Evitar la Ceguera en México.

During the disease, snowbanking is replaced by fibrotic tissue and can evolve into a cyclitic membrane (CM) that can extend over ciliary body, lens, zonule and posterior capsule. CM can lead to vitreous traction, ciliary body and retinal detachment. CM is observed in 12% of eyes with pars planitis seen at our hospital.

In eyes with clear media, snowbanks and CM can be seen with a 20+ D lens and scleral indentation, with a gonioscope or with ultrasound biomicroscopy (UBM). UBM provides excellent images of anterior uvea, vitreous base, and peripheral retina. It has already been reported as a reliable imaging technique, but as far as we know there are no reports of the importance of UBM findings as factors for visual prognosis in PP.

Material and Methods: The aim of this report is to show the value of UBM findings as factors for visual prognosis in patients with PP. A retrospective study was performed in patients who had an UBM ultrasound using a probe of 50-MHz frequency and gain of 105dB.

Results: Will be described at the meeting.

Conclusions: UBM allows imaging of structures of the eye that cannot be seen otherwise.

In patients with suspicious or definite diagnosis of PP, UBM can provide fine details useful for diagnosis and also for follow-up evaluation and it guides the surgeon in choosing the optimal timing and type for surgical intervention and to probably to define prognosis in patients PP.

Echographic findings in the convalescent and recurrent stage of Vogt-Koyanagi-Harada disease (VKH).

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Purpose. To correlate clinical and B scan ultrasound posterior pole findings in VKH patients during the convalescent (CP) and recurrent (RP) phases. To determine if CP and RP findings correlate with visual prognosis

Materials and Method. Transversal, observational, descriptive study of clinical and B scan ultrasound (BSU) posterior pole findings in a group of consecutive VKH patients in the convalescent or recurrent stage

Results. We included 37 eyes of 25 patients, mean age 43 y, 80% were women. Most frequent clinical findings were: pigment migration (94.59%), sunset glow fundus / nummular scars (70.27%), subretinal fibrosis (64.8%). BSU detected subretinal fibrosis in 64.86% of eyes and had a 100% sensitivity and specificity. Eyes with subretinal fibrosis had a 84.61% probability of having VA < 20/70.

Conclusions. In this study BSU was able to detect all subretinal fibrosis cases clinically diagnosed. Subretinal fibrosis was associated to a worst visual prognosis. In CP, RP VKH eyes with media opacity BSU may detect subretinal fibrosis and may help to determine visual prognosis.

Macular Ocular CoherenceTomography (OCT)findings in patientsunderchronictreatmentwithChloroquine and Hydroxychloroquine

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Hobbs in 1959 firstreportedretinaltoxicityduetolongterm use of chloroquine (CQ).Currently, sulfate hydroxychloroquine (HCQ) isthemostwidelyusedantimalarialagent in thetreatment of autoimmunediseasesbecause of itslowerincidence of adverse reactionsalthough, like CQ, may produce ocular toxicitydueto corneal and retinaldeposition. HCQ can haveserioussideeffectssuch as retinopathy, gastrointestinal malaise, pruritus, and visual disturbances. As a weak base, CQ entersacidicorganelles as anunchargedmolecule, becomingprotonated in thematrix of acidicorganelles. Theloss of protonsbyprotonation of CQ causes theneutralization of thelumenal pH of acidicorganelles. Accumulation of protonated CQ in acidicorganelles induces osmoticswelling and therelease of lysosomalhydrolases. Thus, neutralization of acidicorganelles and therelease of lysosomalhydrolaseshavebeenconsidered as themain causes of CQinducedcytotoxicity. Hydroxychloroquinetoxicityappearstofirstaffecttheretinalganglioncells and thephotoreceptors, especially in theperifovealregion. Thedrugalso has affinityforpigmentedcells, includingtheretinalpigmentepithelium, perhaps as a secondaryeffectonthephotoreceptoroutersegments.Earlychloroquineretinopathyisdefined as anacquired paracentral scotomaonthreshold visual fieldtesting, with no detectable retinalfindings, whileadvancedretinopathy has associatedparafoveal RPE atrophy.

OCT is a techniquethatprovidescross-sectionalimaging of tissuemorphology in vivo withcross-sectionalimages and quantitativeinformationonretinalpathologicalabnormalities. Animagewith 10-µm axial resolution and 512 axial scansmay be acquired in seconds.

In 2007 Rodriguez-Padilla et al using a high-speed ultra-high-resolution OCT Stratusreporteddiscontinuityorloss of perifovealphotoreceptorinnersegment/outersegmentjunctions and thinning of theouter nuclear layer in 15 patientsreceivinghydroxychloroquine. Later, Korah and Kuriakose(2008) reported a patientwithbilateral superior paracentral scotomas, fluorangiographicevidence of RetinalPigmentEpithelium (RPE) loss and the OCT revealedanatomicalloss of ganglioncelllayers, causingmarkedthinning of the macula and parafovealregion. Pasadhika (2010) suggestedthat OCT isusefultodetectperipapillary RNFL thinning in clinicallyevidentretinopathy, and selectivethinning of the macular inner retina can be detected in theabsence of clinicallyapparentfunduschanges. Usingspectral-domain OCT, onlytheganglioncelllayer and innerplexiformlayercomplex in theperifovealareawasaffected in thepatientswithhydroxychloroquineexposurecomparedtocontrols.Recently, Marmor (2012)describedthathydroxychloroquine causes earlyparafovealloss of theoutersegmentlinesonSpectralDomainOCT (SD-OCT), withthefirstchangesoftenevident in theinferotemporalquadrant. Parafovealthinning of theouter nuclear layerfollows, beforeretinalpigmentepitheliumdamageis visible. Ourgroupstudied 75 patientsundertreatmentwithChloroquineorHydroxichloroquine. Allpatientsunderwent a complete ophthalmologicalexaminationwith color visionIshihara test, 10-2 automated visual field and fluoresceínangiography and macular OCT (OptovueRtVue Fourier-Domain Ocular CoherenceTomography).

Antimalaricintake time was 8 yearswith a cumultivedose of 602gr. Fundusexaminationfindingswere normal exceptforpatientswithseveretoxicity. Most of thepatientsshowed a ring pattern of parafovealthinningwithanaverage central macular thickness of 239microns. Fluoresceinangiographyan 10-2 automated visual fieldwere normal in themajority of patients.Weconcludedthat

OCT may be anusefultoolforCQ or HCQretinaltoxicityscreeningwith a characteristic ring pattern of macular thinning. Thesefindings are present in most of the cases beforeotherclinicalorancillary test alterations.

In summary,parafovealretinalthickness and volumemeasurementsmay be initialevidence of chloroquinetoxicity. OCT measurementsmust be part of CQ and HCQ toxicityscreeningforearlydetection of chloroquinemaculopathy.

Ultrabiomicroscopy in Patients with Uveitis and its Correlation with Clinical Findings

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Purpose: 1) To analyze the data observed by ultrabiomicroscopy (UBM) and its correlation with clinical findings in patients with different types of uveitis and, 2) To assess the usefulness of UBM to identify changes in the anterior segment and anterior vitreous associated with uveitis.

Methods: Experimental and prospective study. We included patients of the with uveitis regardless of its cause, in whom a complete ophthalmic evaluation of the anterior segment and the anterior vitreous was possible. In all cases, an observer determined clinically the presence of keratic precipitates, anterior chamber cells, synechiae, iris nodules, inflammatory pupillary membrane, changes in ciliary body and anterior vitreous. Subsequently, all patients underwent an UBM study with 35 MHz probe. All the UBMs were done by the same observer who was blinded to the clinical findings. All patients signed an Informed Consent to participate in the study. The statistical analysis was done with independence tests using chi-squared statistics.

Results: We included 32 eyes (27 patients), 11 eyes (34.4%) with idiopathic non-granulomatous anterior uveitis, 7 (21.9%) with pars planitis, 3 (9.4%) with Fuchs' uveitis syndrome, 2 (6.3%) with herpetic queratouveitis, 2 (6.3%) with anterior granulomatous uveitis, 2 (6.3%) with Vogt-Koyanagi-Harada disease, 1 eye (3.1%) with: idiopathic panuveitis, other with infectious panuveitis, other with ocular toxocariasis and other with positive HLA-B27 associated uveitis. There was a statistically significant association between UBM and clinical findings in patients with: keratic precipitates, pupillary membrane, synechiae and anterior vitreous changes. There was less correlation for anterior chamber cells and ciliary body changes.

Conclusion: UBM may be a useful diagnostic technique in patients with uveitis, especially for those in which media opacity prevents adequate clinical assesment. Larger series of patients are necessary in order to confirm these findings.

Session 46

IOIS session: *Emerging infectious uveitis*

CMV Anterior Uveitis

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Cytomegalovirus (CMV) may manifest as acute hypertensive recurrent anterior uveitis (Posner Schlossman syndrome), or chronic anterior uveitis in the immunocompetent. The diagnosis is made by a positive polymerase chain reaction of the aqueous for CMV. Keratic precipitates seen in the acute and chronic uveitis differ in size, shape and distribution, but stromal iris atrophy and the absence of posterior synechiae are common to both. CMV positive chronic anterior uveitis eyes are more likely to occur in males, >57 years at diagnosis, and those with nodular corneal endothelial lesions than CMV negative eyes. CMV uveitis responds to various routes of administration of ganciclovir in about 75% of eyes but relapses equally frequently. Ganciclovir gel resulted in the lowest recurrence rates and is preferred for safety and cost considerations.

Rickettsioses

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Rickettsioses are worldwide distributed zoonoses due to obligate intracellular small gram-negative bacteria. Most of them are transmitted to humans by the bite of contaminated arthropods, such as ticks. Systemic disease typically consists of high fever, headache and skin rash, with or without « tache noire» (dark spot). Case confirmation is based on serology which may take 2-3 weeks. Ocular involvement is common, but it is often asymptomatic and self-limited. Retinitis, retinal vasculitis, and optic nerve involvement are the most common ocular findings. Retinitis typically manifests as white retinal lesions infiltrating primarily the inner retinal layers, typically located adjacent to retinal vessels, varying in number, size, and location, with associated mild vitritis. Retinal vascular lesions may include focal or diffuse vascular sheathing, vascular leakage, retinal hemorrhages, and retinal vascular occlusions. Optic nerve involvement may present in the form of optic disc edema, optic disc staining, optic neuritis, neuroretinitis, or anterior ischemic optic neuropathy. Other ocular manifestations include Parinaud's oculoglandular syndrome, conjunctivitis, keratitis, nongranulomatous anterior uveitis, panuveitis, and endophthalmitis. Doxycycline is the drug of choice for the treatment of rickettsial infection. Corticosteroids may be used in addition to antibiotherapy in cases with severe ocular involvement. Prognosis is usually good but systemic complications or permanent visual impairment may occur. In conclusion, the presence of inner retinitis, retinal vasculitis, or optic neuropathy in a patient with a history of fever and/or skin rash living in or returning from a specific endemic area, especially during the spring or summer, strongly suggests the diagnosis of rickettsiosis.

Ocular Manifestations of Chikungunya

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Purpose: To report the ocular manifestations associated with chikungunya infection.

Methods: Prospective ophthalmologic study of serologically confirmed or PCR confirmed patients with Chikungunya infection presenting with ocular complaints.

Results: Of 25 patients 15 had anterior uveitis, 7 viral retinitis, 2 episcleritis and one optic neuritis. PCR from the aqueous was positive in a case of Fuchs' heterochromic iridocyclitis. Patients received anti-inflammatory therapy and the majority recovered well.

Conclusion: Anterior uveitis is the commonest, retinitis and optic neuritis can also be seen. Physicians need to be aware of the association to diagnose and treat the condition in endemic areas. We will present our experience with review of literature on ocular manifestations of Chikungunya infection.

Ocular Manifestations Of Dengue Fever

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Dengue Fever is a viral epidemic in many parts of the world. With increasing urbanization and air travel, it has become a considerable international concern. Ocular manifestations of dengue fever are uncommon but of great significance due to the possibility poor outcomes. Proposed mechanisms include direct viral infection as well as immunologic phenomena. A wide variety of ocular involvement has been reported. We discuss the common manifestations ranging from bleeding diatheses to uveitides, as well as the investigations and outcomes.

Ocular manifestations of West Nile Fever

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West Nile virus (WNV) infection is a worldwide zoonosis due to a flavivirus transmitted by a mosquito vector. Most human infections are subclinical or manifest as febrile illness, but a small proportion of patients may develop severe neurologic manifestations. Meningoencephalitis is frequently associated with advanced age and diabetes. Ocular involvement is frequently asymptomatic. A bilateral multifocal chorioretinitis, with typical clinical and fluorescein angiographic features, is the most common ocular manifestation of WNV infection, occurring in nearly 80% of patients with severe systemic disease. Other ophthalmic manifestations mainly include anterior uveitis, retinal hemorrhages, focal or diffuse vascular sheathing, vascular leakage, occlusive vasculitis, and optic neuropathy. Although definitive diagnosis is based on specific laboratory tests (detection of specific IgM antibody in serum or cerebrospinal fluid using the IgM antibody-capture enzyme-linked immunoabsorbent assay), the typical pattern of multifocal chorioretinitis is of utmost importance to make early diagnosis while serologic testing is pending. WNV-associated ocular involvement usually has a self-limited course. There is no effective antiviral therapy against WNV infection.

Bilateral acute depigmentation of the iris

Ilknur Tugal-Tutkun

Bilateral acute depigmentation of the iris (BADI) is a new clinical entity of an unknown cause. It is characterized by an acute onset of pigment dispersion in the anterior chamber, symmetrical bilateral

depigmentation and discoloration of the iris stroma without transillumination defects, and pigment deposition in the anterior chamber angle. Young females are more commonly affected. Patients typically describe an upper respiratory tract infection or flu-like illness preceding the acute onset of severe photophobia and red eyes. Topical corticosteroids effectively relieve symptoms and pigment dispersion has a self-limiting course. Iris changes are reversible in the long term.

Session 47

Uveitis Society of Indonesia: *Uncommon clinical presentation of Ocular inflammation*

Suppression effects of *Curcuma longa* towards IL-1 and cyclo-oxygenase 2 expression in Endotoxin Induced Uveitis

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Introduction: Endotoxin Induce Uveitis (EIU) is an experimental inflammation mimics human acute uveitis. IL-1 is a potent inflammatory cytokine, whereas cyclooxygenase (COX)-2 convert arachidonic acid into prostaglandins, which both may have a role in uveitis pathology. Curcuma longa have been widely used as traditional medicine for anti-inflammatory.

Objective: to determine the suppression effects of oral C longa extract towards IL-1 and COX-2.

Methods: An experimental study have been done in rabbits by intravitreal injection of 100 µg lipopolysaccharide of E.coli to developed EIU, which divided into control and treatment groups. After 3 days of injection, the treatment group been given a *curcuma longa* extract (80 mg/kg body weight daily) intra gastric for 3 days. At day 6 all of the rabbits were killed, eyes were enucleated, and stained by immuno-histochemistry using monoclonal antibody of IL-1α and COX-2. The difference of Allred score were analyzed by Mann-Whitney test.

Result: Clinical signs of acute uveitis were prominent at day 3 in the control group than treatment group. The IL-1α and COX-2 were markedly increased in EIU rabbit compared to normal EIU rabbit. The expression of IL-1α and COX-2 in treatment group significantly lower than control group (p=0.001).- This results showed that *curcuma longa* extract suppressed the inflammation due to expression of IL-1α and anti COX-2 in EIU.

Conclusion: Oral *Curcuma longa* extract showed an anti-inflammatory effect against EIU by suppression of IL-1α and COX-2 expressions.

Keywords: *curcuma longa*, EIU,IL1-a, COX-2, rabbits.

Cytomegalovirus Retinitis in Diabetic Patients

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Background: CMV retinitis occur almost exclusively in severe immunocompromised patients, especially HIV-AIDS patients with CD4 less than 100 cells/µl.- The incidence of CMV retinitis in other immunosuppressed states is very rare, such as after renal, liver or bone marrow transplantation.

Purpose : To report two cases of CMV retinitis, proven with polymerase chain reaction (PCR) from vitreous in uncontrolled diabetic patients

Designs : case series

Methods : retrospective chart reviews

Results : Case 1, female 52 years old with history of diabetes since more than 10 years, complained of sudden blurred vision on both eye 2 weeks prior admission. Visual acuity RE 1 meter counting fingers and LE no light perception. Inflammatory process was seen on both eye, AC cells and posterior synachiae, and USG examination revealed vitreous haze Case 2, female 59 years old with history of non-proliferative diabetic retinopathy. VA on left eye 6/12 with macular edema, and patient was treated with triamcinolone acetonide injection intravitreally. After injection, VA dropped to 1 meter counting fingers.- Funduscopy examination revealed peripheral retinal necrosis and vitreous haemorrhage. We performed vitreous tap and PCR examination on both patients, and the results were positive for CMV.- Patients were treated with valganciclovir 2x900 mg, but unfortunately the vision did not improved due to severe retina damage.

Conclusion: Risk for development of CMV retinitis in uncontrolled diabetic patients and after triamcinolone injection should be considered by ophthalmologists

Unusual Clinical Manifestations Of Scleritis

Asyari Fatma, University Of Indonesia

Scleritis is a chronic and potentially blinding inflammatory disease that affects the sclera. it may be diffuse, nodular or necrotizing and may involve the anterior and or posterior segment of the eye. Scleritis is commonly associated with systemic autoimmune disorder and may be the initial and only presenting clinical manifestations of rheumatoid arthritis, relapsing polychondroitis, Wegener granulomatosis, spondylo-arthropathy, polyarthritis nodosa, or giant cell arteritis. Diagnosis mainly clinical but laboratory examination, ocular imaging may help .Treatment must be individualized for the severity of scleritis, response to treatment, adverse effects, and presence of the associated diseases. Unusual clinical manifestations of scleritis do occur and will be presented.

Unusual clinical presentation of intraocular Tuberculosis

Halida Wibawaty, Indonesian Ocular infection and Immunology Society

Intraocular tuberculosis is a rare condition caused by Mycobacterium tuberculosis and represents one percent of all cases of systemic tuberculosis (TB). When it does occur, the most common features are anterior or posterior granulomatous uveitis including retinal vasculitis and neuroretinitis. Here we report 2 cases with unusual presentation of ocular TB. First case :a 38 year-old Javanese lady, presented with gradual loss of vision in the right eye for 3 weeks duration. It was associated with right side headache, nausea and vomiting. Visual acuity (VA) in right eye was perception of light with presence of relative afferent pupillary defect. Both anterior segments were unremarkable. Funduscopy in right eye showed optic disk hyperemic edema appearance. The left eye was normal

with VA of 6/6. Patient was diagnosed as neuritis optic and treated with corticosteroid intravenously. Second day in the ward patient noticed there was cervical lymphadenitis. Erytrocyte sedimentation rate (ESR)was elevated by 38 mm/h, and mantoux test was positive 22 mm, chest radiography was normal. Patient also had a history of contact with TB patient 5 years ago. Patient was diagnosed to have optic neuritis secondary to TB. She was treated with anti TB drugs, systemic corticosteroid was given after 2 weeks. Second case :a 42 year-old chinese man, presented with sudden visual loss in the right eye. No general complain and systemic disease, VA was 1/60 in the right eye and 6/6 in the left eye. Both segments anterior were normal. Funduscopy in right eye showed an supero-temporal BRVO with flame shape hemorrhages, macular edema and cotton wool spots. The left fundus was normal. Patient was diagnosed to have BRVO in the right eye. Three weeks later optic disk swelling was detected in the left eye, right VA was 1/60 and left eye was 6/60, no intraocular inflammation were found in both eyes. He also had a history of contact with TB patient, elevated of ESR and positively of mantoux test. He also treated with anti TB drugs.

Herpetic Keratitis: Clinical Variations, Management and Treatment

Getry Sukmawati, Indonesian Ocular Infection

Introduction: Herpetic Keratitis (HK) appears with much clinical variation, or combines of them. It is often difficult to determine the diagnosis, because the clinical signs covered by another etiology, and may be for the first time, the diagnosis of HK couldn't perform. The treatments depend on the clinical variations, and will be contra indicated for other manifestation, andto prevent recurrence stage.

Purpose: To report HK cases, with Clinical variations, Management and Treatment

Materials and Method: At Infection Immunology Subdivision, Department of Ophthalmology,DR M Djamil Hospital, we was treated the HK (HSV 1) from January 2012 to October 2013, 44 persons (53 eyes). The HK forms consists of Epithelial 8 (9 eyes), Subepithelial 13 (18 eyes), Stromal 5 (7 eyes), combines three forms 8, combines with Kerato uveitis 5 (6 eyes). The first time diagnoses: Secondary Glaucoma 1, Corneal Ulcer 4. The treatment was Acyclovir ointment, Acyclovir oral 5x 400mg, and Corticosteroid eye drop. Amnion Graft Transplantation 3 cases. At this paper we reported 5 HSV Keratitis cases with different forms.

Result: Improvement visual acuity 32 (60,4%), didn't changes 15 (28,3%), decrease 6 (11,3%) eyes. The average treatment until a best visual acuity: 1-3 months. Supporting laboratories finding: Giemsa staining dominant Mononuclear Cell 20, Giant Cellpositive 9, Papanicolou: virus infectious 6 cases. The all cases, decrease of corneal sensibility. Conclusion:The majority cases were subepithelial 18 (34%), bilateral 9 (17%), improvement visual acuity 32 (60,4%).

Key Word: Herpetic Keratitis, Epithelial, Subepithelial, Stromal, Endotheliitis, Kerato Uveitis

Variations in the Clinical Manifestations-of-Ocular Toxoplasmosis

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Abstract Background; to describe the variation of clinical characteristic of ocular toxoplasmosis Methods ; we reviewed the records of 17 patients in with ocular toxoplasmosis who were examined in the last two years (2011-2013). We performed color fundus photography and serologic test. There were 10 (58,8%) males and 7 (41,2%) females.

Results: Seventeen patients (21 eyes) were included in this study, 7 (41.2%) females and 10(58.8%) males. The age range presentation was 10-74 years . Of the patients 3 (17.6%) had congenital and 14 (82.4%) had acquired toxoplasmosis . Four patients involve both of eyes. At the initial examination, 4

eyes with inactive lesions and 17 eyes with active lesion, two of them had new lesions. Almost of the localisation of the active retinochoroiditis were macula (juxtapapillary retinochoroiditis). In congenital toxoplasmosis, we found large lesions and moderate retinal necrosis. In acquired form, new lesion was found adjacent to the scar in 15 eyes. Macular edema, vasculitis, retinal bleeding, retinal neovascularization were also found in acquired form. One patient with disk edema have recurrences in a short time. There are 14 patients have positive serum anti toxoplasma Ig G antibodies, 13(92.8%) with negative IgM antibodies and only one patient, with oldest age have positive serum IgM antibodies. Two patient were suspected for immunocompromised, but the laboratory examination not supported it.

Conclusion; There are some variation in the clinical manifestation of ocular toxoplasmosis, and its may be related with many factors, including parasitic factors, host factors, patient age, route of infection, parasitic load, and environmental factors.

Keyword; ocular toxoplasmosis, ocular manifestation, diagnosis.

Session 48

Saudi Ophthalmological Society: *Non-Infectious posterior uveitis:* Clinical features, current management, and controversies

Pattern of Uveitis in Behçet's Disease in a Tertiary Center over 25 Years: The KKESH Uveitis Survey Study Group

Hassan AL-Dhibi

Aim: To describe the pattern of uveitis in Behçet's disease(BD)in a tertiary center over a 25-year period.

Methods: Out of 888 consecutive uveitis patients(1455 eyes),132(14.9%)patients(232 eyes)with BD were evaluated retrospectively from1986 through 2011at KKESH in Saudi Arabia.

Results: Panuveitis was the most common form of ocular presentation;affecting 118(89.4%).102(77.3%) patients were men.Mean age at onset of the disease was 36.9±11.4years.Episodes were bilateral in100 patients(75.8 %).Baseline BCVA was 20/125(LogMAR=0.8±0.8)in both eyes.Presenting VA was equal or better than 20/50(LogMAR=0.4)in 87(37.5%)eyes and 20/200(LogMAR=1)or worse in 89(38.4%) of affected eyes.Retinal vasculitis(RV) at presentation was found in 61eyes(26.3%),ischemic retina in 59(25.4%)eyes,and macular edema in 42(18.1%)eyes.Therapeutic management was oral systemic corticosteroids in123(93.2%)patients,intravenous steroid in 35(26.5%),immunosuppressant agent such as cyclosporine in 98(74.2%),azathioprine in 65(49.2%),infliximab in12(9.1%),and methotrexate in 6(4.5%)patients.Local steroid and intravitreal triamcinolone were used in14(10.6%),and 5(3.8%) patients,respectively.Most common complications in the anterior segment included;glaucoma in 44(19%)eyes,cataracts in34(14.7%),and posterior synechiae in14(6%)eyes.The most common posterior segment complication was optic nerve atrophy in19(8.2%)eyes.During the course of the disease,60(25.9%)eyes required surgery of which 43(71.7%)eyes underwent phacoemulsification. BCVA was better than 20/50(LogMAR=0.4)in131(56.5%)of affected eyes,and 20/200(LogMAR=1)or worse in 51(22 %)eyes at the last visit.

Conclusions: BD uveitis affects predominantly young men.Bilateral panuveitis associated with RV was the most common ocular manifestation.More than50% of patients maintained a VA of 20/50 or better at the last follow up, and immunosuppressive therapy with oral systemic corticosteroids was the primary management of these patients.

Sympathetic Ophthalmia

J. Fernando Arevalo

Purpose: Sympathetic ophthalmia (SO) is a bilateral diffuse granulomatous intraocular inflammation that occurs in most cases within days or months after surgery or penetrating trauma to one eye.

Methods: Review.

Results: The incidence of SO ranges from 0.2 to 0.5% after penetrating ocular injuries and 0.01% after intraocular surgery. Vitreoretinal surgery and cyclodestructive procedures are considered risk factors. The time from ocular injury to onset of SO varies greatly, ranging from a few days to decades, with 80% of the cases occurring within 3 months after injury to the exciting eye and 90% within 1 year. The diagnosis is based on clinical findings rather than on serological testing or pathological studies. It presents as a bilateral diffuse uveitis. Patients report an insidious onset of blurry vision, pain, epiphora, and photophobia in the sympathizing, non-injured eye. Classically this is accompanied by conjunctival injection and a granulomatous anterior chamber reaction with mutton-fat keratic precipitates (KPs) on the corneal endothelium. In the posterior segment, the extent of inflammation can vary.

Conclusions: Systemic corticosteroids are the first line therapy for SO. If patients are non-responsive to steroid therapy or have clinically significant side effects, cyclosporine, azathioprine or other immunosuppressive agents can be used for long-term immunomodulatory therapy.

Serpiginous Choroiditis

Vishali Gupta

Serpiginous choroiditis typically is a non-infective autoimmune disease with characteristic clinical features and needs management with systemic corticosteroids and immunosuppressive drugs. However in areas endemic for tuberculosis, it may present as multifocal serpiginous choroidopathy or serpiginous-like choroiditis. There are distinct clinical features that can help in differentiating these two entities. This presentation aims to highlight these differentiating features and management protocol for serpiginous choroiditis in endemic versus non-endemic areas for tuberculosis. Further, the illustrative cases shall be shown to demonstrate the course of disease in either setting.

Birdshot Reitnochoroidopathy

Albert Vitale

Birdshot Retinochoroidopathy (BSRC) is an uncommon but well characterized chronic, bilateral posterior uveitis, which is uniquely associated with a human leukocyte antigen (HLA-A29) phenotype. While autoimmune mechanisms are thought to play an important role in its pathogenesis, its etiology remains unknown. Important questions remain in our understanding of BSRC with respect to its pathogenesis, epidemiology, optimal treatment, and prognosis including the determinants of remission and relapse, as well as the best strategy for monitoring disease activity and progression response to therapy. In addition to and discussion of the clinical features and differential diagnosis of BSRC, a discussion of these gaps in our knowledge of BSRC in the context of our current understanding of this disease will be discussed.

Ocular sarcoidosis

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Purpose: To report on clinical manifestations and treatment outcome of ocular sarcoidosis at the tertiary care center in the Middle East.

Materials and Methods: Chart and literature review.

Results: Ocular sarcoidosis has a variety of presentations and can affect both anterior and posterior segments of the eye as well as the ocular adnexa. The most common manifestations in our cohort were posterior uveitis, vasculitis, optic neuropathy and eyelid infiltration.

Conclusions: Ocular sarcoidosis is a rare condition in the Middle East. Ocular imaging and neuroimaging studies are crucial for diagnosis and follow-up. Immunosuppressive treatment improves natural history of the disease.

Vogt-Koyanagi-Harada Disease

M. Alharby

Purpose: To describe ocular clinical characteristics, complications, surgical outcome and treatment among patients with Vogt- Koyanagi-Harad (VKH) disease in a tertiary center over a 25-year period.

Methods: we retrospectively analyzed 194 patients (382) eyes diagnosed with VKH disease in a tertiary center from January 1986 through December 2011.

Results: VKH disease was diagnosed at a median age of 35.1 - 12.8 years (range from 7 to 68 years), occurred in 135 (69.6%) female, and was bilateral in 188 (96.9%) patients. Mean baseline best-corrected visual acuity (BCVA) was 20/125 (LogMar 0.8 - 0.72) in both eyes. Symptoms duration was short (< 3 months) in 110 (56.7%) patients. A single episode occurred in 87 (44.8%) patients and recurrent episodes in 107 (54%) patients. The most common form of presentation was panuveitis in 151 (77.8%) eyes. Retinal detachment (RD) was present in 164 (42.9%) eyes. An exudative retinal detachment (ERD) was diagnosed in 143 (87.2%) eyes, and tractional retinal detachment (TRD) in 21 (12.8%) cases. Oral prednisone was the first line of treatment in 168 (86.6%) patients. Immunosuppressive treatment with cyclosporine was embloyed in 87 (44.8%) patients, azathioprine in 58 (29.9%), intravenous steroid in 50 (25.8%), mycophenolate mofetil in 18 (9.3%), and methotrexate in 12 (6.2%) patients. During the 25 years of this study, 89 (45.9%) patients (136 eyes) underwent surgery. Visual acuity was better than 20/50 in 240 (62.8%)

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OCT characteristics of patients with uveitis with epiretinal membranes, cystoid macular edema, or both

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Purpose: To investigate whether quantitative and qualitative characteristics on spectral domain optical coherence tomography (SD-OCT) correlates with visual acuity and complications of uveitis.

Methods: We retrospectively selected all patients with uveitis who were followed at the USC Eye Institute from July 2010 to July 2012 and had CME, ERM or both CME and ERM. Patients were grouped into three categories: eyes with CME; eyes with ERM; and eyes with CME and ERM. Retinal changes as defined by SD-OCT and central foveal thickness (CFT) were compared among the groups by ANOVA and Kruskal-Wallis tests. Correlation analysis was used to explore whether there is an association between SD-OCT features, visual acuity, and the above mentioned uveitis complications.

Results: 18 eyes had documentation of CME and ERM. 16 eyes had documentation of ERM only. 4 eyes had documentation of CME only. Visual acuity in patients with ERM was significantly better than in eyes with both ERM and CME ($p=0.02$, one tailed; $p=0.051$, two tailed). Visual acuity and CFT correlated with each other in eyes with both CME and ERM if one outlier was removed ($R^2=0.69$, $p<0.001$). Gender ($p=0.89$), anterior chamber inflammation ($p=0.72$), and anterior vitreous inflammation ($p=0.099$) were not statistically significant between the groups. In eyes with both CME and ERM, CFT was increased in eyes with vision worse than 20/40 and decreased in eyes with vision better than 20/40. Eyes with CME and ERM and vision better than or equal to 20/40 were more likely to be older (mean 66.75) than those with vision worse than 20/40 (mean 58.1) ($p<0.05$).

Conclusions: Simultaneous presence of both CME and ERM trends towards worse VA in patients with uveitis. Eyes with both CME and ERM have worse visual acuity compared with eyes with uveitic ERMs. The presence of both CME and ERM in an eye with uveitis is associated with thickening of fovea and lower visual acuity.

Cellular composition of the inflammatory infiltrate in the iris in uveitis associated with juvenile idiopathic arthritis

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Purpose: To investigate cellular infiltration in iris biopsies in uveitis associated with juvenile idiopathic arthritis (JIA) in comparison with other pediatric uveitis entities and non-inflammatory pediatric controls.

Materials and methods: Iridectomy specimens were obtained during elective trabeculectomy from 31 eye of 25 patients: 12 eyes with JIA-associated uveitis, 13 eyes with other uveitis entities and 6 eyes with open angle non-uveitic juvenile glaucoma. Histopathologic and immunohistochemical analyses were performed. A semi quantitative scoring system was used with a scale ranging from 0 to 4 depending on the intensity of staining of positive cells.

Results: Inflammatory infiltrate was present in 8/12 (67%) specimens with JIA-associated uveitis. The cellular infiltrate in JIA specimens was characterized by the presence of CD138 plasma cells and CD68 histiocytes,while the presence of CD20, CD4 and CD8 cells was variable. In general CD4 T cells seemed to be more prevalent in the iris of JIA and other uveitis entities than CD8 T cells. Presence of plasma cells in the inflammatory infiltrates correlated with ANA positivity in anterior uveitis regardless the diagnosis of JIA. One antinuclear autoantibody (ANA) negative JIA-associated uveitis specimen was characterized by the abundance of giant cells typical for a granulomatous process.

Conclusions: Inflammatory infiltrate in the iris in ANA-positive JIA-associated uveitis is primarily characterized by involvement of plasma cells and histiocytes, CD4 T cells are more prevalent in the iris than CD8 T cells.

Autoimmune uveitis: A pilot study of Vitamin D levels and its supplementation effect

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Purpose: Low serum levels of Vitamin D has been found to be involved in the development of autoimmune diseases. The aim of this study was to determine basal blood levels of 25(OH)vitaminD in patients with autoimmune uveitis and the effect of vitamin D supplementation on the course of the disease.

Methods: Prospective, comparative, longitudinal study with follow-up period of six months. All patients received conventional treatment and were divided in 2 groups: Group A: patients with autoimmune uveitis and daily supplementation with 600IU of vitamin D and group B: patients with autoimmune uveitis, without vitamin D supplementation. Basal serum 25(OH)vitaminD levels were measured using High Resolution Liquid Chromatography. All patients underwent complete ophthalmological evaluation in the first visit and every month until the sixth month.

Results: There were 12 patients in each group. The mean serum vitamin D levels were normal in both groups (Group A: 66.9 nmol/L, Group B: 75.9 nmol/L). Mean age was 48.4 years. 88% were female. The most frequent type of uveitis was bilateral idiopathic non-granulomatous anterior uveitis. After six months of treatment, group A had an improvement of LogMar visual acuity that was statistically significant (p=0.0035), and decrease in anterior chamber cells (p=0.0001) compared with group B.

Conclusions: Our pilot study study suggest that in patients with autoimmune uveitis, vitamin D supplementation, regardless to vitamin D levels, may have a beneficial effect in the course of the disease.

In vivo confocal microscopy of dendritic-like cells in patients with Herpetic Anterior Uveitis versus other subtypes of Anterior Uveitis

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Purpose: To compare densities of dendritic-like cells (DLC) in corneal subepithelial nerve plexus in patients with Herpetic Anterior Uveitis (HAU) with other subtypes of anterior uveitis: Fuchs Uveitis Syndrome (FUS), Juvenile Idiopathic Arthritis (JIA) and HLA-B27 related anterior Uveitis, using *in vivo* confocal microscopy.

Methods: Ninety-two eyes of 50 patients were examined *in vivo* with the combination Heidelberg Retina Tomograph II/III and Rostock Cornea Module (HRT RCM, Heidelberg Engineering). The contralateral unaffected eye was used as control. Morphology of DLCs was defined and evaluated statistically.

Results: The difference between mean DLC density of affected eyes with HAU (102.3 ± 35.4 cells/mm2 n=12), that of FUS patients (43.1 ± 33.3 cells/mm2 n=18) and that of JIA patients (44.4 ± 30.8 cells/mm2 n=10) was significant (p=0.0046). DLC density difference between HAU and HLA-B27 patients (65.2 ± 57.6 cells/mm2 n=10) was not significant (p=0.203). Fellow eye, even though clinically unaffected, showed an inflammatory response with DLCs. In two of the groups we noticed a significant difference between affected and contralateral eye (HAU p=0.0010; FUS p=0.0199) whereas in the other two groups both eyes showed high DLCs numbers and the difference was not significant (JIA p=0.3612; HLA-B27 p=0.2243).

Conclusion: The high density and morphology of corneal DLC in HAU patients assessed by confocal microscopy supports the clinical diagnosis especially when compared to FUS and JIA patients. This study suggests that corneal non-invasive confocal microscopy is capable of supporting a clinical diagnosis in uveitis patients.

Development of sustained release disc of Valganciclovir based on PLGA polymer

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Aim:- Development of a poly(lactic-co-glycolic acid) (PLGA) disc of sustained release valganciclovir or periocular implant and high-throughput fluorescence screening for efficient tuning of valganciclovir .

Methodology: In order to avoid repeated ocular injections with Ganciclovir and eliminate systemic side-effects with Valganciclovir we investigated the tuning of Valganciclovir drug release from thin films of poly(lactic-co-glycolic acid) (PLGA), Polycaprolactone (PCL), or mixtures of both. A high throughput fluorescence-based quantificatoin screening assay for the detection of Valganciclovir release was also evaluated.

Results: Our results show that it is possible to quantitate Valganciclovir down to 100 ng/mL in 96-well polypropylene plates, allowing high-throughput screening of numerous thin film formulations. We also demonstrated that the acidic microenvironment within the polyester matrix protects Valganciclovir from the rapid degradation that occurs at physiological pH by increasing the half-life to 100 days, making it an ideal drug delivery system. Linear release profiles were obtained using the pure polymers for 7 d and 60 d formulations, however gross phase separations of PCL and acid-terminated PLGA prevented tuning of drug delivery within these timeframes.

Conclusions: The establishment of a high-throughput Valganciclovir detection method in a plate reader based upon the drug's intrinsic fluorescence is described in this paper for the first time in world literature. We show that the half-life of Valganciclovir is prolonged inside of 1:1 PLGA to PCL thin films to around 100-days.

Do tuberculin testing results predict 5 year recurrence rates in intermediate uveitis, retinal vasculitis and choroiditis in an TB endemic population ?

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Purpose: To correlate tuberculin testing results with recurrence of uveitis, in intermediate uveitis, retinal vasculitis and choroiditis, over a 5 year period in a TB endemic population.

Materials and Methods: Case records of patients with a diagnosis of intermediate uveitis, retinal vasculitis and choroiditis who had undergone tuberculin testing at the baseline visit and had a minimum follow up of 5 years were included. Demographic information, use of ATT, tuberculin test results and recurrence rates were extracted from the case records.

Results : 189 patients were included, mean age was 32 (SD:11) yrs. 140(74%) were males. Median duration of follow up was 7 years (Range 5-23). 73(39%)patients had intermediate uveitis, 101(53%) retinal vasculitis and 15(8%) choroiditis. 162 (86%) had at least one recurrence with a median of 3 recurrences. 50 (27%) received anti-tuberculosis therapy .107 (57%) were tuberculin test positive (> 10 mm). On univariate analysis use of ATT OR: 0.38(95%CI: 0.17,0.89, p=0.025) and larger size of tuberculin reaction OR: 0.94(95%CI: 0.89,0.99,p=0.033) were protective against recurrences . After adjusting for use of ATT larger size of tuberculin reaction was protective OR: 0.87 (95% CI: 0.77, 97, p=0.014) in only the ATT treated group.

Conclusions: Larger size of tuberculin reaction was predictive of lower recurrence rates in ATT treated patients with intermediate uveitis, retinal vasculitis and choroiditis .

Preliminary Results of a Safety and Pharmacokinetic Study of Gevokizumab in Subjects with Behçet's Disease Uveitis

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Purpose: Gevokizumab is a recombinant humanized monoclonal antibody that binds to human IL-1ß and regulates activation of IL-1 receptors. Gevokizumab is intended to treat various autoinflammatory diseases, such as Behçet's disease uveitis (BDU). The objective of this exploratory study was to evaluate safety and further document the pharmacokinetics of gevokizumab in patients with BDU. Clinical activity was also assessed.

Methods: Patients with a history of BDU with posterior segment involvement experiencing an acute ocular exacerbation or considered at risk of subsequent exacerbation were randomly assigned to one of 3 open-label treatment groups receiving different combinations of 30 or 60 mg gevokizumab, IV or subcutaneously every month, on top of stable standardized immunosuppressive therapy and ≤ 20 mg/day prednisone equivalent.

Results: A total of 21 patients (mean age 34 years; 16 men and 5 women; 17 with acute exacerbation at study entry) were enrolled from 8 centers in Korea, Turkey, and Tunisia. Mean duration of BDU was 4 years. All 15 evaluable patients with an acute exacerbation at entry responded to gevokizumab, most within 1 week. First signs of improvement were observed as early as day 1. Two acute patients were not evaluable due to early withdrawal. Observed concentrations of gevokizumab were consistent with the values expected for these dosing regimens. Most adverse events were related to BDU; no serious adverse events related to gevokizumab were reported.

Conclusions: Gevokizumab was well tolerated. Acute exacerbations were rapidly controlled without the need for high-dose corticosteroids. The Phase III "EYEGUARD™" program with gevokizumab is ongoing.

Retinal vascular changes and immune restoration in a cohort of HIV patients on highly active antiretroviral therapy

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Purpose: To investigate whether retinal microvascular changes are correlated with CD4 /CD8 cell count changes in HIV patients on highly active antiretroviral therapy (HAART).

Methods: Prospective,longitudinal hospital-based study. Fifty HIV/AIDS patients on HAART were followed up over 9 months. Patient demographics and history of HIV infection were collected at baseline. Serologic tests for immune status assessment (CD4/CD8 cell counts), and retinal photography were done at baseline and at 9 months. A semi-automated computer-based programme was used to assess retinal vascular parameters of caliber, tortuosity, branching angle, and fractal dimension. Changes of retinal vascular parameter and CD4 and CD8 cell counts were defined as the difference between baseline and 9 months.

Results: Majority of the patients were Chinese (82%) and males (96%). Mean age was 46 years. 35 of 50 patients had CD4 cell counts of <200 cells/µl at baseline. Duration of HAART ranged from 0 to 11 years. There were significant increments in CD4 cell counts (174.40 vs 227.74; p<0.001) and CD8 cell counts (819.90 vs 1014.1; p=0.012) between baseline and the 9-month visit, respectively. After adjusting for age, sex, ethnicity and years of HAART, each 10 µm reduction in retinal venular caliber at baseline was associated with a 191.08 cells/µl increase in CD8 counts (SE 63.54; p=0.004), but not CD4, during the 9 month period.

Conclusion: Retinal venular narrowing was associated with an increase in CD8 cell counts over time. Improved retinal venular health may be predictive of immune restoration in HIV on HAART for at least 9 months.

Macular involvement in patients with Behçet's uveitis

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Purpose: To assess macular involvement in patients with Behçet's uveitis.

Materials and Methods: The study included 65 patients (120 eyes) with Behçet's uveitis. All patients underwent detailed ophthalmic examination, including dilated biomicroscopic fundus examination, fundus photography, fluorescein angiography, and optical coherence tomography. Follow-up ranged from 6 to 46 months (mean 20 months).

Results: At initial examination, 29 eyes (24.1%) had macular involvement including macular edema (16 eyes, 13.3%), serous retinal detachment (SRD; 5 eyes, 4.1%), active retinitis (3 eyes, 2.5%), macular hole (3 eyes, 2.5%), macular atrophy (2 eyes, 1.6%), macular ischemia (1 eye, 0.8%), epiretinal membrane (1 eye, 0.8%), branch retinal vein occlusion involving the macula (3eyes, 2.5%), and branch retinal artery occlusion involving the macula (2 eyes, 1.6%). During follow-up, 22 eyes (18.3%) developed macular complications including macular edema (10 eyes, 8.3%), SRD (4 eyes, 3.3%), active retinitis (2 eyes, 1.6%), severe macular atrophy (2 eyes, 1.6%), macular ischemia (3 eyes, 2.5%), macular hole (1 eye, 0.8%), epiretinal membrane (2 eyes, 1.6%), and subretinal fibrosis (1 eye, 0.8%). Branch retinal vein occlusion involving the macula developed in two eyes (1.6 %). Final best corrected visual acuity in patients with macular involvement ranged from 20/400 to 20/25 (mean 20/80).

Conclusions: Macular edema and other vision-threatening macular complications are common in Behçet's uveitis. Macular damage is often irreversible, causing permanent visual impairment. Early and appropriate treatment of Behçet's uveitis is mandatory to reduce the risk of visual impairment due to macular involvement.

Treatment Strategies in Primary Vitreoretinal Lymphoma: Toward prevention of subsequent central nervous system lymphoma – A European Study-

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An optimal treatment option for primary vitreoretinal lymphoma (PVRL) without signs of CNS involvement on MRI or in cerebrospinal fluid (CFS) remains unknown and we therefore studied 95 patients in a retrospective study engaging 17 participating centres in Europe. The incidence of central nervous system lymphoma (CNSL) was the primary outcome measure and was evaluated in different treatment groups defined and ascribed as local ocular treatment (radiotherapy and/or intravitreal chemotherapy(n=31; 33%)), extensive treatment (intravenous and/or intrathecal chemotherapy and/or cerebral irradiation(n=21;22%)) or a combination of both treatments (n=23; 24%). Additionally, 20 patients were initially not treated for their PVRL. The median follow-up was 57 months. CNSL developed in 45/95 (47%) of all patients; 17/20 (85%) of the untreated group and 32-43% of patients in all treated groups. Incidence of CNSL development was similar among the three treatment groups (p=0.76). Kaplan-Meier ten-year survival curves with CNS manifestations as outcome showed no significant differences when the three treated groups were compared (p=0.91). The five-year cumulative survival rate was similar in all treatment groups (P=0.10). The median progression-free survival (end point CNSL manifestations) was 47 months (range 7-152) in all treated patients. There was no significant difference in overall and progression-free survival among the three treatment groups (p=0.74 and p=0.15, respectively). Treatment complications developed in 9/40 (23%) patients receiving systemic chemotherapy with acute renal failure being the most common (5/40; 13%). Ocular treatment was employed in 53 patients and complications within the eye(s) occurred in 15 patients (28%). In the present series, although treatment per se reduced the frequency of CNSL, the additional benefit of an extensive treatment approach for PVRL in patients without evidence of CNSL on MRI or CSF examinations could not be shown and was associated with more severe adverse effects.

Role of inmunomodulatory therapy with Interferon β or Glatiramer Acetate on Multiple Sclerosis associated uveitis

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Purpose: To analyze the role of combined immunomodulatory and steroid therapy for the management of multiple sclerosis (MS)-associated uveitis.

Methods: Non-randomized, retrospective case series of 13 patients with proven multiple sclerosis and uveitis (minimum follow-up, 12 months). All patients were given immunomodulating treatment (interferon-β or glatiramer acetate) to control the MS course and corticosteroid therapy (oral, topical, or subtenon injections) to manage the ocular inflammatory episodes. Visual acuity, number of ocular inflamatory episodes, as well as the results of medical treatment were assesed in this study.

Results: Intermediate uveitis was the most common form of uveitis (77%), followed by retinal vasculitis (11%), and anterior or posterior forms (5%). As compared to their pre-treatment status, patients under treatment with interferon-β or glatiramer acetate showed a significant decrease of 0.030 episodes of ocular inflammation per month (P=0.02). Corticosteroid therapy succesfully controled uveitis episodes in 85% of patients; and a second immunosuppressive agent was just needed in two cases resistant to corticosteroid therapy.

Conclusion: Corticosteroid therapy achieved adequate control over most episodes of MS-associated uveitis. Treatment of this condition with interferon-β or glatiramer acetate reduced the number of uveitis episodes.

Choroidal thickening prior to anterior recurrence in patients with Vogt-Koyanagi-Harada disease

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Purpose: Choroidal thickness is shown to increase at the onset of Vogt-Koyanagi-Harada disease (VKH). The recurrence in VKH is mostly manifested as anterior segment inflammation (anterior recurrence); however, indocyanine green angiography reveals hypofluorescent dark dots even in eyes with anterior recurrences, suggesting choroidal involvement. The purpose of this study is to examine the relationship between choroidal thickness and the anterior recurrence in VKH. Subjects and

Methods: Twelve eyes of 6 VKH patients with anterior recurrences were studied. Choroidal thickness was measured using enhanced depth imaging (EDI)-optical coherence tomography (OCT) at the following phases: (A) during the remission phase, (B) one month before the anterior recurrence, (C) at the anterior recurrence, and (D) after prednisolone treatments leading to remission.

Results: Regarding Phase A as baseline (100%), the average changing rates of choroidal thickness were 149.3±42.3%, 157.5±46.5% and 106.0±12.2% for Phases B, C and D, respectively. All the 12 eyes presented increases in thickness at the anterior recurrence (Phase C). Importantly, in 10 eyes (83%), the thickening had already developed one month prior to the recurrence (Phase B). Choroidal thickness after treatment (Phase D) recovered to the level equivalent to that at remission (Phase A).

Conclusions: These findings suggest that choroidal thickening is involved with and frequently followed by the anterior recurrence in VKH. Periodical evaluation of choroidal thickness in VKH eyes may help detect and predict its recurrence.

Multimodal Imaging in Primary Intraocular Lymphoma

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Purpose: Primary intraocular lymphoma (PIOL) is a subtype of primary central nervous system lymphoma frequently masquerading as chronic posterior uveitis. The aim of this study was to describe multimodal imaging features of PIOL.

Materials and Methods: We retrospectively included patients diagnosed with PIOL and examined with near-infrared red reflectance (NIR), fundus autofluorescence (AF), fluorescein angiography (FA), indocyanine green angiography (ICGA) and spectral-domain optical coherence tomography (SD-OCT) by means of confocal scanning laser ophthalmoscope (Spectralis, Heidelberg Engineering, Germany).

Results: Nine patients (13 eyes) diagnosed with PIOL were analyzed. Abnormal NIR reflectance was observed in all the eyes and consisted of hyper-reflective dots or spots (100%, 13/13 eyes) and hypo-reflective areas (24%, 3/13 eyes). AF was abnormal in all the eyes examined. We observed hypo- and hyper-AF lesions in 77% (10/13) and 100% (13/13) of the eyes respectively. FA showed the following abnormalities: mottling clusters 92% (12/13 eyes), punctate window defects 85% (11/13 eyes) and inflammatory signs in 62% (8/13 eyes). ICGA revealed small and large hypocyanescent lesions in 75% (9/12) and 25% (3/12) of the eyes respectively. The abnormalities detected on SD-OCT were: vitreal cells 54% (7/13 eyes), focal hypereflectivity in the outer nuclear layer 69% (9/13 eyes), outer layers granularity 100% (13/13 eyes), subretinal material 69% (9/13 eyes), subretinal fluid 23% (3/13 eyes), small PEDs 69% (9/13 eyes), large PEDs 31% (4/13 eyes).

Conclusions: multimodal imaging in PIOL can lead to earlier diagnosis and treatment.

Sterile Vitritis in the Setting of a Boston Keratoprosthesis

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Purpose: To revisit the clinical paradigm attributed to Keratoprosthesis (KPro) patients presenting with idiopathic culture-negative vitreous inflammation.

Materials and Methods: Between 2000 and 2013, 38 KPro patients at Mass Eye and Ear Infirmary developed vitreous inflammation between 2 days and 8.5 yrs after surgery. 23/38 patients had no obvious cause for vitreous cells. 20 had Type I and 3 had Type II KPros. 6/23 had an auto-immune disease. Prior to the episode, all patients were on a fluoroquinolone, 16/23 on prednisolone acetate, and 9/23 on Vancomycin. On presentation, 17/23 received retrotenons triamcinolone acetate and 11/23 had a vitreous tap. In these 11, vitreous samples were negative except for 1 patient with S. epidermidis.

Results: 7/23 presented with signs and symptoms similar to infectious endophthalmitis but were culture-negative. Vision decline was variable (median loss of 6.5 lines on Snellen chart, range 0-24). Median time to best vision was 13.5 weeks. 5/23 did not recover baseline vision. 11/23 patients had repeat bouts of vitritis. 17/23 later developed RPM (13), glaucoma (8), CME (3), RD (2).

Conclusions: Many cases of vitreous inflammation after KPro have no identifiable trigger. The paradigm for sterile vitritis after KPro implantation includes sudden, painless loss of vision with full recovery of vision upon treatment with periocular steroids. However, this may not apply to all cases. Patients with keratoprostheses can present with vitritis that mimics infectious endophthalmitis, yet be culture negative. Full recovery of baseline visual acuity is not guaranteed. Idiopathic vitritis may be a part of a common pathway of chronic inflammation after KPro.

Correlation between stress, cytokines and uveitic activity

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Purpose: To demonstrate the correlation between emotional stress, pro-inflammatory and anti-inflammatory cytokines in the activity of anterior uveitis.

Material and Methods: 15 active anterior uveitis (AAU) patients and 7 inactive anterior uveitis (IAU). 5 psychiatric stress tests (PST): Q-LES-Q, GHQ28, STAI, SASS and Sheehan were applied in all cases. Tear samples were obtained at the same time. The pro-inflammatory cytokines IL-1b, IL-6, IL-8, TNF-a, and the anti-inflammatory cytokines: IL-10 and IL-12p70 were determined by cytometric bead arrays. Data were analyzed with U Mann-Withney tests and Spearman correlation test.

Results: We found an increased statistical difference ($p<0.05$) in the levels of pro-inflammatory cytokines between AAU (IL-1b:17.0120.49pg/ml, IL-6:29.9264.79pg/ml, IL-8:240.9178.9pg/ml), and IAU (IL-1b:3.878.71pg/ml, IL-6:2.755.49pg/ml, IL-8:121.938.25pg/ml).- There was not statistical difference in levels of TNF-a, IL-10 and IL-12p70 between the two groups. In psychiatric tests there was a statistical difference ($p<0.05$) in all parameters related with stress between AAU and IAU. The correlation between levels of cytokines and the clinical score obtained from PST showed a statistical difference ($p<0.05$).

Conclusions: The increased levels of emotional stress in the AAU patients are correlated with increased levels of pro-inflammatory cytokines. There was no difference between anti-inflammatory cytokines. This study demonstrates the importance of the multidisciplinary approach in patients with AAU at least by ophthalmology and psychiatry specialist.

Long-term effects of tocilizumab therapy for uveitic macular edema

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Purpose: To report the long-term efficacy and safety of tocilizumab (TCZ) treatment for uveitic macular edema (UME) refractory to immunomodulatory therapy.

Methods: Five refractory patients with UME who received TCZ between January 2012 and october 2013 were identified by retrospective chart review. All patients received 8 mg/kg TCZ at 4 week intervals. Main outcome measures: Central foveal thickness (CFT) measured by optical coherence tomography, degree of anterior and posterior chamber inflammation (Standardization of Uveitis Nomenclature Working Group criteria), and visual acuity (logarithm of the minimum angle of resolution [log-MAR]) were recorded during TCZ therapy at months 1, 3, 6, and 12.

Results: Eight eyes from 5 patients (all females) were included. Mean age was 51.4 years. Mean follow-up was 15 months (range, 12-18). Before TCZ, all patients failed conventional IS therapy and had received at least 1 another biologic agent. Uveitis diagnoses were: Birdshot chorioretinopathy (n=3), juvenile idiopathic arthritis-associated-uveitis (n=1), and idiopathic panuveitis (n=1). Mean baseline CFT (95% confidence interval) was 602 ± 236 µm in baseline, 386 ± 113 µm at month 1 (p= 0.006), 323 ± 103 µm at month 3 (p= 0.026), 294.5 ± 94.5 µm at month 6 (p= 0.014), and 266 ± 74.4 at month 12 (p = 0.012) of follow-up. Median log-MAR best-corrected visual acuity (BCVA) improved from 0.66 ± 0.57 in baseline to 0.47 ± 0.62 at month 12 (p = 0.035). TCZ was withdrawn in 2 patients due to sustained remission at 12 months. No serious adverse events were reported.

Conclusions: These data suggest that TCZ is effective for treating UME in otherwise refractory cases.

Fuchs Uveitis Syndrome: clinical findings and virus association

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Introduction: Fuchs Uveitis Syndrome (FUS) is a common intraocular disease, accompanied by insidious visual loss. The most probable causes are rubella virus (RV) and cytomegalovirus (CMV). While a CMV associated anterior uveitis (AU) can be treated with Ganciclovir, there is no causal therapy for the RV associated AU. We investigated if the RV and CMV associated AU can be distinguished by clinical findings and if there is relation to the FUS in our caucasian patients.

Methods: In this retrospective study we analyzed clinical findings of patients seen in our department between 2002 and 2012 with AU and intraocular antibody formation (Goldman/Witmer coefficient >3) against RV or CMV. The records of patients with intraocular RV and CMV infections were quantitatively compared for clinical findings.

Results: We investigated 107 eyes. In 86 eyes we detected intraocular immunoglobulin G (IgG) synthesis against RV and in 21 eyes against CMV. Absence of external inflammatory signs (p=0.0477), diffusely scattered corneal precipitates (p=0.0045), iris atrophy (p=0.1161), heterochromia (p=0.0001), vitreous haze (p=0.0001) and cataract formation (p=0.0303) were found more frequently in the RV associated AU. Extraocular inflammation, few localized corneal precipitates and intraocular pressure above 30 mm Hg (p=0.0001) were more commonly seen in CMV associated AU. The clinical records of both viral associated AU, differed significantly with the exception of iris atrophy (p=0.1161).

Conclusions: Our results indicate that RV and CMV associated AU differ distinctly. The RV associated AU shows clinical findings of a FUS, whereas the clinical findings of the CMV associated AU match better with a Posner-Schlossman syndrome.

Incidence Rate and Risk factors for Contralateral Eye Involvement among Patients with AIDS and Cytomegalovirus Retinitis Treated with Local Therapy

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Purpose: To calculate the incidence rate of contralateral eye involvement among patients with AIDS and unilateral cytomegalovirus retinitis (CMV retinitis), who were treated with repetitive intravitreous ganciclovir injections without concomitant systemic therapy, in the era of highly-active antiretroviral therapy(HAART), and to identify the risk factors for developing contralateral disease.

Materials and Methods: The clinical records of 119 patients with newly-diagnosed, unilateral CMV retinitis seen at a tertiary medical center between January 2004 and December 2011 were included. The main outcome measurement was the occurrence of contralateral eye involvement. The relationship between potential risk factors and the main outcome was analyzed using Kaplan-Meier analyses and Cox proportional hazard models.

Results: Over a mean follow-up period of 1.6 years, the overall incidence rate of contralateral involvement was 0.17/person-year. The cumulative incidence of contralateral involvement at 3 months, 6 months, and 1 year was 16%, 25% and 28%, respectively. The 25th percentile of time to contralateral involvement was 218 days. According to the multivariate analysis, the most recent CD4 T cell count ≤ 11 cells/mm3 was associated with an increased risk of developing contralateral retinitis (hazard ratio [HR] = 2.4, P = 0.035). Receiving HAART during the follow-up period reduced the risk of contralateral retinitis by 74% (HR = 0.26, P = 0.003).

Conclusions: In comparison to the incidence of contralateral involvement among patients treated with local therapy reported in the pre-HAART era, the incidence of this event has been reduced by approximately one half in the HAART era. Receiving HAART during the follow-up period was the strongest protective factor in reducing the risk of contralateral disease. Patients with a low CD4 T cell count at enrollment were at a greater risk for contralateral involvement.

Evaluation of Ocular Disease Activities using Behcet's Disease Ocular Attack Score 24 Before and After Infliximab

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Purpose: To evaluate the disease activity of ocular Behçet's disease (BD) before and after infliximab therapy using Behcet's Disease Ocular Attack Score 24 (BOS24).

Methods: We recently established a novel scoring system of the disease activity of ocular BD, BOS24, that consists of a total of 24 points summing up 6 parameters of ocular inflammatory symptoms, including anterior chamber cells, vitreous opacities, peripheral fundus lesions, posterior pole lesions, subfoveal lesions and optic disc lesions. Using BOS24, the ocular disease activities before and after initiation of infliximab were retrospectively scored in a total of 150 cases of ocular BD.

Results: The numbers of ocular attacks per patient decreased significantly from 3.17±2.00 during the 6 months before starting infliximab (baseline) to 0.53±1.10 and 0.66±1.07 during 1 to 6 months and 7 to 12 months after infliximab ($P<0.001$ vs. baseline, respectively, Wilcoxon's signed rank test). The accumulated BOS24 in 6 months (BOS24-6M) before infliximab therapy were 18.80±17.46, whereas those after infliximab were 2.60±6.73 in 1-6 months and 2.83±5.62 in 7-12 months, respectively ($P<0.0001$ vs. baseline, respectively, Wilcoxon's signed rank test). The average score of BOS24 per ocular attack was 5.77±3.69 in 6 months before infliximab and 4.76±3.38 in 1-6 months and 4.16±2.61 in 7-12 months after infliximab, respectively (($P<0.05$ and <0.001 vs. baseline, respectively, Wilcoxon's signed rank test).

Conclusions: Using BOS24, infliximab therapy was shown to reduce not only frequencies of ocular attacks but also severities of each ocular attack in BD. BOS24 is a promising tool for evaluating ocular BD activities

Clinical Manifestations of Patients with Intraocular Inflammation and Positive QuantiFERON–TB Gold In-Tube Test in a Country Non-endemic for Tuberculosis

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Purpose: To evaluate clinical manifestations of patients with uveitis and scleritis of unknown origin and positive QuantiFERON–TB test Gold In-Tube (quantiferon) in a country not endemic for tuberculosis.

Material and Methods: Multicentre retrospective cohort study. Methods: Retrospective review of the clinical, laboratory and imaging data of 77 patients. Main outcome measures consisted of ocular and systemic features as well as results of laboratory examinations.

Results: Out of all, 60/71 (85%) were living for at least 6 months in tuberculosis-endemic regions. Location of uveitis was variable; posterior uveitis 29/77 (38%) was the most frequent. Two clinical entities were commonly noted, retinal occlusive vasculitis (21/77; 27%) and serpiginoid choroiditis (n=11/77, 14%). Anti-tuberculosis treatment was completed in 32 patients, 29 (91%) of them achieved complete remission. Mean quantiferon level was 7.5 U/ml; 71% had values above 2 U/ml and 41% above 10 U/ml. We observed no associations between Quantiferon levels and clinical and/or imaging features. Previous tuberculosis infection was diagnosed in 5/77 (6.5%) patients, while hilar/mediastinal lymphadenopathy was found in 25/76 (33%) patients. Of these, 12 were consistent with the diagnosis of sarcoidosis, 9 were typical for (prior) tuberculosis and 4 were compatible with both diagnoses.

Conclusions: Ocular features of patients with idiopathic uveitis and positive quantiferon were diverse, but retinal occlusive vasculitis and serpiginoid choroiditis were common. The quantiferon levels were usually highly elevated and 33% of patients exhibited lymphadenopathy, suggesting frequently the diagnosis of sarcoidosis. Ocular inflammation reacted favorably to anti-tuberculosis treatment, although only a small minority had documented (prior) tuberculosis

Incidence of macular epiretinal membrane formation in uveitis

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Purpose: The evaluation of incidence of macular epiretinal membrane (ERM) formation in patients diagnosed with various types of uveitis.

Materials & methods: In a retrospective observational study, the files of patients diagnosed with uveitis during the last 5 years (2009-2013), were reviewed. Patients with incomplete files were not included in the study. Optical coherence tomography (OCT) was performed in cases with funduscopic findings compatible with macular involvement. The association with the type of uveitis was examined.

Results: Out of 314 patients (who satisfied the inclusion criteria) diagnosed with uveitis,143 had findings of suspected macular pathology in fundus examination (45,5%) and OCT was performed. In 50 of them (35%) the presence of ERM was documented during the active phase of disease or during follow-up. Therefore, macular epiretinal membranes were present in 15,9% of cases with uveitis included in the study. Inflammatory macular ERMs were observed both in infectious and non-infectious uveitis, with either anterior or posterior segment involvement of the inflammation.

Conclusions: Macular epiretinal membrane formation is a relatively frequent complication of uveitis. Attention must be paid as it constitutes a significant cause of visual acuity reduction even in cases in which the inflammation is under control.

Vision-related quality of life and depression in herpetic compared to HLA-B27 associated anterior uveitis

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Purpose: To investigate the vision-related quality of life (VR-QOL) and the prevalence of depression in patients with herpetic (infectious) compared to HLA-B27 associated (non-infectious) anterior uveitis (AU).

Materials and Methods: This study was conducted in 2012 at the ophthalmology department of the University Medical Center of Groningen. Thirty-six patients with herpetic AU (herpes simplex virus or varicella zoster virus) and sixty-one patients with HLA-B27 associated AU participated. All patients filled out the National Eye Institute Visual Functioning Questionnaire-25 (NEI VFQ-25), Beck Depression Inventory and social support lists. Analyses were conducted on various patient and ocular characteristics. We compared our NEI VFQ-25 scores with those previously found in the literature.

Results: The NEI VFQ-25 mean overall composite score (OCS) was 88.1±10.6 in the herpetic group and 88.1±9.8 in the HLA-B27 group (p=0.890). Compared with other ocular diseases the OCS in both patient groups is relatively high, but lower than in a normal working population. The mean general health scores were 59.0±19.0 in the herpetic group and 47.5±20.6 in the HLA-B27 group (p=0.007). In the HLA-B27 group, patients with a systemic disease scored significantly lower on VR-QOL and general health. Depression was found in one (2.8%) patient in the herpetic group and in seven (11.4%) patients in the HLA-B27 group (p=0.252).

Conclusions: We concluded that in both groups the VR-QOL is moderately affected. However, in the HLA-B27 group, the presence of a systemic disease affects the VR-QOL and general health considerably, and may be associated with an increased risk of depression.

Efficacy of high dose methotrexate in pediatric auto-immune uveitis.

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Purpose: To analyze the efficacy of high dose (>15mg/m2/week) methotrexate (MTX) in relation to time to disease remission.

Methods: Retrospective analysis of 46 pediatric patients with uveitis with or without underlying systemic disease treated with MTX at the University Medical Center Groningen (The Netherlands) between 1993 and 2013.

Results: Mean age at onset of uveitis was 6.6 years (1.7 – 18). Male:female ratio was 24/22. In 36 patients, bilateral disease was found. Most patients (n=27) had anterior uveitis. JIA was the underlying systemic disease in 23 patients. In 40 patients, MTX use had been sufficiently long for analysis. In 28 of these patients, disease remission was achieved in (median) 26.7 (range 2.5- 146) months. Patients treated with a lower maximum dose of MTX had a longer time to disease remission (median 26.1, range 2.8 – 147.1 months) than patients treated with a higher dose of MTX (median 19.7, range 2.5 – 29.8 months) (p-value 0.02).

Conclusion: In this retrospective study on pediatric auto-immune uveitis, high dose MTX seems to result in a quicker disease remission.

Sensitivity and specificity of the laboratory diagnosis of infectious uveitis; complementarity of PCR and Goldmann-Witmer coefficient

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Purpose: To determine the sensitivity and specificity of PCR and Goldmann-Witmer coefficient (GWC) for the diagnosis of infectious uveitis caused by cytomegalovirus (CMV), herpes simplex virus (HSV), varicella zoster virus (VZV), rubella virus and *Toxoplasma*.

Methods: The laboratory results and clinical data of 441 uveitis patients (451 eyes) from whom first diagnostic paired serum and aqueous humor samples were taken between January 2009 and March 2012, were reviewed. Sensitivity and specificity of the PCR and GWC assay were determined for specific uveitis entities identified based on clinical appearance, test outcome and response to treatment.

Results: Of the 451 AH samples 126 (28%) had a positive result. CMV was positive in 7 (6%) AH samples, HSV in 27 (22%), VZV in 29 (23%), rubella virus in 36 (29%) and *Toxoplasma* in 26 (21%). Overall, PCR and GWC contributed in 42% and 84% to the diagnosis. Sensitivities were 48% for PCR and 55% for GWC in herpetic anterior uveitis, 72% and 82%, respectively, in herpetic post/panuveitis and 60% and 50%, respectively, in CMV retinitis. For rubella virus uveitis sensitivities were 9% for PCR and 90% for GWC, and for *Toxoplasma* chorioretinitis 19% for PCR and 54% for GWC. When combining PCR and GWC sensitivities increased to 75% for herpetic anterior uveitis, 88% for herpetic post/panuveitis, 100% for CMV retinitis, 97% for rubella virus-associated uveitis and 58% for *Toxoplasma* chorioretinitis. Specificities were 100% for all entities and assays.

Conclusions: Combining PCR and GWC increases the sensitivity of intraocular fluid analysis most notably for herpes viruses.

Patterns of primary and recurrent intraocular inflammation in congenital toxoplasmosis

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Objective: To analyze patterns of active intraocular inflammation in a large cohort of children diagnosed with congenital toxoplasmosis(CT) through neonatal screening in southeastern Brazil, followed during the first five years of life.

Methods: Out of 146,307 screened newborns(~95% of livebirths for 6 months), 190 had CT(1 in 770 live born infants) and 178 were examined in the first 2 months of life.

Results: Retinochoroidal(RC) lesions were early detected in 142 newborns(79%), with 85(47.8%) displaying active lesions. Those primary active lesions were of variable number and size, being bilateral in 57 babies(32%) and accompanied by vascular sheathing in 32(18%). Large lesions simulating acute retinal necrosis were observed in 3(3.5%). Keratic precipitates and inflammatory cells in the anterior chamber were invariably absent, but vitreous opacities were present in 16 babies(20%). All were treated during the first year of life. Follow-up disclosed a total of 46 episodes of reactivation of retinochoroiditis in 38/165 children(23%), invariably in the absence of symptoms. These lesions were unilateral in 42 (91.3%), involved the macula in 9 (19.5%) and were satallite to preexistent scars in 34(73.9%). Slit-lamp examination revealed only vitreous but not anterior chamber cells. Reactivations had a peak in the forth year of life, affecting 22/160(13.8%) children.

Conclusion: In young children with CT, primary and recurrent active RC lesions frequently present without significant anterior segment inflammation. Recurrences have a peak in preschool children and in the absence of symptoms. Close follow-up may be warranted to allow prompt treatment of centrally located active lesions.

Optimal Delivery of Sirolimus to the Posterior Segment of the Eye: Preclinical and Early Clinical Findings

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Purpose: To identify properties of an intraocular formulation of sirolimus (DE-109) that would potentially contribute to its efficacy and safety for the treatment of noninfectious uveitis of the posterior segment (NI-PSU).

Materials and Methods: Seven studies—5 in New Zealand White (NZW) rabbits and 2 in humans—were conducted as part of early development of DE-109 to explore its pharmacologic properties and safety.

Results: Once injected, sirolimus formed a highly hydrophobic depot resistant to rapid ocular clearance. In single-dose studies (22, 66 or 220 µg) in NZW rabbits, sirolimus was released from the depot continuously and in a dose-dependent fashion. This resulted in a concentration gradient of vitreous > retina/choroid > sclera > whole blood. At single doses of 22, 66, or 220 µg, drug concentrations ≥10 ng/g were maintained in the retina/choroid for approximately 2 months with a 220 µg dose. In single-dose studies in patients with diabetic macular edema and multiple-dose studies in patients with age-related macular degeneration (up to 352 µg), peak serum concentrations of sirolimus were <2 ng/mL at Day 2, below the daily trough range (5–15 ng/mL) considered necessary for systemic immunosuppression (Mudumba et al, Oct 2012). There was no accumulation of sirolimus in whole blood after repeated bimonthly doses of 352 µg in humans.

Conclusions: Sirolimus, delivered intravitreally, has physicochemical properties that prolong its clearance from the vitreous, with a predictable pharmacokinetic profile and minimal systemic exposure with no tissue accumulation. This makes it a potentially favorable treatment option for inflammation in NI-PSU.

Early surgical debridement in the management of infectious scleritis after pterygium excision

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Purpose: To report outcomes of infectious scleritis after pterygium surgery, managed with early scleral debridement and antibiotic therapies.

Methods: Retrospective chart review of 13 consecutive cases of infectious scleritis after pterygium excision between 1999 and 2009.

Results: Median follow-up: 14 months. Twelve patients underwent prompt surgical debridement after infectious scleritis diagnosis (median: 2.5 days). Debridement was delayed in 1 patient. Median hospital stay was 3 days. Best-corrected visual acuity improved in 10 patients, remained stable in 1 patient, and decreased in 2 patients following treatment. Complications included scleral thinning requiring scleral patch graft, flat anterior chamber, and posterior synechiae. One eye progressed to phthisis bulbi. No patients required enucleation.

Conclusions: In contrast to the generally poor outcomes in the literature, early surgical debridement of pterygium-associated infectious scleritis appears to offer improved prognosis.

Rapid fire presentations abstracts

Outcome of cataract extraction and lens implantation following the bag-in-the-lens technique in uveitis: a retrospective study

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Purpose: To report the outcome of cataract surgery using the bag-in-the-lens technique in patients with uveitis and to evaluate the occurrence and frequency of postoperative complications.

Methods: A retrospective study of medical records of 34 eyes of 24 patients with a history of uveitis who underwent cataract surgery. Best corrected visual acuity (BCVA), level of inflammation, intraocular pressure (IOP) and presence of complications were registered at every visit. We reviewed the outcome of surgery at one month and one year, taking note of every complication in the file.

Results: Mean preoperative BCVA was 0,3 (counting fingers – 0,7) mean postoperative BCVA at one month was 0,7 (0,05 – 1,25) and at one year was 0,9 (0,2 – 1,6). Overall occurrence of complications was at 9,4 % for the visit one month after surgery, consisting of cystoid macular edema, deposits on the surface of the intraocular lens (not obscuring vision), inflammatory relapse and moderate rise in IOP. One year after surgery, overall complication rate was 76 %, mainly consisting of deposits on the surface of the intraocular lens and inflammatory relapse, other complications being more rare.

Conclusion: Cataract surgery using the bag-in-the-lens technique results in good visual recovery, comparable with classic lens-in-the-bag techniques. There is an absence of posterior capsule opacification (PCO), relapse rates are similar and incidence of cystoid macular edema is slightly lower than reports in the literature. Overall, it seems a safe technique to use in eyes suffering from uveitis, providing the benefit that no PCO can be formed.

Utility of high frequency ultrasound biomicroscopy (UBM) in the treatment of HLA B27 associated parsplanitis with complicated cataracts

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Purpose: To study the utility of high resolution ultrasound biomicroscopy in the treatment of HLA B27 associated parspanitis with complicated cataracts.

Methods: Retrospective analysis of 7 eyes (7 patients) with HLA-B27 positive uveitis and complicated cataract.

Results: 7 eyes of 7 patients were studied. All affected patients were males. 2 patients had ankylosing spondylitis and 3 had non specific arthritis. All had complicated cataract with shallow anterior chamber. 3 eyes had peripheral anterior synechae and one had bandshaped keratopathy. Fundus was not visible in all the eyes. Ultrasound B-scan of all the eyes was normal. UBM scan of all the eyes showed bulky lens causing shallow anterior chamber with peripheral anterior synechae. Since all eyes showed parsplana membranes causing traction on the ciliary body on UBM, the decision to do lensectomy and vitrectomy under oral steroid cover was taken. All patients had satisfactory improvement in their post-operative vision with aphakic correction.

Conclusions: Parsplanitis in HLA B27 uveitis is a new entity detected on UBM. Secondary angle closure in these cases may occur due to the forward shift of the bulky lens and iris diaphragm with subsequent formation of peripheral anterior synechae. Routine phacoemulsification with in the bag intraocular lens implantation is difficult in such situations and will not treat the exact pathology at parplana region. Investigation with UBM to localize the pathology and subsequent appropriate treatment will save the vision.

Topical Ganciclovir gel alone or associated with intravitreal Foscarnet for Cytomegalovirus anterior uveitis

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Purpose: To report the effectiveness of topical 0,15% Ganciclovir gel alone (each 2 hours daytime), or associated with a single 2400 µg intravitreal Foscarnet injection, for Cytomegalovirus (CMV) anterior uveitis (UA).

Patients and methods: Prospectively 4 Caucasian Spaniard immunocompetent patients (1 female, median age: 47,7 years) with chronic unilateral UA, and episodes of elevated intraocular pressure while on topical corticosteroids, were treated. In two patients who received a previous 6 month course of Valganciclovir, aqueous humor CMV real time polymerase chain reaction (PCR) (threshold: 57 copies/ml) were: undetectable in two different samples (pre Valganciclovir: 430 copies/ml) and 57 copies /ml (pre: 489 copies/ml) respectively. The PCR results in the other two not previously treated patients were: 6235 (undetectable one montn before) and 2415 copies/ml.

End point: The outcome measure of the efficacy was the interruption of corticosteroid therapy.

Results: Only the PCR negative patient could decrease Prednisolone acetate 1% from two drops daily to one, with no relapse along 6 months of gel therapy. In the other 3 patients, despite of an initial decrease in the anterior chamber inflammation, mainly in the higher genomic DNA load patients, topical corticosteroid therapy could not be interrupted without relapse, either along a 3 months course of Ganciclovir gel, nor after adding a single Foscarnet intravitreal injection.

Conclusion: Frequent topical Ganciclovir gel therapy, seems to be ineffective, alone or associated with a single dose of intravitreal Foscarnet, in our treated patients with CMV UA and their effectiveness were not affected by CMV DNA load.

Effect of tumor necrosis factor-alfa blockers on cytokines secretion in children with noninfectious uveitis

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Purpose. To evaluate the effect of tumor necrosis factor (TNF)-α blockers on cytokines secretion in children with noninfectious uveitis.

Methods. Cytokines levels were measured by enzyme-linked immunosorbent assay or flow cytometry in serum (192 samples) and tears (171 samples from affected eyes) out of 73 children with uveitis (71 associated with juvenile idiopathic arthritis, 2 – with Behcets disease) before and during therapy with Infliximab or Adalimumab.

Results. During anti-TNF treatment TNF-α was revealed more often in patients who achieved remission than with persistent inflammation (46.9% and 77.4% in serum; 83.3% and 58.1% in tears respectively, $p<0.05$). Decrease in Interleukin (IL)-8 levels in both fluids was detected, more prominent in children with remission of uveitis. Tears IL-8 levels more than 400 pg/ml were revealed more often in active uveitis than in remission (70.6% and 50%, $p<0.05$). Simultaneously increase in frequency of detection and levels of IL-10 and less prominent IL-4; slightly decrease of IL-1 and IL-2 were also found. IL-6 in serum and Interferon (IFN)-γ in tears were revealed more often in patients with successful than with ineffective treatment (IL-6 91.7% and 70.6%; IFN-γ 76.5% and 56.3% respectively, $p<0.05$).

Conclusions. Low TNF-α serum and tears levels during anti-TNF treatment are more favorable for remission of uveitis than full suppression of the cytokine secretion therefore TNF-α measurement is indicated. Despite selective target, TNF-α blockers influence systemic and local cytokines secretion mostly in direction to decrease proinflammatory and increase antiinflammatory mediators. Different degrees of various cytokines changes were detected. Il-8 and Il-10 may serve as markers of response of uveitis to anti-TNF treatment.

ROP16 is a pathogenic marker in human ocular toxoplasmosis

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Background: ROP16 is a protein kinase of Toxoplasma gondii identified in the mouse model of infection as a virulent marker, but it is unknown if this finding is relevant in human toxoplasmosis. Genetic analysis of the putative virulent Toxoplasma ROP16 locus and prevalence analysis of antibodies against a peptide from the ROP16 virulent protein was performed in human clinical samples in Colombia.

Methods: We obtained Toxoplasma ROP16 locus DNA sequence in samples from 12 patients with ocular toxoplasmosis, 1 from a patient with congenital toxoplasmosis, 22 from soldiers operating in jungle, 2 from urban soldiers and 10 from meat for human consumption. A specific ELISA for antibodies against the ROP16 virulent peptide was performed in 26 serums from patients with ocular toxoplasmosis and in 60 serums from patients with a chronic asymptomatic infection Results: We found a striking nucleotide sequence divergence of the ROP16 sequences. 10 of 12 (83.3%) sequences from patients with ocular toxoplasmosis belonged to the group of ROP16 sequences of virulent strains whereas 7 of 7 (100%) ROP16 sequences from meat were clustered with non-virulent strains. The ELISA for antibodies against ROP16 virulent peptide was positive in 71% (15/26) of patients with ocular toxoplasmosis and in 10% (6/60) of patients without ocular toxoplasmosis.

Conclusions: Antibodies against virulent ROP16 peptide are present in the great majority of Colombian patients with ocular toxoplasmosis.

Clinical outcome of viral and non-viral hypertensive uveitis

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Purpose: To review the clinical outcome of patients with hypertensive uveitis.

Methods: Retrospective review of uveitis with complete follow-up since first attack with at least one episode of intraocular pressure (IOP) > 25 mmHg, and 6 months follow-up. Recorded data: uveitis type, etiology (grouped in viral (VU) and non-viral uveitis (NVU), IOP at presentation of uveitis, first elevated IOP, maximal IOP, medical and/or surgical treatment.

Results: 68 patients were included: 28 VU (18 PCR : Fuchs: 3/5, herpes: 9/17, CMV: 6/6) and 40 NVU. Patients with VU were older (50.5y/39.8y, p=0.01), had significant higher mean baseline IOP (36.33/30.68 mmHg, p=0,009), maximal mean IOP (and 40.07/34.25 mm Hg, p=0.0128) and unilateral disease 100%/72.5% p=0.007) than NVU. Final IOP could successfully be lowered under 25 mmHg in VU (95%) and non-viral uveitis (82.14%, (p=0.568). Secondary glaucoma (based on glaucomatous aspect of visual field or/and OCT) occurred in VU (17.86%) and NVU (32.5 %) (p=0,286).

Conclusion: Patients with viral hypertensive uveitis were older, had higher first and maximal IOP and more frequent unilateral disease than non-viral hypertensive uveitis. Final IOP could be lowered in most patients in both groups, but glaucoma developed in a significant number of patients in both groups.-

The Impact of Retinal Vasculitis on Visual Acuity in Ocular BehçetDisease as Determined by

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Purpose: To identify fluorescein angiography (FA) findings significantly associated with visual acuity (VA) in Behçet retinal vasculitis.

Methods: We reviewed medical records of 68 patients who have Behçet retinal vasculitis.

Results: There was posterior pole involvement of retinal vasculitis in 63 eyes (73%) and isolated peripheral involvement in 23 eyes (27%). The mean initial VA of eyes with posterior pole-involved vasculitis was significantly worse than that of those with peripheral vasculitis (LogMAR VA: 0.55±0.57 vs. 0.08±0.15; p<0.0001). Subgroup analysis revealed a more severe and diffuse pattern of vascular leakage in posterior pole-involved vasculitis compared to peripheral vasculitis (p<0.0001) but no significant difference in optic disc hyperfluorescenc (p=0.11). In multivariable regression analysis, retinal vascular leakage (β=0.35; 95% confidence interval [CI], 0.16 to 0.53; p<0.0001), optic disc hyperfluorescence(β =0.15;95% CI, 0.01 to 0.28, p=0.03), and macular leakage(β =0.11; 95% CI, 0.004 to 0.22, p=0.05) were identified as angiographic findings significantly associated with worse initial VA (adjusted *R2*=0.41).

Conclusions: Posterior pole involvement of retinal vasculitis is associated with more severe inflammatory activity of the retinal vessels andhas a significant impact on visual prognosis. During the follow up, the change of leakage showed a marginally significant correlation with change of VA between the initial and at 2 year time point within a 6 month window in posterior pole-involved vasculitis(correlation coefficient τ = 0.199, p=0.092), but no significant correlation in peripheral vasculitis(p=0.75).

Late posterior segment relapses in a series of Vogt-Koyanagi-Harada disease

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Purpose: To determine the time course and clinical characteristics of exudative retinal detachment (ERD) in eyes with late relapsing episodes of Vogt-Koyanagi-Harada (VKH) disease.

Material and Methods: We reviewed the data on 19 subjects who presented a posterior segment reactivation among 45 subjects diagnosed with VKH disease. The main outcome measures were: demographics (race, gender), clinical course (nature of the relapse), treatment (both initial and at the time of relapse) and findings on spectral-domain OCT (SD-OCT) imaging in eyes with VKH and posterior segment relapsing disease.

Results: Relapses of ERD were noted within 10 months after presentation in most of the subjects (84%, 16/19) who experienced a posterior reactivation. A subset of four subjects developed delayed (>12 months after onset) relapses of ERDs at a median of 19 months (range 16 to 25 months). In the 4 subjects with recurrent posterior segment disease, focal or multifocal localized areas of subfoveal retinal detachment (N=4) were seen, together with anterior uveitis (N=2). Treatment at onset of VKH with intravenous corticosteroid pulse therapy followed by oral corticosteroids for at least 6 months (N=3) did not prevent late posterior segment relapses. For the fours subjects with delayed relapses, the use of an additional immunosuppressive agent was introduced (N=4) either because response to corticosteroids was insufficient or as steroid sparing (ie to lower dose to avoid toxicity) and no further relapse was seen (N=2) at 6 and 48 months of follow up.

Conclusions: While posterior relapses are not rare in the first year after presentation, ophthalmologists should also be aware that late ERDs do occur. Late posterior relapses showed the same features that at presentation, albeit less pronounced. Prolonged high dose corticosteroids treatment (>3 months) at presentation of disease or the need of corticosteroid sparing agents may act as markers for late relapses.

Intracameral Levofloxacin for Intra Operative Prophylaxis of Acute Endophthalmitis Post Cataract Surgery: Safety Profile

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Purpose: To evaluate the safety of intracameral levofloxacin for intra-operative prophylaxis in cataract surgery.

Materials and Methods:This study is a randomized controlled trial. In December 2009 until May 2010, 62 patients underwent phacoemulsification and IOL implantation were randomized to received intracameral levofloxacin or only BSS at the end of the surgery. All surgery was uneventful and was done by one surgeon. Evaluation of endothelial density, corneal pachymetry and flare meter value were done before surgery, 7 days and 28 days after surgery. Any endopthalmitis was noted.

Results: Mean age in both groups were comparable (60.1 vs 62.1 years old). There was no different (p=0.855) in endothelial density pre operation, 7 days and 28 days after surgery in levofloxacin group were 2445.3, 2124.6 and 2270.5 respectively. In BSS group there werer 2387.4, 2080.3 and 2290.1 respectively. There was no different (p=0.745) in corneal pachymetry pre operation, 7 days and 28 days after surgery in levofloxacin group were 535.7, 528.8 and 537.0 respectively. In BSS group there werer 525.9, 517.5 and 536.3 respectively. There was no different (p=0.278) in flare meter pre operation, 7 days and 28 days after surgery in levofloxacin group were 3.8, 7.0 and 3.4 respectively. In BSS group there werer 3.4, 11.38 and 3.1 respectively. There were no endopthalmitis events in both groups.

Conclusion: Intracameral levofloxacin prophylaxis given intra-operatively is safe based on endothelial cell count, pachymetry and flare meter.

Long term evaluation of non-infectious uvetic macular edema treated with Ozurdex

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Purpose: To evaluate the long-term visual prognosis and complications of patients who received intravitreal Ozurdex injections for the treatment of non-infectious uveitic macular edema (UME).

Methods: A retrospective study of 32 patients with UME refractory to systemic and intraocular therapies were treated with Ozurdex. Vitrectomized (PPV) versus non vitrectomized (non-PPV) patients were analyzed. The main variables analyzed were the reduction in central retinal thickness (CRT), best corrected visual acuity (BCVA) and intraocular pressure (IOP). Activity status of uveitis and side effects were also assessed. Statistical analysis was adjusted by the presence of vitrectomy, reinjection of Ozurdex during follow-up and number of treatments for high IOP.

Results: The median age of patients was 46,7 years (range, 18–61). The mean follow-up time was 38,5 months. The CRT (95% confidence interval) was 571.9 microns (476.1–667.9) in non-PPV patients and 509,63 (428,3; 590,9) in PPV patients at baseline, its maximum decrease was at first month, 320,53 (266,09; 374,9) and 278,74 (224,6; 332,8) respectively which was maintained all over the follow-up. LogMar BCVA improved from 0,912 (0,685; 1,139) at baseline to 0,651 (0,428; 0,873) at 3 months in non-PPV patients and from 0,875 (0,682; 1,067) to 0,522 (0,35; 0,694) in PPV patients. IOP showed statistically differences of 3,82 mmHg (p=0,012) between non-PPV and PPV patients from third to twelfth month 4,5 mmHg (p=0,001) In 22 eyes (50%), reinjection of the implant was performed at a mean of 4.8 months. Ocular hypertension (50%), hypotony (7.1%), anterior chamber displacement of the implant (4.7%), cataract surgery (7,1%) and glaucoma, which required filtration surgery (4.7%), were the most common adverse events.

Conclusions: Our results indicate that treatment with Ozurdex for UME has favorable long-term safety profile. IOP shows statistically differences between PPV and non-PPV patients.

Increased serum IL-23 and IL-21 levels in patients with Behcet disease associated Uveitis

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Purpose: To compare the serum interleukin (IL) levels between the patients with extraocular manifestations of Behcet disease and Behcet disease-associated uveitis.

Material-Methods: Prospective study involving 12 patients with extraocular manifestations of Behcet disease and 16 patients with Behcet disease-associated uveitis. Inclusion criteria for all patients consist of initial diagnosis at the time of examination,positive HLAB51 tissue typing and without receiving any immunosuppressive or immunomodulatory therapy for at least 6 months. The serum levels of IL-17, 21, 23, 6 and 10 were analyzed with enzyme linked immunosorbent assay. Statistical analysis were performed with SPSS 15.0. 2-sample t-test.

Results:Serum IL-23 and IL-21 levels of patients with Behcet disease-associated uveitis were significantly elevated as compared to the patients with extraocular manifestations of Behcet disease. ($p = 0.001 < 0.05$, $p = 0.001 < 0.05$ respectively)

Conclusions: IL-23 and IL-21 may play a critical role in the pathogenesis of Behcet disease- asociated uveitis. However, IL-6 is significant for patients with extraocular manifestations of Behcet disease.

Low Dose Dasatinib Efficiently Blocks PDGF-induced Orbital Fibroblast Activation: a Potential Novel Therapeutic Agent in Fibrotic Disease?

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Purpose: Graves' ophthalmopathy (GO) comprises inflammation, expansion and fibrosis of orbital tissue. Excessive orbital fibroblast activity, driven by locally produced platelet-derived growth factor (PDGF), plays a central role in GO. Current treatment options are limited. Tyrosine kinase inhibitors (TKI) imatinib mesylate and nilotinib have been shown to block PDGF receptor in in vitro and animal models of fibrosis. Due to their highly variability in clinical outcome and adverse effects, dasatinib, a new generation TKI with higher pIC50, is considered as an option. The aim of this study is to compare prophylactic and therapeutic effect of imatinib mesylate and dasatinib on PDFG-BB-induced orbital fibroblast activation.

Materials and methods: Orbital fibroblasts from four GO patients and five healthy controls were used. Prophylactic studies were performed by overnight incubation with TKI before followed by 24h stimulation with PDGF-BB (50 ng/ml). For therapeutic studies, TKI and PDGF-BB were co-added. Proliferation was assessed by colorimetric assay. Hyaluronan and cytokine production were measured by ELISA.

Results: Dasatinib dose-dependently inhibited PDGF-BB-induced orbital fibroblast proliferation, hyaluronan, and cytokine (CCL2, IL-6, IL-8) production far more efficient than imatinib mesylate in the prophylactic setting. Under therapeutic conditions, the lowest concentration dasatinib tested (0.04 µg/ml) significantly inhibited as it did prophylactically, with the exception of IL-8 production that was only significantly reduced at 2.5 µg/ml. Imatinib mesylate (0.04 µg/ml) was unable to block fibroblast activation in the therapeutic setting.

Conclusions: Our study indicates that dasatinib is a potent inhibitor of the PDGF-signaling cascade in orbital fibroblasts and might be a promising therapeutic agent in GO.

The role of thrombin in proliferative vitreoretinopathy

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Purpose: Proliferative vitreoretinopathy (PVR) is a difficult to treat inflammatory and fibrotic disorder complicating retinal detachment. Understanding of the activating processes involved in PVR is still incomplete. We believe that coagulation proteins may be involved. In recently published studies we demonstrated that factor Xa and, more potently, thrombin induce the production of a broad panel of pro-inflammatory cytokines and growth factors by RPE, resulting in the differentiation of RPE into a mesenchymal cell type via autocrine PDGF-R signaling. In our current study we demonstrate that thrombin activity is significantly higher in the vitreous of patients with established PVR compared to control groups. We also show that this vitreous contributes to PVR-associated changes in RPE cell behavior.

Materials and Methods: Thrombin activity in vitreous was determined with a thrombin-specific substrate in absence/presence of hirudin. RPE cells were cultured with vitreous or thrombin and changes in cytokine and growth factor expression levels were determined by RQ-PCR. Proliferation of RPE was determined with the MTT assay.

Results: Thrombin activity was significantly ($P < 0.05$) higher in vitreous of patients with established PVR compared to all control groups. RPE cells cultured with vitreous of PVR patients showed significantly ($P < 0.05$) higher mRNA expression levels of cytokines and growth factors like IL6, IL8, PDGFA and PDGFB, compared to control groups. All increased expression levels of cytokines and growth factors were significantly ($P < 0.05$) inhibited by hirudin. Vitreous did not affect RPE proliferation.

Conclusion: These results clearly demonstrate that thrombin activity is elevated in vitreous of PVR patients and that this vitreous contributes to PVR-associated changes in RPE cell behaviour. These data demonstrate that thrombin may therefore be an interesting therapeutic target in the prevention of PVR development.

Primary retinal vasculitis. does it exist

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Purpose: primary retinal vasculitis (PRV), defined as a retinal vasculitis without systemic disease associations or infection, is an ophthalmic disease entity since 1880 (Eales). As some of the systemic vasculitis entities can be life threatening, it is questionable if PRV can be accepted as a diagnosis, or continued reinvestigation is warranted.

Material and methods: case series of 179 uveitis patients with a follow-up of > 1 year, visiting a tertiary uveitis clinic during 2010, in whom vasculitis was the dominant feature of their uveitis. Files were analysed for date and diagnosis of (non)infectious or systemic diseases associated with retinal vasculitis.

Results: After initial routine screening, 72 patients had been labeled PRV. By 2010, mean follow-up was 7.3 years (range 1-27). Within 5 year of follow-up, 54% of the patients were diagnosed with a specific disease known to be associated with retinal vasculitis. In patients with longer follow-up, an additional 23% of patients got a specific label by year10, another 14% of patients got a specific diagnosis after 10 years of follow-up. At least 91% of PRV will be relabeled during their follow-up.

Conclusion: Most or perhaps all patients initially labeled as PRV will get an systemic (non)infectious inflammatory diagnosis, known to be linked with retinal vasculitis. Of course, patients could have multiple autoimmune diseases and can get infected by new agents during their follow-up. Nevertheless, repeated rescreening seems to be indicated in patients with retinal vasculitis, to rule out severe systemic diseases. The term retinal vasculitis ´of unknown origin´ is certainly not as eloquent but in our opinion more transparant than primary retinal vasculitis.

Fulminant bilateral neuroretinopathy of unknown etiology in a young immunocompetent patient

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Introduction: Acute bilateral blindness is a dramatic condition that requires an extensive diagnostic evaluation and emergent treatment.

Case Report: A 25-year-old Caucasian male, immunocompetent, presented with acute onset unilateral visual loss, rapidly progressive, accompanied by pain with ocular movements. Second eye presented with similar evolution a few days later; patient went blind (no light perception) despite desperate therapeutic mesures that included broad-spectrum antibottics, antivirals and immunossupressant drugs. An extensive evaluation for infectious, inflammatory, toxic and hipercoagulable etiologies was negative. Fundoscopy showed generalized atrophy of optic disc and retina. SD OCT, FAF and electrophysiologic testing confirmed destuction of the outer retina and bilateral optic atrophy. Brain MRI was unremarkable. Three months post neuroretinal involvement patient was admitted with choreoatetotic movements, pyramidal signs and EEG changes. Etiology remains unclear.

Conclusion: We present a dramatic case of fulminant bilateral blindness of unknown etiology. Despite the mutidisciplinary evaluation – ophthalmology, neurology, internal medicina, infeccious diseases – and therapeutic resources available, final outcome could not be prevented.

Outcome of patients with non-infectious retinal vasculitis – long term follow-up

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Purpose: to report the clinical features, etiology and the long-term outcomes of patients with non-infectious retinal vasculitis(RV).

Materials and Methods: We reviewed medical records of 45 patients with RV (90 affected eyes) diagnosed with retinal vasculitis with follow up longer then 6 months.Patients in which infectious etiology such as TB was found were excluded. Clinical presentations, Imaging, associated systemic diseases, and treatment were recorded

Results: 51% of the patients were male.The mean age was 39.2 years .The mean follow-up was 50.3 months (range 6-210). 22% of patients had a known systemic disease on presentation the most common was bechet's disease(BD). 40% were diagnosed with a systemic disease during work-up,the most common was also BD. 5% were diagnosed with an ocular disease(BSCR) and 33% were defined as idiopathic. 54% of eyes had an initial visual acuity of 6/12 or better.The most common clinical findings were vitritis in 52% of patients followed by vascular sheathing. The retinal veins were involved in 44.6% of the eyes and the arteries in 12.1%. 21.6% of eyes had both arteries and veins involved.96% of patients were treated with systemic therapy. 87% were treated with systemic steroids and 73% were treated with at least one type of immunosuppressive medication. The most common agent used was cyclosporine A in 45% of the patients.At the end of follow up 39.5% of patients did not require systemic therapy.65% of patients who initially received systemic steroids were able to stop the drug ($P<0.0001$). 50% of patients were still on systemic immunosuppressive therapyAt the end of follow-up 35% of eyes improved in 3 or more lines in BCVA and 49% of eyes had stable visual acuity.

Conclusion: A newly diagnosed systemic disease was found in 40% of patients. Under proper management in a uveitis clinic setting long term outcomes were good with the majority of patients keeping stable or improved vision.

Identification of vitreous biomarkers for postoperative endophthalmitis

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Purpose: To identify biomarkers for postoperative endophthalmitis (POE).

Material and Methods: Vitreous fluid from 45 patients with POE, 30 with macula hole, 30 with pucker and 28 with infectious uveitis were investigated by Surface-enhanced laser desorption-ionisation time-of-flight (Seldi-tof) to generate protein profiles. Peptide clusters were identified using the Biomarker Analysis Cluster Wizard software and statistically evaluated by Expression Difference Mapping software. Relevant proteins were separated by SDS-PAGE and cut out of the gel. The isolated peptides were identified by liquid chromatography tandem mass spectrometry. The expression of putative POE biomarkers was confirmed by ELISA assay. The data were correlated to vitreous culture results.

Results: Seldi-tof analysis revealed significant upregulation of a cluster of three peptides with a mass-to-charge ration of 3377, 3448 and 3492 in 43 of 45 POE samples ($P < .000$; Kruskall-Wallis). The two vitreous samples lacking the peptides were culture negative. The peptides were not detected or with a 200 to 300 times lower intensity in the control groups. Mass spectrometry identified the cluster as human alpha-defensins or human neutrophil peptides 1 to 3 (HNP1-3). Subsequent ELISA analysis of all POE vitreous samples and 10 samples each of the control groups also showed a significant increase in HNP1-3 expression in the POE versus each control group ($P < .001$; Kruskall-Wallis with correction for multiple testing).

Conclusions: Intravitreous HNP1-3 may represent a biomarker for postoperative endophthalmitis, however, semi-prospective validation experiments are warranted. Intravitreous HNP1-3 analysis may eventually be used to differentiate between sterile and bacterial endophthalmitis.-

Beneficial effect of immunosuppressive therapy in patients with APMPPE, ampiginous and serpiginous choroiditis

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Purpose: To investigate the effect of immunosuppressive therapy in patients diagnosed with acute posterior multifocal placoid pigment epitheliopathy (APMPPE), ampiginous and/or serpiginous choroiditis.

Materials and Methods: Retrospective review of 46 eyes in 26 patients. Recorded data were visual acuity (VA, in LogMAR) at baseline and final follow-up, diagnosis, therapy strategy, recurrences, discontinuation of treatment. For statistical analysis the worst eye at onset was used.

Results: Median age was 25.4 years (range 18.2 - 75.0). Median follow-up was 3.3 years (range 0.26 - 26.6). APMPPE was diagnosed in 12, ampiginous in 8 and serpiginous in 6 patients; 54% was female, and 77% had bilateral involvement. Treatment was started in 19 patients (73%), of which 16% received steroids only, 74% received cyclosporine, 10% azathioprine. In 21% of eyes monotherapy was given, 58% followed a step-down strategy and 21% a step-up strategy. In 10 out of 26 patients one or more recurrences were seen. At final follow-up only 4 patients had ongoing treatment. Median (range) VA at baseline was 0.40 (0 – 2.0) and at final follow-up 0.12 (-0.1 – 1.3). A significant VA improvement was seen in the treated group ($p = 0.02$) but not in the untreated group ($p = 0.116$) and in the patients with step-down strategy ($p = 0.021$) compared to the other strategies.

Conclusions: APMPPE, ampiginous and serpiginous choroiditis can be considered as diagnostic entities within one clinical spectrum, with the mildest course in APMPPE. Patients receiving immunosuppressive therapy showed more VA improvement than observed cases. A step-down strategy seems more beneficial than monotherapy.

Poster presentations

Assessment of the Effects of Topical Cyclosporine on Conjunctival Goblet Cell Density in Severe Dry Eye Disease Induced by Mustard Gas

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Purpose: To evaluate the treatment effectiveness of topical cyclosporine A 0.05% on conjunctival goblet cell density in severe dry eye patients exposed to mustard gas.

Materials & Methods: In this prospective clinical study 19 eyes of 19 patients exposed to mustard gas with dry eye unresponsive to artificial tears therapy enrolled the study. Before and after treatment with topical cyclosporine A 0.05% twice daily for 3 months, they were evaluated using the OSDI for improvement in symptoms of the disease as well as Tear Breakup Time, Schirmer testing and superior bulbar conjuctival goblet cell density measurement for improvement in signs.

Results: The mean OSDI score before treatment was 42.8±6.1. -After 3 month treatment with topical cyclosporine it reduced to 36.4±5.2 ($p<0.001$). The mean TBUT at baseline was 2.5±1.3 seconds which increased to 4.9±2.1 seconds ($p<0.001$). Value of mean Schirmer test 1 rose from 4.2±1.2 to 5.8±1.6 after treatment ($p<0.001$). Mean goblet cell density of all cases was 23.3±17.1 at baseline. It increased to 47.7±16.1 at the end of the study ($p<0.001$).

Conclusions: Treatment with topical cyclosporine A 0.05% increases goblet cell density in the bulbar conjunctiva in severe dry eye patients exposed to mustard gas and improves the symptoms of the disease as well.

Disaster in cosmetic surgery; Inadvertent Formalin Injection during Blepharoplasty

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Abstract: We report a case where Formalin was accidentally injected into the eyelids of a 71 year old woman undergoing blepharoplasty, causing full thickness necrosis of both upper lids and ocular complications that required multiple reconstructive surgical procedures.

Introduction: Accidental drug injection in medicine is not a common incident; however the complications can be disastrous and tragic. Formalin, a 35% to 40% aqueous solution of formaldehyde, is routinely used as a tissue fixative in operation rooms when sending tissues for pathology investigations. Upon contact with tissues, formalin binds with proteins and denatures them while also causing DNA cleavage and RNA structure inhibition.(1) In some operating rooms, this colorless fluid is kept in empty vials of lidocaine that are labeled as formalin. There are several previous reports of accidental formalin injection in blepharoplasty, cataract and maxillofacial surgery. (2-6) This report describes another case of inadvertent formalin injection in blepharoplasty surgery which led to severe ocular complications.

Case report: A patient was referred to Farabi Eye Hospital, Tehran, Iran with a history of upper eyelid blepharoplasty 40 days earlier. She was a 71 year old woman with full thickness necrosis of both upper lids. At her first operation, the surgeon was mistakenly handed a syringe filled with formalin instead of lidocaine which was then injected subcutaneously into both upper lids. The injection was severely painful and the patient had severe pain during the procedure, however the surgeon did not understand the cause of ineffective injection of presumed anesthetic injection during the surgery. At her presentation to us, the visual acuity was hand motion in the right eye and light perception in the left eye. The upper eyelids of both eyes were severely edematous with a thick membranous necrotic tissue (Figure 1). Both globes were frozen which presumably had resulted from extra-ocular muscle and nerve involvement (Figure 2) . On slit lamp examination, there was significant corneal exposure due to inadequate eyelid closure, corneal epithelial defects and severe corneal edema with bilateral anterior chamber reaction and hypopyon. The anterior segment displayed signs of severe toxicity and ischemia including corneal anesthesia, fixed and dilated pupil in the right eye (minimally reactive in the left eye) and bilateral cataracts. Fundus details were poorly visible and there was bilateral papillitis. For evaluation of optic nerves, visually-evoked potential (VEP) was performed and showed severe delay bilaterally. In order to control corneal exposure, bilateral blepharorrhaphy was performed through the eyebrow and upper and lower lid margins so that the sutures could be opened to evaluate the cornea as needed (Figure 3). Systemic methylprednisolone 500 mg per day was prescribed for 3 days and then changed to oral prednisolone 50 mg/day to help reduce tissue edema in the eyelids and around the optic nerve. Ciprofloxacin tablets 500 mg two times a day and chloramphenicol eye drops were prescribed prophylactically along with artificial tears to control the dry eye. After 5 days, betamethasone eye drops were added. After 14 days, the corneal epithelial defect was healed and by one month, corneal sensation had improved and the patient's vision improved to count fingers at 4 meters in the right eye and 2 meters in the left. However, eyelid problems were too extensive to allow any kind of surgery at that time. During this first 2-month, both eyes were closed with blepharorrhaphy and opened every 3-4 days to evaluate the cornea and vision. After 2 months, the necrotic eyelid tissue which had shrunk was removed under local anesthesia. The bed of the tissue was full of purulent necrotic material all the way through to the bone with some necrotic periosteum along the superior orbital rim. On the opposite side, necrotic material over the eyelid extended all the way to the conj

Case report - A 20-year-old woman with neuroretinitis, chorioretinitis and Kyrieleis arteriolitis

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Introduction: We report an atypical case of ocular toxoplasmosis, which is the most common of infectious posterior uveitis.

Case report: A 20-year-old woman presented with sudden onset of decreased vision in her right eye. She had 1 week of redness, photophobia, pain, and decreased vision. She reported no underlying disease. She lived with two cats. On examination, her VA was 20/160, 20/25. Her IOP was 23, 15 mmHg. On her right eye,she had 1 cell and flare,white stellate keratic precipitates and trace anterior vitreal cells. She had blurred temporal margin of right optic disc and macular star. There was focal chorioretinitis along inferotemporal branch and segmental arterial sheathing (Kyrieleis arteriolitis) without scar. Her left eye was normal. FFA showed hypofluorescence in early phase from blockage of retinitis then staining in late phase. There was no vascular leakage from Kyrieleis arteriolitis. Her CXR, Anti-HIV, VDRL, FTA-ABS, HBsAg, and CBC were negative. Aqeous PCR for CMV, EBV, HSV1, HSV2, VZV were undetectable. Toxoplasma gondii IgM and IgG returned positive. Ocular toxoplasmosis right eye was suspected because the other cause of infections were rule out and the Toxoplasma IgM and IgG results, combined with the patient's history of living with cats. She was started on oral trimetroprim-sulfamethoxazoleand Clindamycin for 6 weeks. After starting on antibiotics for 48 hours, she was received prednisolone. Her vision was better to 20/50, IOP 15, right quiet anterior chamber, also chorioretinits and Kyrieleis arteriolitis were much improved.

Conclusions: We present atypical finding of ocular toxoplasmosis, including mild vitritis, neuroretinitis combined with chorioretinitis and Kyrieleis arteriolitis,which periarterial plaques without associated leakage or vascular obstruction, could be diagnosed by FFA. Trimethroprim-sulfamethoxazole combined with clindamycin is effective,moreover, this regimen has a better safety profile and save cost.

Prevalence of HIV-associated ophthalmic disease among patients presenting to infectious disease center in Tokyo

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Purpose: To investigate prevalence and characteristic of ocular complications in patients with human immunodeficiency virus (HIV) infection in Tokyo.

Patients and Methods: Subjects were HIV-infected patients who were examined ocular manifestations at Infectious Disease Center Tokyo Metropolitan Komagome Hospital between January 2000 and December 2009. Ocular complications, demographic information, and laboratory data at the time of ocular assessment were analyzed from medical records retrospectively.

Results: Five hundred forty four patients (488 men and 56 women) visited department of ophthalmology and assessed ocular manifestations. The age ranged from 18 to 75, average was 43.3 years. One hundred eighty eight patients (34.6%) had ocular complications related to HIV infection. HIV-related microangiopathy was the most frequent (95 patients), followed by cytomegalovirus retinitis (41 patients). The mean CD4 T cell count was 55.6 cells /μL in patients with ocular complications, whereas 151.4 cells /μL in patients without ocular complications. There was significant difference between them ($p<0.01$, Mann-Whitney U test). Among 490 patients received antiretroviral therapy ART, 13 patients experienced immune recovery uveitis after the initiation of ART.

Conclusions: Ocular complications were developed in one third of HIV-infected patients. It is important to care these patients in cooperation with infection control doctors in order to manage the ocular disease according to the general immune conditions.

Family history of autoimmune diseases in patients with juvenile idiopathic arthritis and uveitis

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Purpose: To study the prevalence of autoimmune diseases (AD) in family members of patients with uveitis associated with juvenile idiopathic arthritis (JIA) and analyze the relation with the clinical forms of JIA.

Methods: Retrospective review of medical charts of a series of 80 patients with uveitis associated with JIA in a tertiary center. We analyzed demographic data, clinical forms of JIA, family history and coexistence of other AD.-

Results: The group consisted of 65 girls and 15 boys age 2 to 21 with mean age of onset of JIA of 3.3 years and uveitis of 4.6 years.- 60 (75%) patients had oligoarthritis (of these 51 with positive ANA antibodies), 11 (13.8%) psoriatic arthritis, and 9 (11.2%) polyarthritis with negative rheumatoid factor.

7 (8.8%) patients suffered from other AD (4 children with psoriasis, 1 autoimmune hepatitis, 1 celiac disease, and 1 diabetes mellitus type 1). 32 (40%) patients had family history of AD, which included: psoriasis (12 cases), rheumatoid arthritis (5), systemic lupus erythematosus (5) JIA (5), celiac disease (3), ankylosing spondylitis (3), type 1 diabetes (2), ulcerative colitis (2), multiple sclerosis (2), autoimmune thyroiditis (2), anterior uveitis (1), and discoid lupus erythematosus (1).

Conclusions: Patients with JIA and uveitis are at increased risk of developing other AD and often present positive family history, of which psoriasis, rheumatoid arthritis, JIA, and systemic lupus erythematosus are most common. Family history of AD is more frequent among patients with polyarthritis and psoriatic arthritis than in oligoarthritis.

Evaluation of the recurrence rate for ptergium treated with conjunctival autograft

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Purpose. The aim of this study was to evaluate the recurrence rate for the conjunctival autografts in the treatment of primary pterygium.

Material and Methods. Thirty-six eyes of 36 patients with the diagnosis of primary pterygium underwent surgical excision and treated with conjunctival autografts. Complications, recurrence rate, and final appearance of the cases were evaluated prospectively. Data were analysed using SPSS software 15.0 (SPSS, Inc., Chicago, IL). Comparisons for categorical variables were done using x2 tests, although Fisher's exact test was used when data were sparse. Significance was set at $p< 0.05$ using two-sided comparisons.

Results. Complications were observed in five cases; three eyes with Dellen ulcer and two case with a Tenon's cyst in the superior temporal quadrant. The onset of recurrence was 4.5 months. Higher complication rates were detected among patient group below 54 compared to patient group aged over 54 years, 22.2% v 5.6%, respectively ($p=0.338$). Complications were more frequent among male patients compared to female group, 16.6% v 5.6%, respectively ($p=0.603$). Recurrence was detected in four (8%) cases with the average recurrence time of 4.5 months.

Conclusion. We suggest that conjuntival autografting is an effective technique in primary pterygium in terms of low recurrence rate. Increasing patient age is associated with significantly less risk of recurrence and complication.

Choroidal Neovascular Membrane Secondary to Toxoplasmic Retinochoroiditis

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Introduction: We report the diagnosis and treatment of a case with toxoplasmic retinochoroiditis complicated by choroidal neovascular membrane.

Case Report: A 14 year-old boy was diagnosed as having ocular toxoplasmosis in his left eye regarding his retinochoroidal lesions and serological investigations. -At presentation his best corrected visual acuity (BCVA) was counting fingers. His retinal examination revealed subretinal hemorrhage and macular elevation adjacent to a wide retinochoroidal scar. Optical coherence tomography showed retinal edema with retinal pigment epithelium detachment. Fundus fluorescein anjiography -revealed a choroidal neovascular membrane under the macula. He was treated by monthly intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents for five months. -His final BCVA was 0.2 Snellen lines and no recurrence was noted during his 2 years follow-up period.

Conclusion: Choroidal neovascular membranes can develop in patients with retinochoroiditis due to ocular toxoplasmosis which can be successfully treated by intravitreal anti-VEGF injections.

Macular Hole Surgery in Ocular Behçet's Disease

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Introduction: We report the surgical treatment of macular hole in a patient with ocular Behcet's Disease.

Case: A 31 years old male patient being followed up in our Uveitis Clinic for five years had an instant decline in his best corrected visual acuity (BCVA) from 0.8 to 0.1 snellen lines. The optical coherence tomography (OCT) revealed a recently developed macular hole in his left eye. Surgical treatment was decided and he underwent vitreoretinal surgery with internal limiting membrane (ILM) peeling, long-acting gas tamponade and face down head positioning for 5 days. His macular hole was noted to be successfully closed by OCT examination at the end of the first week postoperatively, and his BCVA improved to 0.8 snellen lines. No recurrence was noted during the postoperative follow-up period of 9 months.

Conclusion: Macular hole can occur as a sequela of macular involvement in ocular Behçet's Disease. Vitreoretinal surgery with ILM peeling and gas tamponade with head positioning leads to closure of the hole and helps to preserve central visual acuity in affected cases.

Clinical characteristics of patients diagnosed with presumed diabetic iritis

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Purpose: To describe clinical features of new-onset anterior uveitis associated with severe hyperglycemia.

Methods: Retrospective analysis of 24 eyes of 16 patients (13 men, 3 women; mean age 47 years) who presented with new-onset anterior uveitis associated with severe hyperglycemia between December 2001 and April 2013.

Results: Ocular findings at presentation included posterior synechiae (14 eyes, 58%), fibrin (11 eyes, 46%), keratic precipitates (8 eyes, 33%), Descemet folds (6 eyes, 25%), and hypopyon (3 eyes 13%). High intraocular pressure (> 21 mmHg, 8 eyes, 33%) and diabetic retinopathy (non-proliferative, 8 eyes, 33%) were also noted. The mean fasting blood glucose was 349 mg/dl and the mean hemoglobin A1c was 12.6%. Five patients were unaware of their hyperglycemic state, and the remainder had either poor control or discontinued diabetes treatment. Systemic examination and ancillary testing did not reveal any other possible causes for anterior uveitis. Ocular inflammation was controlled in all cases using local corticosteroid therapy (drops and subconjunctival injections) in addition to proper internal medicine intervention for diabetes. At 3 months, the visual acuity (VA) was improved or maintained in 17 eyes (90%), while the VA was <0.5 in 3 eyes due to cataract and/or diabetic macular edema. There were no recurrences with a mean follow-up of 22 months.

Conclusions: We observed new-onset anterior uveitis in association with severe hyperglycemia in 16 patients. Patients were either undiagnosed or had poorly-controlled diabetes. Ocular inflammation was severe, but easily managed with local therapy in addition to proper diabetes treatment.

Immunogenicity of a novel anti-IL-17A antibody, secukinumab, in healthy subjects and patients

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Purpose: To assess the immunogenicity of secukinumab (AIN457), a high-affinity fully human monoclonal antibody (mAb) that selectively binds to and neutralizes IL-17A, under development for treatment of inflammatory diseases.

Materials and Methods: Samples for immunogenicity assessment were obtained pre-dose, during treatment, and during follow-up periods from subjects (both healthy volunteers and patients) from more than 20 clinical studies across various indications. Subjects were exposed to a range of secukinumab dosing regimens, which included single doses such as 25mg s.c. in psoriasis patients and multiple 7x10mg/kg i.v. doses in multiple sclerosis patients over a 6-month period, respectively. The immunogenicity assessment followed a 3-tiered approach: 1) samples were screened for anti-drug antibodies (ADA); 2) a confirmatory assay was performed to identify true positives; 3) true positive were quasi-quantified via titration. A Biacore-based assay was used mainly during the early stages of the psoriasis and the arthritis secukinumab program (up to Phase IIB), and a MSD-based bridging immunoassay was applied during the later stages (Phase III and other indications).

Results: Overall, more than 2000 subjects have been tested for ADAs within secukinumab trials. None of the subjects tested developed sustained ADAs. In total, 4 subjects (3, Biacore; 1, MSD-based assay) met the definition of treatment-related, transient positive immunogenicity showing low ADA titers. None of these had evidence of loss of efficacy, altered pharmacokinetics, or reported immunogenicity-related adverse events.

Conclusions: Based on currently available data, secukinumab appears to carry a low risk of immunogenicity. More data from larger clinical studies are required to strengthen this encouraging finding in greater patient populations.

Contamination of topical anestesic solutions with Kyotococcus sedenterius

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Purpose: A microbiologic investigation was carried out for an epidemic among patients admitted to Ahi Evran University Research and Teaching Hospital, Ophtahalmology Clinic with the symptoms of redness, purulent secretion and periorbital edeme between the time period of July 2013 to October 2013. Solution containing topical anestesic sucked into a paper containing floresein was analysed microbiologically for the probability of contamination.

Material-method: One microliter of the solution in routine use in the clinic was inoculated onto blood agar, eosin-metylen-blue agar and chocolate agar and incubated for five days at37°C both aerobically and microaerophilic conditions. Strain identification and antimicrobial susceptibility testing was performed by VITEK 2 Compact (bioMerieux, France) automated system.

Results: At the second day of the incubation tiny, white-grey colored colonies on chocolate agar and blood agar were detected. Gram-positive coccus and diplococcus were seen on Gram-staining of the smear. Identification and antimicrobial susceptibility of the strain was performed by VITEK 2 Compact (bioMerieux, France) and identified as *Kyotococcus sedenterius*.

Conclusions: *Kyotococcus sedenterius* is an aerobic, catalase-positive, oxidase-negative,- Gram-positive organism, generally considered as clinically important only in immuncompremised patient causing endocarditis, pneumoniae, peritonitis. The limitation of this study is that we could not obtain samples from the patients and compare the microbiological test results with the solution. Although, we identified *Kyotococcus sedenterius* from the topical solution, we could not identify the source of outbreak clearly. It is emphasized that changing the intensity of the solution at least weekly and treating in accordance with the rules of sterility is important to prevent future outbreaks.

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Fuchs' Uveitis Syndrome and laser flare photometry measurements

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Purpose: To evaluate the symptoms, clinical findings and laser flare photometry measurements in patients with Fuchs' Uveitis Syndrome (FUS).

Materials and Methods: Eleven eyes of eleven patients with FUS were evaluated retrospectively. Affected eyes of patients were compared with healthy fellow eyes. Delay in diagnosis, detailed slit lamp and dilated fundus examinations, laser flare measurements (KOWA FM-6000, KOWA Company, Ltd, Tokyo, Japan), history of ophthalmic surgeries and intraocular pressures were noted. Statistical analysis were evaluated with SPSS 11.5 programme.

Results: Mean age of patients was 40±11.4 years. Median delay in diagnosis was 22 months. All patients were affected unilaterally. The most common presenting symptom was blurred vision. Typical keratic precipitates were detected in all patients. Anterior chamber cells were seen in only four patients at presentation. Mean laser flare measurements of affected eyes and healthy eyes were 11.2±2.5 ph/ms and 6.0±2.3 ph/ms respectively. Repeated laser flare measurements in 3 different visits of six eyes followed without treatment did not incerease (p>0,05). Four eyes with FUS underwent cataract surgery and laser flare measurements were found similar before and after cataract surgery.

Conclusions: Mildly elevated laser flare measurements in FUS do not elevate during follow up period without treatment and also these values do not decrase even if a treatment regimen is given. These outcomes justify follow up of patients with FUS without treatment.

Mediterranean fever (MEVF) gene mutations in Behçet patients with and without ocular involvement.

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Purpose: The frequent appearance of Familial Mediterrenian Fever (FMF) and Behçet's Disease (BD) within similar human populations, presence of clinically mistreated cases, emergence in the same family even in the same patient and acceptance of both diseases as auto inflammatory diseases brings to mind the possibility of common genetic background. It is already known that FMF has a relation with MEVF gene. This study aims to determine the relationship between BD and MEditerrenian FeVer (MEVF) gene with the hypothesis of both diseases have the same genetic background.

Materials and Methods: Between November 2010 and June 2011, 51 (51%) male and 49 (49%) female patients with BD and 18 (39.1%) male, 28 (60.9%) female healthy volunteer included in the study. MEFV gene mutations were evaluated with sequence analysis.

Results: While the mean age was 40.7 (21-65) years in the patient group and 36.2 (23-59) years in control group ($p>0.05$). MEFV mutations (P369S, R761H, E148Q, R202Q, K695R, M694I, F479L, A744S, M680I, M694V, V726A) were 55% in Behçet's patients and 57% in control group ($p>0.05$). The most observed mutation was R202Q (36% in patients group, 19.1% in control group). We thought R202Q mutation may be a counfounding factor because of high mutation levels in control group. When we excluded R202Q mutation, MEFV mutations were 0 in patient's group and .2 in control group ($p=0.015$). There was no statistically significant difference according to ocular involvement. The only clinical relationship with MEFV mutations was M694V mutation which was higher in patients with deep venous thrombosis.- -

Conclusions: There may be a correlation between BD and MEFV gene mutations. M694V mutation may be related with deep venous thrombosis. MEFV gene mutations are not associated with ocular involvement. Wider population based prospective cohort studies are required to determine MEFV gene mutation ratio in BD patients and healty persons in our country.

Sustained bilateral effect of unilateral dexamethasone implant injection in a case of intermediate uveitis with macular edema

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Introduction:The 0.7-mg dexamethasone drug delivery system (Ozurdex®; Allergan Inc., USA) was approved by the US FDA for treating posterior noninfectious uveitis. Few reports showed favorable visual outcomes in non-vitrectomized and vitrectomized eyes with uveitis and macular edema. Our case-report is the first to show a bilateral simultaneous effect of a unilateral ozurdex injection in a case of idiopathic intermediate uveitis presenting with bilateral vitritis and macular edema.

Case report: A 26-year-old female with a history of recurrent attacks of idiopathic bilateral anterior uveitis, vitritis and RE macular edema was examined due to vision deterioration in her RE. Treatment included cellcept 2gr/day (a fixed dose for last 10 months). BCVA was 20/70 RE and 20/30 LE. Clinical examination revealed RE significant vitritis and LE very mild vitritis, OCT showed normal macular appearance in both eyes. The patient was offered ozurdex injection to her RE due to the severe vitritis, but returned only 1 month later. Further vision deterioration was noticed in both eyes; VA was 20/100 RE and 20/40 LE, and both eyes developed significant macular edema. Systemic corticosteroids were offered as macular edema involved both eyes, but the patient refused and asked for local treatment. Ozurdex injection was given to her RE. Two months post injection, vitritis and macular edema completely resolved in both eyes. Sixteen months post injection, no recurrence of vitritis or macular edema was visible and BCVA significantly improved to 20/27 RE, 20/25 LE.

Conclusions: Unilateral ozurdex injection may have a bilateral effect with vitritis& macular edema resolution and visual acuity improvement.

Fuchs' heterochromic iridocyclitis associated with Stargardt's disease

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Introduction: Fuchs' heterochromic uveitis (FHU) is a chronic nongranulomatous uveitis that affects patients between the ages of 20 and 40 years. Stargardt's disease is an autosomal recessive disease characterized by an atrophic macular dystrophy. We here report a patient with Stargardt's disease and unilateral FHU.

Case report: A young male was referred for decreased vision in both the eyes since 5 years. He complained of occasional floaters in both the eyes. His best-corrected visual acuity was 20/100 in both eyes. His color vision with Ishihara pseudoisochromatic chart was 16/16 in both eyes. Slit lamp examination of left eye showed stellate keratic precipitates, anterior chamber reaction, iris hypochromia with nodules, posterior sub capsular cataract and vitreous debris. Fundoscopy showed retinal pigment atrophy at the fovea surrounded by yellow fleck like lesions at the border of the atrophy. Angiography was suggestive of silent choroid with transmitted hyperfluorescence at fovea due to retinal epithelial atropy suggestive of Stargardts disease.

Conclusion: This is the first case report of an association of FHU with Stargardt's disease. An association of FHU with retinitis pigmentosa has been described in the literature. A hereditary factor closely linked to RP and FHU was not reflected in these patient's pedigree. The cause for such association is still undetermined. Apart from the retinitis pigmentosa, we found viral, toxoplasma and sarcoidosis association with FHU. We did not find any association of FHU with Stargardt's disease or other hereditary macular degenerations on Medline search.

Granulomatous Panuveitis in a case with Juvenile Idiopathic Arthritis and Tuberculosis History

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INTRODUCTION: Diagnosis of ocular tuberculosis (TB) can be difficult in cases with previous infection. Herein we report a case with juvenile idiopathic arthritis (JIA) and TB history with granulomatous panuveitis.

CASE REPORT: A 20 year-old female presented with relapsing iritis for months in both eyes (BE), with posterior synechiae, complicated cataract and blurred fundi. Visual acuity (VA) was 20/100 (BE). She was diagnosed of JIA in her childhood, and pulmonary with spinal TB post complete treatment when 18.

JIA-related iritis was first impressed. Systemic methotrexate with topical steroid were given. After cataract extraction, VA improved to 20/40. Biomicroscopy revealed multiple punched-out chorioretinal scars with active infiltration (BE). Strong positivity was shown in skin tuberculin test. Anti-tubercular chemotherapy was initiated, while methotrexate held. However, iridocyclitis aggravated 4 weeks later. AC-tap TB-PCR was negative. Methotrexate was resumed and anti-TB medications discontinued.

Low-grade iritis ensued for the next 4 years. Granulomatous uveitis workup excluded sarcoidosis or syphilis. AC-tap of TB-PCR was still negative. Mantoux skin test showed 21-mm induration. Fluorescein angiogram disclosed diffuse punched-out scars without leakage. Interferon gamma release assay (IGRA) was positive. Therefore, anti-TB medications were given for 18 months when she was 28. Iridocyclitis gradually abated 12 months after anti-tubercular treatment. Her VA became LP (RE), and NLP with phthistical change (LE).

CONCLUSIONS: In highly-suspicious ocular TB case with previous systemic infection, anti-TB therapeutic trial should be aggressively applied. Nevertheless, delayed clinical response, and Jarisch-Herxheimer-like reaction can further puzzle the clinician. Delayed diagnosis and treatment can therefore result in poor visual prognosis.

Chronic anterior uveitis in paediatric patients

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Purpose To describe clinical features and visual prognosis of chronic anterior uveitis in paediatric patients. Methods The medical records of 35 paediatric patients who met criteria for chronic anterior uveitis (SUN) were reviewed to identify clinical features, complications, visual outcome and treatment between 1996 and 2012 at the University of Buenos Aires.

Results: There were 35 patients, 21 (60%) girls, mean age 7,4 years (r: 2-15) and mean follow up 79,2 months (r: 12-192). Out of 35, 26 (74,2%) presented bilateral uveitis. ANA was positive in 19 (54,2%) patients while arthritis was found in 18 (51,4%). Metotrexate was given in 25 (71,4%) patients. Fourteen patients (40%) were treated with biologics agents: 11 with Adalimumab, 3 with Etanercept, 1 with Infliximab and 1 with Rituximab. Final visual acuity better than 20/40 was found in 49 out of 61 (80%) eyes. Most common complications were band keratopathy in 20 eyes, cataract in 16 eyes and posterior sinechiaes in 13 eyes. Facoemulsification with IOL was performed in 10 eyes. Regresion of uveitis after a mean time of treatment of 8 years was achieved in 6 patients.

Conclusion: In our series, chronic anterior uveitis was related to Juvenile Idiopathic Arthritis only in half of patients. Therefore, not all chronic anterior uveitis in children are associated with JIA. Regarding treatment 40% of our patients had to receive biologic agents to improve the inflammation.

Cataract Surgery with Intraocular Lens Implantation in Patients with Vogt Koyanagi Harada Syndrome

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Purpose: To describe the results of cataract surgery in patients with Vogt Koyanagi Harada syndrome.

Methods: The medical records of patients with VKH syndrome who underwent cataract surgery between June 1998 and November 2012 were retrospectively analyzed.

Results: Thirty seven eyes of 26 patients were included. Mean age was 49.38 ± 15.62 years (19-80 years). Preoperative best corrected visual acuity (BCVA) was less than 20/200 or worse in 30 eyes (81.08%), while postoperative BCVA was greater than 20/40 in 25 eyes (67.56%). Phacoemulsification was performed in all patients. Small pupils managed by synechiolysis with an iris kuglen (19 eyes) or iris hooks (18 eyes). Pars plana vitrectomy (PPV) and posterior capsulotomy were carried out in 18 eyes of 16 patients. All patients underwent intraocular lens (IOL) implantation. The difference in the proportion of patients with postoperative inflammation relapse between those who had hydrophilic acrylic IOL, hydrophobic acrylic IOL and PMMA implantation was not statistically significant (Fisher exact test: hydrophilic vs hydrophobic: 0.14; hydrophilic vs PMMA: 0.11; PMMA vs hydrophobic: 0.39). None of the IOLs needed to be explanted. Severe postoperative inflammation was recorded in 6 eyes.

Conclusion: Phacoemulsification with IOL implantation associated with PPV and posterior capsulotomy in combination with a suitable perioperative medical management yielded a good visual outcome in patients with Vogt Koyanagi Harada syndrome. The comparison of the occurrence of postoperative inflammatory relapses between those patients who underwent hydrophilic acrylic, hydrophobic acrylic and PMMA was not statistically signicant.

Diffuse choroidal thickening in patients with Vogt-Koyanagi-Harada Syndrome

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The effect of Epidermal growth factor receptor inhibitors on the growth inhibition of intracellular *Toxoplasma gondii* in the RPE cells

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Purpose: The spontaneous signal transducer and activator of transcription (STAT)6 phosphorylation and the following specific gene expression of the host cells are major strategy for the survival of the intracellular *Toxoplasma gondii* against the parasiticidal events through the STAT1 phosphorylation by the provoked interferon-gamma in the infection. We examined to find out the effect of several tyrosine kinase inhibitors (TKIs) on the growth inhibition of intracellular *T. gondii* and the relationship with STAT1 and 6 phosphorylation in the retinal pigment epithelial cell line, ARPE-19.

Methods: We counted the number of *T. gondii* per parasitophorous vacuolar membrane (PVM) after the treatment with several TKIs within RPE host cells at 12-hr interval for 72 hrs. In addition, the inhibition of phosphorylation of STAT6 after treatment was checked in the western blot and immunofluorescence assay.

Results: Among the tested TKIs, Afatinib (pan ErbB/EGFR inhibitor, 5uM) inhibits the growth of *T. gondii* of 98.0%, which is comparable to pyrimethamine (5uM) of 96.9%, and followed by Erlotinib (ErbB1/EGFR inhibitor, 20uM) of 33.8% and Sunitinib (PDGFR or c-Kit inhibitor, 10uM) of 21.3% in the counting number of *T. gondii* per PVM within the host cells. In early stage of the infection (2, 4, and 8 hr after *T. gondii* challenge), Afatinib inhibits the spontaneous phosphorylation of STAT6 in the western blot and immunofluorescence assay, but still the STAT1 phosphorylation is not affected by interferon-gamma stimulation. On the while, Jak1/Jak3, the upper hierarchical kinase of the cytokine signaling, are strongly phosphorylated at 2 hr and then disappear entirely after 4 hr.

Conclusions: Some TKIs, especially EGFR inhibitors, might play an important role in the inhibition of intracellular replication of *T. gondii* through the inhibition of direct phosphorylation of STAT6 by *T. gondii* itself.

Twenty-five gauge pars plana vitrectomy for vitreous opacity associated with uveitis resistant to medical treatment

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OBJECTIVE: The diagnosis of primary intraocular lymphoma is difficult in many cases, even with conventional cytological tests using vitreous samples. This study examined the results of pars plana vitrectomy for nonclearing vitreous opacities associated with uveitis and malignant masquerade syndrome that is resistant to corticosteroid treatment.

METHODS: Ten consecutive patients (18 eyes) with vitreous opacities were studied. All patients were resistant to or intolerant of corticosteroid therapy. All eyes underwent 25-gauge pars plana vitrectomy, followed by evaluation of visual acuity and recording of the grade of inflammation and complications. Specimens of undiluted vitreous were collected at the time of pars plana vitrectomy and interleukin (IL)-10 and IL-6 concentrations were determined.

RESULTS: Vitreous specimens were obtained from 3 patients with suspected intraocular lymphoma and 7 patients with uveitis considered unrelated to neoplasm. Twelve eyes (57%) improved by 2 or more lines of Snellen visual acuity within 6 months. Four eyes (22%) remained unchanged, within a line of preoperative Snellen visual acuity, and two eyes (11%) worsened by 2 or more lines of Snellen visual acuity. Severe postoperative inflammation did not recur in any eyes. In all 7 patients with uveitis, IL-10/IL-6 ratio was less than 1. In 2 of the 3 patients, the vitreous IL-10 concentration was higher than the vitreous IL-6 concentration. One patient was eventually diagnosed with Hodgkin's lymphoma.

CONCLUSIONS: Diagnostic pars plana vitrectomy appears to have beneficial effects on restoring vision and stabilizing vitreous inflammation.

Thermal Imaging in Ocular Inflammation

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Purpose: The purpose of this study was to evaluate thermographic pictures of ocular inflammatory and non-inflammatory conditions using commercially available thermal camera.

Method: A non-contact thermographic camera (FLIR P 620) was used to take thermal and non-thermal pictures of 3 cases of scleritis (a necrotising, a non-necrotising and a posterior), one case of postoperative anterior uveitis, a case of meibomian gland dysfunction-keratitis (MGD keratitis), a case of conjunctival benign reactive lymphoid hyperplasia (BRLH), a case of central serous chorio-retinopathy (CSCR) and a participant with healthy eyes as a control. Images were transferred to computer and using analyzing software gross ocular surface temperature and temperature over area of interest was calculated. Temperature of affected eye and non affected eye was compared.

Result: Patient with fresh non-necrotizing scleritis who was not on treatment revealed significant higher temperature compared to fellow healthy eye. Patient with necrotizing scleritis on immuno-modulatory therapy revealed low temperature in necrotized area. Slightly higher temperature was noted in posterior scleritis. Paradoxically, MGD-keratitis depicted lower temperature on thermograph in clinically more affected eye. Conjunctival BRLH showed a cold lesion. Eye with CSCR showed slightly lower temperature. Healthy eyes of control showed no difference in temperature.

Conclusion: This small study has shown interesting results and prompted further exploration of thermography in ocular inflammatory and non-inflammatory conditions.

Takayasu disease and scleritis

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Purpose: To present three rare cases of Takayasu arteritis (TA) with scleritis and to emphasis on basic clinical examinations.

Methods: All the case records with diagnosis of Takayasu disease and scleritis presented to our clinic were reviewed. Patients demographics, past medical history, clinical presentation, investigations and treatment details were noted.

Results: We found 3 cases of TA and scleritis. First case presented with scleritis and later developed choroidal infarction. Second case had scleritis as the only ocular presenting feature. Third case presented with choroidal folds in both the eyes and had huge exudative retinal detachment (ERD) in the left eye. Surprisingly this patient had no significant pain. All three patients had history of absent radial pulse on left arm. First and second patients were successfully managed with steroids and methotrexate therapy. In third patient ERD was refractory to anti-inflammatory treatment.

Conclusions: Scleritis can be a presenting feature of Takayasu arteritis which may bring patient to the ophthalmologist first. Simple basic examination such as pulse and blood pressure measurement can give clue to suspect this rare disease.

Intravitreal Methotrexate in Leukemic Retinopathy - a case report.

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Introduction: Leukemic retinopathy, a rare condition, is not only a diagnostic challenge in an immune-compromised patient but also difficult to manage. We present an unfortunate young male's journey from 20/20 vision to no perception of light and ultimately loss of life in a span of just 3 months.

Case report: A 29/M known case of chronic myeloid leukemia presented with mild defective vision in both the eyes, was found to have bilateral retinal infiltrates and vascular sheathing. Initial deceptive response to valaciclovir eventually progreesed to develop hypopyon. Anterior chamber tap for cytology, molecular and bacteriological diagnostics were all negative. Patient went on to develop total bilateral retinal infiltrates. Option of external beam radiotherapy (EBRT) was denied by oncologist since patient was on maximum possible chemotherapy (triple intrathecal therapy) with normal blood counts. Intravitreal methotrexate in worse eye resulted in mild reduction of cellular infiltrates. But ultimately patient developed intractable glaucoma and succumbed to death due to CNS metastasis.

Conclusion: Use of methotrexate in ocular lymphomas have been well reported in literature but its administration in leukemic retinopathy should be studied further. More work needed to include ocular involvement as an indication for EBRT and to co-relate mortality with ocular involvement in leukemic retinopathy.

Occlusive vasculitis: A challenging diagnosis

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We bring you the case of a Guinean 36 years old male with the precedent of a bilateral optical neuropathy episode in 2006.

The patient consults us due to an episode of bilateral occlusive retinal vasculitis which is only active in left eye at the moment of the evaluation. In following visits he also refers oral ulcers without known origin, acne, and a digestive bleeding which remains unexplained despite the realization of a colonoscopy. A positive PPD test (3 cm.) was demonstrated, as well as a persistent rise of acute phase reactants. The test for lupic anticoagulant was positive, but in the other hand there was a negative result for ANA. We also found high calcium levels in blood and the patient was negative for HLAB51. Serology were requested for Brucella, Toxoplasma, syphilis, hepatitis B and C, HIV and CMV. They were all negatives except for the last one. ECA, and liver enzymes were normal in repeated test.

Due to the atypical course of the disease, we have requested a TC to confirm the presence of hilar adenopathy or parenchymal lung involvement, being sarcoidosis our first diagnostic option.

Orbital infections:clinical features, etiologies, and outcome

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Purpose: To describe clinical features,etiologiesandoutcome of orbital infections.

Materials and Methods: Retrospective review of 28 cases of orbital infections examined atthe Ophthalmology department of FattoumaBourguiba University Hospital,Monastir, Tunisia between January 1995 and December 2012. All patients underwent a complete ophthalmic examination, otorhinolaryngology examination andorbital and cerebral computed tomography (CT). All patients received antibiotic therapy with or without surgical drainage. Mean follow-up was 5 weeks (range, 1 week- 4 months).

Results: Mean age of our patients was 35.9 years. Thirty-six percent of patients were younger than 15 years. A male predominance was noted (54%). Of 28 patients, 32.2% hadpreseptal cellulitis, 39.2% had diffuse orbital cellulitis, 14.3% hadsubperiosteal abscess, and 14.3% had orbital abscess. No case of cavernous sinus thrombosis wasrecorded. Staphylococcuswas the most frequently isolated germ (62.5% of cases). All patients received intravenous antibiotics. Surgical treatment was performed in 39.2% of patients. Recovery without sequelaewas observed in 92.8 % of patients. The mean final visual acuity was 20/25.

Conclusions: Orbital infection is a serious, vision-threatening infection. Early diagnosis and appropriate treatment are essential to improve prognosis.

Branch retinal vein occlusion in young patients

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Purpose: To analyze the characteristics of branch retinal vein occlusion (BRVO) in young patients (< 50 years).

Materials and Methods: Retrospective chart's review of 40 patients (47 eyes). All patients underwent detailed ophthalmic examination, fluorescein angiography, and optical coherence tomography.

Results: BRVO in young patients accounted for 29% of all BRVO cases. Underlying inflammatory or infectious disease was found in 12 patients (30%) (Behçet disease 9, sarcoidosis 1, tuberculosis 1, and toxoplasmosis 1). Systemic hypertension, diabetes, and hyperlipidemia were found in 13, 3, and 5patients, respectively. Final visual acuity was < 20/200 in 19% of eyes.

Conclusions: Inflammatory or infectious diseases and systemic hypertension are important risk factors for BRVO in young patients.

Neuroretinitis: a rare feature of tubulointerstitial nephritis and uveitis syndrome

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Introduction: We report a 17-year-old female with biopsy proven TINU syndrome who developed neuroretinitis.

Case report: A 17-year-old female presented to our hospital with fatigue, arthralgia and fever associated with non-granulomatous anterior uveitis in the left eye. Blood tests revealed renal failure and a renal biopsy showed acute tubulointerstitial nephritis. Findings were consistent with tubulointerstitial nephritis and uveitis (TINU) syndrome. The patient received systemic corticosteroids for 2 months as well as dexamethasone and mydriatic drops. Bilateral nongranulomatous anterior uveitis occurred 10 days after prednisone discontinuation, and was treated with topical steroids; however, uveitis recurred several weeks later. Bilateral anterior chamber inflammation was associated with neuroretinitis in the right eye. Extensive posterior synechiae precluded fundus examination of the left eye. The posterior segment manifestations responded to systemic prednisone, which was slowly tapered. The final visual outcome was favorable.

Conclusions: TINU syndrome is an uncommon condition characterized typically by bilateral anterior uveitis, which is likely to relapse. It also may manifest with neuroretinitis, either at onset or during recurrence of ocular inflammation.

Herpesvirus detection and cytokine levels (IL-10, IL-6, and IFN-γ) in ocular fluid from Tunisian immunocompetent patients with uveitis

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Purpose: To investigate the incidence of HHVs in aqueous humor samples of immunocompetent patients with suspected viral uveitis and cytokine (IL-10, IL-6, and IFN-γ) expression profiling.

Materials and methods: Forty-seven aqueous humor samples were collected from immunocompetent patients with viral uveitis. Samples were assayed for HHV-1 to HHV-8 by in-house real-time polymerase chain reactions. IL-6, IL-10, and IFN-γ were quantified with a cytometric bead array. Relations between viral detection, cytokine profiles, and clinical data were studied. At least one viral genome was detected in 21 aqueous humor samples analyzed.

Results: Varicella-zoster virus (VZV) was detected in 14 of the positive samples, cytomegalovirus (CMV) in 8, HSV-1 in 1, Epstein-Barr virus (EBV) in 4, and HHV-6 in 2. More than one viral genome was detected in seven aqueous humor samples. Aqueous humor samples positive for HHV-DNA contained significant levels of IL-6, IL-10, and IFN-γ, compared to HHV-DNA negative samples. High levels of IL-6 were detected in patients with CMV-DNA in their aqueous humor samples. Significantly higher levels of IL-10 and IFN-γ were found in positive samples for VZV, EBV, and HHV-6 DNA than in negative aqueous humor ones.

Conclusions: VZV was the principal etiologic agent of uveitis in this Tunisian series, with CMV the second most common agent. Knowledge of immunoregulatory interactions and dynamic changes in viral uveitis may be a key to understand the pathogenesis leading to more-effective treatments.

Priphlebitis mimicking frosted branch angiitis following eye blunt trauma: case report

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Introduction: We report a case of a patient with acute frosted retinal periphlebitis after eye blunt trauma.

Case report: A 14-year-old otherwise healthy female patient presented with sudden decrease in visual acuity in the left eye after contusive trauma one dayearlier. At examination, best-corrected visual acuity (BCVA) was 20/20 in the right eye (RE) and 20/100 in the left eye (LE). Results of slit-lamp and fundus examination of the RE were unremarkable. Results of slit-lamp examination of the LE revealed subconjunctival hemorrhage, mild hyphema, pupillary sphincter ruptures, and iridodialysis in the left eye. Fundus examination showed prominent sheathing of inferotemporalretinalvenules associated with area of retinalwhitening in the posterior pole, retinal and preretinal hemorrhages. Fluorescein angiography revealed delayed filling of inferotemporal branch retinal vein and late staining of sheathed retinal venules, and late hyperfluorescencein the area of retinal whitening seen clinically.Indocyanine green angiography shows a choroidalrupture. Optical coherence tomography (OCT) showed serous retinal detachment (SRD) involving the posterior pole with associated subretinal fibrin. The patient was treated by oral prednisone 1 mg/Kg/day with gradual tapering. One month after presentation, BCVA of the LE did not improve, and fundus examination revealed resolution of retinal whitening, branch retinal vein sheathing, and retinal hemorrhages. OCT shows resolution of SRD with macular atrophy, pseudo macular hole, and epiretinal membrane formation.

Conclusions: Frosted branch angiitis has been reported in association with infectious and autoimmune disease. It may be related to immune mechanism following vascular damage by severe trauma.

Bilateral pseudo-lymphomatousconjunctival hyperplasia: case report

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Introduction: To describe the clinical and histopathological characteristics of a pseudo-lymphomatousconjunctival hyperplasia.

Case report: A 33-year-old otherwise healthy woman, presented with bilateral lower eyelid induration of 9-month duration. Ophthalmic examination showed fleshy-salmon-pink conjucnctival tumors located at the upper and lower tarsal conjunctiva of both eyes. The orbito-cerebral computed tomography scan revealed no abnormalities. Histopathological evaluation with immunohistochemical markers of conjunctival biopsy revealedpseudo-lymphoumatoushyperplasia without signs of malignancy.

Conclusions: Pseudo-lymphomatousconjunctivalhyperplasia can mimic conjunctival lymphoma. A definitive diagnosis can be reliably established employing immunohistochemical methods.

Macular hole and Behçet disease

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Purpose: To report 4 cases of macular hole in patients withBehçet's uveitis.

Materials and Methods: All patients underwent detailed ophthalmic examination, fluorescein angiography, and optical coherence tomography.

Results: We report 4 young patientsdiagnosed with Behçet's uveitis who developed a macular hole. Two patients were treated by vitrectomy with internal limiting membrane peeling and gas tamponade. The macular hole was closed in 1 patient with improvement of visual acuity, and persisted in the second patient.

Conclusions: Macular hole is a rare complication ofBehçet's uveitis that can lead to severe visual impairment. Early diagnosis and aggressive treatmentofBehçet's uveitis might prevent such severe complication.

Acute visual loss associated to rickettsial disease

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Purpose: To characterize and analyze ocular involvement associated with visual loss in a cohort of patients with rickettsial disease.

Materials and Methods: Retrospective study of 16 eyes of 14 patients. All patients underwent detailed ophthalmic examination, fluorescein angiography, and optical coherence tomography.

Results: Mean initial visual acuity (VA) was 20/63 (range, 20/800-20/25). White retinal lesions infiltrating inner retina was the most common finding occurring in 14 eyes (87.5%). It was associated with a serous retinal detachment (SRD),accurately detectable by optical coherence tomography, in 11 eyes (78.6%). Other findings included optic neuropathy in 7 eyes (43.75%), cystoid macular edema in 1 eye (6.25%), branch retinal artery occlusion in 1 eye (6.25%),and choroidal neovascularization in 1 eye (6.25%). Thirteen patients were treated with a 2-week course of oral doxycycline 200 mg/day. Mean final VA was 20/40.

Conclusions: Innerretinitis, associated with mild vitritis and SRD, and optic neuropathy are the most common vision-threatening ocular manifestations of rickettsial disease.

Indocyanine green angiography findings in patients with nonfamilial amyloidosis

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Purpose:To assess indocyaninegreen angiographic findings in patients with nonfamilialamyloidosis.

Patients and Methods: Prospective study including seven patients (14 eyes) with nonfamilial amyloidosis. All patients underwent detailed ophthalmic clinical examination, fundus photography, and indocyanine green angiography (ICGA). Fluorescein angiography (FA) was performed in four patients.

Results: Of the seven patients, four (57.1%) were male. Mean age was 49.5 years. Six patients had renal amyloidosis and one patient had systemic amyloidosis. Mean bestcorrectedvisual acuity was 20/25. Fundus and FA findings included cotton-wool spots (28.5%), retinal hemorrhages (14.3%), retinal pigment epithelial changes (21.4%), serous retinal detachment (7.1%), optic disc edema or staining (7.1%), area of peripheral retinal capillary non-perfusion (7.1%), disseminated peripheral punctiformhyperfluorescence (21.4%), and subretinal pooling (7.1%). Fundus examination results were unremarkable in eight eyes (57.1%). ICGA showed abnormal findings in all eyes. These included diffuse or focal/multifocal choroidal vascular staining appearing at the late phase and prevailing in peripheral fundus (100%), hyperfluorescent fleecy lesions appearing at the late phase and also prevailing in peripheral fundus (28.5%), hypofluoresent areas of variable sizes (85.7%), and pinpoints (71.4%).

Conclusions: Our results show that a subclinical, fairly typical choroidal involvement, detectable only by ICGA, is common in patients with nonfamilial amyloidosis. ICGA may be useful in better understanding the pathogenesis of amyloidosis choroidopathy and in establishing a diagnosis of amyloidosis in atypical or incomplete clinical presentations.

Acute Retinal Necrosis Associated With Central Retinal Artery Occlusion Followed After its Resolution by Keratouveitis

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Introduction: We describe herein a patient with ARN associated with central retinal artery occlusion (CRAO) who developed after complete recovery of ARN ipsilateral keratouveitis.

Case report: A 53-year-old female complaining of loss of vision in the right eye. Ophtalmic examination revealed granulomatous anterior uveitis,2 vitreous cells and haze in the RE, areas of necrotizing retinitis in the posterior pole and temporal periphery, and an area of ischemic retinal whitening in the posterior pole along with diffuse narrowing of retinal vessels and segmental fuzzy vascular sheathing in the RE. Fluorescein angiography revealed a marked delay of retinal artery filling consistent with CRAO in the RE. A diagnosis of ARN was made. PCR on aqueous humor sample was positive for HSV type 1. The patient was treated with oral valacyclovir associated with oral prednisolone. Necrotic lesions completely healed within 2 months. Five months after the resolution of ARN episode, the patient presented with disciform keratitis, mutton-fat keratic precipitates, 2 cells and 1þ flare in anterior chamber, and sectoral iris atrophy. The patient was treated with topical corticosteroidsand oral valacyclovir. She has been maintained on a preventive doseof valacyclovir 500 mg, once a day for 3 additionalmonths. Visual acuity of the RE at last follow-up was20/400.

Conclusions: CRAO should be considered as apotential, severe manifestation of occlusive vasculitisassociated with ARN. Patients with ARN also shouldbe closely monitored after healing of retinal lesions forthe development of isolated keratouveitis or anterioruveitis.

Ocular involvement and visual outcome of Herpes Zoster Ophthalmicus: review of 45 patients from Tunisia, North Africa

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Purpose: To characterize and analyze ocular involvement and visual outcome of Herpes Zoster Ophthalmicus (HZO) in patients from Tunisia, North Africa.

Methods: retrospective chart review of 45 patients (51 eyes) with HZO.All patients have received antiviral therapy.

Results: Mean age was 44.5 years. Thirty patients (66.7%) were aged over 50 years. Twenty-four patients (53.3%) were maleand 21 patients were female (46.7%). Mean initial best- corrected visual acuity (BCVA) was 20/50. Ocular involvement included oculomotor nerve palsy (5.8%), lid edema (58.8%), subconjunctival hemorrhage (45.1%), vesicular conjunctivitis (25.8%), corneal hypoesthesia (31.3%), epithelial keratitis (9.8%), stromal keratitis (15.6%), an association of superficial and stromal keratitis (5.8%), anterior uveitis (60.7%), intraocular pressure elevation (23.5%), and optic neuritis (1.9%).Anterior uveitis and keratouveitis were more likely to be associated with age ≥ 50 years (p=0.001 and 0.02, respectively). Ocular complications included neurotrophickeratopathy (1.9%); corneal opacity in 3 eyes (5.9%), secondary glaucoma (33.3%), optic atrophy (1.9%),and postherpetic neuralgia was recorded in 13.3% of patients. Mean final BCVA was 20/32. It was < 20/200 in 7.8% of eyes and ≥ 20/40 in 78.4% of eyes.

Conclusions: Our study provided epidemiologic and clinical data on HZO in a Tunisian population. Anterior uveitis and keratitis were the most common ocular complications. The overall prognosis is good, with about 3/4of the treated patients maintaining a VA of 20/40 or better.

Inflammatory choroidal neovascularization: review of 21 patients

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Purpose: To report clinical features and visual outcome in patients with inflammatory choroidal neovascularization (CNV).

Materials and Methods: Retrospective study of 22 eyes of 21 patients. All patients underwent detailed ophthalmic examination, fluorescein angiography, and optical coherence tomography. Thirteen patients underwent indocyanine green angiography. Mean follow-up was 12 months.

Results: Mean age was 33.2 years. Fifteen patients were female (71.4%)and 6 patients (28.6%) were male. Mean initial best-corrected visual acuity (BCVA) was 20/125. Main causes of inflammatory CNV included sarcoidosis (22.7%), punctate inner choroidopathy (18.2%), and toxoplasmosis (18.2%). CNV was subfoveal in 10 eyes (45.4%). Multiple CNVfociwere recorded in one eye. Sixteen (76.2%) patients were treated with intravitreal injection of bevacizumab. Mean number of injections was 1.13. Six patients (28.6%) were treated with systemic corticosteroids, one patient (4.8%) with conventional immunosuppressive therapy, and one patient (4.8%) with periorbital triamcinolone acetonide injection. Mean final BCVA was 20/50.

Conclusions: CNV is an uncommon complication of uveitis and remains a cause of significant visual impairment in patients with uveitis.Intravitrealbevacizumab led to significant mean visual improvement.

Optic neuritis and oculomotornerve palsy revealing acute disseminated encephalomyelitis: Case report

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Introduction: We report a case of optic neuritis and oculomotornerve palsy revealing acute disseminated encephalomyelitis (ADEM).

Case report: A 7-year-old patient presented with sudden decrease in visual acuity in the right eye. Best corrected visual acuity (BCVA) was 20/200. Ophthalmic examination revealed a sixth nerve palsy, partial third nerve palsy with afferent pupillary defect. Fundus examination revealed optic disc edema. Fluorescein angiography showed optic disc staining. MRI of the brain showed multiple cerebral T2-hyperintense signals.The patient was diagnosed ashaving ADEM and was treated with intravenous methylprednisolone followed by oral prednisone. At 1-month follow-up, BCVA was 20/20 with resolution of oculomotor nerve palsy and optic disc edema.

Conclusions: ADEM is a monophasic clinical syndrome, characterized by immune-mediated demyelination of the central nervous system. Treatment options for ADEM consist of anti-inflammatory and immunosuppressive agents. The disease is usually self-limiting and the prognostic outcome favorable. ADEM should be considered in the differential diagnosis of optic neuritis and oculomotor nerve palsy in childhood.

Clinical spectrum of presumed ocular tuberculosis in Tunisia, North Africa

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Purpose: To analyze the spectrum of presumed tubercular uveitis in Tunisia, North Africa.

Materials and Methods: We retrospectively reviewed the clinical records of 40 patients (69 eyes) diagnosed with presumed tubercular uveitis.

Results: Mean age at presentation was 42.7 years. Twenty-five patients were women (62.5%). Posterior uveitis (35.4%) and intermediate uveitis (32.3%) were the most common forms, followed by panuveitis(20%) and anterior uveitis (12.3%).Ocular findings included vitritis(67.7% of eyes), multifocal choroiditis(23.1% of eyes), multifocal serpiginoidchoroiditis(21.5% of eyes), periphlebitis (21.5% of eyes), and mutton-fatkeraticprecipitates(20% of eyes). Uveitis was bilateral in 71.1% of patients. Extraocular tuberculosis was recorded in 15% of patients.Antituberculosis therapy(ATT) was prescribed in 33 patients (86.8%). Mean duration of antituberculosis therapy was 6.8 months (range, 6-12 months). Systemic corticosteroidsand periocular steroids were used in 20 patients (52.6%) and 4 patients (10.5%), respectively. Most common complications included posterior synechiae (50% of eyes), macular edema (21.7%), and optic disc or preretinal neovascularization (13%). After amean follow-up of 11.2 months (range, 6- 58 months),inflammation was controlled, with a significant improvement in visual acuity (P=0.028). Recurrences developed in two patients (5.3%). Mean best-corrected visual acuity improved from 20/100 to 20/32.

Conclusions: Ocular tuberculosis usually presents with uveitis involving the posterior segment. The most common chorioretinal changes include multifocal non serpiginoid or serpiginoid choroiditis and periphlebitis in nearly 50% and 20% of affected eyes, respectively. Visual recovery is common following ATT with or without associated corticosteroid therapy.

Adult Coat's disease and uveitis

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Introduction: Presumed aquired retinal angiomatosis (Adult Coat's disease) and it's association with uveitis is rarely seen. Herewith we present an interesting patient presented to us with history of cervical cancer and hypopyon uveitis who was found to have adult Coat's disease.

Case report: A 56/F presented to us with 1mm of hypopyon, 360 degree posterior synechia, mature cataract in the left eye. B scan revealed dot vitreous echoes and retina on. Patient's baseline uveitis workup was negative and oncologist ruled out possibility of metastasis. Patient was managed with oral and topical steroids. After control of inflammation she underwent IOL implantation. In immediate postoperative period she developed sever AC reaction and iris bombe. After controling inflammation and IOP, fundus examination revealed yellow, crystalline, extensive subretinal deposits and peripheral retinal vascular changes suggestive of Adult Coat's disease. Patient gradually developed exudative retinal detachment. Due to very poor visual prognosis further interventions deferred.

Conclusion: Adult Coat's disease can present as a masquerade. In our case history of cervical cancer added to confusion.

Long term follow-up of patients with early acute Vogt-Koyanagi-Harada disease treated with high-dose systemic corticosteroids

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Purpose: To report long term follow-up of patients with early acute Vogt-Koyanagi-Harada (VKH) disease treated with high-dose systemic corticosteroids.

Materials and methods: Retrospective study including 30 patients (60 eyes) with early acute VKH disease (< 15 days). All patients underwent detailed ophthalmic examination. Fluorescein angiography (FA), indocyanine green angiography, and optical coherence tomography were performed for all patients at presentation, and when needed during follow-up. Mean follow-up was 26 months (Range, 24-38).

Results: Mean age of our patients was 32years. Twenty patients (66.7%) were female and ten patients (33.3%) were male. Patients were treated with oral corticosteroids (66.7%) or intravenous methylprednisolone followed by oral corticosteroids (33.3%). Mean duration of corticosteroid therapy was 8 months (Range, 6-12). Only 2 patients (6.7%) evolved into chronic disease and needed additional immunosuppressive. Final BCVA was ≤ 20/200 in 6.7% of eyes, and > 20/40 in 86.7% of eyes.

Conclusions: Early diagnosis and prompt treatment with high-dose systemic corticosteroids for at least 6 months allows favorable long term visual outcome in patients with acute VKH disease.

Clinical profile, visual outcome and treatment of posterior scleritis with focus on misdiagnosed cases in a tertiary center in India

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Purpose: To analyze the clinical profile of posterior scleritis cases in a tertiary eye care hospital in India.

Materials and methods: Retrospective analysis of all cases of posterior scleritis presenting to a tertiary eye care hospital between 2002-2012

Results: 47 eyes of 44 patients were analyzed. Mean age of the patients were 41.79 years (range 17 – 70 years). Unilateral involvement was seen in 41 (93.1%) patients whereas 3 (6.8%) patients had bilateral disease. Of all patients 25 (56.81%) patients were misdiagnosed initially and referred as clinical entities other than posterior scleritis which include central serous chorioretinopathy, optic nerve related disorders, choroiditis, choroidal mass, conjunctivitis etc. Delay in initiation of treatment because of misdiagnosis was calculated and visual outcome in such patients were analyzed. Common clinical presentations were diminution of vision 28(63.6 %), ocular pain 24 (54%), redness 23 (52.2%). In 13 (52%) cases among misdiagnosed cases (N=25), ocular pain was absent or minimal. Ultrasound B-scan (USG) was the most helpful diagnostic ancillary test for diagnosis of these cases. However in 20% of misdiagnosed cases USG (N= 25) alone was not sufficient and required additional imaging to confirm the diagnosis. Rheumatoid arthritis was most common cause of systemic association. 33 patients (77%) were treated with oral steroid and 14 (31.8%) patient required treatment with immunosuppressives. Only 8 (18.8%) patients required intravenous steroid administration. Recurrence of inflammation was noted in 7 eyes.

Conclusion: Posterior scleritis, one of the most under diagnosed clinical condition requires high degree of suspicion and clinical correlations for diagnosis.

Preliminary results of a Safety and Pharmacokinetic Study of gevokizumab in subjects with Behçet's Disease Uveitis.

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Purpose: Gevokizumab is a recombinant humanized monoclonal antibody that binds to human IL-1β and regulates activation of IL-1 receptors. Gevokizumab is intended to treat various autoinflammatory diseases,such as Behçet's disease uveitis (BDU). The objective of this exploratory study was to evaluate safety and further document the pharmacokinetics of gevokizumab in patients with BDU. Clinical activity was also assessed.

Methods: Patients with a history of BDU with posterior segment involvement experiencing an acute ocular exacerbation or considered at risk of subsequent exacerbation were randomly assigned to one of 3 open-label treatment groups receiving different combinations of 30 or 60 mg gevokizumab, IV or subcutaneously every month, on top of stable standardized immunosuppressive therapy and ≤20 mg/day prednisone equivalent.

Results: A total of 21 patients (mean age 34 years; 16 men and 5 women; 17 with acute exacerbation at study entry) were enrolled from 8 centers in Korea, Turkey, and Tunisia. Mean duration of BDU was 4 years. All 15 evaluable patients with an acute exacerbation at entry responded to gevokizumab, most within 1 week. First signs of improvement were observed as early as day 1. Two acute patients were not evaluable due to early withdrawal. Observed concentrations of gevokizumab were consistent with the values expected for these dosing regimens. Most adverse events were related to BDU; no serious adverse events related to gevokizumab were reported.

Conclusions: Gevokizumab was well tolerated. Acute exacerbations were rapidly controlled without the need for high-dose corticosteroids. The Phase III "EYEGUARD™" program with gevokizumab is ongoing.

Sarcoid uveitis in southern Europe. A descriptive analysis.

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Purpose: To describe demographical and clinical features, diagnostic tests, treatment and complications in sarcoid uveitis patients from Spain.

Material & methods: A retrospective descriptive non comparative study was carried out at a tertiary referral centre between 1989 and April 2011. Patients with sarcoid uveitis were identified from database and clinical records reviewed. Data regarding age, gender, evolution time, visual acuity (VA), ocular and extraocular clinical findings, diagnostic tests, treatment and complications were recorded for further analysis.

Results: Biopsy proven sarcoid uveitis were diagnosed in 26 patients during the study period. Mean age at diagnosis was 52 /-19.9 years. Nineteen women and 7 men, 84.6% Caucasians, with a mean evolution time of 4.7±6.1 years. Among affected eyes, initial VA was ≤0.1 in 80.1%. Panuveitis was the most frequent anatomical type (65.6%) and 73.1% were bilateral. ACE level was abnormal in 33.3%, chest X ray in 26.3% and chest CT in 54.5%. ACE determination together with Ga67 scintigraphy showed 81.8% sensitivity. Steroids were prescribed to all patients, 34.6% required classic immunosuppressives and 11.5% anti-TNF-alpha. Cataract (57.7%) and glaucoma (57.7%) were the most common complications and macular edema was present in 23% of affected eyes.

Conclusions: Adult Caucasian women with bilateral chronic granulomatous panuveitis are the most frequent profile of sarcoid uveitis in our population. ACE levels in combination with Ga67 scintigraphy seems enough sensitive for presumptive diagnosis. Despite apparent inflammatory control with steroids and methotrexate in most of the cases, complications are common leading to poor visual prognosis.

Evalution of microorganisms related with conjunctivitis and antimicrobial susceptibility

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Purpose: Bacterial conjunctivitis is characterized with rapid onset of conjunctival-redness, swelling of the-eyelid, and-mucopurulent discharge, diffuse pinkness of the conjunctiva, -In this study presence of bacterial pathogens among patients suffering from ocular discharge and pain was evaluated.

Methods: A total of 280 swab samples from patients admitted to Ahi Evran University Research and Teaching Hospital, OphthalmologyClinic,, with the symptoms of conjuctival redness, mucopurulent discharge were examined during the study period between January to August 2013. Swap samples were transported to the laboratory promptly, and inoculated onto -blood agar, chocolate agar, and Eosin Metylene Blue agar and incubated for three days at37 °C. Bacterial identification was performed by VITEK 2 Compact fully automated bacterial identification system. Antimicrobial susceptibility testing was performed using Kirby-Bauer disk diffusion method and by VITEK 2 Compact- according to CLSI.

Results: Among 280 conjunctival swab samples 18.5% bacterial strains were isolated.The distribution of the bacteria,*S.aureus* 3.2 %*S.pneumoniae* 1.07%*Moraxella* spp.1.78 %, 1 *Haemophilus* spp. 0.35 % *E.coli* 0.7%, *Pseudomonas aeruginosa* 0.7 % coagulase negative Staphylococcus (CNS) 10.7%, respectively. Among *S.aureus* strains 88.8% were found to be resistant only penicillin and methicillin/ vancomycin resistant strain was not detected. Methicillin resistance rate was 68.5% among CNS isolates. The most susceptible antibiotics against *E.coli* and *P.aeruginosa* were as follows; imipenem,aminoglycosides and piperacillin-tazobactam, respectively.

Conclusion: Culture remains controversial in the diagnosis of eye infections. Due to the high frequency of Gram-positive bacteria often found be as a component of the normal flora, evaluation of the clinical relevance of culture, delicate, avoid delays in the transport of laboratory samples to increase the likelihood of bacteria growth should be considered.

A rare case of *post-kala azar ocular leishmaniasis*

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Introduction: Post-kala azar dermal leishmaniasis is well-known in dermatogy as a fulminant immunologic and cutaneous reaction. Post-kala azar ocular leishmaniasis has been reported only a few times in the literature and represents a sight threatening condition which needs to be rapidly recognized and treated to avoid permanent visual loss. The pathogenesis of post-kala azar ocular leishmaniasis remains unclear. According to some report, ocular leishmaniasis panuveitis is thought to be part of HAART-induced immune restitution syndrome. The inflammatory reaction is often severe in these cases leading to blindness.

Case report: Here we present the case of a 40-year-old man, HIV positive on HAART, with a presumed diagnosis of post-kala azar bilateral granulomatous panuveitis. This patient, previously diagnosed with a visceral leishmaniasis in 2008, was seen at Moorfields Eyes Hospital with a rapidly progressive panuveitis. His initial visual acuity was counting fingers in both eyes. Complete investigations were negative (including aqueous and vitreous analysis). On anti-leshmaniasis therapy and systemic steroids, the visual acuity of the left eye improved to 6/9 but remained poor in the right eye. Based on the medical history, on the improvement on therapy and the exclusion of other common infections, a presumed diagnosis of post-kala azar ocular leishmaniasis was made.

Conclusions: In conclusion, a major immune reaction against lingering parasites may play a key role in the pathogenesis of this sight threatening and rapidly progressive condition. Both the infection and the immune reaction should be kept in mind and targeted when treatment is planned.

Pregnancy and abortion effect on chronic uveitis - a case report

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Introduction: It has been reported that pregnancy decreases activity of uveitis. We report an interesting case of a chronic intermediate uveitis which worsened during 1st trimester of her pregnancy and improved after abortion.

Case report: A 26/F presented with history of chronic intermediate uveitis and florid retinal neovascularization along superior arcade in left eye. Patient was put on oral steroids and inflammation brought under control. Patient developed pregnancy. Oral steroids were gradually tapered and pan-retinal photo coagulation was partially done after posterior subtenon's injection of steroid. After a week patient presented with worsening of vision. Examination revealed hypopyon and grade 3 vitritis. Infectious uveitis was suspected and AC tap was planned. But patient lost follow to follow up and returned after 2 weeks with history of spontaneous abortion. Patient had stopped all medications given for ocular problem. Examination revealed absence of hypopyon and decrease in vitreous haze. Patient was followed up for few days without steroids. The inflammation slowly returned to its prepregnancy level. Oral steroids and topical steroids were restarted.

Conclusion: Effect of pregnancy on non-infectious uveitis is still poorly understood phenomenon. In contrast to previous reports we presented a case of worsening of uveitis during pregnancy and improvement of uveitis after abortion.

Is cataract surgery safe in scleritis?

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Purpose: To report the outcomes of cataract surgery in patients with immune mediated scleritis

Methods: Retrospective chart review.

Results: 18 eyes of 16 patients M:F (4:12), were included. Visual acuity at presentation ranged from 20/30 to HM. All patients had a previous diagnosis of non-necrotising diffuse anterior scleritis. Three patients were diagnosed cases of rheumatoid arthritis while the etiology in all other cases was unknown. All patients received oral corticosteroids and four patients were on steroid sparing immuno-supressants. The scleritis was graded as quiescent at the time of cataract surgery.The time from diagnosis of scleritis to cataract surgery ranged from 2 to 82 months. Eight eyes underwent phacoemulsification; seven eyes underwent extra capsular cataract extraction, four eyes underwent manual small incision cataract surgery. Scleral incisions were placed in eight eyes. Eleven patients had postoperative visual acuity better than 20/60. Complications included increased anterior segment inflammation in three eyes in the immediate postoperative period. No reactivation of scleritis was noted in the early post-operative period.The mean follow up period was one month to seven years.

Conclusions: In our series, cataract surgery improved visual acuity without significant worsening of the clinical course of scleritis. We conclude that in inactive disease, cataract surgery can be safely undertaken.

Efficacy of intra-vitreal OzurdexTM in uveitic eyes with cystoid macular edema

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Purpose: To assess the efficacy of intra-vitreal OzurdexTM implant in the management of anterior or posterior uveitis with persistent cystoid macular edema.

Methods: Retrospective Chart Review

Results: Nine eyes of seven patients with uveitis and persistent cystoid macular edema underwent intra-vitreal Ozurdex Implant. Seven eyes of nine had posterior uveitis. Reduction of intra-ocular inflammation was noted in eight eyes. Decreased foveal thickness in optical coherence tomography was noted in all eyes at one-month follow-up. One patient had post procedure raised intraocular pressure, controlled with 2 anti glaucoma medications. Overall, improved patient satisfaction with decreased dependence on frequent instillation of topical and oral medications was noted.

Conclusions: Intravitreal OzurdexTM implant led to reduction of intra-ocular inflammation and reduction of foveal thickness.

Switching to golimumab after other anti-TNF failures in refractory uveitis.

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Purpose: To analyze the efficacy and tolerance of golimumab in patients with uveitis treated unsuccessfully with other anti-TNF.

Material & methods: Retrospective case series of uveitis patients refractory or intolerant to classic immunosuppressives and other anti-TNF drugs. Age, sex, uveitis etiology, previous treatments, and presence/absence of macular edema were recorded along with remission at final follow up.

Results: Five patients were included: Two juvenile idiopathic arthritis (JIA), one Ankylosing spondylitis (AS) and two Behçet disease (BD) uveitis patients. JIA were 2 girls 18 and 25 years with secondary failure to successive previous etanercept and adalimumab. Both required 3 dexamethasone implants for relapsing macular edema. After switching to golimumab, remission was achieved in both and macular edema resolved during 10 and 18 months of follow up, respectively. On the other hand, a 37 years man with unilateral recalcitrant anterior-intermediate AS-associated uveitis, previously refractory (etanercept, adalimumab, abatacept) or intolerant (infliximab, severe infusion reaction) were switched to golimumab, with mild favourable effect. Macular edema relapsed after golimumab commencement and new flare appeared in the fellow eye at 6 months. Two BD-associated uveitis men, 28 and 31 years relapsed during successive infliximab (secondary failure) and adalimumab (primary failure) treatment and then switched to golimumab. Partial remission was achieved in both, however continuous mild relapses including macular edema in one of them were observed after 7 and 5 months, respectively. No adverse events were detected during golimumab treatment in any case.

Conclusions: Golimumab can be an effective and well tolerated alternative in JIA refractory uveitis with previous failure to other anti-TNF drugs. However, golimumab efficacy in anti-TNF refractory or intolerant patients with other uveitis etiologies, as AS or BD, is not clear in our experience.

Scleritis posterior with panuveitis associated to influenza vaccine

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Introduction: Posterior scleritis establishes a slight subgroup within scleral inflammations. The 50% of scleritis are associated to autoinmune systemic diseases. However, up to a 7% cases are associated to infections, virus included. In a short percentage of the cases there is an important intraocular affectation that dissembles the diagnostic and it is in these cases where the B-scan ultrasound plays a fundamental role.

Case report: A male patient, 52 aged, assisted the Ophtalmology emergency department with red eye, pain and progressive loss of vision in his left eye in a week. He was diagnosed with conjunctivitis at the primary attention clinic five days before. The treatment applied was antibiotic and corticoids eye drops which it wasn´t effective.

He suffered from arrhythmia, valve disease and ictus, immunizing against the influenza 10 days before.

A diagnosis of panuveitis was made in the Ophtalmology emergency department initially. It is done B Scan ultrasound that shows pseudotumoral image. Therefore, it is applied as esclerouveitis pseudotumoral. The systemic complete research managed in collaboration with the Rheumatalogy service shows only an increase of the acute stage reactants.

We apply steroid systemic and usual topic treatments with remission complete after 10 months.

Once revised periodically, two years later patient felt asymptomatic and free of systemic associations.

Conclusions: The debut of this inflammatory ophthalmologists acute process days after the innoculation for antigens surface of the influenza virus in a patient without systemic immunologic pathotlogy leads us to thing that these attenuated virus are the guilty of the disorder.

Successful treatment of scleritis and panuveitis with rituximab in rheumatoid arthritis patients

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Purpose: To report on two patients with diffuse anterior scleritis and panuveitis who responded very well to rituximab treatment.

Materials and methods: Observational case series.

Results: Two patients presented at a uveitis clinic with diffuse anterior scleritis bilaterally. The first patient is 40 yrs old, with quiet palindromic rheumatoid arthritis on NSAIR treatment. Relapsing keratoscleritis developed, and later panuveitis. She was treated with corticosteroids, later with methotrexate, mycofenolat mofetil and adalimumab. This year rituximab was introduced; after the first application there were no signs of active inflammation in terms of scleritis or panuveitis. Follow up is 8 months. Second patient is 76 yrs old with rheumatoid arthritis for many years, treated with ethanercept, methotrexate and corticosteroids. Diffuse anterior scleritis developed bilaterally, with panuveitis in one eye, poorly responsive to high dose corticosteroids treatment. Ethanercept, as a possible cause of scleritis, was stopped, but this had no effect on the regression of scleritis. Rituximab was applied; after the first application there are no signs of inflammation. Follow up is 6 months.

Conclusion: There is a paucity of data in the literature regarding the efficacious treatment of inflammatory ocular disease, scleritis, peripheral ulcerative keratitis. Our results indicate very good and quick therapeutic response of aggressive, recalcitrant scleritis with panuveitis after the first course of treatment with rituximab.

Benign Reactive Lymphoid Hyperplasia presented with unilateral ptosis

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Purpose: To evaluate two patients presenting with ptosis in benign reactive lymphoid hyperplasia.

Method: The medical records of two patients with unilateral ptosis who were referred to Akdeniz University Ophthalmology Department were examined.

Results: Conjunctival hyperemia and follicular hypertopia and upper eyelid edema and mechanical ptosis were seen unilaterally in both of the patients. Incisional biopsy were performed in both patients. The lesions were characterized by polyclonal lymphoid cell infiltration and pathological diagnosis were benign lymphoid hyperplasia. Systemic steroid treatment was performed and the lesions were disappeared in two months. Systemic analysis was performed and no lymphoproliferative diseases were found. The patients were decided to be examined 6-months periodically.

Conclusion: Benign reactive lymphoid hyperplasia should be kept in mind in cases with acquired unilateral ptosis and careful inspection is essential for accurate diagnosis in such patients.

Visual outcome of ocular toxoplasmosis in an University Center in Argentina

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Purpose: To evaluate the visual outcome of patients with diagnosis of ocular toxoplasmosis (OT) in an University Center in Argentina.

Methods: Retrospective case series study. Clinical records of patients with diagnosis of active retinitis due to OT at Hospital Universitario Austral were included. Collected data included age, gender, visual acuity at baseline (VA), VA at the end of the episode, anterior inflammation, 2 or more vitreous haze, ocular inflammatory associated signs, primary or recurrent active retinitis, type of lesion, location, complications, and number of recurrences.

Results: 52 patients with OT were found. Active retinitis was observed in 39 patients with a total of 47 active retinitis events. Average age of occurrence of active retinitis events was 34.76 ± 17.26 years. Primary active retinitis was present in 22 patients whereas 25 have recurrent disease. VA at presentation was better than 20/40 in 22 episodes out of 47 (46.80%), whereas VA less than 20/200 was observed in 10 patients out of 47 (21.28%). Twenty four complications were detected in 15 patients. Exudative detachment occurs in 6 events with active retinitis in a central location out of 13 and in 2 events out of 26 where the lesion was peripheral (P=0.006). Final VA was better than 20/40 in 33 cases (84.61%) and less than 20/200 in 5 patients (12.82%) . Only 1 patient out of 10 with 1 complication had a final VA less than 20/200. Four out of 5 patients with 2 or more complications had a final VA less than 20/200. The difference of the final VA in these groups was statistically significant (P=0.022). Recurrences were observed during the studied period in 11 patients out of 29. Seven patients had 1 recurrence and 4 patients had two or more.

Conclusions: Final visual acuity was less than 20/200 in 12.82% of the patients. Greater number of complications was associated with worse final visual acuity. Twenty eight percent of patients developed at least one recurrence.

Ocular syphilis: case series (2000-2009) from two tertiary care centers in Montreal

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Purpose: To review ocular syphilis cases diagnosed and treated between 2000 and 2009 at Maisonneuve-Rosemont Hospital and Notre-Dame Hospital, Montreal, and to describe the demographics, clinical presentations, proportion of co-infection with HIV, treatment and outcome.

Materials and methods: Medical records of patients with positive treponemic serologic testing and who visited the ophthalmology department at Maisonneuve-Rosemont Hospital and Notre-Dame Hospital for ocular manifestations related to syphilis between the years 2000 to 2009 were retrospectively reviewed. Several data were compiled.

Results: 91 patients (80% males) were included in the study. The majority of cases were found in men aged 51-60 years old (26%) and 41-50 years old (17%). Around 30% of the patients were men who have sex with men (MSM). Snellen BCVA was converted to logMar notation. Pre-treatment mean was 0.42 (BCVA around 20/50) while post-treatment mean was 0.34 (BCVA around 20/40). The most common ophthalmologic diagnoses were all types of uveitis (anterior being the most frequent one with a proportion of 31%). Coinfection with HIV was found in 34 % of patients. Lumbar puncture was done in 55% of patients and VDRL serology was positive in 11% of those patients. The mainstay of treatment was intravenous penicillin in 75% of the patients. In about 85% of patients treated, no history of reinfection was noted.

Conclusions: Syphilis is known as the great masquerader. There has been a significant increase in the past ten years. It is primordial to keep this diagnosis in mind, especially since the treatment is readily available and has an excellent outcome.

Dexamethasone Intravitreal Implant in the Treatment of Recalcitrant Uveitic Macular Edema in the Absence of Active Inflammation

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Purpose: To examine the observational efficacy of the dexamethasone (DEX) intravitreal implant (Ozurdex®) in the treatment of non-infectious uveitic macular edema in patients with otherwise quiescent uveitis.

Materials and Methods: Retrospective chart review of twenty seven consecutive patients with persistent macular edema recalcitrant to standard short-term therapy despite quiescent non-infectious intermediate and posterior uveitis. Each patient was treated with a DEX 0.7 mg implant. Primary outcome measure was resolution of macular edema as measured by decrease in central macular thickness. Secondary outcome was change in visual acuity at 1, 2, and 3 months post-injection.

Results: Twenty seven eyes of twenty seven patients were included for analysis, with six of these patients receiving bilateral DEX implants. There was a statistically significant reduction in mean central macular thickness at 1 month post-DEX implantation (mean 278.9um, range 206-352) compared to baseline (mean 478.7 um, range 330-667um) ($p<0.0001$). There was a statistically significant improvement in visual acuity at 3 months (LogMAR 0.42; 20/50-1) compared to baseline (LogMAR 0.61; 20/80) ($p=0.0007$). There were no major complications following DEX implantation.

Conclusion: The DEX implant may be a safe and effective modality in the treatment of uveitic macular edema in otherwise quiescent uveitic patients.

Ultra-wide field fluorescein angiography in patients with uveitis

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Purpose: To evaluate the fluorescein angiography (FA) findings of uveitis patients by using Ultra-wide field FA (UWFA) with Optos®200Tx (Optos, Scotland, UK).

Methods: The UWFA was performed on 22 eyes of 11 patients diagnosed as uveitis (4 male, 7 female, average age; 44.7 years-old, 4 patients with sarcoidosis, 2 patients with Vogt-Koyanagi-Harada disease, and 5 patients with uveitis by unknown cause) at Nagoya City University hospital between May 2011 and May 2012.

Results: UWFA with Optos®200Tx allows us to obtain clearer and much wider FA images than that with conventional fundus camera. Vascular leakage and staining were observed in the peripheral fundus of all tested eyes by UWFA. There were four cases in which no marked change was found by ophthalmoscope, while diffuse leakage from the vessels in the far peripheral retina was found. In addition, it was able to take FA images in the eyes with poor mydriasis which was sometimes caused by posterior synechia of the iris.

Conclusions: FA findings in the peripheral fundus could be obtained by UWFA, which gave us more information including new findings of the inflammatory change caused by uveitis. UWFA could be utilized for one of the methods to evaluate the status of uveitis and the effect of the treatments.

Bilateral diffuse uveal melanocytic proliferation (B-DUMP) and B-cell lymphoma. A case report

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Introduction: To report a case of bilateral diffuse uveal melanocytic proliferation (BDUMP), a rare paraneoplastic syndrome, causing visual loss in a patient diagnosed with B-cell lymphoma

Case report: A 62 year old female, presented to the uveitis clinic complaining of blurring of vision in the left eye for one year with deterioration over the past six months.

On examination corrected vision was 6/6 in the RE and 6/18 in the LE with no signs of inflammation in the anterior and posterior segment of both eyes. Mild cataract was noted in both eyes.

Gray or grayish-brown lesions were found in the fundus in BE, and FFA revealed hyperfluorescence due to window defects associated with the retinal pigment epithelium damage that corresponded with the pigmented lesions. OCT showed areas of complete retinal pigment epithelium loss alternating with areas of thickened retinal pigment epithelium that corresponded to the window defects seen during FFA and absent autofluorescence seen during AF photography.

Patient was referred to the oncology service and later diagnosed with a B-cell lymphoma. She is currently receiving chemotherapy.

Conclusion: Neoplasms associated with BDUMP have been mostly carcinomas including ovarian, lung, gall bladder, cervical, kidney, pancreatic, breast, esophageal, and colorectal cancers. It may also be associated with melanocytic proliferation in other tissues. The cause is unknown but it has been postulated that there are factors released by the cancer or produced by the body in response to the cancer that causes the melanocytes to proliferate. Association with a B-cell lymphoma has not been previously reported

Diagnostic utility of mediastinal- lymph node biopsy in patients with Sarcoidosis related uveitis

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Purpose: To evaluate the role of mediastinal lymph node biopsy as a diagnostic tool in suspected ocular sarcoidosis.

Materials and Methods: consecutive patients followed at the Immunology Ocular Unit of Reggio Emilia hospital, affected by bilateral panuveitis and suspected sarcoidosis were evaluated with chest high-resolution computerized tomography (HRCT) and mediastinal lymph node biopsy.

Results: during a period of 12 months a precise histological diagnosis of sarcoidosis was obtained in 13 patients (2 males, 11 females, mean age 64 yrs). The mean diagnostic delay was 37 months. In 8/13 (61%) patients and 4/13 (31%) patients angiotensin-converting enzyme (ACE) and lysozyme were increased, respectively. Chest X-ray was positive only in 2/13 (15%) cases, while in 100% of cases both HRCT and biopsy resulted positive.

Conclusions: the histological exam of lymph nodes taken during mediastinoscopy is a useful tool to confirm the diagnosis of definite ocular sarcoidosis even in presence of negative chest radiography, and can make differential diagnosis with other forms of uveitis, aiding in therapeutic management of the patients.

Association analysis of HLA-DRB1 alleles with the development and clinical manifestations of sarcoidosis in a large Japanese cohort

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Purpose: The etiology of sarcoidosis is still uncertain, but the disease is currently thought to be triggered by various genetic as well as environmental factors. It is well established that sarcoidosis is associated with the human leukocyte antigen (HLA) class II genes, especially HLA-DRB1. The purpose of this study was to identify HLA-DRB1 alleles associated with the development and clinical manifestations of sarcoidosis in a large Japanese cohort.

Materials and Methods: Five hundred and twenty-four Japanese patients with sarcoidosis and 561 Japanese healthy controls were recruited. Genotyping of HLA-DRB1 was performed by Luminex reverse sequence-specific oligonucleotides using Labtype SSO kit from One Lambda Inc. (Canoga Park, CA).

Results: A total of 33 HLA-DRB1 alleles were identified in this Japanese population. The frequencies of HLA-DRB1*0803 and DRB1*0901 were significantly increased in patients with sarcoidosis compared with healthy controls (DRB1*0803: 17.3% vs. 7.5%, Pc = 1.2 × 10-10, OR = 2.58; DRB1*0901: 19.4% vs. 13.7%, Pc = 0.013, OR = 1.51). The carrier frequency of the HLA-DRB1*0803 allele was found to be 4.05-fold higher in sarcoidosis patients with cardiac involvement than in healthy controls (24.7% vs. 7.5%, Pc = 1.3 × 10-10).

Conclusions: This study suggests that HLA-DRB1*0803 and DRB1*0901 play an important role in the development of sarcoidosis in the Japanese population, and HLA-DRB1*0803 may have an effect on cardiac involvement of sarcoidosis patients.

Caterpillar hair induced pars planitis

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Purpose: To report two cases of pars planitis associated with caterpillar hair entry in to the eyes.

Case reports: Two patients reported to our outpatient department with history of pain, redness and irritation and were diagnosed with corneal intrastromal caterpillar hair with anterior chamber reaction and were treated accordingly. On close follow up over a period of 1 year they developed vitritis and pars plana exudates in the affected eye. All the laboratory investigations were with in normal limit and ultrasound biomicroscopy showed presence of cilia. Intraocular inflammation in both the patients responded well to oral steroid.

Conclusion: The presence of intracorneal hair was a significant risk factor for the intraocular penetration and subsequent intraocular inflammations. So a meticulous history and examination aided with complete removal of hair and prompt use of steroids help in preventing grave manifestations of caterpillar hair injury.

Case series of CMV hypertensive uveitis with few atypical cases.

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Purpose: To study cases of hypertensive anterior uveitis caused by cytomegalovirus in immunocompetant patients.

Materials and methods: We retrospectively reviewed case records of 6 immunocompetent patients diagnosed with "CMV hypertensive uveitis" examined between 2007 and 2013. All the patients were positive for CMV by Polymerase chain reaction (PCR). Selected cases were screened for other infectious agents like mycobacterium tuberculosis (M TB) and Varicella Zoster (VZV). Patient's demographics, history, number of flare ups, data from clinical examination, investigations and treatment was noted.

Result: 8 eyes of 6 patients, 5 males and a female have been studied. M TB and VZV genome was also found along with CMV in 2 eyes. Average maximum elevation of IOP noted was noted to be 44mmHg. Duration of symptoms ranged between 1 month and 6 years at presentation. Central granulomatous, pigmented or hyalinised KPs were noted in 3 patients. Moth eaten or honey comb iris atrophy was seen in 2 eyes. Number of flare ups reduced after starting oral ganciclovir therapy in all patients. One patient positive for CMV and VZV developed scleral thinning at the site of bleb and needed immunomodulatory therapy along with scleral patch graft.

Conclusion: Granulomatous hypertensive anterior uveitis with hyalinized or pigmented KPs and moth eaten iris changes may suggest CMV etiology. It is also prudent to consider AC tap for CMV-PCR in hypertensive uveitis even though clinical picture is not suggestive of viral anterior uveitis provided other causes of secondary glaucoma has been ruled out.

Early introduction of systemic immunosuppressive therapy in paediatric intermediate uveitis: a better outcome?

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Purpose: Untreated, intermediate uveitis may significantly alter the vision. Limited numbers of studies in the literature treat of paediatric intermediate uveitis and its optimal management. The purpose of this study is to describe a short series of children with intermediate uveitis and evaluate if an earlier introduction of systemic immunosuppressive agent could influence their visual outcome.

Materials and Methods: This is a retrospective analysis of patients under 16 years old, diagnosed with intermediate uveitis between 1999 and 2011 at the Maisonneuve Rosemont Hospital and Ste-Justine Children Hospital in Montreal, Canada.

Results: Our study includes 19 patients (34 eyes). The mean age was 8.5 years old and 58% of patients were male. 79% of our patient were bilaterally affected. At the diagnosis, the best corrected visual acuity (BCVA) of 71% of the afflicted eyes was 20/40 or better; between 20/50 and 20/150 in 18% and 12% of the eyes were legally blind (BCVA ≤ 20/200). After 5 years of follow up, 91% of the eyes had a BCVA of 20/40 or better; 11% had a BCVA between 20/50 and 20/150 and none of the eyes were blind. Among 4 therapeutic options, 26.3% of the patients received no systemic treatment; 42% received a periocular injection of corticosteroids; 50% received systemic corticosteroids and 25% received a second line immunosuppressive agent. The main complication in our series was the cataract in 32% of the patients. 16% of our patients developed ocular hypertension and 11% presented a cystoids macular oedema.

Conclusions: In our series, systemic immunosuppressive drugs have been used with success in a good proportion of patient. However, they have not reduce the frequency of the complications such as cataracts and glaucoma.

Posterior Scleritis: Presentation, Clinical Course and Visual Outcome

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Purpose: To describe the clinical features, systemic association and visual outcome in a consecutive series of patients with posterior scleritis.

Materials and Methods: Descriptive case series of patients diagnosed with posterior scleritis between 2009 and 2012. Data collected included medical history, age, gender, duration of symptoms, associated systemic diseases, diagnosis and treatment prior to referral, medical management, visual outcome, recurrences and follow-up period.

Results: Included were 14 female patients and one male patient. Mean age at diagnosis was 40 years (range: 8 -80 years).- Mean follow-up period was 17 months. The majority of patients (93.3%) presented with anterior and posterior scleritis and all were referred with a diagnosis other than posterior scleritis. Mean duration of symptoms before diagnosis was 46 days. Posterior segment signs were observed in 13 patients (86.7%) and included papillitis in 53.3%, choroidal folds in 33.3 % and retinal striae in 20%. Two patients had no detectable clinical signs of the disease. Associated systemic disease was seen in 40% of the patients. Visual acuity was preserved in all the patients. Half of the patients were treated with dual immunosuppressive agents whereas 40% received steroids only. Third of the patients suffered from posterior scleritis recurrences and 80% of the patients remain on long-term immunosuppressive therapy.

Conclusions: Posterior scleritis is a rare and under-diagnosed disease that can present with preserved visual acuity and without signs in the posterior segment. High level of suspicion is required and a B-scan ultrasound examination is to be considered in anterior scleritis or unexplained severe eye pain.

Optic neuritis and rapidly progressive necrotizing retinitis as the initial signs of subacute sclerosing panencephalitis: A case report with clinical and histopathologic findings

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Introduction: The purpose of this study is to report a case of subacute sclerosing panencephalitis (SSPE) presenting first with optic neuritis and rapidly progressive necrotizing retinitis at the posterior pole.

Case report: A 15-year-old girl was referred after rapid loss of vision due to optic neuritis and macular necrosis in the right eye. Fluorescein and indocyanine green angiography revealed optic disc hyperfluorescence, hypofluorescence corresponding to the retinal necrosis, and retinal vascular staining and leakage at the posterior pole. Contralateral involvement with rapidly progressive optic neuritis and macular necrotizing retinitis prompted retinochoroidal biopsy of the right eye, which revealed necrosis of inner retinal layers and perivascular lymphoplasmocytic infiltration with intact choroid and outer retina without any findings of inclusion bodies, microorganisms, or atypical cells. The diagnosis was based on histopathologic findings consistent with SSPE, and detection of elevated measles antibody titers in cerebrospinal fluid and serum and was confirmed by development of typical EEG pattern at 6 months and neurological symptoms at 4 years of follow-up.

Conclusion: Clinicians need to be aware that optic neuritis and necrotizing retinitis maybe the presenting features of SSPE.

Hereditary Retinal Degenerations Masquerading as Posterior Uveitis

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Introduction: The masquerade syndromes comprise a group of disorders that occur with intraocular inflammation and are often misdiagnosed as a chronic idiopathic uveitis. Hereditary Retinal Degenerations (HRD) are a group of diseases that lead to progressive degeneration of the photoreceptor cells and may have signs of intraocular inflammation such as cells in the vitreous and cystoid macular edema (CME). HRD are one of the causes of nonmalignant masquerade syndromes. We report two patients with HRD masquerading as Posterior Uveitis.

Case report: Case 1: 21 year old woman with bilateral subretinal white spots, refractory CME and vitreous cellularity. HLA-A29. During 18 months has been treated with high-dose prednisone, azathioprine and methotrexate, resulting in secondary Cushing's syndrome. Case 2: 38 year old woman with bilateral subretinal white spots, refractory CME and vitreous cellularity. HLA-A29 . For two years, the patient was treated with systemic corticosteroids, methotrexate and intravitreal Ranibizumab with no response. The patients were diagnosed with Posterior Uveitis and referred to our hospital for evaluation and treatment. The results of the history, physical examination, diagnostic tests and genetic studies are consistent with HRD. Antiinflammatory and immunosuppressive treatments were suspended. We report the response of CME to treatment with systemic acetazolamide and topic brinzolamide.

Conclusions: Hereditary Retinal Degenerations are disorders that may present with vitreous cellularity and chronic cystoid macular edema and may be misdiagnosed as white dot syndromes. The antiinflammatory and immunosuppressive therapy is unnecessary and ineffective in such cases of nonmalignant masquerade syndromes.

Cirrus SD-OCT performance measuring choroidal thickness in acute central serous chorioretinopathy and healthy eyes

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Purpose: To evaluate the SD-OCT Cirrus(Carl Zeiss Meditec, Dublin, CA) without EDI performance to examine choroidal thickness in healthy subjects and in acute central serous chorioretinopathy (CSC) patients.

Methods: Prospective study, in healthy subjects and in acute CSC patients, examinated during April 2013 at the Ophthalmology Service of the University Hospital of La Candelaria. Each patient underwent one high definition line raster scanning using SD-OCT without enhancement software. Two independent observers measured manually choroidal thickness from the posterior edge of the retinal pigment epithelium to the choroid/scleral junction at 500µm intervals up to 2500µm nasal and temporal to the fovea.

Results: Ten consecutive patients with acute CSC (10 eyes) and nine healthy subjects (9 eyes) were examined. The mean age of CSC group was 47±14.41 years. In patients with CSC only in three cases (30%) all section points were measurable and in 50% of cases at least 8 section points were measured. Only in one case, was impossible to measure any point. However, in healthy patients at least 8 section points were measurable in all cases. The mean subfoveal choroidal thickness of eyes with CCS (351,75 ± 80,57µm)was thicker than in healthy subjects (278,60 ± 66,59µm).

Conclusions: The submacular choroid is thicker in patients with acute CSC. This finding provides additional evidence that CSC may be caused by increased hydrostatic pressure in the choroid. SD-OCT Cirrus (Carl Zeiss Meditec, Dublin, CA) without EDI can measure choroidal thickness with minimal interobserver variability in CSC, but with limitations.

Choroidal granulomas visualization by Enhanced Depth Imaging Optical Coherence Tomography

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Purpose: To assess the possibility of visualizing choroidal granulomas by Enhanced Depth Imaging Optical Coherence Tomography (EDI-OCT) and to describe their OCT characteristics.

Materials and Methods: Combined indocyanine green angiography (ICG) and EDI-OCT images of sarcoid, tubercular and Vogt-Koyanagi-Harada choroidal granulomas were reviewed. Lesions were classified according to ICG as full-thickness (FT) or non-full-thickness (nFT) and as "small" or "large". EDI-OCT scans were evaluated by two independent operators to identify visible lesions, to classify them as FT or nFT and to record their characteristics. The agreement between ICG and OCT and the interobserver agreement were assessed by Cohen K test. A correlation between lesion size and OCT features was determined by Fischer test.

Results: 34 lesions from 8 patients were analyzed. 100% of the granulomas were detectable by EDI-OCT. Lesions were classified as FT in 85.3% and 73.5% of the cases on ICG and OCT respectively (K=0.64). Interobserver agreement was good for all the OCT characteristics (K>0.8). 100% of nFT lesions were located in the inner choroid. 100% of the lesions generated a backscattering effect. "Large" granulomas prevalently resulted: FT (p=0.02), roundshaped (p=0.02), hyporeflective (p<0.01), homogenous (p=0.02), with defined margins (p<0.01).

Conclusions: EDI-OCT resulted suitable for the detection of choroidal granulomas. OCT features seemed influenced by the granulomas size, except for backscattering. Backscattering could be helpful for the identification of these lesions on OCT.

Spectral domain ocular coherence tomography features in paediatric cases of active and healed toxoplasmic retinochoroiditis

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Purpose: To present atypical spectral domain ocular coherence tomography (SDOCT) features in a case series of 3 paediatric patients with active or healed toxoplasmic retinochoroiditis.

Materials and Methods: Observational series of 3 paediatric patients with toxoplasmic retinochoroiditis. Serial SDOCT scans showing features of toxoplasmic retinochoroiditis in the acute and resolved stages in 2 cases and an unusual pattern of scarring following toxoplasmic retinochoroiditis in the third.

Results: We report the novel finding of a subretinal fluid cavity associated with a macular lesion. The subretinal fluid resolved to leave a well-demarcated rectangular outer retinal cavity, which is also a previously undescribed finding. In case 2 there is a hyperreflective focus sitting on the inner retina overlying an old scar adjacent to a new inflammatory focus, with outer retinal disorganisation connecting the 2 lesions. Vitreo-retinal interface hyperreflective foci have been described in adults but not specifically in children. Case 3 shows a resolved lesion resulted in an elevated scar and an established epiretinal membrane leading to a spoke-like appearance. This is not consistent with any of the usual patterns of scarring following healed toxoplasmic retinochoroiditis.

Conclusion: The SDOCT appearances described in these cases of toxoplasmic retinochoroiditis, both in the active and healing phase show features that have not previously been reported in children, which may assist in making an earlier diagnosis. We also present SDOCT features that have not been previously reported as a feature of active or healed toxoplasmic retinochoroiditis.

Vogt-Koyanagi-Harada disease in Mexican Mestizo children

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Purpose: Describe clinical characteristics, treatment and outcome in Mexican Mestizo children with Vogt-Koyanagi-Harada disease (VKH)

Material and Methods: Retrospective review of 15 clinical files of children with VKH seen in a 16 yr. period at Asociación Para Evitar la Ceguera en México.

Results: 11 female, ages 11.46±3.83 years (range 2-16), follow-up 61.47±84.28 months, delay in diagnosis 4.44±4.73 months. Stages at admission: 11 in uveitic stage, 2 recurrence and 2 in convalescent. -5 patients presented prodromic manifestations. Initial VA mean 20/40- (range CF-20/20). Final VA mean of 20/30 (NLP-20/20). Prodromal manifestations: tinnitus (13.3%), hipoacusia (6.7%), headache 33.3%). Initial manifestations: serous retinal detachment (46%), iridocyclitis (73%), KP's (66%), posterior and anterior synechia in 40% and 26%. Convalecent stage manifestations:- sunset glow (90%), numular scars (83%), peripapillary atrophy (50%), pigment dispersion (53%) and subretinal fibrosis (16%). Vitiligo (13.3%), poliosis (3.3%). 60% received systemic steroids and/or immunosuppressive drugs, in 4 patients IV steroids were used in the uveitic stage, periocular steroids in 66%. 23% requiered surgery: cataract extraction, Ahmed valve implant, vitrectomy, iridectomy and pupiloplasty. Complications: cataract (40%), glaucoma (10%), ocular hypertension (OHT) (13%). 20% recurred were correlated with no --immunosuppressive therapy either at admittance or during follow up. ($p<0.002$ and $p<0.016$) Final VA ≤ 20/200 was related to subretinal fibrosis ($p<0.017$) and OHT ($p<0.010$).

Conclusion: This is the largest pediatric VKH report in the literature with the youngest patient. Better VA was achieved in patients who received IV steroids and immunosuppresive treatment. Worst visual prognosis was related to subretinal fibrosis and OHT.

Combined Depth Imaging of Choroid

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A) Aim: Purpose:To study the structural visibility using Spectral Domain – Optical Coherence Tomography in patients with uveitis using normal, Enhanced Depth Imaging (EDI) and Combined Depth Imaging (CDI) techniques.Methods: Fifty Eight (58) eyes of fifty (50) patients (21 males, 29 females) between age group 9 – 82 years with uveitis identified clinically underwent SD – OCT using normal, EDI and CDI scanning techniques. SD – OCT scanning was done in the same area of interest for each patient. Results: There was no statistical difference between detection of vitreous changes in normal and CDI techniques (p &amplt; 0.05). Also, there was no statistical difference between choroidal visibility in patients with EDI and CDI techniques (p &amplt; 0.05). Conclusion: CDI technique alone might provide a good structural visibility compared to normal and EDI scanning done separately in patients with uveitis with posterior segment pathology.

Inmune recovery uveitis after HAART treatment

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Introduction: Inmune recovery uveitis (IRU) is an intraocular inflamatory reaction that occurs in patients with an inactive CMV retinitis area, when the linfocitic counts increases after HAART therapy. It has a variable incidence, with a prevalence around 20 %. The disorder usually begins at 8 weeks after treatment was started. IRU is usually treated with cortecoesteroids, but depot presentations are controversial by the risk of reactivation. Also Valganciclovir can be used in IRU as a treatment cause reduce the antigenic charge.

Case report: Male, 47 years old, presented to us with cachexia, chronic diarrea, fever and decrease of VA from three month. In his medical history, we found the diagnosis of HIV in 1996, with no treatment or follow up. At the ophthalmological examination we found VA OD: 0,3 OI: 0,4. At fundoscopy we found a CMV active retinitis area, phlebitis and paramacular woolen spot on OD. Blood test marked a T CD4 : 51 cel/µl Antigenemia CMV 430 cel/200.000. Remeaning test was negative. Retinitis by CMV was stablished as a diagnostic. Valganciclovir and HAART therapy was started. 3 months later he came refering a decrease of VA OD (OD: 0,1, OI 0,6). We found vitritis and macular edema. We thought in a IRU and start treatment with transeptal triamcinolone.

Conclusions: The IRU is an entity currently less frequent due to better screening and treatment programs for HIV patients, so these pictures we can go unnoticed and therefore migdiagnose and increase the complications.

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Atipical Neurorretinitis course in chilhood

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Introduction: neuroretinitis (NR) is an inflammatory disorder characterized by presenting a papilledema with macular star formation . There are multiple causes associated, the most likely an infection . Other causes may be described like postviral autoinmune diseases, although most often are idiopathic . Usually it is a self-resolutive process, over a period of 8-12 weeks, presenting final VA>20/40 in 90% of cases.

Case report: female patient, 11 years old, that is send to us as a consultation for papilledema in the right eye (OD) of 3 days duration . The patient had a viral disease previously with left lateral cervical lymphadenopathy . Her VA was 0.3, showing a marked papilledema, lipid exuding toward the macular área. Neuroretinitis was diagnosed and systemic examination was performed, which was normal . Initially acquired an expectant attitude, but later was treated empirically with corticosteroids and systemic antibiotics due to increased edema and exudation. After a year of evolution, the patient has VA 0.4, with chronic pallid swelling of the optic nerve and alteration in the IS / OS segment in the macula.

Conclusions: benign evolution was described for most of these patients, but sometimes the NR can result into a serious complications . In any of these cases (like the one we have presented a very severe papilledema) could be applied early and empirical treatment, although most patients show excellent recovery without treatment, thereby trying to minimize the damage.

Solitary choroidal granuloma as an initial manifestation of systemic sarcoidosis

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Introduction: Sarcoidosis is a multisystemic non-caseating granulomatous disorder of unclear etiology. The incidence of ocular involment in sarcoidosis has been estimated to be 25-63%. Posterior segment findings are seen in approximately 25% of patients with ocular involment. The incidence of choroidal granulomas in ocular sarcoidosis is about 5,5%.

Case report: A 73-year-old white man presented with a 4-week history of painless blurred vision and metamorphopsia in his right eye. The personal and family history was unremarkable. No afferent pupillary defect was detected. Intraocular pressure was within normal limits. Anterior segment examination revealed cataracts and wide anterior chamber with no cells or flare. The vitreous was clear with no cells or opacities. Funduscopy of the right eye evidenced a retinochoroidal elevation in the macula with exudation and subretinal fluid. Ultrasound B-scan confirmed a localized retinochoroidal elevated lesion with high surface reflectivity and absence of internal reflectivity and a serous retinal detachment surrounding the lesion. The fluorescein angiography findings were hypofluorescence from blockage of the choroidal vasculature with late leakage and staining. Laboratory tests showed an elevated serum angiotensin-converting-enzyme (ACE 86U/L) and Mantoux test was negative. SPECT-CT study with 67Gallium evidenced uptake suggestive of sarcoidosis. Bronchoscopy with lymph nodes biopsy showed noncaseating granulomatous inflammation.

Conclusions: In our case, the ocular examination was the tool for the diagnosis of a systemic disease such as sarcoidosis, which presented a solitary choroidal granuloma as the only clinical manifestation, despite its low incidence. Early diagnosis led to early and specific treatment, which improved the prognosis.

Recurrent uveitis associated with streptococcal pharyngitis and serous otitis media in a pediatric patient

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Introduction: Poststreptococcal syndome uveitis is a disease of young patients (more than 50% younger than 15 years). Immune mechanisms could be involved in the pathogenesis of this disorder. Although it commonly presents as an anterior nongranulomatous uveitis, posterior segment findings are observed in some patients.

Case report: A 6-year-old male presented to the emergency department having pain, redness and blurred vision in his left eye. He reported history of otitis media. Slit-lamp examination revealed acute nongranulomatous anterior uveitis and dilated fundus examination demonstrated a bilateral papillitis. Patient was consulted with pediatricians and a physical examination was performed. Laboratory tests showed elevated C-reactive protein and anti-streptococcal lysin O titles.

The patient was diagnosed with streptococcal pharyngitis and bilateral serous otitis media. Other investigations revealed no other systemic abnormalities. The patient was treated with topical corticosteroids, mydriatics and sistemyc antiobiotics, and the inflammatory activity was controlled. Three months later, he presented with a recurrence of otitis media and anterior uveitis in his left eye. The patient received treatment and it was temporarily effective. Finally he underwent adenoidectomy, tonsillectomy and insertion of ventilation tubes (grommets) . Over a 3-month follow up, there has been no recurrence.

Conclusion: Uveitis is an infrequently reported manifestation of poststreptococcal syndrome. It is not well recognized by general ophthalmologists, because ocular manifestations usually appear several weeks after the onset of systemic disease. Therefore, poststreptococcal syndrome uveitis should be looked for in acute bilateral nongranulomatous uveitis, especially in children and young patients.

Macular characteristics of patients with ankylosing spondilitis without uveitis history

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Purpose: To evaluate macular charecteristic of patients with ankylosing spondylitis without any uveitis history.

Materials and Methods: In Uvea-Behçet's Division of Deparment of Ophthalmology of Afyon Kocatepe University Medical Faculty, 46 ankylosing spondilitis patients examined. Central subfield thickness, Cube volume, cube avg thickness measurements done by optical cohorence tomography.

Results: 8 female 38 male patients. Mean age was 40,28 ± 11,36 (19- 66) years. Mean central subfield thickness was 258,33 ± 17,48 microns. Mean cube volume was 10,39 ± 0,44 mm3. Mean cube avg thickness was 288,71 ± 12,13 microns.

Conclusions: It seems that there is no macular characteristics changes in ankylosing spondilitis patients without uveitis history.

Granulomatous uveitis secondary to previous practice tattoo

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Introduction: Anterior uveitis is described in the literature as granulomatous reaction after the increasingly common practice of tattooing. We report the case of a patient of 48 years who presented bilateral granulomatous anterior uveitis and ultimately related to the practice of a previous tattoo .

Case report: 48 year old patient presented to the emergency of ophthalmology clinker hospital with blurred vision and bilateral painful red eye . On examination was found bilateral VA reduction (right eye 20/25 and left eye 20/30) and bilateral granulomatous anterior uveitis . During questioning, the patient said he had a red tattoo on left supramalleolar area for a year and had introduced progressively inflammatory signs in it. Tattoo biopsy showed a granulomatous reaction . Within the study of it was generally a blood test was normal, negative PPD, normal chest radiograph, negative viral serology, ANA and rheumatoid factor negative and negative sarcoidosis study . He was treated with topical corticosteroids and cycloplegic with inflammatory clinical improvement . Is pending tattoo removal.

Conclusions: Tatto is a common practice in our population. Oftalmologyst must be aware to the skin backgrounds of the uveitic pacients. Tattoo could be a increasing causes of ocular inflamation.

Polyangeitis Nodosa. Atypical onset with ocular involvement.

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Introduction: We report the case of a man of 79 years with a bilateral sclerouveitis as unusual onset form of Polyarteritis Nodosa.

Case report: The patient presented, in absence of systemic symptoms, with a subacute bilateral orbital-episcleral inflamatory process. It subsequently was complicated with glaucoma secondary to elevated episcleral venous pressure, and ciliochoroidal effusion. He was treated with high-dose oral corticosteroids with complete resolution. Recurred after two months as episcleritis and bilateral nongranulomatous anterior uveitis associating carpal and proximal interphalangeal oligoarthritis, panniculitis, constitutional symptoms, and elevated acute phase reactants. A skin biopsy was diagnostic of polyarteritis nodosa.

Conclusions: We illustrate a unusual form of debut of the patient with polyarteritis nodosa. Although there was no evidence of intraocular inflammation until the second outbreak, due to the nature of the disease is possible that in the pathogenesis of choroidal detachment, besides congestion transmitted to vortex veins and reduced in the transscleral diffusion, there was some hematoocular barrier disruption at the level of choriocapillaris by subclinical inflammatory phenomenon. It is appropriate to consider systemic vasculitis in the differential diagnosis of uveitis, especially in the presence of orbital connective tissue inflammation.

Presumed Ocular Tuberculosis

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Purpose: To present a case series of presumed ocular tuberculosis (TB) with different clinical manifestations.

Materials and Methods: Retrospective review of the patients diagnosed with presumed tuberculous uveitis at Hospital Egas Moniz uveitis clinic from January 2011 to June 2013. Presumed ocular TB was defined as the presence of suggestive ophthalmologic findings, positive test result for latent TB (tuberculin skin test or/and QuantiFERON TB Gold Test) and positive response to antituberculosis treatment (ATT). The presence of pulmonary TB, the time to diagnosis, the predominant site of ocular inflammation, the initial and final corrected distance visual acuity (CDVA), the therapy performed, the complications and relapses were assessed.

Results: Ten patients were included with a mean age of 56.82 (range 37-78 years) at diagnosis. Three patients presented with anterior uveitis, two patients with multifocal choroiditis, two with serpiginous-like choroiditis, two with retinal vasculitis and one patient with optic disk tuberculoma. In most patients (70%) ocular involvement was bilateral. No patient had evidence of pulmonary TB. The patients underwent a 6 to 9 month course of ATT. Six patients underwent concomitant systemic corticosteroids. Average delay from ocular disease onset to uveitis clinic referral was 98.38 months. Mean initial CDVA was 0.39 and at the last follow-up was 0.78. The main complications were cystoid macular edema (3 patients) which improved after ATT and cataract (3 patients). There were no recurrences with a mean follow-up time of 6.4 months after ATT.

Conclusions: TB should be part of the differential diagnosis in patients with suggestive uveitis and no evidence of pulmonary involvement. Prolongued ATT (9 months) with or without systemic corticosteroids was effective in controlling ocular inflammation and reducing recurrences.

Development of a Bayesian belief network for the differential diagnosis of anterior uveitis

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Purpose: To construct a Bayesian network-based decision support system to help in the differential diagnosis of anterior uveitis, based on demographic characteristics, clinical examination and ancillary test results.

Materials and Methods: data of the demographic characteristics, clinical findings and laboratory results were obtained after performing a systematic review of the literature. Case series including more than 20 patients with a single etiology of anterior uveitis, or more than 50 patients with anterior uveitis of any cause were included. Searches were performed in Medline, EMBASE, LILACS and Proceedings of the Association for Research in Vision and Ophthalmology. Finally, in order to define the prevalence of each of the different causes of anterior uveitis in the Moorfields population, we reviewed the notes of all patients that received a diagnosis of anterior uveitis during 2012, and classify them according to their diagnosis.

Results: Prevalence of each of the demographic characteristics, clinical findings and ancillary tests results in each of the diagnosis was calculated by meta-analysis of the case series findings. Using this, and the prevalence of each of the conditions in our population, a Bayesian network was developed using the Elvira software.

Conclusions: The Bayesian network developed may help clinicians with the differential diagnosis of anterior uveitis. Additionally, it can help with the selection of the diagnostic tests performed, by avoiding those that will not change post-tests probabilities. Prospective validation is required before this Bayesian network can be used clinically.

The value of electrophysiological testing in the diagnosis and management of unusual "posterior uveitis" cases.

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Introduction: When the underlying pathophysiology and natural history is uncertain in posterior uveitis, electrophysiological testing can not only provide diagnostic information, but also objective functional data to assist evaluation of disease severity and response to treatment.

Case reports: Five cases with unusual posterior segment clinical picture are presented where electrophysiological assessment helped reveal the nature of the underlying pathology, degree of retinal dysfunction, disease progression or the response to treatment. A 32-year-old female with unilateral paravenous chorioretinal atrophy (PVCRA), a child with idiopathic retinal vasculitis and neuroretinitis (IRVAN), a 39-year-old man with diffuse unilateral subacute neuroretinitis (DUSN), a patient with birdshot chorioretinopathy (BCR), and a case with ambiguous signs of punctate inner choroidopathy (PIC). Full-field electroretinography (ERG) was performed to incorporate the Standard responses recommended by the International Society for Clinical Electrophysiology of Vision. Macular function was assessed with pattern ERG and optic nerve function with pattern VEP. Our patients had good, stable visual acuities (i.e. 6/6-6/9) during the follow-up period. However, the degree of retinal dysfunction varied. The PVCRA patient had generalised rod, cone and RPE dysfunction with macular involvement. The IRVAN patient had severe peripheral retinal ischaemia with mild generalised cone dysfunction. The DUSN case had macular dysfunction. The retinal function of the BCR patient deteriorated with disease progression but showed dramatic improvement following treatment with prednisolone and mycophenolate mofetil. The "unusual" PIC patient revealed generalised rod/cone dysfunction. The ERG results are discussed in the context of the relevant literature.

Conclusion: The objective data provided by electrophysiological examination can assist diagnosis and management in challenging cases of "posterior uveitis".

Acute- retinal epithelitis or krill disease: A case report

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Introduction: This very rare condition was first described by Krill and Deutman in 1972. Acute retinal pigment epitheliitis (ARPE) is a self-limited disease of the RPE that typically occurs in young, otherwise healthy adults. The acute occurrence and its self-limiting course has suggested that a viral infection could be the origin of the disease.

Case report: A 33 year-old male was referred for sudden blurred vision of his left eye. Best-corrected visual acuity in his right eye was 10/10 and 1/10 in his left eye. He reported viral syndrome with fever and arthralgia fifteen days before. On ophthalmoscopic examination, there was a yellow foveal lesion with vitelliform appeareance. OCT revealed an abnormal foveal hyperreflectivity involving the outer nuclear layer and photoreceptors, with disruption of the IS/OS junction of the photoreceptors and the inner band of the RPE layer. The macular campimetry had small central defect in left eye. The inner segment and outer segment layers typically showed restoration of normal anatomy with disease resolution in two month. AFG performed inicially was normal but one month later, whilst the sub-retinal deposits were resolving, showed point transmission hyperfluorescent suggesting alterations of the pigment epithelium. The visual acuity is 20/20 after one year, but patient referred subjective central scotoma.

Conclusions: ARPE has a self-limited course, usually with complete resolution over a 6- to 12-week period. Patients usually regain good vision without treatment. A viral infection could be the origin of the disease with transient dysfunction of the retinal pigment epithelium.

Punctate Inner Choroidopathy (PIC): unilateral relapses, bilateral choroidal neovascularization (CNV) and response to Dexamethasone Implant and Bevacizumab

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Purpose: To describe a relapsing PIC and its therapeutic approach

Case Report A 45 years old myopic woman, was diagnosed in April 2008 of bilateral PIC. Both subfoveal CNV and subretinal fibrosis, despite of oral prednisone treatment (0,4 mg/kg/24hr) and 3 intravitreal Bevacizumab injections (0,05 ml,1.25mg), complicated her left eye course (Visual acuity -VA- 0,025). Tuberculosis chemoprophylaxis during 6 months with Isoniazid was done because of a 20 mm Mantoux test and a 0.79 Uds Quantiferon-Tb Gold (>0.35). New small posterior pole choroidal lesions and a yuxtafoveal CNV, without vitreous cells or anterior chamber inflammation, appeared in her right eye 4 years later. The treatment with oral prednisone 1,5 mg/kg/24hr and an Ozurdex implant quickly healed the choroidal lesions, but the CNV only get closed with a single dose of intravitreal bevacizumab. One year later after a new similar relapse, the combined treatment of Ozurdex with one intravitreal bevazizumab injection were rapidly effective. Also a standard antituberculous treatment was added. No more relapses 6 months later, right eve VA= 0,8.

Conclusions: The early treatment with high doses of intravitreal (Ozurdex), associated or not with oral, corticosteroids, in conjuntion with intravitreal bevacizumab for choroidal CNV treatment, had been effective to prevent second eye macular fibrosis in our patient. The PIC course is rarely recurrent especially in one eye only, and the preventive treatment remains to be elucidated. There might be an etiologic association between PIC and a latent mycobacterium tuberculosis infection in our patient.

Acute Retinal Necrosis

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Introduction: Acute Retinal Necrosis is a rare potentially blinding syndrome. The most common therapeutic approach includes prompt treatment with intravenous acyclovir followed by prolonged oral therapy and systemic corticosteroids. In serious cases or when there is no response to conventional therapy, intravitreal injections of foscarnet can be used. Nowadays, vitrectomy is recommended as an early approach.

Case report: First case: 56-year-old male with decreased vision and floaters in the left eye. Best corrected visual acuity (BCVA) was hand movements. Fundoscopy revealed dense vitritis and vitrectomy was performed. Vitreous polymerase chain reaction (PCR) was positive for VZV. Intravenous acyclovir and oral methylprednisolone were started. After vitrectomy, fundoscopy showed peripheral retinal necrosis and whitish, segmentad, nodular plaques within the walls of the retinal arteries, compatible with Kyrieleis' arteriolitis, which subsequently faded over 1 month therapy. Final BCVA was 20/70.

Second case: 64-year-old male with decreased vision and pain in the right eye. On examination, BCVA was 1/10, vitritis, circumferential retinal necrosis, papiledema and vasculitis were noted. PCR was positive for VZV. Intravenous acyclovir and oral methylprednisolone were started, a vitrectomy and intravitreal injections of foscarnet were performed. 2 months later a secondary retinal detachment (RD) occured. The patient was submitted to 23 gauge pars plana vitrectomy.

Conclusion: Early vitrectomy is useful in preventing the progression and the RD. Intravitreal injections of foscarnet are a safe and effective adjunctive therapy.-

To our knowledge, the association between VZV retinitis and Kyrieleis' arteriolitis is rare and has only been described once. Kyrieleis' arteriolitis in the setting of VZV retinitis may be reversible after appropriate treatment.

Not everything that glitters at the fundus is an infection

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Introduction: To describe the findings of a masquerade syndrome.

Case report: A 52 year old myopic (-10 D) woman with HIV infection (CD4 868 cells/µl), was refered because of visual acuity (VA) loss in her right eye (RE), 5 days after an orbital surgery. The VA was light perception with 3 afferent papillary deffect. A 3 vitreus flare with many white cells, condensations and fiber tracts, toghether with a well demarcated area of posterior pole retinal whitening, was seen on opthalmoscopy. After 3 days of trimethoprim-sulfamethoxazole, valganciclovir and oral prednisone(0,5mg/kg) treatment, both vitreous debris and retinal perivascular whitening improved. Fundus examination also showed: periarteritis, patchy constriction of temporal arteries, faint macular cherry-red spot and inferior subhyaloid white debris. Fluorescein angiography showed a delay in the filling time of the superior temporal vein, faint hypofluorescence with minimal perimacular late staining. SD optical coherence tomography (OCT) disclosed a profound loss of the normal architecture with located hyaloid separation. The RE visual field showed a 30º absolute scotoma. The left eye examination was normal. Luetic, toxoplasmic plasma serology and aqueus humor herpes virus PCR analysis were negative. So and because of peribulbar betamethasone injection was used in the surgery, the diagnosis of toxic retinopathy by inadvertent intraocular injection, was done. Along the first year the RE VA was of moving hands, the retina became atrophic and thin, with arteriolar attenuation and peripapillary bone spicule pigment. Also a non progressive flat, posterior pole located tractional retinal detachment was seen on OCT examinations.

Conclusions: Intraocular betamethasone produces irreversible retinal damage

Retinal Vascular Occlusions In Patients With Behçet's Uveitis

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Purpose: To assess the prevalence and analyze the clinical features of retinal vascular occlusions in patients with Behçet's uveitis.

Methods: This retrospective study included 114 patients (195 eyes) with Behçet's uveitis, full filling the diagnostic criteria of International Study Group for Behçet's disease (ISGBD). The follow-up period ranged from 6 to 180 months (mean: 32.730.5 month).

Results: Retinal vascular occlusions occurred in 11 eyes (5.6%). Best-corrected visual acuity ranged light perception to 20/40. Retinal vein occlusion was more common than retinal arterial occlusion (4.6% vs 1%). Among eyes with retinal vein occlusion, there were 7 cases of branch retinal vein occlusion (BRVO) and 2 cases of central retinal vein occlusion (CRVO). Branch retinal arterial occlusion was noted in 2 eyes (1%). Vaso-occlusive events occurred in patients during relapses and periods of active ocular inflammation. Final Best-corrected visual acuity ranged from 20/400 to 20/40.

Conclusion: Patients with Behçet's uveitis are at risk of retinal vascular occlusion. Retinal vein involvement is more common than retinal arterial occlusion, and may occur predominantly in patients with active or uncontrolled ocular inflammation.

Careful follow-up and appropriate management is required to improve the visual prognosis of affected patients.

Factors Associated with Anatomic and Visual Outcomes in Acute Retinal Necrosis

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Purpose: To examine the factors associated with anatomic and visual outcomes in Japanese patients with acute retinal necrosis (ARN).

Methods: One-hundred-and-four patients with ARN were followed for more than 1 year at nine referral centers were reviewed. Retinal involvement at initial presentation was classified into four groups: zone 1 (posterior pole, n=22), zone 2 (midperiphery, n=54), zone 3 (periphery, n=25), and unknown (n=3). Forty-eight eyes underwent prophylactic vitrectomy before development of retinal detachment (vitrectomy group); 56 eyes were treated conventionally without prophylactic vitrectomy (observation group).

Results: The retina was attached in 28 (58.3%) of 48 eyes in the vitrectomy group and 42 (75.0%) of 56 eyes in the observation group at final visit (P=0.071). At 1 year, 56 eyes (53.8%) had a best-corrected visual acuity (BCVA) of 20/200 or worse. Multivariate logistic regression analyses identified that zone 1 disease (odds ratio=4.983) and optic nerve involvement (odds ratio=5.084) were significantly associated with BCVA of 20/200 or worse. Among zone 3 eyes, significantly (P=0.012) more eyes in the observation group than the vitrectomy group had an attached retina.

Conclusions: Prophylactic vitrectomy did not improve the final BCVA in any eyes. Zone 3 eyes had better outcomes without prophylactic vitrectomy.

PCR of aqueous humor in atypical cases of ocular toxoplasmosis

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Introduction: Acquired Ocular Toxoplasmosis (OT) is usually unilateral, so in cases of bilateral involvement with no past history differential diagnosis should be made. PCR of the Aqueous Humor (AH) is a simple and safe test in the early confirmation of the diagnosis in cases with anterior chamber inflammation.Two cases of bilateral ocular OT confirmed by Polymerase Chain Reaction (PCR) of the AH are presented.

Case Report: Two African young male patients presenting with blurry, decreased vision. Biomicroscopic examination revealed anterior chamber reaction, vitritis, a retinochoroidal scar and an active satellite retinal lesion. The fellow eye showed pigmented retinochoroidal scars, in one patient affecting the macula. Anterior chamber paracentesis was performed and they were started on Trimethoprim-sulfamethoxazole and methylprednisolone. PCR was positive for *Toxoplasma gondii* and Anti-*T. gondii* IgG was elevated in both patients. The patient with the macular lesion was continued on profilaxis with TMP/SMX.

Conclusions: PCR testing is a useful tool for early diagnosis of OT in atypical cases with anterior chamber inflammation.

Eyelid Edema As Initial Manifestation Of Hyperthyroidism

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Purpose: To describe a case of recurrent eyelid edema associated with hyperthyroidism.

Case report: A 53 year-old healthy man presented with a painless swelling of the upper eyelid of the left eye of one month duration. The patient was previously misdiagnosed as having chronic blepharitis. The severity of lid swelling increased gradually and became bilateral. On examination, the patient exhibited bilateral eyelid edema with blepharoptosis and moderate skin redness. Proptosis was not present. The patient was orthophoric and his ocular motility was full. His best-corrected visual acuity was 20/20 in both eyes and ophtalmoscopy was unremarkable. Magnetic resonance imaging examination showed infiltration of the orbital fat without rectus muscles inflammatory involvement.

-The patient was diagnosed as having hyperthyroidism and was treated with oral corticosteroids associated with antithyroid drugs. The eyelid edema partially resolved over a period of three months, however the patients exhibit subsequent relapses with bilateral involvement of the eyelids.

Conclusion: Eyelid edema may be a revealing manifestation of hyperthyroidism and may be a challenging diagnosis. Careful examination and appropriate workup are helpful to establish the correct diagnosis and to rule out other inflammatory orbitopathies and masquerade syndromes.

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Optic neuropathy secondary to severe preseptal cellultis in a child

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Case report: Preseptal cellulitis is generally regarded to be innocuous compared to orbital cellulitis. Prompt treatment with antibiotics usually results in complete resolution. In children, presentation may be severe with devastating visual complications. We report a case of a severe preseptal cellulitis in a child complicated by amblyopia and optic neuropathy.

An 11 month old baby presented with a week history of severe upper and lower lid swelling and redness. Examination showed left upper and lower lid swelling and erythema with mechanical ptosis obscuring the visual axis. Pupillary reflexes were brisk bilaterally with normal intraocular pressure. The eye was white and patient was systemically well. CT scan showed a preseptal cellulitis with no paranasal, orbital and brain involvement. Broad spectrum intravenous antibiotics were started but the response was slow. The globe remained unaffected. An incision and drainage was performed and antibiotics were tailored to the culture results. After 10 days, the child showed objection to occlusion of the right eye suggesting early development of amblyopia. There was left relative afferent papillary defect suggestive of optic neuropathy. Parents refused pulsing with high dose steroid but complied with eye patching therapy. The preseptal cellulitis subsequently improved and child was tolerating the eye occlusion better.

Conclusion: Preseptal cellulitis in children can be severe. Although the globe is not directly involved, the eye and vision can still be compromised. Amblyopia and optic nerve damage secondary to globe compression from lid swelling are potential complications in pediatric cases as shown in this case study.

The various presentations and manifestations of ocular tuberculosis.

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Case reports: We present a series of patients with different ocular presentations, managed as ocular tuberculosis (TB).

Case 1

54 years old female with persistent vitritis; post cataract surgery. Her eye was white with no frank signs of endophthalmilitis. She did not respond to antibiotics or steroids. Mantoux test was 12mm; quantiferon test unequivocal. Inflammation resolved after anti TB treatment

Case 2

60 years old female with bilateral granulomatous anterior uveitis and vitritis. She has a previous history of pulmonary TB (2 years ago) and bowel tumour; in remission. No recent TB contact. Mantoux was 15mm. Inflammation and vision resolved with anti TB.

Case 3

35 years old male with recurrent left eye anterior and intermediate uveitis. Intravitreal Ozurdex was given which showed initial good response. Two months later he developed severe vitritis with reduced left eye vision. Endophthalmitis investigations were negative. Mantoux 15mm, ESR 42. His eye improved with anti TB treatment.

Case 4

21 years old female with right eye vision of counting fingers. Fundus showed optic disc swelling, macular star with multiple choroiditis. Mantoux was negative. Anti TB was commenced based on clinical findings. Her vision improved to 6/6 with resolution of fundus signs.

Case 5

30 years old male with a history of TB contact and left eye reduced vision. Fundus examination revealed vitritis, retinal haemorrhages, sclerosed vessels and macula oedema. Mantoux was 20mm. Fluorescein showed vasculitis with capillary fallouts. Good response to laser and anti TB treatment.

Case 6

33 years old male with right eye poor vision with vitritis, hyperaemic disc, macular oedema and extensive subretinal exudates. Mantoux was negative. Anti TB was started. Patient showed good response and subretinal exudations resolved.

Conclusion: Ocular tuberculosis has variable manifestations. Diagnosis therefore often relies on good clinical judgments. Investigations are useful but usually unreliable.

The Utility of PET Imaging in Uveitic Patients

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Purpose: To elicit the utility of PET imaging in identifying systemic inflammation in active uveitis patients that may lead to biopsy site and the diagnosis.

Materials and Methods: Retrospective, interventional case series of patients presenting to the Uveitis and Retinal Services at the Walter Reed National Military Medical Center in the Washington DC area between 2007 and 2013. Patients with uveitis of unknown etiology were evaluated with a preliminary basic lab screening, screening chest radiographs or chest CT. They were then evaluated with PET imaging. Guided by clinical course or PET imaging, interventional biopsy of lymph nodes or vitrectomy was performed for tissue diagnosis.

Results: Twenty-two patients were evaluated &ampnbsp;with active uveitis had PET imaging. 5/22 had positive PET imaging findings. Four of the five patients with positive PET scans were diagnosed with sarcoidosis. A frontal lobe mass was identified in the other patient which was later diagnosed with primary CNS lymphoma. In two of the patients with positive PET findings, the hypermetabolic foci were in locations that could be biopsied. These two patients had a tissue diagnosis of sarcoidosis.&ampnbsp;

Conculsions: Despite other positive reports, PET imaging had limited utility in this small series, aiding in the diagnosis of five of the twenty-two patients. Due to its cost and time intensive nature, PET imaging may be most beneficial in unusual uveitic presentations, including patients with recurrent or recalcitrant uveitis or when preliminary lab and radiologic studies do not lead to a definitive diagnosis. ImmunoPET, however, &ampnbsp;where antibodies are used to target tissue and apply and monitor therapy is a new experimental modality that may offer promise in the treatment of uveitic patients and this will be discussed.

Idiopathic bilateral posterior scleritis: A report of two cases

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Introduction: Posterior scleritis is an inflammation of the posterior sclera with a significant threat to vision. A detailed history, ocular examination and investigation of underlying systemic disease should be done with a multidisciplinary approach.

Cases report: We present a 23 years old man and 41 years old woman studied in our service because of photophobia and reduced bilateral vision without pain. Both patients didn´t present afferent pupillary defects.- Exploration after pupils dilatation showed bilateral serous retinal detachment and optic nerve swelling without cotton-wool spots. The optical coherence tomography scan confirmed the retinal detachment over the macula; ultrasound scan confirmed the swelling of posterior sclera. The axial computerized tomography confirmed the scleral thickening with no orbital infiltration. After a complete study including full blood count, liver and renal fuction, C-reactive protein, erythrocyte sedimentation rate, antinuclear antibody (ANA), antineutrophil cytoplasmic antibody (ANCA), anti-double stranded DNA antibody, rheumatoid factor, syphilis and coxiella serology and Mantoux study, no underlying disorder was identified. In both cases, intravenous methylprednisolone at high doses (1 gr/day in three days) was followed by a starting dose of 1 mg/kg/day with weekly reduction of 30 mg/week. After four weeks of treatment the swelling disappeared and median final vision was 20/20.

Conclusion: In some cases of posterior scleritis, there is no pain when clinical presentation so careful clinical examination and B-mode ultrasonography are essential for diagnosis and to exclude infectious diseases. Idiopathic posterior scleritis responds to steroids but recurs frequently and an effective therapy can be instituted to control inflammation and avoid destructive complications.

A case of acute zonal occult outer retinopathy complicated by uveitis

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Introduction: Acute zonal occult outer retinopathy (AZOOR) occasionally presents retinal vasculitis; however, it rarely does apparent findings of uveitis. We report here a case of AZOOR presenting retinal vasculitis accompanied with vitreous opacity and retinal exudates.

Case report: A 28-year-old female. She visited us with complains of temporal visual field defect and photopsia OD. Visual acuity was 1.2 OU. Despite of no inflammatory findings in the anterior segment, mild vitreous opacity, redness of optic disc, vascular sheathings, and retinal exudates were observed OD. Leakages from retinal capillaries were detected with fluorescein angiography. Goldmann visual field examination revealed the presence of relative scotoma and enlargement of Mariotte's blind spot. Decrease of amplitudes in multifocal electroretinogram and defects of the junction between photoreceptor inner and outer segment (IS/OS) were also detected corresponding to visual field defects. Since these findings could not be fully explained by inflammatory findings, the right eye of the patient was diagnosed as AZOOR. Inflammatory findings gradually diminished with no medication; however, the visual acuity OD suddenly decreased to 0.1 after 8 months. Development of central scotoma and expansion of IS/OS defects into the macular area were detected without any ophthalmoscopic changes in her right fundus. Following a steroid pulse therapy, her visual acuity increased to 0.5 and the IS/OS in the macular area recovered well.

Conclusions: The presence of uveitis and the response to the steroid therapy suggest inflammatory mechanisms in the development of AZOOR in this case.

CMV Retinitis in a Patient with Hypogammaglobulinemia associated with thymoma (Good's Syndrome)

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Introduction: Good's syndrome is a rare immunodeficiency syndrome characterized by hypogammaglobulinemia accompanied by thymoma. Patients with Good's syndrome have combined B and T cell defect and usually present with recurrent infection including systemic CMV infection. We here report an unusual case of Good's syndrome patient presented with CMV retinitis.

Case: A 65-year-old Thai female patient presented with rapidly progressive blurred vision in the past week. Her fundoscopic examination revealed peripheral granular retinal necrosis with subtle retinal hemorrhage. CMV was detected by RT-PCR. Therefore, CMV retinitis was diagnosed. She has history of Good's syndrome presented with thymoma, subsequent thymectomy, and recurrent infection. Laboratory investigation showed hypogammaglobulinemia. She received intravenous immunoglobulin (IVIg) every 4 weeks to correct the hypogammaglobulinemia. Despite proper serum IgG level, she has experienced recurrent CMV viremia. Intravitreous gancyclovir and systemic gancyclovir were given to the patient with satisfactory response. IVIg dose was increased to every 3 weeks with the hope to minimize the recurrence of CMV infection.

Conclusion: CMV retinitis can be found in patients with Good's syndrome. Currently, anti-viral therapy aims at treating CMV retinitis. However, because of underlying combined B and T cells immune defect, patients are likely to develop recurrent infection. IVIg replaces only antibody deficiency, but the underlying T cell defect which mainly predisposes patients to viral infection cannot be corrected. A better strategy to reconstitute T cell defect is needed to prevent recurrent CMV retinitis and thus prevent permanent visual loss in this group of patients.

Bilateral occlusive retinitis treated with intravitreal triamcinolone acetonide

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Introduction: To study the clinical outcome in a patient with bilateral occlusive retinitis having macular involvement treated with intravitreal triamcinolone acetonide

Methods: Interventional case report of 30 yr old male who presented with bilateral occlusive retinitis. He was on oral steroids with acyclovir since 1 month. Best corrected visual acuity at presentation was CF 3m in right eye and 20/120 in left eye. SD-OCT showed macular edema in both eyes (>350 microns in each eye). Anterior chamber tap was done. PCR for HSV, VZV and CMV was negative and so acyclovir was stopped. Oral steroid were continued and he underwent intravitreal triamcinolone acetonide injection (4mg in 0.1 ml) in the right eye followed by the left eye, 3 weeks later, when the macular edema on SD-OCT in the left eye further increased with deterioration of vision to CF 3m.

Results: Both eyes showed a dramatic improvement in visual acuity, fundus appearance and SD-OCT (<210 microns) with a single injection of triamcinolone acetonide. At the end of 3 months, the vision in the right eye improved to 20/30 and in the left eye to 20/60. The areas of retinitis healed significantly.

Conclusions: Intravitreal triamcinolone acetonide is a useful adjunct to oral steroid in patients with refractory occlusive retinitis especially when involving macula.

Vogt-Koyanagi-Harada disease in childhood

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Purpose: To report clinical findings and visual outcome of Vogt-Koyanagi-Harada (VKH) disease in childhood (patients younger than 16 years old).

Materials and Methods: Retrospective study including 5 children (10 eyes) with VKH disease. All patients underwent detailed ophthalmic examination, fluorescein angiography, and optical coherence tomography. Mean follow-up was 12 months (range, 6-24).

Results: Mean age of our patients was 8 years (range, 6-12). Three patients (60%) were male and 2 patients (30%) were female. All patients were diagnosed at the chronic recurrent stage. Mean initial visual acuity was 20/63 (range, 20/800-20/25).Ophthalmic findings included anterior granulomatous uveitis (60%), band keratopathy (20%), posterior synechiae (40%) intraocular pressure elevation (20%), cataract (40%), sunset glow fundus (100%), and subretinal fibrosis (10%). Poliosis and vitiligo were recorded in 2 patients (40%). All patients were treated with oral corticosteroids and immunosuppressive therapy (cyclosporine=3,azathioprine =1, methotrexate=1). Three eyes (60%) underwent cataract surgery. Mean final visual acuity was 20/63 (range, 20/200-20/25).

Conclusions: VKH disease is an uncommon cause of uveitis in children. The disease is often recognized late in the course of the disease. The use of immunosuppressive therapy or biologic agents is necessary.Delay of diagnosis and treatment may lead to poor prognosis due to chronic recurrent inflammation and complications.

Role of detecting CD4/CD8 ratio in aqueous humor of patients with uveitis

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Introduction: The characterization of different T-lymphocyte populations (CD4 andCD8) during an ocular inflammation episode may be useful in reaching a diagnosis of uveitis with T-lymphocyte involvement in difficult situations.

Purpose: To study the role of CD4/CD8 ratio in anterior uveitis..

Method: In this prospective, comparative, observational case series study, we investigated the CD4/CD8 ratio in aqueous humors of 20 patients, which included idiopathic anterior uveitis, viral anterior uveitis, presumed tubercular anterior uveitis, sarcoidosis and controls (senile cataract). We analyzed the CD4/CD8 ratio in aqueous humor by flow cytometry, in patients with an acute episode of anterior uveitis.

Results: No lymphocytes were detected in the aqueous humor of the controls; the CD4/CD8 ratio was >1 in idiopathic anterior uveitis and presumed tubercular anterior uveitis. Viral uveitis showed a CD4/CD8 ratio of <1 while in patient with ocular sarcoidosis the CD4/CD8 ratio was more than 7.

Conclusion: CD4/CD8 ratio analysis in aqueous humor in patients with anterior uveitis can be a simple, inexpensive method of investigation to aid in diagnosis.

Bilateral interstitial keratitis with hypopyon due to herpes simplex virus 2 (HSV2): A rare presentation

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Purpose: To report a case of bilateral interstitial keratitis with hypopyon due to HSV-2

Methods: An 18 year old female presented with decreased vision in both eyes. She had already undergone cataract surgery. Distant vision was 2/60 and CF-CF in the right eye and left eye respectively. She had bilateral central chronic corneal edema involving the posterior stroma and descemets membrane with early scarring and 360° deep vascularisation. Anterior chamber showed 3 cells in right eye and hypopyon in the left eye. Slit-lamp examination further revealed pseudophakia with posterior capsular opacities in both eyes. Investigations done ruled out syphilis and rubella. HLA-typing was negative. Polymerase chain reaction (PCR) for herpes simplex virus-1, cytomegalovirus, varicella zoster virus were negative but was positive for herpes simple virus-2. In view of this, patient was put on systemic antivirals and topical steroids.

Results: Following treatment her vision improved to 6/18 and 1/60 in the right eye and left eye respectively with resolution of the edema confirming HSV-2 infection.

Conclusion: Simultaneous bilateral interstitial keratitis with hypopyon uveitis is a rare entity. PCR can help to confirm the diagnosis. Bilateral interstitial keratitis due to HSV-2 has not been reported.

Bilateral Herpes simplex Uveitis - Case Report

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Introduction: Herpes simplex- associated uveitis is usually considered a unilateral eye disease, and rarely considered as a differential diagnosis whenever there is bilateral eye involvement. Here we report four cases of bilateral anterior herpetic uveitis.

Case reports: We evaluated two female and two male patients, between 28 and 51 years of age, who presented to our service with the typical clinical manifestations of uveitis such as blurred vision, red eye, ocular pain, tearing and photophobia. On ophthalmologic examination we found intraocular hypertension, endothelial pigmented KP, cells in the a/c, paralytic mydriasis, iris atrophy with positive retroillumination and variable anterior vitreous cellularity. Three of them had been misdiagnosed as having noninfectious uveitis and had received systemic immunomodulatory medications. According to the clinical findings, and supported with Herpes-specific antibody titers and aqueous humor sample for PCR in two of the patients, all of them were then diagnosed with bilateral anterior herpetic uveitis.

Conclusions: Most of our patients were initially misdiagnosed as having noninfectious uveitis and were treated with immunomodulatory medications, which could have favored the extension of the ocular infection bilaterally. Although not very often found, bilateral herpetic uveitis should always be considered among the differential diagnoses, when patients present with signs and symptoms of uveitis of infectious origin involving both eyes.

Peripheral immune response in human toxoplasmosis depends on clinical condition but not on the antigen

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Background: The peripheral immune response is incompletely known in human toxoplasmosis.

Methods: The specific lymphocyte proliferative response and cytokine profile production regarding Toxoplasma P30 (2017 from virulent and non-virulent strain) and ROP18 protein-derived peptides (from clonal lineages I, II and III) were determined in 19 patients having ocular toxoplasmosis, five suffering chronic asymptomatic infection, 9 with congenital toxoplasmosis and 8 Toxoplasma negative people. A Beckman- Coulter FC500 flow cytometer was used for determining antigen-specific T-cells (CD3 CD4 or CD3 CD8 cells) in peripheral blood culture. IFN and IL10 levels were determined in culture supernatants.

Results: Specific CD4 and CD8 T-cell response to total antigen and P30- and ROP18-derived peptides was observed in infected people. Ocular toxoplasmosis patients had a preferential Th2 response after antigenic stimulation. Non-virulent peptide 2017 was able to shift response towards Th1 in congenitally-infected children and virulent peptide 2017 induced a Th2 response in chronically-infected, asymptomatic people.

Conclusions: An immune response in human toxoplasmosis after ex vivo antigenic.

Depressive Psychosis in Chronic Uveitis

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Introduction: In cases of recalcitrant uveitis the patients sometimes suffer from depressive psychosis which complicates the situation. It may even lead to loss of life. We have come across such a case where a medical college professor ended his life after suffering from bilateral uveitis for a long time.

Case report: A 60 year old medical college professor suffered from recalcitrant anterior uveitis for 10 years. He was diabetic and hypertensive. He had a history of immunosuppressive therapy for carcinoma prostate 12 years back. His BCVA was 3/60 BE, IOP 22 mm Hg BE, lental opacity, endothelial dusting with cells & flare . He was on topical Prednisolone 6 hourly and Brimonidine. If Prednisolone was reduced to 8 hourly, inflammation flares up along with rise of IOP. Underwent cataract surgery with perioperative steroid coverage. Instillation of Prednisolone 6 times causing further raised IOP that needed additional topical Brinzolamide to control IOP. Each bout of inflammation damaged his visual acuity. He refused to take either systemic steroid or immunosuppressive. The recurrence of inflammation led him to be in depressive mood out of fear that he is going to be blind. Out of frustration he ended his life by jumping from the 5th floor from the hospital where he used to work.

Conclusion: In case of recalcitrant uveitis where the patient is quiet aware regarding the visual outcome, the uveilogist should give him psychological support during counseling. Otherwise once the patient starts suffering from depressive psychosis, the fatal events may arise as the case we have mentioned.

Recurrent granulomatous anterior uveitis in pacient with a high suspicion of berylliosis.

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Introduction: Both sarcoidosis and tuberculosis (TB) can affect the eye with various manifestations, including iritis. Chronic berylliosis is a systemic granulomatous disease in patients with occupational exposure to beryllium with prolonged latency. In the literature no uveitis by berylliosis is described.

We report a patient with a high suspicion of berylliosis and recurrent anterior uveitis.

Case report: 40 year-old male without known previous clinical history, except beryllium exposure due to his job as prosthetic dentistry. He presented a posterior subcapsular cataract in the right eye (RE), and episodes of non synechial, granulomatous anterior uveitis in both eyes (BE).

The study made by Internal Medicine found an interstitial pattern with mediastinal lymphadenopathies plus TB residual traits. Mantoux negative. Elevated ACE (Angiotensin-converting enzyme). Positive HLA-B51. Bronchoalveolar lavage without the presence of acid-alcohol resistant bacilli. Videothoracoscopy lung biopsy exhibits anthracosilicosis nodules typical of pneumoconiosis; granulomatous lesions or microorganisms were not found.

After two years follow-up, two outbreaks with similar characteristics in the RE and four in the LE have just been diagnosed and are nowadays being controlled with topical steroids.

Conclusions: The diagnosis of sarcoidosis is histological and is made by exclusion, once infectious and non-infectious causes are excluded. In this patient TB was ruled out, and sarcoidosis was not confirmed. Although this cause has never been described before, we suggest that this patient's uveitis could be related to a chronic berylliosis. Given the systemic granulomatous nature of this disease and its immunopathogenesis (based on the response of CD4 T cells), we believe that this association is possible.

To report the efficacy and safety of intravitreal dexamethasone implant (Ozurdex) in treatment of non-infectious uveitis

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Materials and Methods: We retrospectively analysed cases who underwent intravitreal implantation of Ozurdex for uveitis from May 2012 to Dec 2013. Best corrected visual acuity (BCVA), OCT central macula thickness (CMT), intraocular pressure (IOP), anti-glaucoma medication usage were recorded, in additional to any significant adverse event.

Results: To date, 9 eyes in 7 patients were identified. 5 had idiopathic intermediate uveitis, 2 being bilateral. One had idiopathic retinal vasculitis with cystoid macula oedema (CMO) and one had chronic anterior uveitis and CMO secondary to previous multiple ocular surgeries. Mean follow up was 6 months (range 2-12 months). At baseline, the average CMT was 372 microns and BCVA 0.60. At 1 month, all patients showed regression of CMO with CMT 280.1 and an increase of BCVA to 0.35, vasculitis also regressed. By 3 months, 3 of the patients showed reacculumation of CMO and the mean CMT increased to 351 micron, VA 0.31. 2 patients received repeated injection by 6 months. 2 patients had raised IOP during the follow up period (22-34mmHg) and controlled by topical agents. 1 patient developed an immediate postoperative vitreous hemorrhage which resolved spontaneously by week 4. 1 patient had phacoemulsification after the second Ozurdex injection.

Conclusions: Dexamethasone implant can improve the vision, control vasculitis and decrease CMO in patients with non infectious anterior and intermediate uveitis. Data collection is ongoing but interim results show that most patient relapse by 4 months. There is a place for the use of Ozurdex in the treatment of persistent CMO in these patients.

A Case Of Panuveitis With Buerger's Disease

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Introduction: We report a a rare case of panuveitis associated with Buerger's disease.

Case report: A-31 years old male patients was referred to our clinic due to visual loss in his right eye.He had unilateral anterior uveitis, vitritis and retinal vasculitis. Past history revealed he had brain vasculitis, renal vasculitis and migratory thrombophlebitis.He had succefully treatment of topical and subtenon steroid injection.

Conclusions: Buerger's disease is characterized by the development of segmental- -panvasculitis of the medium and small arteries.Mainly found in young males and smokers, is a clinical trombotic occlusions. Ocular finding in this disease atherosclerosis of retinal -and -conjunctival arteries were reported.We -first reported case of panuveitis associated with Buerger's disease.

Our experience in viral retinal necrosis

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Purpose: To analyze the clinical features, treatment and outcome of patients diagnosed with acute retinal necrosis (NRA), progressive outer retinal necrosis (PORN) and cytomegalovirus (CMV)

Materials and methods: A retrospective, case series of 8 patients (10 eyes). Were analyzed the best corrected visual acuity (BCVA) before and after the treatment, the age, the race, the sex, the immune status, the early symptoms and the anterior and posterior segment manifestations and the time takes to to diagnosis the resolution. Results: We present eight patients; six (75%) were diagnosed with NRA, one (12.5%) was diagnosed with bilateral case with PORN and one case (12.5%) was diagnosed with CMV in both eyes. Initial average BCVA was 0.3 and final average BCVA was 0.6. Decrease in visual acuity was the initial symptom in 4 patients (50%), floaters in 3 cases (37,5%) and pain in one patient (12.5%). The average time to diagnosis was 7 days. Two of eight (25%) patients were treated with intravitreal injections of aciclovir and foscarnet, one (12,5%) with intravitreal injections of ganciclovir and foscarnet, and the rest (62.5%) with endovenous aciclovir only. Prophylactic laser coagulation was performed in all patients. Retinal detachment (RD)occurred in 3 eyes that were repaired by vitrectomy. Other complications were cataract, epiretinal membranes and optic nerve atrophy.

Conclusions: In our series emphasizes the good prognosis of the NRA when diagnosis is made before 7 days. In the case of CMV retinitis and PORN is necessary to keep antiviral therapy until the patient recovers immunity.

Infectious keratitis following LASIK

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Purpose: To describe clinical findings and visual outcome of infectious keratitis following laser in-situ keratomileusis (LASIK).

Materials and Methods: Retrospective review of five patients (5 eyes)referred to our department with microbial keratitis following LASIK. All patients underwent detailed ophthalmic examination. Corneal scrapping at the edge of the infiltrates or beneath the falp, with microscopic examination and culture, were performed in all cases. Follow-up ranged between 1 to 8 months.

Results: Mean age of our patients was 31.6 years (range, 24-44). Four of them were female. Three patients had femtosecond laser-assisted LASIK and two had microkeratome-assisted LASIK.All patients presented with blurred vision and pain in the affected eye. The mean interval between LASIK and presentation with keratitis was 10.6 days (range,2-21 days). Mean initial visual acuity (VA) was 20/125. Findings of theslit-lamp examination included central focal infiltrates in all cases, corneal epithelial defects (3 eyes) and edema of the flap (2 eyes). Only two patients underwent flap lift. The causative germ was identified in two patients (streptococcus in one eye, candida in one eye).All patients were treated with a combination of antimicrobial agents, based on the suspected bacterial and/or fungal origin. Resolution of the infection was obtained within 3 to 8weeks,in 4 eyes.Final VA was 20/20 in one eye, and less than 20/200 in one eye.

Conclusions: Infections occurring after LASIK surgery are a serious and increasing complication.In our patients, multiple central corneal infiltrates were the most common feature. Prompt identification with appropriate management of keratitis is mandatory to improve visual outcome.

Fundus autofluorescence in diagnosis and follow-up of white-dot syndromes

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Purpose: In uveitic diseases changes in fundus autofluorescence (FAF) pattern as a sign of a diseased RPE/photoreceptor-complex are found mostly in the spectrum of white-dot syndromes (WDS). Ocular tissues involved in the pathogenesis of WDSs include RPE, outer retinal layers and choroid. We analyzed the reliability and contribution of FAF changes for the detection and localization of disease activity in WDS.

Material and Methods: We included 15 eyes of 11 patients diagnosed with multifocal choroiditis (MFC, n=3), punctate inner choriopathy (PIC) (n=2), serpiginous choroidopathy (SPC, n=3), tuberculosis-associated serpiginouslike choroidopathy (TB-SPLC, n=1), APMPPE (n=1), and MEWDS (n=1). For detection of disease activity and lesion size FAF, fluorescein angiography (FA), indocyanine green angiography (ICGA), and spectral-domain OCT (Spectralis HRA; Heidelberg Engineering) were performed.

Results: In SPC, TB-SPLC, and MEWDS lesion activity on FAF was represented by hyperfluorescence and blurred borders that correlated with active lesions on FA/ICGA and OCT. Overall there was no significant difference in lesion size within the macular region as measured with FAF, FLA and ICGA. However, in MFC patients hyperfluorescent areas on FAF did not correspond to small lesions on FA and ICGA representing a more widespread involvement of the RPE/photoreceptor-complex than seen on FA/ICGA. During follow-up two patients (1 SPC, 1 TB-SPLC) developed an active lesion within the fovea that could only be seen on FA and ICGA but not on FAF.

Conclusion: FAF is a valuable addition in the diagnostic procedure of WDSs and can reveal more information than suspected by other means of imaging. Nevertheless, FAF is not sufficient as a sole imaging tool for diagnosis and follow-up purposes, as in particular foveolar lesions might not be discovered.

Advanced Imaging in Retinal Vasculitis

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Purpose: Recent advances on optical imaging techniques enable imaging the retinal microvasculature at the capillary level using a commercially available retinal function imager (RFI, Optical Imaging Ltd,Rehovot,Israel). Herein we present the feasibility and applicability in diagnostic imaging of the retinal blood flow (BF) velocity in patients with retinal vasculitis using a commercially available RFI instrument.

Materials and Methods: The RFI is a fundus camera-based device with an attachment of a specific camera that captures reflectance changes as a function of time under stroboscopic illumination. This device was originally designed to measure the BF velocity directly and noninvasively (without using any contrast agent) in secondary and tertiary retinal vessels while using the hemoglobin in the red blood cells as an intrinsic motion-contrast agent. In a pilot study we measured the retinal blood flow velocity with the RFI in 9 patients (m:f=2:7) with a mean age of 51±11 years. Seven if these patients suffered from Birdshot Chorioretinopathy and two patients had a retinal vasculitis of unknown origin. We compared these data with a healthy control group.

Results: In the control group the arterial blood flow velocity was 4,1±0,9 mm/s and in the venous vessels 2,9±1,0 mm/s. Comparing these data with the retinal BF velocities of the study group, we achieved significant differences. The vasculitis patients disclosed an arterial blood flow velocity of 2,5 ±1,6mm/s ($p<0,001$) and a venous BF velocity of 1,8±1,0 mm/s ($p<0,001$).

Conclusions: We could demonstrate for the first time, that in patients with retinal vasculitis the arterial as well as the venous blood flow velocity is significantly reduced, when measurend with the Retinal Function Imager. Thus, this device could offer the advantage to represent a diagnostic tool and, in addition, to assess the effectiveness of treatment.

Outcome of cataract surgery in patients with uveitis

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RESUME

Purpose: To describe the outcome of cataract surgery in adult patients with uveitis and to compare with the literature.

Methods: Retrospective and observational study. Clinical and surgical data from 30 patients with uveitis (40 eyes) who underwent cataract surgery with intraocular lens implantation between March 1991 and October 2011. Remission of inflammation was achieved at least 3 months prior to surgery and anti-inflammatory prophylaxis was given in every case

Results: Phacoemulsification was performed in 87.5% of eyes and extracapsular surgery in 12.5%. There were no intraoperative complications in this case series. The postoperative visual acuity (VA) was ≥20/40 in 77.5% of eyes and VA <20/40 in 23%. Compared to presurgical VA 80% improved, 17.5% remained the same and 2.5% worsened. The most common postoperative

complication was posterior capsule opacification (40%), followed by ocular hypertension (10%) and epiretinal membrane (10%); 40% did not develop complications.

Conclusions: Cataract surgery is a safe and effective procedure on restoring the visual function in patients with uveitis. However there was a higher rate of complications in our patients than previously reported series of patients without ocular pathology, despite the completion of a period of remission before surgery and anti-inflammatory prophylaxis. The results of this study are comparable to those offered in the literature in patients with uveitis, making assume that protocols and surgical procedures used are correct.

Key words: cataract, cataract surgery, uveitis.

Observational multicenter study of intravitreal dexamethasone implant in Uveitis: Baseline characteristics, clinical outcomes and reinjection frequency

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Purpose: To identify the characteristics, clinical outcomes and treatment patterns of intravitreal dexamethasone implant (IDI) in Uveitis.

Materials and Methods: Retrospective, observational, multicenter study in 4 european hospitals (2 United Kingdom, 2 Spain). Indication, uveitis type, diagnosis, visual acuity (VA), intraocular pressure (IOP), phakic status, number of injections, time to reinjection and complications rate were collected.

Results: Seventy-nine eyes (61 patients) were included. Cystoid macular oedema (CMO) (61.4%), vitritis (24.6%), and combined CMO vitritis (11.6%) were the most common indications. Most frequent anatomical locations were intermediate uveitis (37.9%), posterior uveitis (24.5%) and panuveitis (20.2%), and most frequent diagnosis were idiopathic (43%), Birdshot chorioretinopathy (15.1%), sarcoidosis (7.5%) and multiple sclerosis (7.5%). Mean number of injections was 1.7±0.9 (mean±standard deviation) with a mean follow up of 15.4±9.9 months. Single injection was performed in 51.8% of cases, 30.3% required 2 injections, and 17.6% ≥3 injections. Baseline VA and vitreous haze score (VHS) was 0.71±0.4 and 0.69±0.8, at 1st month was 0.53±0.5 and 0.1±0.3, 3rd month 0.45±0.4 and 0.19±0.4, 6th month 0.50±0.5 and 0.24±0.5 and 12 months 0.42±0.5 and 0.15±0.3 respectively. Raised IOP (≥21 mmHg) was observed in 45.5% of the cases and 44.9% required treatment during the follow up period. The percentage of pseudophakic patients increased from 50.6% at baseline to 55.3% at final follow up.

Conclusions: The use of IDI in uveitis provides good outcomes with regards to VA and VHS measurements but requires repeated injections. The reinjection frequency has to be considered during choice of intraocular steroid treatments.

Hypertensive anterior uveitis. Retinal and leptomeningeal relapse of a plasmacytoma

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Purpose: To describe a patient with several relapses of retinal secondary extramedullary multiple myeloma, preceded by a iridocyclitis.

Case report: A 47 years old woman with multiple myeloma who after two bone marrow transplants: autologous (2004) and allogeneic (2005), was diagnosed in April 2010 of a granulomatous iridocliclitis and shortly after of a retinal myeloma recurrence. The opthalmoscopy showed: yellowish white retinal infiltrates, hemorrhages, edema and retinal vein irregularities, located in the upper temporal cuandrant of the right eye (RE). The lesions gradually evolved into a retinal mass of 6x4 mm in size on ocular ultrasound. One month later both leptomeningeal and spinal cord (L4-L5) relapses were diagnosed. Both brain and orbital CT and MRI were normal. After treatment with systemic and intrathecal chemotherapy along with local (L4 L5) radiotherapy, the retinochoroidal mass, the edema and the vascular abnormalities disappeared completely, leaving a yellowish retinal perivenous infiltrates. In February 2011 a new allogeneic bone marrow transplantation associated with cranial radiation were done. In October 2012 a RE hypertensive granulomatous iridocliclitis was followed by a new retinochoroidal relapse, shortly accompanied by a VI nerve paresis with plasma and cerebrospinal fluid relapses. Both aqueous humor herpes virus PCR and flowcytometric analysis, were negative. After intrathecal and systemic chemotherapy, both iridocyclitis and chorioretinal lesion completely disappeared and have not recurred (October 2013).

Conclusion: Retinal extramedullary multiple myeloma can start as an uveitis syndrome and may precede a systemic relapse.

Tuberculosis presenting as retinal vasculitis

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Introduction: Retinal vasculitis is an inflammatory disease of the retinal vessels. It may occur as an isolated idiopathic condition or associated with autoimmune or infectious diseases (CMV, tuberculosis (TB), toxoplasmosis and syphilis). Intraocular TB has an incidence of 2 % and can have different clinical manifestations including retinal vasculitis. The diagnosis may be difficult and presumptive being based on clinical findings and evidence of systemic TB infection.

Case report: Caucasian 15 years-old boy with sudden painless visual loss in his left eye (LE). Best-corrected visual acuity (BCVA) was 10/10 in the right eye (RE) and 4/10 in LE. Fundoscopic examination showed signs of peripheral vasculitis in RE and macular edema, superior and inferior temporal hemorrhages and prominent sheathing of retinal vessels in LE. Angiography revealed temporal venous occlusion, macular edema and mid-periphery ischemia in LE. Investigation included chest X-ray, full blood count, liver functions, PCR, SV and Mantoux test were normal. The interferon gamma release assay was positive. After treatment with corticosteroids and antituberculosis, there was progressive clinical improvement. At angiographic control was found bilateral retinal vasculitis with peripheral capillary dropout and retinal neovascularization. Photocoagulation of ischemic areas was performed. His final BCVA was 20/20 bilaterally.

Conclusion: Tubercular retinal vasculitis is characterized by vitritis, retinal hemorrhages, neovascularization and neuroretinitis. Fluorescein angiography contributes to the diagnosis and tuberculin test for the pathogenesis, sometimes intraocular fluids samples are needed. Close follow-up and preemptive treatment (antituberculosis, corticosteroids and photocoagulation) is imperative to manage possible disease complications and iatrogenic effects as ethambutol optic neuritis.

MicroRNA-146a and Ets-1 gene polymorphisms are associated with pediatric uveitis

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Purpose: To investigate the association of microRNA-146a (miR-146a) and V-Ets oncogene homolog 1 (Ets-1) gene polymorphisms with pediatric uveitis in a Han Chinese population.

Methods: Five single-nucleotide polymorphisms (SNPs), miR-146a/rs2910164, miR-146a/rs57095329, miR-146a/rs6864584, ets-1/rs1128334 and ets-1/rs10893872 were genotyped using a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay. The expression of Ets-1 in peripheral blood mononuclear cells (PBMCs) from genotyped healthy controls was tested by real-time PCR.

Results: Two SNPs (rs2910164 and rs10893872) were associated with pediatric uveitis in the present study. The frequencies of the rs2910164 GG genotype and G allele were significantly increased (Pc=3.11×10-4; Pc=2.75×10-6) while the CC genotype and C allele were significantly decreased (Pc=0.001; Pc=2.75×10-6) in patients compared with normal controls. The frequencies of the rs10893872 CC genotype and C allele were significantly increased (Pc=3.89×10-4; Pc=0.01) while the CT genotype and T allele were significantly decreased (Pc=0.004; Pc=0.01). The SNP rs2910164 GG genotype and G/C allele were also associated with the presence of microvascular leakage as detected by fundus fluorescein angiography in pediatric uveitis (Pc=0.01; Pc=0.005, respectively). Ets-1 expression in rs10893872 CC carriers was significantly higher than in TT individuals (Pc=0.038). There was no association of the other three SNPs with pediatric uveitis. No association was detected between the five SNPs and patients who were subdivided according to their RF or ANA status or whether they had JIA.

Conclusions: This study shows that miR-146a and Ets-1 are both associated with pediatric uveitis in Han Chinese. SNP rs10893872 may affect the genetic predisposition to this disease by modulating expression of Ets-1.

Bilateral Optic Nerve Swelling as Presenting Sign for Vogt -Koyanagi -Harada syndrome: Case Report

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Introduction: Vogt-Koyanagi-Harada syndrome (VKH), a multisystemic autoimmune disease affects tissues containing melanin. It is characterized by severe bilateral panuveitis associated with serous retinal detachments and meningeal irritation with or without auditory disturbances.

Case Report: A 41-years-old Philippine female previously healthy presented with progressive loss of vision left eye and severe headache after a chemical splash 3 days prior to symptoms. Physical examination showed bilateral edematous optic nerves and a shallow retinal detachment extending from the optic nerve to the center of macula OS. The detachment became bilateral within 2 days with a drop of BCVA from 20/30 to CF bilaterally. No abnormities were detected on brain CT. The lumbar puncture had a normal opening pressure, clear fluid, and mild pleocytosis. B scan showed posterior choroidal thickening and multiple exudative retinal detachments. Within 2 weeks she developed multiple focal cream colored, discrete, deep lesions at the level of the choroid and bilateral exudative retinal detachments involving the macula. No vitritis and no cutanous findings were seen. The patient was diagnosed with VKH and treated with IV solu-medrol 1 gm QD for 3 days followed by prednisone 1 mg/kg/day p.o. with improvement of signs and symptoms. The patient was started on Azathioprine 125 mg qd and cyclosporine 75 mg bid to subsequently control the inflammation.

Conclusion: Early and aggressive systemic corticosteroid is very useful to control the acute manifestations of VKH. Immunosuppressive treatment is needed to control the ongoing inflammation.

Adalimumab and Acute Acquired Incomitant Esotropia in a Patient Treated For Uveitis: Case Report

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Introduction: Adalimumab (Humira) is a recombinant human immunoglobulin monoclonal antibody that binds specifically to Tumor Necrosis Factor alpha (TNF alpha). It is approved for the treatment of rheumatoid arthritis and Crohn's disease and recently gained wide popularity in the treatment of chronic non-infectious intraocular inflammations not responding to classical immunosuppressive therapies. There is evidence that anti-TNF alpha treatment are implicated in the development of demyelinating neurologic events.

Case report: A 49-year-old male presented with severe ocular pain and double vision of 2 weeks duration while taking anti-tumor necrosis factor alpha (anti-TNF alpha) adalimumab for pars planitis refractory to standard therapies. On examination, the patient had horizontal, binocular diplopia that was worse at distance. His right esodeviation was incomitant and was 30 prism diopters (PD) for distant and 25 for near. His visual acuity was 20/50 OD and 20/25 OS. Slit lamp examination showed 2 anterior chamber cells and flare in both eyes.

The patient was diagnosed with acquired incomitant esotropia secondary to adalimumab.

The symptoms resolved after discontinuation of the medication.

This is the first report of this potential side effect with anti-TNF alpha monoclonal antibody.

Conclusion: Physician should pay close attention to the onset of neurological symptoms that wouldn't be explained by other factors in patient taking anti-TNF alpha. Discontinuation of the offending drug is the first management.

Topical ganciclovir for cytomegalovirus corneal endotheliitis

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Purpose: To evaluate the efficacy of topical ganciclovir treatment in cytomegalovirus (CMV)-associated anterior segment infections.

Methods: Seventy-four eyes (67 patients) with positive results of the CMV polymerase chain reaction from aqueous humor tapping were enrolled. All eyes were treated with continuous topical 2% ganciclovir eye drops after positive results of the CMV PCR. The therapeutic assessments were analyzed in three aspects of trabeculitis, iritis, and endotheliitis, measured by intraocular pressure (IOP) control, anterior chamber reaction, and corneal endothelial cell density (ECD) preservation, respectively.

Results: All eyes showed undetectable level of CMV DNA at repeated taps. The follow-up time was 31.76 ± 13.15 months. Under topical ganciclovir treatment, 28 eyes (37.8%) experienced IOP crisis (IOP ≥ 30mmHg) and 10 eyes (13.6%) needed further glaucoma surgery. The occurrence of iritis was detected in 19 eyes (25.7%). Among them, none presented with corneal edema or keratic precipitates and most episodes of iritis were not accompanied by IOP elevation. The initial and last ECD measurements were 1553 ± 727 cells/mm2 and 1479 ± 681 cells/mm2, respectively. The mean percentage of individual endothelium change was -0.78%.

Conclusion: Topical 2% ganciclovir had the capacity to clear viral load in anterior chamber, prevent iritis recurrence, assist intraocular pressure control, and preservation of corneal endothelium. Under uninterrupted topical application of 2% ganciclovir, CMV-associated endotheliitis had the most favorable remission rate followed by iritis and trabeculitis.

Ocular findings in Takayasu's arteritis is milder in a Turkish series

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Introduction: Takayasu's arteritis (TAK) is an inflammatory, granulomatous vasculitis affecting aorta and its major branches. According to the type of vascular involvement, Takayasu's retinopathy (TR) and hypertensive retinopathy (HR) may be observed. Complications related to chronic immunosuppression and steroid therapy are also not infrequent in TAK and complications including amarosis fugax, iris neovascularization, glaucoma, cataract, uveitis and anterior ischemic optic neuropathy have been reported.

Methods: We screened 43 patients with TAK (41 female, 2 male, mean age 42.5±11.3 years, mean disease duration 5.6±5.1 years), followed at Marmara University Hospital Rheumatology clinics, for the presence of ocular complications. Thirty-eight patients were on low-dose (< 10 mg/d prednisolone) corticosteroids, 24 were on azathioprine, 16 were on methotrexate and 2 patients were on leflunomide.

Results: None of the patients suffered from an ocular disease activity or complication causing permanent reduction in visual acuity. Six patients (14%) had HR (grade 1-2) and only one patient (2%) had TR (grade 1). Six patients (14%) had posterior subcapsular cataract, one patient (2%) was bilaterally pseudophacic and 36 (84%) had no cataract.

Discussion: The prevalence of TR was reported to be higher (15% and 13.5%) in previous two similar studies, while prevalence of HR (16% and 30.8%) and steroid-related cataract (23%) was similar to our study. We did not observe any of the other above-mentioned serious complications.

Conclusion: This is the first study to report a low prevalence of TR and related complications in TAK. This finding can be explained in three possibilities: our unselected study population from a rheumatology clinic, rather than an ophthalmology clinic (usually with a selection bias), might have a milder eye disease, good control of general disease activity might have attenuated ocular disease in our patient group or TAK may have a milder course in Turkey.

Clinical Features of Herpes Virus-induced Anterior Uveitis

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Purpose: We compared the background of the patients of herpes simplex virus (HSV), varicella zoster virus (VZV), and Cytomegalovirus (CMV) anterior uveitis in patients with unilateral granulomatous anterior uveitis.

Methods: We retrospectively reviewed patients diagnosed with unilateral hypertensive anterior uveitis who visited The University of Tokyo Hospital from 2004 to 2011. The cases of uveitis with retinitis or optic neuritis were excluded. Patients with active skin lesions of herpes zoster ophthalmicus (HZO) were clinically diagnosed as VZV anterior uveitis. In other patients, anterior chamber taps were performed to determine the cause of uveitis. The aqueous samples were used for polymerase chain reaction (PCR) assay of the 3 types of herpetic virus DNA (HSV, VZV and CMV). The background of patients was reviewed from the clinical records retrospectively.

Results: HSV, VZV and CMV anterior uveitis was 18 patients, 34 patients and 22 patients, respectively. Male gender ratio of HSV, VZV and CMV were 61.8, 44.4 and 86.4% ($p=0.019$, Chi-square test). Mean of age were 53.2, 61.0 and 62.6 years old, respectively (n.s., Student's t-test). History of the recurrence of anterior uveitis were 55.6, 26.5 and 100%, respectively ($p<0.0001$, Chi-square test).

Conclusions: Clinicians should be aware that not only HSV and VZV, but also CMV can cause unilateral granulomatous anterior uveitis, and those prevalence rates might be similar level. Characteristics of the patients with CMV anterior uveitis are history of recurrence and male gender.

Vogt-Koyanagi-Harada Syndrome: Review of 32 cases diagnosed in our area.

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Purpose: To describe and analyze the clinical profile, management and outcomes of 32 cases of Vogt-Koyanagi-Harada (VKH) Syndrome diagnosed between 1995 and 2013 in our reference area in Barcelona, Spain.

Materials and Methods: Retrospective chart review.

Results: The study included 32 patients. The most common initial complaint was headache (81%), followed by bilateral vision loss (72%). Average time to diagnosis was 36.9 days. Audiometry and Lumbar puncture were positive in 70% of the cases. All patients received treatment with topical dexamethasone and oral prednisone, 6 (19%) of them requiring an intravenous megadose, and 9 (28%) requiring combination of an immunosupressant drug. 28 patients (87,5%) presented Uveomeningeal VKH, and 4 patients (12,5%) presented complete VKH. Complications included glaucoma, cataract, epiretinal membrane and choroidal neovascularization, 8 patients (25%) required ocular surgery. On follow up, 15 patients (48%) evolved to healing, 11 (34%) evolved to a recurrent form, and 6 (17%) to a chronic form. Best corrected vision improved 5.3 Snellen lines in average in 43 eyes (67.8%), remained stable (/- 1 Snellen line) in 17 eyes (26%) and decreased in 4 eyes (6%).

Conclusions: The results of this series are similar to those in the published literature. Nevertheless, the proportion of complete forms of the disease is smaller than in older references and there are more cases of healing with less cases of chronification. This is possibly related to an early energical treatment preventing the disease from fully developing. Adequate treatment with prompt addressing of the complications provides VKH with a generally good visual prognosis.

Could we begin to de describe the relentless placoid chorioretinitis as an indepent entity?

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Introduction: Relentless placoid chorioretinitis is an unusual clinical entity with characteristics of acute placoid posterior multifocal pigment epitheliopathy (APPMPE) and serpinginous choroiditis but with a different clinical course.

Case report: A 17-years-old man had blurred vision and floaters of three days evolution in the left eye. His medical history was remarkable for bronchial asthma and unknows origin of viral symptom. His visual acuity was 20/20, the anterior segments were few cells in anterior chamber. Finding from fundus examination showed several creamy white placoid lesions at the level of retinal pigment epithelium (RPE) and choroid in the medium inferiornasal periphery and scattered lesion in the far periphery. The angiography showed early hypofluprescence with later hyperfluorescence of placoid lesions. Oral prednisone, 60 mgr per day, was administrated. One week later the patient presented news lesions along the infratemporal and superiortemporal arcades that no involved the fovea, just in the areas of lightly hypofluoresence in the fluorescence angiography one week before. Two weeks later after the first medical examination, his VA decreased to 20/60 and a new cream white lesion was seen in the macula, optical coherence tomography (OCT) showed an hyperreflectivity of RPE with a disruption of the photoreceptors layer, the treatment was an intravitreal injection of ranibizumab, the inflammatory activity decreased. During the next weeks the AV improved to 20/25, and then a gradual tapering of prednisone to 15 mgr per day was performed. Six months after the patient was free of new inflammatory lesions. The autoflourescence showed a high hypofluorescence of the no-inflamatory lesions and clearly hyperfluorescence in the active lesions

Conclusions: These features suggest that it is a different disease from serpinginous choroiditis or APMPPE.

Bilateral acute depigmentation of the iris

Ilknur Tugal-Tutkun

Bilateral acute depigmentation of the iris (BADI) is a new clinical entity of an unknown cause. It is characterized by an acute onset of pigment dispersion in the anterior chamber, symmetrical bilateral depigmentation and discoloration of the iris stroma without transillumination defects, and pigment deposition in the anterior chamber angle. Young females are more commonly affected. Patients typically describe an upper respiratory tract infection or flu-like illness preceding the acute onset of severe photophobia and red eyes. Topical corticosteroids effectively relieve symptoms and pigment dispersion has a self-limiting course. Iris changes are reversible in the long term.

Punctate Outer Retinal Toxoplasmosis and Kyrieleis vasculitis

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Introduction: Punctate Outer Retinal Toxoplasmosis (PORT) is an atypical presentation characterized by multiple gray white lesions at the level of the outer retina and retinal pigment epithelium with minimal vitreous inflammation.

Case report: A 35-year-old man without personal medical history with painful red left eye associated with blurred vision. Visual acuity was 0,6. Minimal inflammatory reaction was observed in anterior chamber. The ocular fundus showed a white-yellow lesion of retinochoroiditis perimacular temporal-inferior with slightly raised and blurred edges, little vitreous inflamatory reaction and perilesional calcified nodular vasculitis (Kyrieleis vasculitis). No other retinochoroidal scars were presented at the initial examination. Titers of immunoglobulin G were positives and titers of immunoglobulin M were negatives to toxoplasma. Other diagnostic possibilities were ruled out. The patient was treated with empiric treatment with pyrimethamine, sulfadiazine, folinic acid and prednisone. He had an allergic reaction to sulfadiazine and the treatment was changed to pyrimethamine, clindamycin, folinic acid and prednisone. The clinical course was favourable, the ocular fundus showed a lesion with pigmented edges without activity.

Conclusions: The interest of this case lies in the simultaneous appearance of two atypical debut presentations of ocular toxoplasmosis (PORT and Kyrieleis vasculitis) without previous scars to support the diagnosis of congenital toxoplasmosis and without serological confirmation of acute infection that improves with the correct treatment. Recognition of this unusual presentation of toxoplasmosis allows an effective treatment even before serological confirmation and complementary studies.

Aflibercept for inflammatory CNV partially responsive to ranibizumab

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Porpuse: To analyze the efficacy of intravitreal injections of aflibercept for inflammatory choroidal neovascularization (CNV) due to muiltifocal choroiditis non-responsive to ranibizumab.

Methods: Review of ophthalmic charts of 3 eyes of 3 female patients diagnosed of inflammatory CNV with suboptimnal response to intravitreal ranibizumab and the outcome following intravitreal aflibercept after suffering a partially reponse to ranibizumab.

Results: Patient 1 received 5 intravitreal injections of ranibuzumab through a six month follow-up, resulting in a final visual acuity (VA) of 0.9. The anatomical response was suboptimal. Thereafter the patient received three bimonthly intravitreal injections of aflibercept resulting in a final VA of 1,0. Patient 2 received monthly intravitreal injections of ranibiuzmab for 5 months resulting in a final VA of 0,90. The anatomical response was suboptimal. Thereafter the patient received three bimonthly intravitreal injections of aflibercept resulting in a final VA of 1,0. Patient 3 was treated with 5 monthly injections of ranibizumab, with a final VA of 0,30 and persistent macular thickening. After three monthly injections of aflibercept her VA improved to 0,50 and complete resolution of exudation was evidenced.

Conclusions: Aflibercept might be a useful alternative in cases of inflammatory CNV partially responsive to ranibizumab.

Choroidal neovascularization as unusual ophthalmic manifestation of cat-scratch disease in 8-year-old girl

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Purpose: To report an unusual case of choroidal neovascularization (CNV) appeared during the primary Bartonella Henselae infection in a 8-year old girl.

Case report: A 8-year old girl was referred to our clinic complaining of a central scotoma in the right eye. Fundus examination revealed a bilateral disc edema and in the right eye neuroretinitis with macular star and CNV, which was confirmed by fluorescein angiography (FA). The optical coherence tomography (OCT) revealed the presence of a macular serous retinal detachment. Laboratory analysis showed rising IgM and IgG titers for Bartonella Henselae. Cat scratch disease was diagnosed, and a 8-week course of Azithromycin was initiated. In addition, an intravitreal injection of Ranibizumab was performed in the right eye to treat the CNV. One month later we needed to restart systemic antibiotic for others 5 months, due to the persistence of papillitis

Conclusions: Cat scratch disease should be considered among different causes of inflammatory CNV secondary to infectious uveitis. The combination of systemic antibiotic treatment with intravitreal anti-VEGF therapy allowed us to obtain the complete resolution of neuroretinitis, associated to the scarring of choroidal neovascular membrane, with a final visual acuity of 20/20 in both eyes.

Rituximab Treatment for Refractory Necrotizing Idiopathic Scleritis

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Introduction: Rituximab has been used with success in the treatment and resolution of systemic non infectious diseases associated with scleritis. We report a case of refractory necrotizing idiopathic scleritis which healed with 2 Rituximab pulses (rheumatoid arthritis scheme) associated with oral cyclophosphamide (CFM).

Case Report: a 70 years old woman had been treated because of pain and redness in her left eye since 5 months ago without any benefit. She had a diagnosis of necrotizing scleritis at the temporal quadrant in her left eye (OS). Systemic workup is negative for syphilis, tuberculosis, rheumatoid factor (RF), anti-neutrophil cytoplasm antibody (ANCA), anti-citrullinated peptide antibodies (anti-CCP), angiotensin converting enzyme (ACE), antinuclear antibodies (ANA), between others. When we receive the patient we doesn't treat with systemic corticosteroids because her diabetes is not well controlled and her hypertension either. So we start 500 mg intravenous pulses each 30 days with CFM without any response. After the third CFM pulse a new necrotizing focus appeared in the temporal side of the other eye. We change to oral CFM at a dose of 100 mg with no response either. The lesions resolve only after the second intravenous pulse of 1000 mg of rituximab and remained quiescent without any treatment after 2 years.

Conclusions: We didn't find any case published about idiopathic necrotizing scleritis treated with rituximab. In this case the result was very satisfactory. We think that this treatment could be an alternative for this potentially sight threatening eye disease. Further investigations are needed.

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Dry Eye Disease: What the patients say and what we observe... are they

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Purpose: Clinical and symptomatic evaluation of dry eye disease in four different age groups.

Material and Methods: The authors present a prospective study where they evaluate the best corrected visual acuity (BCVA) and eye anterior segment. The patients answer an enquiry evaluating symptoms, fluctuation during the day, aggravating factors, labour abstention and the impact on quality of their lives, rating them on a 1 to 5 scale. Exclusion factors are well defined. It was excluded the contact lens-user report due to the low number of patients included. It was used SPSS Statistics Program®, with statistic significance considered $p<0.05$.

Results: 178 patients, 62.2% female, four age groups: < 20 years (21.6%), 21-44 years (24.3%), 45-64 years (45.0%) and > 65 years (9.1%). The median BCVA was 0.92. Anterior and posterior blepharitis are related with clinical issues worst in the morning. Break-up time with fluorescein dye is increased when conjuntivochalasis is worse. Increasing the lissamine green dye is associated with worsening in quality of life. < 45 years patients with dry eye observation complain about burning, red eye and itching. Active adults complain about visual acuity fluctuation and eye fatigue. Tearing is typical in > 65 years patients. All aggravating factors are important to dry eye patients and have an essential impact on their lives.

Conclusions: Dry Eye Disease has an estimated prevalence of 20%. In Portugal, there is no database. Children and young adults can be underestimated due to the low studies involving them. It is important to listen the patient issues due to high correlation with the ophthalmic examination, helping in diagnosis and treatment increasing the patient satisfaction.

Choroidal involvement in patients with systemic lupus erythematosus

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Purpose: To assess indocyanine green angiographic findings in patients with systemic lupus erythematosus (SLE).

Materials and Methods: Prospective cross-sectional study including 30 patients (60 eyes) with active SLE. All patients underwent detailed ophthalmic clinical examination, fundus photography, fluorescein angiography (FA), and indocyanine green angiography (ICGA).

Results: Of the thirty patients, twenty eight (93%) were female. Mean age was 34 years. Mean bestcorrected visual acuity was 20/25. Fundus and FA findings included vascular tortuosity (3.3%), cotton-wool spots (18%), retinal hemorrhages (5%), retinal pigment epithelial changes (6.6 %), drusen-like deposits (6.6%), branch retinal vein occlusion (1.6%), venous macroaneurysm (1.6%), optic disc edema (3.3%), peripheral retinal capillary non-perfusion (1.6%), disseminated peripheral punctiformhyperfluorescence (6.6%), telangiectasis (10%), optic disc staining (25%), and point of leakage (6.6%). Fundus examination results were unremarkable in 51.6% of eyes. ICGA findings included areas of hyperfluorescence of variable size and predominating in the posterior pole (93.3%), pinpoints (76%), areas of hypofluoresence (83.3%), choroidal vascular staining (26%),dilated fuzzychoroidal vessels (36%), and hyperfluorescent fleecy lesions in 6 eyes (10%).

Conclusions: Our results show that a subclinical, non specificchoroidal involvement, detectable only by ICGA, is common in patients with SLE. ICGA may be useful in better understanding the pathogenesis oflupus choroidopathy and in evaluating its severity.

Unilateral serous retinal detachment as first manifestation of syphilis

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Introduction: Syphilis is a sexual transmitted disease caused by Treponema pallidum. Ocular involvement may appear at any state of the disease and is one of the most common manifestations of neurosyphilis. In a patient infected by syphilis and human immunodeficiency virus (HIV), posterior uveitis is the most common ocular presentation.

Case Report: A 35-year-old man complained of redness, pain and blurred vision for 5 days in the left eye (LE). Ophthalmoscope exploration showed a focus of choriorretinitis on upper and nasal area, snowballs and serous retinal detachment. Analytical tests were requested, obtaining positivity in nontreponemal and treponemal tests with positive anti-HIV antibodies. He received intravenous penicillin and subtenon corticosteroids. After one day of treatment the patient suffered an allergic pustular rash. The desensitization protocol was not successful so he was treated with doxycycline instead. Two months later the lesions had disappeared.

Conclusions: Unilateral serous retinal detachment as first manifestation of syphilis is very uncommon. Posterior uveitis involvement in syphilis mainly occurs in HIV infection this is why HIV tests are always required in patients with positive treponemal test. Jarisch-Herxheimer reaction must be excluded when systemic symptoms appear during the first 24 hours after initiation Penicillin therapy. Doxycycline is the preferred second-line agent for the treatment of syphilis. The level in cerebrospinal fluid achieved is higher than the peak level of other alternative drugs expected from the current dosage recommended for treatment of latent or neurosyphilis.

Perioperative treatment is the key to the succsee of treatment of juvenile chronic arthritis (JCA) and its associated uveitis complicated cataract surgery

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Purpose: To study the importance of perioperative treatment of patients with JCA associated uveitis who develop cataract.

Methods: Retrospectively analyzed the clinical data of 10 patients(19 eyes) with JCA associated uveitis who develop cataract including history of present illness, past medical history, detection of HLA-B27 and X-ray examination of sacroiliac joint and spine. In addition, analyzed the treatment, outcome and complication of these patients.

Results: Four of the ten patients (7 eyes) were male, the other six patients (12 eyes) were female. The episode ages of JCA and uveitis were 8±7 and 9±5; according to the laboratory examination, all patients were ANA( ), ASO(-), only one patient was RF( ).Five eyes had cataract surgery when patients are 8-16 years old, five eyes had cataract surgery when patients are 16-26 years old, the other eyes had cataract surgery when patients were 26 years of age or older. Seven patients(14 eyes) were diagnosed of JCA before the surgery,and treated with orally ciclosporin A, local cycloplegia agent, glucocorticoid eye drops for 6-12 months, and have maintenance treatment after surgery for half a year. The vision of all the patients improved to some extent. Three patients(5 eyes)- were preoperatively diagnosed of congenital cataract not JCA, iritis- attacked seriously with pupil membranous adhesion within a month after the surgery, and drug can not control it. Three of these eyes developed secondary glaucoma and vision turn to CF before eyes. Two of these eyes atrophied and only -have light sensation.

Conclusions: Most JCA with uveitis are chronic recurrent anterior uveitis, and it often develops insidiously within 5 years after clinical manifestations of JCA appeared. Cataract is one of its main complications. Asking for details of the history, and according to the typical clinical presentation, history of arthropathy and ANA positive results can make a definite diagnosis. Seriously treating JCA concurrent cataract, preoperative and postoperative reasonable use of corticosteroids and other immunosuppressive agents and close follow-up count for much.

Screening of key genes and inflammatory signalling pathway involved in the pathogenesis of HLA-B27-associated acute anterior uveitis by gene expression microarray

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Objective: To investigate the genes and signalling pathways located upstream of the inflammatory processes in human leukocyte antigen (HLA)-B27-associated acute anterior uveitis by gene expression microarray.

Methods: Experimental study. HLA-B27-positive and –negative monocytes isolated from human peripheral blood were stimulated with Vibrio cholera lipopolysaccharide (LPS).Gene expression microarrays were used to identify the differentially expressed genes.Differentially expressed (DE) genes were testified by RT-PCR and analysed by a series of bioinformatics-based techniques.

Results: Gene expression microarray analysis revealed marked differences between HLA-B27-positive AAU and HLA-B27 negative healthy control peripheral monocytes in the genes that are upregulated in response to LPS stimulation with 1105 genes and 25 genes respectively. Gene Ontology enrichment(GO) and pathway analysis indicated that genes participating in protein transport and folding were essential to the inflammatory process. The LPS receptor-TLR4 induced Toll-like receptor(TLR) signalling pathway and pathway related to Vibrio cholerae infection are located upstream of the network and contribute to the overall response. Among the DE genes, PIK3CA, PIK3CB, AKT3, and MAPK1 may play critical roles in inflammation.

Conclusions: Equivalent LPS stimulation induces a different response in HLA-B27-positive peripheral monocytes compared to normal control, suggesting that the TLR pathway is involved in the pathogenesis of HLA-B27-associated AAU. Blocking this pathway and other pathways by siRNA interference of candidate genes may contribute to the development of a treatment for this type of AAU.

A case of human thelaziasis in child

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A 3-year-old female were brought to Beijing Chaoyang Hospital by her parents on 06/28/2013 with a history of rubbing her right eye and the complaint of a foreign body sensation in the affected eye. The patient was otherwise healthy, and the history of infectious disease was denied. Cats and dogs were raised in her neighborhood, but there were no pet dogs or cats in the household. The patient also did not give any history of exposure to infected areas or contaminated water. On examination, the VA of the patient was 0.8 in both eyes. Conjunctival congestion and chemosis could be found, and flakes of mucopus were seen in the fornices. A thread-like worm was observed wiggling in the lower conjunctival sac of the right eye. Orbit, eyelid, lacrimal apparatus, eyeball, cornea, sclera, anterior chamber, iris, pupil, lens, posterior chamber and fundus were found to be normal. The cream-colored, motile worm was immediately removed and sent to the laboratory. Conjunctive sac flushing and antibiotic eye drops was given to the patient afterwards. All symptoms were relieved on the next day, the patient stopped scrubbing the right eye, and conjunctival congestion was reduced. No worm or ovum could be found in the eye or in the saline been used to irrigate the conjunctive sac. The worm was fixed in 10% formalin and examined by the department of parasitology at Capital Medical University. It was then identified as Thelazia.

The worm was ivory white and thread-like. The length of the worm was about 1.6cm and the breadth was within the range of 0.3-0.6mm. Macroscopically, transverse cuticular striations were seen in the whole body of the worm except both ends. The edge of the striation was sharp and serrated. The keratinized buccal cavity was trapezoid and located in the obtuse anterior end, while the posterior end was ventrally coiled and relatively cuspidal. Hollow translucent caudal spicule, which could be differentiated from the eyelashes, was shown on the posterior portion.

Inhibiting Effect of-Radix Hedysari Polysaccharide (HPS)-on Endotoxin-Induced Uveitis in Rats

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Purpose: To investigate the anti-inflammatory effect of Radix Hedysari Polysaccharide (HPS) on the clinical indicators also the expression of Toll like receptor-4(TLR4) and its downstream transduction molecules on endotoxin-induced uveitis in rats.

Methods: EIU was induced by intraperitoneal injection of lipopolysaccharide (LPS 200 μg) in male Wistar rats. HPS (400mg/kg), DXM (1mg/kg) or an equivalent volume of normal saline was injected intraperitoneally, respectively, 1 hour before the LPS induction. The clinical manifestation was observed and scored at 2 h intervals by slit microscope. The inflammatory reaction degree was inspected by routine histological examinations, and expression of TLR4, MyD88 in iris-ciliary body complex was detected through double-labeled immunofluorescence study. Real time RT-PCR was used for observing the effects of HPS on TLR4 complex, MyD88and NF-κB p65 mRNA expression. The protein expression of TLR4, MyD88 and NF-κB p65 were examined by Western blot.

Results: HPS treatment had similar therapeutic results with dexamethasone on significantly reducing the clinical severity of EIU as well as fibrin exudations and inflammatory cell infiltrations in the eye. Correspondingly, according to the result of immunofluorescence, HPS treatment significantly suppressed the expression of TLR4, MyD88 in iris-ciliary body complex. HPS treatment could also remarkably reduce the mRNA and protein expression of TLR4 complex, MyD88and NF-κB p65.

Conclusion: HPS can suppress intraocular inflammation of EIU by inhibiting TLR4 and its downstream signal transduction pathway.

Fundus autofluorescence in active ocular toxoplasmosis

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Purpose: To characterize the fundus autofluorescence (FAF) findings in patients with active ocular toxoplasmosis (OT).

Methods: Full clinical examination and FAF imaging was undertaken in 36 eyes of 35 patients with active OT. FAF was performed using a Topcon fundus camera with an excitation filter peak at 560 nm and a barrier filter centered at 655 nm. Patients with severe media opacity and/or far peripheral location of lesions were excluded from the study.

Results: twenty-one men and 14 women were included. The mean age at presentation was 30.9 years (range 12 - 76 years). Forty-eight percent of patients had atypical presentations, 12 (34.3%) had macular involvement and 7 (20%), juxtapapillary lesions. Different patterns were identified, depending on the degree of exudation and retino-choroidal involvement, grading from subtle amorfous fluorescence (45.7%) to more intense, discrete coalesced hyperautofluorescence. During follow-up, a rim-shaped hypoautofluorescent area progressed in a centripetal fashion until disappearance of the hyperautofluorescence in most cases. In typical presentations, FAF easily alowed to differentiate scars from the active focus. FAF imaging clearly defined active focal toxoplasmic lesions in cases of presumed papillitis and neuroretinitis

Conclusion: FAF is a useful and no invasive tool in the management and documentation of OT, easily disclosing the extent of retino-choroidal damage, and offer additional information about associated alterations.

Evaluating the effect of cavum vitreum injection of triamcinolone acetonide (TA) to treat uveitic macular edema by optical coherence tomography

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Objective: (1) To study the effect of cavum vitreum injection of triamcinolone acetonide (TA) to treat macular edema (ME) resulting from uveitis and evaluate its therapeutic effects. (2) To investigate the correlation between optical coherence tomography (OCT) and fluorescein angiography (FA) features and visual acuity (VA). (3) To determine the impact of OCT/FFA patterns on visual improvement over time.

Methods: 17 eyes of 14 patients followed for uveitis with macular oedema and adequate media clarity from January 2010 to December 2012 were included in this retrospective-study. Optical coherence tomography and Fluorescein fundus angiography were performed before and after treatment of TA injection. We examined the relationship between BCVA and central macular thickness.

Results: 16 eyes (94.1%) of 13 patients had an improvement of their VA, except one eye with-posterior-capsular-opacity. The mean BCVA before and 3 month after the TA injection were 0.713±0.156(LogMAR) and 0.274±0.222(LogMAR) respectively. Mean retinal thickness at the central fovea detected by OCT were 237.12±50.78μm, 236.59±49.72μm and 235.76±51.08μm at 1, 3 and 6 month after the TA treatment. The uveitis macula edema reduced in all eyes 6 month after the treatment. There was a correlation between VA and central thickness on OCT

Conclusion: OCT is effective in detection of macular oedema. It allows determination of the distribution of fluid and quantification of retinal thickness which is correlated with the visual acuity of the patient. Macular edema is the main cause of severe visual impairment in uveitis. Intravitreal injection of triamcinolone acetonide can eliminate the macular edema and improved the visual acuity, but long term effects remain to be further studied.

Cytomegalovirus corneal endotheliitis in immunocompetent patients: two case reports

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Introduction: Cytomegalovirus (CMV)-related corneal endotheliitis is an inflammation of the corneal endothelium caused by CMV. It is characterized by keratic precipitates, with or without corneal edema, destruction of the endothelium, and a mild anterior chamber reaction. Here we report two cases of cytomegalovirus (CMV) corneal endothelitis in the immunocompetent patients treated with systemic ganciclovir.

Case report: Two healthy male patients presented with unilateral recurrent hypertensive iritis were referred to our hospital due to poor IOP control for a period. On examination, both cases showed coin-shaped keratic precipitates (KPs) with stromal edema and decreased endothelial cell count in the affected eyes. Minimal anterior chamber reaction was also noted. Aqueous polymerase chain reaction (PCR) test revealed positive results for CMV DNA. Under the diagnosis of CMV endotheliitis, these two cases were treated with intravenous ganciclovir for 1 week and shifted to oral valganciclovir for 11 weeks. After 3 months of treatment, coin-shaped keratic precipitates (KPs) were completely resolved and IOP got well controlled in both cases. There was no recurrence during the follow-up 6 months.

Conclusion: CMV has been reported as a causative agent of corneal endotheliitis. We reported two cases of cytomegalovirus (CMV) endotheliitis in the immunocompetent patients. Both cases responded well to systemic ganciclovir.

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The histology of NRAS transgenic mice and BDUMP

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Purpose: To describe the histologic finding in transgenic NRAS mice eyes and to compare to the histology of eyes of patients with BDUMP

Methods: heterozygous mice that had a constitutively activated NRAS were sacrificed and their eyes enucleated, fixed, embedded,, sectioned and stained with HandE.

Results: There was obliteration of the normal choroid by melanocytes and extension of the melanocytes into the trabecular meshwork and extrascleral space

Discussion: the findings seen in the eyes of these transgenic mice are similar to those described in the literature in eyes of patients with Bdump

Severe Anterior Uveitis in Patients with Urinary Tract Infection

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Introduction: To present a case series of patients manifesting with severe anterior uveitis and to illustrate its association with urinary tract infection.

Case Report: Three women presented with severe signs and symptoms of anterior uveitis and likewise tested positive for urinary tract infection (UTI). They were treated with topical and periocular steroids as well as Ofloxacin 200mg/tab BID for 7 days. Upon follow-up, there was significant improvement of ocular inflammation.

Conclusion: Uveitis with UTI can present with more severe signs of inflammation and vision threatening complications. Treatment with appropriate antibiotic is needed and must be considered in patients with concomitant UTI.

A new interesting way of handling infectious keratitis by Corneal Cross Linking (CXL).State of the art.

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Purpose: To summarize the published data and evaluate the effectiveness of this treatment on infectious keratitis.

Material and Methods: A Medline search was performed to identify all articles describing treatment of CXL in infectious keratitis. According to protocol for a Cochrane systematic metaanalysis, all the articles included in this study were classified as a level of evidence of 3. (Level 3= non analytic studies). To assess the risk of bias of each study, we evaluated the similarity of groups at baseline, the description of primary and secondary outcomes and the presentation of the results. Furthermore, the adequacy of reporting data and the missing follow up was evaluated.

Results: The total number of eyes treated with CXL was 104. The infectious keratitis was associated to bacteria in 58 eyes (57%), Gram in 44 (43%), among these 4 Mycobacterium (3.6%), and Gram – in 14 eyes (13%), Fungus in 13 eyes (12 %,), Acanthamoeba in 7 eyes (7%). In 26 eyes (25%) the microbiological culture was negative or not performed. The mean time of re-epithelization after CXL was 20.7±28.1 days (min 3-max145). 16 eyes underwent deep or lamellar keratoplasty. Corneal transplantation was more frequent in fungus followed by Acanthamoeba, Gram and Gram-.

Conclusion: CXL could be a new interesting way of handling infectious keratitis .The absence of control groups and the high risk of bias in studies suggest performing a new study where the standard treatment is compared to CXL and the severity of keratitis and infecting organism was homogeneus.

Intravitreal dexamethasone

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Case Report: We report a 8-year-old boy with pars planitis associated with cystoid macular edema (CME). He was treated with methotrexate combined with mycophenolate mofetil without improvement of CME and vitritis. He received an intravitreal sustained-release dexamethasone implant. During 4 months follow-up CME and vitritis were resolved. No significant side-effects were observed. At the fifth month increased vitritis associated with CME was detected.

Conclusions: Intravitreal sustained-release dexamethasone implant controls inflammation for short-term in children with pars planitis without significant side-effects.

A rare case of Blau syndrome from Indonesia

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Introduction: Blau syndrome (MIM 186580) is a rare autoinflammatory granulomatous disease that involve skin rashes, arthritis and uveitis. This disease occurs secondary to a single amino acid mutation of the NOD2/CARD15 gene on chromosome 16p12-q21. It is first reported in 1985 and fewer than 100 cases are known. This is the first case report of Blau Syndrome from Indonesia.

Case report: An 8-year-old boy was consulted to ophthalmology department with suspicion of juvenile idiopathic arthritis. He had a history of skin rash since 3 months old and spread to all over the body and trunk at 4 years old. Joints swelling appeared when he was 5 years old, symmetrically in the knee, wrist, ankle, and they were causing movements restriction. Redness of the eye, blurred vision and pain in both eyes started since he was 7 years old. In both eyes, his visual acuity was hand movement; cornea was hazy due to band keratopathy, iris bombe, busacca nodules, 360° posterior synechiae, neovascularization of the iris, and cataract. Posterior segment was in normal limit. The genetic result showed a c.1000>C>T p. (Arg334Trp) mutation in exon 4 of the NOD2 gene associated with Blau Syndrome. His parents and younger sibling don't have any similar clinical signs and symptoms. He was treated with oral and topical steroids. Steroid treatment induced high intraocular pressure and Cushing syndrome. Tapering off the steroid and adding the methotrexate managed the condition. The skin and joint swelling was improved and uneventful cataract surgery was done in the left eye. The visual acuity was not improved and he developed a retinal detachment.

Conclusion: Early recognition of Blau syndrome is necessary because late presentation of inflammation of the eye could lead to blindness and surgical intervention in such late stage have a grave prognosis.

FAF and SS-OCT in patients with ampiginous choroiditis

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Purpose: To analyze the choroidal thickness (CT) underneath the typical retinal atrophic lesions in cases of ampiginous choroiditis (AC).

Methods: Multimodal imaging findings obtained with swept source optical coherence tomography scans (SS-OCT), color photographs and fundus autofluorescence (FA) of patients with AC were analyzed. CT was mesured with the manual caliper of the SS-OCT. RESULTS: Three eyes of three patients diagnosed with AC were reviewed. The most peculiar finding was a thinner CT under the atrophic areas. The exactly same point without atrophy (SPWA) of the contralateral eye of each patient was used as control. Case 1: the three analyzed areas showed decreased CT (184 µm, 35 µm and 48 µm) compared with the SPWA of the fellow eye (237 µm, 147 µm and 152 µm). Case 2: the average CT of temporal atrophic area was 68 µm, whereas SPWA measured 135µm. Case 3: no differences between both eyes were evidenced, with CT in the AC of 329 and 282 µm, and 302, 282µm in SWPA respectively.

Conclusions: CT underneath the typical retinal atrophic lesions may be decreased due to choriocapillaris atrophy. If this change is primary or secondary to the retinal atrophy should be further investigated in prospective studies.

Outcomes of surgical management in patients with uveitic cataract

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Purpose: To assess the visual outcome of cataract extraction in patients with uveitis and to determine the postoperative complications responsible for the decrease in visual acuity.

Design: A prospective, non comparative study. A total of 116 eyes fulfilled the enrollment criteria.

Methods: 116 eyes with uveitis were operated for cataract. The patients were followed up for 3 months post surgery. All patients had well controlled uveitis for at least 3 months prior to the surgery with either anti-inflammatory medications or immunosuppressives. The postoperative complications limiting the visual acuity were noted at 1 month and 3 months post surgery.

Results: Patients were divided into those with anterior disease (n=63), intermediate disease (n=14), posterior disease (n=5), panuveitic group (n=34). Overall, the visual improvement was seen in 107 (95.5%) patients. In the anterior disease group, 98.4% of eyes showed an improvement in vision (median 5 Snellen's lines) with 93.4% with a VA of 6/12 or better at 3 months. In the Intermediate group, 100% shows an improvement in vision (median 4 snellen's lines) with 92.9% with a VA of 6/12 or better and in the Posterior group, 100% shows an improvement in vision (median 7 snellen's lines) with 100% with a VA of 6/12 or better at 3 month. In the PAN group, 87.1% of eyes showed an improvement in vision (median 6 snellen's lines) with 66.7% with a VA of 6/12 or better at 3 month. The causes for non improvement of visual acuity at 3 months was due to posterior capsular opacification (n=16, 14.3%) involving the pupillary area, persistent uveitis (n=24, 21.4%) with cystoid macular oedema (n=7,6.3%), and epiretinal membrane formation(n=11,9.8%).

Conclusion: The outcomes of cataract extraction in patients with uveitis were satisfactory. Phacoemulsification with PCIOL implantation is safe and is associated with less severe postoperative inflammation. It is imperative to have a quiet eye before performing cataract surgery to have good visual outcomes with lesser postoperative complications and since persistent uveitis is one of the commonest complications seen resulting in macular oedema and posterior capsular opacification, all eyes with persistent uveitis should be aggressively managed with anti-inflammatory medications.

Cataract extraction in eyes with uveitis: visual outcome and complications

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Introduction: Cataract is a common complication of uveitis and its treatment. This study investigates the outcome of cataract extraction in patients with uveitis.

Materials and methods: Retrospective review of the medical records of adult patients with uveitis, who underwent cataract extraction between the years 1991-2008.

Visual acuity, intraocular inflammation data, surgical data and complication rate, were collected.

Results: 89 patients (114 eyes) were found. Mean age was 48.58±18.06. 49.1% of the eyes had panuveitis, 42.1% anterior uveitis, 6.2% posterior uveitis and 2.6% intermediate uveitis. 84 eyes (76.4%) received perioperative anti inflammatory prophylaxis. Surgical procedures included 53.5%phacoemulsification, 31.6 CE, 14%lens aspiration and 0.9%ICCE. IOL was implanted in 112 eyes (98.2%): Hydrophobic acrylic(36.4%), hydrophilic acrylic(30%), PMMA(26.4%) and heparin coated PMMA(6.4%). Mean follow-up time was 41.46 months. BCVA at the last follow-up visit improved by 0.59log MAR compared to preoperative BCVA(p=0.001).

BCVA improved by 2 or more lines in (80.7%) at the last follow-up visit. Severe degree of intraocular inflammation has increased from 2.6% preoperatively to 64.8% at the first postoperative day then dropped to 16.7% at 1 month postoperatively, 12.6% at 3 months and 8.9% at the last follow-up visit. Complications rate was: CME(22%), PCO(63%). ERM(28.9%). YAG laser capsulotomy was performed in(32.5%).

Conclusion: Most eyes with uveitis achieve significant improvement in visual acuity following cataract extraction, which remains stable over a long follow-up. Postoperative intraocular inflammation increases at the first month after surgery and then subsides. The high rate of postoperative complications in uveitic eyes renders special attention preoperatively at surgery and postoperatively.

Efficacy of Anti-Tumor Necrosis Factor-alpha Therapy in Refractory Non-infectious Childhood Uveitis

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Purpose: To evaluate the efficacy and safety of anti-tumor necrosis factor-alpha (anti-TNF-α) agents including infliximab and adalimumab in the treatment of refractory non-infectious childhood uveitis.

Materials and Methods: The medical records of 9 eyes of 6 children (M/F:1/5; mean age 12.8 ±5.3 years) diagnosed with refractory non-infectious uveitis and treated with anti-TNF-α agents between 2007 and 2013 were reviewed retrospectively. Visual acuity and uveitis relapse rates were evaluated before and after commencement of anti-TNF-α treatment.

Results: Diagnoses included idiopathic intermediate uveitis in 2 (33%) and Behcet's panuveitis in 4 (67%) children. Mean age at onset of uveitis was 11.2±5.3 (7 to17) years. All children received and were resistant to therapy with one or more immunosuppressive agent, previously. Three children were treated with infliximab (5 mg/kg, IV at 0, 2, and 6 weeks, then every 8 weeks) and 3 with adalimumab (24 mg/m2, sc, every 2 weeks). Overall, mean treatment period for anti-TNF-α agents was 16.5 ± 7.1 (6-27) months, and treatment response was observed in all children. Basal uveitis relapse rate was of 3.7±1.5/year before anti-TNF-α treatment and none of eyes had attack during treatment period. Potential vision was preserved in all of the 9 eyes and best-corrected distance visual acuity was increased at least two logMAR lines in 6 out of 9 eyes (67%). No adverse effect requiring cessation of anti-TNF-α agents was observed.

Conclusions: In line with the previous data, our findings also suggest that infliximab and adalimumab may be tried in the treatment of non-infectious childhood uveitis resistant to other therapeutic approaches. However, because of severe side effect profile of these medications, they should be reserved and monitored in selected cases.

Key words: anti-TNF-α agents, adalimumab, infliximab, childhood uveitis

Bilateral Acute Transillumination of Iris: Case Report

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Purpose: To report a case with bilateral acute iris transillumination (BAIT), pigment dispersion, and sphincter paralysis.

Methods: Case report

Results: A 33-year-old woman with acute iridocyclitis refractory to systemic and topical corticosteroid treatment was referred to our clinic for another opinion. She was on topical prednisolone asetat (8 times a day) and systemic methylprednisolone (1mg/kg/day) for 2 weeks. Her visual acuity was 20/25 in both eyes with intraocular pressures of 30 mmHg in the right and 32 mmHg in the left eye. Ophthalmic examination revealed bilaterally 4 pigment dispersion in the anterior chamber, symmetrical diffuse iris transillumination, pigment deposition on the corneal endothelium and trabecular meshwork. Pupils were mydriatic and poorly responsive to light. Systemic corticosteroid was discontinued and topical corticosteroid was reduced to 4 times a day. Topical hipotensive dorzolamide/timolol-fixed combination two times a day was started. With the decrement of intraocular pressure to normal limits, pigment dispersion decreased gradually and disappeared completely within 2 weeks. However, midriatic pupillae poorly responsive to light and iris transillumination resisted. These findings suggested the diagnosis of BAIT.

Conclusion: Clinicians should recall BAIT syndrome to mind in the differential diagnosis of iridocyclitis and pigment dispersion to avoid unnecessary diagnostic evaluation and treatment.

Key words: bilateral acute iris transillumination (BAIT), pigment dispersion, uveitis

Intermittent Bilateral vitritis: what lies behind

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History: We present a 32 year old male with blurred vision OE (4/10) followed by another episode of blurred vision OD(8/10) and floaters 15 days later. It remitted in 1 month to 10/10 ODE.

Two months later, OD relapsed to 5/10. For one year the patient had intermittent ocular complaints : vision fluctuation in both eyes with several episodes of vitritis. Ophthalmic evaluation was performed as needed. He is now stable at 10/10 ODE.

Past Ocular History: myopia, contact lens wearer

Past Medical History: Age of 21 an episode of pain in the inferior left member/fever/non conclusive diagnostic. Age of 31 a diagnosis of phlebothrombosis of the same member. Medicated on aspirin ® 100 mgr/day. Age of 32 erithema nodosum at the left inferior member plus fasciitis of the left foot previous to ocular symptoms.

Social history: smoker 3 cig./day

Examination on first admission: OD 10/10; OE 4/10; tonometry : 16 mmHg OU; slit lamp examination: quiet anterior segment.

On dilated fundoscopic examination: OD/normal; OE/vitritis 4, floaters

Automated perimetry: normal OU

FA: OD/ normal; OE /late superotemporal macular leakage

Macular OCT:normal OU

Ancillary tests all normal but for:

ESR=41mm (<15)

Lupus anticoagulant sillica cotting: 1.63(<1.20)

Anticardiolipin antibody Ig M: reactive

Treatment: topical and systemic prednisolone as needed/aspirin 100mg; now on deflazacort 6mg aspirin® 100mg

Diferential Diagnosis:

Vasculitis

Collagen disease

Sneddon's syndrome

Inherited thrombophilia

Conclusion: At least one documented clinical episode of venous thrombosis two laboratory lupus anticoagulant/anticardiolipin IgM present in plasma, no known underlying autoimmune disorder suggest Primary Antphospholipid Syndrome in this patient.

Bilateral vitritis with relapsing vision fluctuation is an uncommon presentation.

Care must be taken to avoid complications of vascular inflammation and visual loss.

Ocular Findings in Autoimmune Lymphoproliferative Syndrome (ALPS)

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Purpose: Autoimmune lymphoproliferative syndrome (ALPS) is a rare inherited disorder that is characterized by a defect in Fas mediatiated apoptosis that results in altered immune tolerance, perseverance of autoreactive T cells, and propensity to autoimmunity and lymphoma. The purpose of this study is to report the eye findings in patients with autoimmune lymphoproliferative syndrome (ALPS).

Methods: Medical records of ALPS patients seen for ophthalmic screening at the National Eye Institute between 2003 and 2013 were reviewed. Demographic data and ocular examination findings were recorded for all patients.

Results: Thirty seven genetically confirmed ALPS patients were identified. Median age at teh time of ocular exam was 28.3 years (11-69), majority were male (70%) and Caucasian (87%). Twenty three patients had normal ophthalmic exminations. Of the 14 (38%) that had remarkable ocular findings, the most common finding was ocular inflammatory diseases in 5 patients (13.5%) including episcleritis (n=1), scleritis (n=1) and uveitis (n=3). All patients with uveitis had posterior segment inflammation and required long term systemic immunosuppressive treatment.

Conclusions: Ocular findings can be diverse and relatively common in ALPS patients. More importantly, autoimmune uveitis that require long term immunosuppressive therapy can be seen in a small proportion of patients.

Clinical Outcome of Fluocinolone Acetonide Intravitreal Implant for Vogt-Koyanagi-Harada Disease

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Purpose: To investigate the clinical outcome including efficacy and safety of fluocinolone acetonide (FA) intravitreal implant for Vogt-Koyanagi-Harada (VKH) Disease

Materials and Methods: Multicenter, prospective, randomized controlled clinical trial which evaluated FA implant for the treatment were acquired, and post-hoc subgroup analyses were performed for the patients with VKH disease. Clinical outcomes were compared between implant-treated eyes and the fellow eyes.

Results: Of 664 patients, 34 patients were diagnosed with VKH disease, and completed 36-month follow-up except 2 patients. Mean subject age was 38.7±12.6 years, and 12 (35.3%) were men. The recurrence rates were significantly reduced (32.4%) in implanted eyes than in the fellow eyes (79.4%) ($p<0.001$). Uveitis recurred 0.62±1.05 times in the implanted eye and 3.09±3.06 times in the fellow eye ($p<0.001$). Dose of systemic steroids were significantly reduced, 11.6 mg/day preoperatively, and 2.3mg/day postoperatively ($p<0.001$). Visual acuity (VA, logMAR) in the implanted eye were 0.284±0.395 preoperatively, and 0.393±0.403 postoperatively ($p=0.156$), and there was no significant difference between pre- and postoperative VA. After implantation, intraocular pressure increased more than 21mmHg in 28 (82%) of the study eyes and 10 (29%) of the fellow eyes ($p<0.001$), of which 16 (57%) of the study eyes and 1 (10%) of the fellow eyes required a filtering surgery. Cataract progressed in 15 (88%) of 17 study eyes and 11 (58%) of 19 fellow eyes ($p=0.042$). Finally, 16 (94%) of the study eyes and 9 (47%) of the fellow eyes underwent cataract surgery.

Conclusions: In this post-hoc subgroup analysis, FA intravitreal implant reduced the recurrence rate of VKH disease, as well as the required dose of systemic steroid. Major complications included cataract progression and increase in intraocular pressure among significant portion of the subjects.

Atypical vogt koyanagi harada syndrome – our experience

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Purpose: To report the clinical features and the visual outcomes in Vogt Koyanagi Harada (VKH) syndrome with atypical presentations

Materials: Thirteen eyes of eight cases of Vogt Koyanagi Harada syndrome, which presented to a tertiary eye care centre in India were retrospectively reviewed.

Methods: The case records were analyzed for patient demographics, clinical signs, investigations, management and complications with final visual outcome. Only patients with at least 6 months of follow-up were included in the study. Fundus fluorescein angiography (FFA) and ultrasound B-scan was done for all patients. Spectral domain Optical coherence tomography (Heidelberg spectralis) was done for selected patients.

Results: There were 47 patients of Vogt Koyanagi Harada syndrome from January 2005 to September 2013 were analysed. In this eight patients were found to have atypical presntation Six (75%) out of the 8 patients were females. Clinical presentation was panuveitis in 7 eyes and posterior uveitis in 6 eyes. The typical FFA, ICGA and SDOCT features confirmed the presence of VKH syndrome. One patient developed choroidal melanoma during the chronic phase of the disease. Two patients had associated scleritis in addition to VKH. One patient had ischemic optic neuropathy and 1 patient had neuroretinitis. All patients were treated with oral steroids /- immunosuppressants. All patients had good visual outcome except 1 with ischemic optic neuropathy.

Conclusion: High index of suspicion along with ancillary investigations helps us in diagnosing atypical cases. To the best of our knowledge, malignant choroidal melanoma in case of VKH has not been reported earlier.

A case of bilateral posterior ischaemic vasculitis secondary to kikuchi's disease with left foot drop

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Introduction: We are reporting A case of Bilateral posterior ischaemic vasculitis secondary to Kikuchi's disease with left foot drop

Case report: A 24 yr female presented with blurred vision in both eye since one week, history of fever with lymphadenopathy since 6 weeks undiagnosed and refractory to treatment. FFA showed Early and late hypofluorescence with sluggish filling with lack of perfusion in superotemporal arteries and perivascular leak. On investigations she had raised LDH. Lymph node Biopsy in favour of Kikuchi's disease. Nerve biopsy suggestive of vasculitis, Muscle biopsy neurogenic atrophy with focal myopathic features. Managed with systemic steroids, immunosupressants and Panretinal photocoagulation.

Conclusion: Kikuchi's disease can present as an unusual cause of decreased vision in association with fever, skin rashes and posterior triangle cervical lymphadenopathy that can mimick Infective / autoimmune disease. Aggressive approach with systemic steroids and immunosuppressive therapy helped us to control the disease

Choroidal Thickness in Ocular Sarcoidosis using Enhanced Depth Imaging Optical Coherence Tomography

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Purpose: To evaluate the choroidal thickness in patients with ocular sarcoidosis using enhanced depth imaging optical coherence tomography (EDI-OCT) and comparing it with normal subjects.

Method: Eighteen eyes of 9 patients with ocular sarcoidosis (8 women, 1 man, mean age: 59,12±18,49 years) were enrolled in this study. Their subfoveal choroidal thickness was measured using EDI-OCT in the quiescent phases of sarcoidosis uveitis, and compared with the age, sex, and spherical equivalent-matched normal subjects (6 women, 3 men, mean age: 59,0±12,42 years).

Results: The mean subfoveal choroidal thickness was 281.76±88.1 µm in patients with sarcoidosis, and 338.82±72.02 µm in controls. Significant differences were found at points between nasal 1500 µm and temporal 1000 µm to the fovea between patients and control group (p=0,04, at fovea).

Conclusions: Patients with ocular sarcoidosis had thinner choroids in the quiescent phases when compared to normal subjects.

Pattern of acute retinal necrosis in a referral center in Tunisia, North Africa

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Purpose: To describe the clinical features and the visual outcome of acute retinal necrosis (ARN) syndrome in a referral center in Tunisia.

Materials and Methods: The charts of 12 patients (12 eyes) with newly diagnosed ARN syndrome were retrospectively reviewed.

Results: The mean age was 35.7 years (range: 17-70 years). Eight of the patients were men and 4 were women. All patients were immunocompetent. Peripheral retinitis was associated with macular involvement in 3 eyes (25%). Polymerase chain reaction (PCR) results showed Herpes simplex virus-1 in 4 eyes (33.3%), Varicella-Zoster virus in 3 eyes (25%), and were negative in 5 eyes (41.7%). All patients were treated with intravenous aciclovir, followed by oral valaciclovir for a mean duration of 3.8 months. Intravitreal injections of ganciclovir were given in 2 eyes. The mean follow-up was 6.25 ± 4.67 months (range, 3 to 16 months). During the follow-up, no patient developed ARN in the fellow eye, but retinal detachment (RD) occurred in 3 eyes (25%). Final visual acuity was 20/40 (0.3 log MAR) or better in three eyes (25%) and 20/200 (1 log MAR) or worse in seven eyes (58.3%). Factors associated with poor visual outcome were duration between onset and treatment > 14 days (p=0.015), macular involvement (p=0.045), development of RD (p=0.018) and 25-50% of retinal involvement (p=0 .045).

Conclusion: ARN carries a poor visual prognosis in Tunisia. RD developed in one-fourth of cases despite antiviral treatment. Early diagnosis and prompt management are mandatory to improve visual outcome.

Fuchs uveitis, a review of 36 cases from Tunisia

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Purpose: To characterize and analyze the spectrum of Fuchs uveitis (FU) in a referral center in Tunisia.

Materials and Methods: Retrospective study of the charts of 36 patients (40 eyes) with FU. Results: The mean age was 34 years (range: 13 - 63). Male to- female ratio was 0.9. Four patients (11%) had bilateral involvement. The mean interval between onset of symptoms and diagnosis was 16 months. The initial mean visual acuity was 20/63. Clinical findings at presentation included keratic precipitates (85%), diffuse iris atrophy (97.5%), heterochromia (11.1%), iris nodules (6.9%), elevated intraocular pressure (27.5%), cataract (35.7%), and vitritis (85%). Cataract surgery was performed in 10 eyes (25%). Six eyes (15%) required trabeculectomy for refractory glaucoma. Mean final visual acuity was 20/32.

Conclusions: FU is a common uveitic entity in our setting. Heterochromia was seen in only 11.1% of our patients. Diffuse iris atrophy, keratic precipitates and vitritis were the most frequent findings. In the absence of posterior synechiae, the association of these signs strongly suggests FU.

Ocular complications of chickenpox in adults: A report of 3 cases

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Purpose: To describe 3 cases of ocular complications of chickenpox in adults.

Case report 1: A 35-year-old man presented with a vision blurring of the right eye (RE), 4 weeks after chickenpox. Visual acuity (VA) was 20/40. Examination showed 2 vitreous haze, 3 clock hours peripheral retinal necrosis and arteritis, consistent with acute retinal necrosis. After antiviral therapy associated with steroids, VA improved to 20/20.

Case report 2: A 40-year-old man presented with red painful eyes, one week after varicella onset. VA was 20/200 OU. Examination showed stromal keratitis associated with geographic corneal ulcer OU. Treatment consisted of oral valaciclovir and topical corticosteroids. The patient developped a recurrence few weeks after treatment discontinuation, which was successfully treated with valaciclovir and steroid drops. Final VA was 20/63 in the RE and 20/40 in the left eye (LE).

Case report 3: A 39-year-old man with a history of renal transplantation and immunosuppressive therapy was hospitalized for varicella and was receiving antivirals. One month later, he complained of decreased vision OU. VA was 20/200 in the RE and 20/100 in the LE. Slit-lamp examination revealed granulomatous hypertensive anterior uveitis OU. Topical steroids, mydriatics and hypotensive drops were given. A year later, the patient developed anterior uveitis associated with bilateral iris patchy atrophy. Uveitis resolved with topical antivirals and corticosteroids.

Conclusions: Chickenpox may have sight-threatening ocular complications in adults regardless of their immune status.

Endophthalmitis following anti-VEGF injection: analysis of our cases.

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Purpose: To describe clinical findings, culture results, treatment and visual outcome in six patients with endophthalmitis following intravitreal injection (IVI).

Material and Methods: Retrospective analysis of 6 eyes of 6 patients with endophthalmitis following IVI. All patients were treated with intravitreal antibiotic injection at presentation followed by pars plana vitrectomy (PPV) at the earliest possible date. Analysed parameters included initial and final visual acuity, time to diagnosis and treatment and microbiologic culture results.

Results: We were able to identify the causative agent in 4 of the 6 patients. Endophthalmitis symptoms – red eye, ocular pain and visual acuity impairment – appeared 24 to 48h after IVI in four patients with positive culture to Streptococcus species and in one patient with a negative culture. Symptoms appeared 15 days after IVI in the other patient with a negative microbiologic result. All of them were treated with intravitreal antibiotics (vancomycin and ceftazidime) at admission and PPV 24-144h after hospitalization. Visual acuity on presentation ranged from light perception (LP) to count fingers at 50 cm. At the end of the six-month follow-up, visual acuity ranged from LP to 0.1 on a decimal scale.

Conclusions: Gram-positive Streptococcus is responsible for endophthalmitis in multiple cases. These bacteria are oropharynx commensal and aerosol contamination is a significant route for infection. The visual prognosis for aggressive endophthalmitis remains poor despite prompt intervention. Careful prepping of the patient before intravitreal injection continues to be the most important measure to prevent infection.

Inflammatory ocular reaction to intravitreal rituximab in primary intraocular lymphoma: case report

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Introduction: Previous reports have demonstrated the efficacy and safety of intravitreal injections of rituximab for primary intraocular lymphoma (PIOL) treatment.

Case report: A biopsy confirmed, primary central nervous system lymphoma (PCNSL) was diagnosed in a healthy 32-year-old woman. For 5 years before she has been treated with corticosteroids, methotrexate and bilateral vitrectomy for an unresponsive intermediate uveitis, with late retinal infiltrates. Large CD20-positive cells representing 70% of the sample, were detected in aqueous humor (AH) multicolor flowcytometric immunophenotyping (MFI). With the diagnosis of PIOL and PCNSL she received intrathecal methotrexate and systemic chemotherapy (methotrexate and vincristine) -from May to November 2013. Biweekly bilateral Intravitreal rituximab (1mg/0.1 mL) was interrupted after the second injection, (June 2013) because of red and painful eyes with severe anterior chamber (AC) inflammation, accompanied of widespread retinal vascular sheathing. Four weeks later red eyes, sheathing and retinal infiltrates had improved. No complication appeared after a new bilateral rituximab intravitreal injection. They were administered because of the presence of many cells in AC with keratic precipitates. No improvement was achieved, and a new AH MFI disclosed the presence of large numbers of CD3 T lymphocytes, with conserved CD4/CD8 ratio, and residual CD20-positive diffuse large B-cell lymphoma. Retinal infiltrates and AC cells disappeared completely, with no relapses (October 2013), after adding whole brain and ocular radiotherapy (24 Gy) (August 2013).

Conclusions: Our patient not only showed no response to intravitreal rituximab administration, but she developed both a severe anterior segment and retinal vessels inflammation. In our vitrectomized patient, aqueous MFI analysis has allowed to differentiate between lymphomatous inflitration and secondary inflammatory reaction to intravitreal rituximab.

Intravitreal bevacizumab injection therapy in a case with choroidal neovascular membrane secondary to toxoplasmosis retinochoroiditis

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A 57-year old man presenting with visual loss in left eye was diagnosed as choroidal neovascular membrane secondary to inactive-toxoplasmosis retinochoroiditis scar. He underwent intravitreal bevacizumab injection as primary therapy. The choroidal neovascular membrane regressed partially and the initial visual acuity improved from 1/10 to 3/10. Intravitreal bevacizumab injection appears to be effective in the treatment of choroidal neovascular membrane secondary to toxoplasma retinochoroiditis.

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The Clinical Features and Treatment of Cytomegalovirus Endotheliitis

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Idiopathic choroidal neovascular membrane: A case report

El Hamichi Sophia

Viral anterior uveitis: diagnosis by PCR and Goldman Witmer coefficient

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Purpose: 15% of anterior uveitis are secondary by viruses. Rubella virus have been associated with Fuch´s heterochromic uveitis, Citomegalovirus virus (CMV) with Posner-Schlossman syndrome and Varicella-Zoster virus (VZV) or Herpes Simplex virus (HSV) with chronic uveitis with or without keratitis or ocular hypertension. We assess the role of virus infection in patients with idiopathic anterior uveitis.

Methods: 14 consecutive patients who suffer idiopathic anterior uveitis with or without keratitis or ocular hypertension were analized by PCR and Goldman-Witmer coefficient for Rubella, CMV, HSV and VZV virus.

Results: We established the viral etiology in 64.3% (9/14) of patients. For the first time in Spain we documented 3 cases of rubella uveitis. The Goldman Witmer coefficient was positive in 100% (9/9) of diagnosed patients, whereas PCR was positive in 44.4% (4/9). Serum IgG antibodies for the four viruses were detected in 57.1% (8/14) of patients.

Conclusions: PCR and Goldman Witmer coefficient allow to diagnose nearly 65% of patients with anterior uveitis of unknown etiology, particularly hypertensive and chronic. We report for the first time the presence of rubella virus as the etiological agent of Fuchs Heterochromic Uveitis in Spain.

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Non-protozoal ocular parasitosis in the developed world

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Introduction: Ocular parasitosis in human is more prevalent in areas where environmental factors favor the parasitism between man and animals. In recent years, globalization has facilitated the spread of certain ocular parasitic diseases from endemic to nonendemic areas. This report includes a brief description of the diverse forms of ocular non-protozoal parasitosis attended recently in our Hospital, highlighting diagnosis and management.

Case report: Five different non-protozoal parasitosis were recorded in the last 18 months. Two of the cases were toxocara infections, one in the form of endogenous endophthalmitis in a child of 5-year-old.

Other reported cases included eyelash pediculosis, subconjunctival Loa loa filarial worm and myiasis of the conjunctival fornices.

Although presumptive diagnosis is initially based on the clinical suspicion supported by serological tests, definitive diagnosis require parasitic removal and identification.

Extraocular exploration and specimen collection are necessary in some cases, as in the case of philariasis where is required the analysis of the peripheral blood or the ganglionary aspiration.

Further examinations should rule out coinfections such as intestinal parasitations, HIV or malaria, leading to important epidemiological implications.

Conclusion: Non-protozoal parasitosis of the eye can appear as mild disturbances or as a sight threatening phenomena. However, ophthalmologists should be aware of the appropriate diagnose and management of these infections due to the visual effect that can produce.

Has the economic crisis in Greece affected the rate of herpetic eye disease? Report from a tertiary referral center.

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Purpose: To report the rate of patients with herpetic eye disease among the patients with ocular inflammation examined in a tertiary referral center in Greece and to investigate if an increase was found during the economic crisis 2009-2013.

Materials and methods: Retrospective review of the files of patients with ocular inflammation examined and treated in the Ocular Inflammation Department of the University Hospital of Ioannina, Greece. The number of patients with various forms of herpetic eye disease was reported (keratitis, uveitis, keratouveitis, sclerouveitis, scleritis, episcleritis) and the rate of herpetic eye disease was calculated during the years of the economic crisis 2009-2013.

Results: The rate of herpetic eye disease was 10.20% in 2009, 16.96% in 2010, 15.97% in 2011, 22.07% in 2012 and 19.89% in 2013 (11 from 12 months). An increase was observed in the rate of herpetic eye disease during the economic crisis in the referral center that was not statistically significant (p=0.073).

Conclusions: During the years of the economic crisis an increase of the rate of herpetic eye disease was observed in the tertiary referral center of Ioannina, Greece, even though this result was not statistically significant with a borderline p value (p=0.073).

Cilioretinal oclusion in a patient with optic disc edema and "white dot syndrome"

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Introduction: "White dot syndrome" describe a group of inflammatory diseases of retina and choroid.

Case Report: A 19-year-old caucasian female presented with blurred vision in OD accompanied by pain sensation in the right frontal region and lateral wall of right orbit with 5 days of evolution. Past medical history was relevant for previously known OS decreased vision, rhinitis 2 months earlier and anticonceptives ingestion for the last 3 years. BCVA was 10/10 OD and 8/10 OS. There was OS RAPD. OD fundus examination revealed optic disc edema, pale retina edema in the area of supply of cilioretinal artery and multiple white dots in the retinal vascular arcades and periphery. OS presented with pale optic disc. Neuro-imaging showed left optic nerve atrophy. OD SD-OCT showed optic disc edema and edema of the internal retinal layers in the cilioretinal artery supply area. OS presented with internal retinal layers atrophy in papilo-macular bundle. OD FA displayed patent cilioretinal artery and optic disc edema; no alterations in OS. OD ICG showed hipofluorescent lesions in the early and late phases accompanied by hipofluorescent region peri-papilary; no alterations in OS. Electrophysiology tests were normal. Visual field examination demonstrated blind spot enlargement accompanied by peripheral scotoma in both eyes. An extensive evaluation for infectious, inflammatory, vasculitic and hipercoagulable etiologies was negative. Patient was treated with 5 day metilprednisolone pulse and anti-aggregant therapy. An oral corticotherapy maintenance regime was administered. Final visual acuities were 10/10 OD and 8/10 OS.

Conclusion: "White dot syndrome" demands an extensive ophthalmologic and systemic evaluation, being most frequently a diagnostic challenge.

Decisive role of histopathology of lens capsule in the diagnosis of fungal chronic postoperative endophthalmitis

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Purpose: To report two cases of chronic refractory postoperative endophthalmitis with repeated negative cultures of vitreous samples, for which histopathological examination of the lens capsule defined fungal etiology.

Method: Retrospective analysis of clinical, microbiological and histopathological records of two patients with chronic postoperative endophthalmitis managed at a single referral center.

Results: Both patients had chronic endophthalmitis (six and eight weeks) after uneventful phacoemulsification with intraocular lens implantation. Initial treatment consisted of intravitreal and systemic antibiotics, with partial improvement. After subsequent worsening and successive negative cultures of vitreous samples, pars plana vitrectomy, intraocular lens explantation and en bloc capsulectomy were performed. Histopathological examination in both cases revealed multiple septate hyphae sequestered between anterior/posterior lens capsule. Treatment with intravitreal and oral antifungals eventually controlled the infectious process in both patients.

Conclusion: Chronic postoperative fungal endophthalmitis can manifest with repeated negative cultures associated with the sequestration of the microorganism in the capsular bag, similarly to what occurs in Propionibacterium acnes endophthalmitis. Careful histopathological examination of the lens capsule in these cases may be essential for a definitive diagnosis, thus guiding appropriate treatment.

Posterior subtenon triamcinolone acetonide injection for local control of Vogt-Koyanagi-Harada syndrome

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Objective: To analyze indications, efficacy and complications of posterior subtenon injection of triamcinolone acetonide (STTA) for control of intraocular inflammation associated with Vogt-Koyanagi-Harada syndrome (VKH).

Method: Retrospective chart review of all consecutive patients with VKH receiving STTA in a single uveitis referral center.

Results: STTA (20-40mg in 0.5-1mL) was performed on 25 eyes of 15 patients, through a transconjunctival approach in the superotemporal quadrant, with a follow-up of 7-272 months (mean: 68.7 months). Main indications for STTA were severe intraocular inflammation refractory to systemic corticosteroids and intolerance to systemic corticosteroids. In 11 eyes (44%), injection was performed during the acute stage of disease and, in 14 eyes (56%), in chronic-recurrent stage. All eyes in the acute stage had regression of exudative retinal detachment. Those in chronic-recurrent stage had improvement of intraocular inflammation and macular edema. Visual acuity increased in 16 eyes (64%) after STTA and decreased in 4 (16%). Onset/progression of cataracts were observed in 11 eyes (45.8%). Significant elevation of Intraocular pressure was found in 5 eyes (20%), none of which required anti-glaucoma surgery. 1 eye (4%) developed eyelid hematoma. Tapering of oral corticosteroids was possible in 8 of 9 patients (88.8%) after a single STTA. At least one subsequent injection was needed in 9 eyes (36%).

Conclusion: STTA may be an important adjuvant for local control of VKH, particularly in patients with intolerance to systemic corticosteroids. Risks and benefits should be weighed for each case.

Acute retinal necrosis after myelitis associated with Epstein-Barr virus

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Introduction: Case report of acute retinal necrosis (ARN) following myelitis associated with Epstein-Barr virus (EBV).

Case report: A 53-year-old female presented at our uveitis service complaining of decreased vision in the right eye (OD) for 7 days. She reported acute onset of urinary retention and paraparesis six weeks earlier. At that time, she was treated elsewhere with intravenous methylprednisolone followed by oral prednisone, for a presumed nonspecific myelitis, but with no clinical improvement. Initial examination revealed visual acuity (VA) of 20/40 in OD and 20/20 in the left eye (OS). Intraocular pressure was within normal. There was minimal inflammation in the anterior chamber and vitreous of OD. Fundus examination showed multiple confluent areas of peripheral retinal necrosis, associated with vascular sheathing in OD. OS was normal. The patient was then admitted and treated with IV acyclovir, with a fast taper of oral prednisone. Further workup revealed only HIV coinfection. However review of laboratory results from the other hospital disclosed a positive polymerase chain reaction (PCR) for EBV in cerebrospinal fluid, which had been overlooked. Systemic symptoms progressively improved and VA eventually reached 20/20 in OD, after 21 days of IV acyclovir.

Conclusions: EBV is a rare etiologic agent for ARN and can also be associated with prior infection of the central nervous system. The unopposed use of systemic corticosteroids in these patients may facilitate viral spread to the retina. Early antiviral treatment with antiviral is critical.

Intraocular inflammation associated with dengue in the 2013 epidemic

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Objective: To describe a series of patients with intraocular inflammation associated with dengue during the 2013 epidemic in Belo Horizonte, southeastern Brazil.

Methods: Retrospective chart review of patients with intraocular inflammation associated with dengue consecutively seen at a single uveitis referral center in southeastern Brazil, from January to June 2013.

Results: Three patients with uveitis associated with dengue were identified. All had symptoms consistent with recent infection, supported by positive serological results for dengue, and with exclusion of other uveitis etiologies. One of these patients only reported history of dengue after being specifically inquired. Decreased visual acuity (VA) was the main complaint for all patients, presenting in the first 10 days after onset of systemic symptoms of dengue fever. VA at presentation ranged from 20/20 to 20/800. Bilateral ocular involvement was the rule, and main ocular manifestations included posterior uveitis/retinal vasculitis with cystoid macular edema (4 eyes of 2 patients; one with severe occlusive disease), cotton wool spots (4 eyes of 2 patients), and optic disc edema (2 eyes of 1 patient). Treatment consisted of systemic corticosteroids in 2 patients (1 with intravenous methylprednisolone), laser photocoagulation of ischemic areas (two eyes of 1 patient), and oral acetazolamide (1 patient). Intraocular inflammation eventually subsided, with final visual acuity ranging from 20/20 to 20/40.

Conclusion: Although rare, intraocular inflammation associated with dengue can be severe/sight-threatening, and may respond to high dose systemic steroids. In epidemic areas, specific investigation of symptoms of dengue fever in patients with uveitis is warranted.

Recent trends in cytomegalovirus retinitis in a uveitis referral center in Brazil

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Objective: To investigate clinical and epidemiologic profile of patients with cytomegalovirus (CMV) retinitis in a uveitis referral center in Southeastern Brazil.

Methods: Retrospective chart review of patients with CMV retinitis consecutively seen at the Uveitis Service of Hospital Sao Geraldo / HC-UFMG between January 2009 September 2013.

Results: 20 patients with CMV retinitis were identified; 11 (55%) were male and 9 (45%) female. All but one patient had HIV coinfection, with a mean CD4 count of 49.7 cells/mL (median 35 cells/mL). One of these patients was also receiving cyclophosphamide for treatment of multiple myeloma, with subsequent detection of HIV coinfection after diagnosis of CMV retinitis. The HIV-negative patient was using mycophenolate mofetil and tacrolimus after kidney/pancreas transplantation. Among patients with previously known HIV status, 3 (16%) had recently been diagnosed (still not receiving highly active retroviral therapy- - HAART), 11 (58%) had abandoned HAART and 5 (26%) had failure to current HAART regimen. Retinitis was unilateral in 11 patients (55%) and bilateral in 9 (45%). Treatment consisted of intravenous gancyclovir in all but one patient, who received valgancyclovir. Three patients (15%) also received intravitreal gancyclovir. Maintenance therapy was stopped after immune recovery (CD4 count>150 cells/mm). Retinal detachment developed in 5/29 eyes (17%). Final visual acuity of <20/400 was observed in 19/29 affected eyes (66%), with 8 eyes (28%) evolving with no light perception.

Conclusion: CMV retinitis is still an important opportunistic infection in individuals with AIDS, particularly in those abandoning or failing HAART. Many eyes still evolve with markedly decreased vision despite therapy.

Early ocular ultrasonography in infants with congenital toxoplasmosis

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Purpose: To report results of early ocular ultrasonographic evaluation of a cohort of infants with congenital toxoplasmosis in southeastern Brazil.

Materials and Methods: Cross-sectional qualitative and quantitative analysis of ultrasonographic (B-scan) findings in infants with congenital toxoplasmosis, after population-based neonatal screening detecting IgM in dried blood samples.

Results: B-scan was performed in 142 eyes of 71 infants, with a median age of 60 days. 61 eyes (43.0%) had active retinochoroidal lesions. Main ultrasonographic changes were inflammatory vitreous echoes in 55 eyes (38.7%) of 33 infants (46.5%), macular irregularity in 20 eyes (14.1%) of 12 infants (16.9%), choroidal thickening in 15 eyes (10.6%) of 8 infants (11.3%), posterior vitreous detachment in 10 eyes (7.0%) of 13 patients (18.3%), optic disc elevation in 9 eyes (6.3%) of 7 patients (9.9%) and retinal detachment in 9 eyes (6.3%) of 8 patients (5.6%). Microphthalmia, defined as axial length<16mm (according to a published nomogram), was found in 33 eyes (23.2%).

Conclusion: Ultrasonographic examination is useful for better characterization of intraocular inflammation and complications associated with congenital toxoplasmosis, as well as for objective assessment of the presence of microphthalmia.

Assessment of a presumed metastatic choroidal lesion of follicular lymphoma by swept-source optical coherence tomography

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Purpose: To analyze the tomographic characteristics of a solitary choroidal in a patient with systemic follicular lymphoma.

Material and Metods: A 68 year-old patient diagnosed of systemic follicular lymphoma stage III-A under evaluation by the department of Haematology was referred to our unit because of visual impairment in his left eye.

Results: Dilated fundus examination revealed the presence of an amelanotic mass within the superior temporal quadrant of the macular region. The scans through the lesion obtained with swept-source optical coherence tomography evidenced a hyporeflective lesion displacing both the Sattler and Haller layers, with accumulation of hyperreflective material between the lesion and Bruch's membrane. Subretinal fluid without intraretinal cystoid changes was also evidenced.

Conclusions: Swept-source optical coherence tomogramphy may be an elective diagnostic approach to evaluate choroidal lesions in oncologic patients. The peculiar findings for each diagnostic possibilities enables the physician to make an accurate differential diagnosis.

Spectral Domain OCT in Active and Healed Toxoplasma Retinochoroiditis

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Purpose: To evaluate the role of Spectral-Domain OCT (SD-OCT) in the diagnosis, management, follow-up and prognostication of toxoplasma retinochoroiditis

Materials and Methods: 15 eyes of 8 consecutive patients with active and healed toxoplasma retinochoroiditis lesions were studied. A detailed ophthalmic examination including indirect ophthalmoscopy, slit-lamp biomicroscopy, and Spectral Domain OCT (SD-OCT) evaluations were done. The SD-OCT Scans were directed to the macula and to the area of lesions observed during clinical examination.

Results: In Active Lesions, thickening of the post hyaloid overlying the lesions was seen in 14/15 eyes (93.33%), hyper-reflective spherical deposits within the vitreoretinal interface in 11/15 eyes (73.33%), hyper-reflectivity of the retinal layers with disorganization & thickening in 15/15 eyes (100%), acoustic shadowing and thickening of the underlying RPE-choroidal layers seen in 13/15 eyes (86.67%), RPE-Bruch memb reflective complex was focally increased or contained focal splits in 7/15 eyes (46.67%), Epiretinal Membrane was seen in 8/15 eyes (53.33%). During follow-up, there was progressive decrease in size of the hyper-reflective spherical deposits, collapse onto the retinal surface and disappearance, disorganization and thinning of the retinal layers, atrophy of the RPE and normalization of choroid thickness with hyper-reflectivity.

Conclusions: SD-OCT is a very useful non-invasive tool that helps in characterizing the complex toxoplasma retinochoroiditis lesions, studying their evolution and using this information to prognosticate the outcome.

Takayasu's Arteritis

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Introduction: Takayasu's arteritis (Pulseless Disease) is a potentially life-threatening systemic disease which can sometimes present first to the ophthalmologist, so early recognition is important. Case

Report: 18 year old boy presented with sudden loss of vison in left eye. Left eye was NPL, fundus of left eye showed CRAO, right eye fundus showed vascular tortuosity, copper wiring and lattice degeneration with holes. Carotid Doppler showed thrombus in proximal & mid part of LCCA. MR Angio showed Takayasu's arteritis involving Lt CCA, B/L Subclavian, Rt Vertebral and Lt ICA. Serum triglycerides,VLDL were elevated,HDL was decreased. Patient was given IVMP 3 injections, and advised (by vascular surgeon) subcut. inj heparin, clopidogril aspirin, atorcip-F, angimax. Subsequently lost to follow-up for 17 months, patient presented again with distortion right eye since 3 days. BCVA was 6/18p in right eye and NPL in left eye. Fundus exam showed right eye retinal hges, macular star, CW spots, lattice deg, vascular tortuosity, while left eye showed optic atrophy with sclerosed vessels. OCT showed right eye neurosensory elevation, CME (464µ), left eye chorioretinal atrophy (113µ). BP was 162/100mm Hg. BSF and PP were WNL. Serum homocysteine was elevated. ACA IgM and IgG were negative, Lupus Anti-coag was absent, Vasculitis Profile (C-ANCA, P-ANCA, GBM) was negative. ECG showed LVH with strain. ECHO showed LVH with normal LVEF. MR Angiography showed almost complete occlusion of several arteries in the body. Cardiac, carotid and peripheral angiography confirmed the extensive subtotal occlusion of arteries. Patient was advised stenting of Renal arteries by the Interventional Cardiologist. Patient was also advised Urgent Immunologist review. Patient underwent right eye intravitreal bevacizumab injection and subsequently prophylactic LIO laser around lattice degeneration.The physician, vascular surgeon advised Tab Amcard, Tab Combiplat, Tab Wysolone, Tab Stiloz, Tab Asomox, Tab Razel-F and Tab Folfit. Post bevacizumab Injection the right eye macular edema and neurosensory elevation resolved and BCVA improved to 6/6. The patient subsequently underwent Left Renal artery Angioplasty for systemic hypertension and Immunomodulatory therapy with Methotrexate and Medrol. At last follow-up, 2.5 years after initial presentation, BCVA of right eye was maintained at 6/6, with dry macula.

Conclusions: Macular Edema secondary to venous occlusion in Takayasu's arteritis responds well to intravitreal Anti-VEGF injection, early recognition and systemic management of this serious disorder is critical.

Intraocular T Lymphoma

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Purpose: to report clinical features, diagnosis, treatment and outcome of patients with intraocular T lymphoma (IOTL).

Methods: retrospective case series.

Results: Six immunocompetent Caucasians (5 females, 10 eyes) with IOTL were collected from 4 clinical centres. Mean age was 51 years (25 to 82 years). Initial location was a primary IOTL (PIOTL) (n=2), systemic (n=2), eye and systemic concomitant (n=2) (total systemic n=4, 66.6%), in central nervous system (CNS) (n=1), visceral (n=2, liver, bone marrow), visceral CNS (n=1), (adrenal and meningeal), total CNS (n= 2, 33,3%). Symptoms and signs included blurred vision (n=6), ocular discomfort or pain (n=2), conjunctiva hyperaemia (n=1), bilateral involvement (n=5), vitreoretinal involvement (n=5), iris followed by vitreous involvement (n=1). Serous retinal detachment (5 eyes/4 patients), creamy white retinal lesions (n=6), macular oedema (2 eyes/1patient), optic neuropathy, retinal venous occlusion (n=1). Diagnosis was based on vitreous (n=5) and iris (n=1) histopathology/ cytology, immunohistochemistry (n=3) and polymerase chain reaction (PCR) (n=3). Mean survival from diagnosis was 14.4 months (2-36 months with one patient still alive and one patient in remission for 36 months who died from another cause).

Conclusion: serous retinal detachment and vitreoretinal involvement resulting from peripheral metastatic T lymphoma were frequently observed in our patients with IOTL. Prognosis was very variable.

Dexamethasone Intravitreal Implant in Patients With Recalcitrant Macular Edema Due to Noninfectious Uveitis

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Purpose: To evaluate the efficacy and safety of a single dose intravitreal dexamethasone implant (DEX implant) in eyes with recalcitrant or recurrent macular edema (ME) secondary to non-infectious uveitis.

Methods: This retrospective study included 9 patients (11 eyes) who received a DEX implant for the treatment of ME due to non-infectious uveitis. All patients had recalcitrant or recurrent ME despite systemic/periocular corticosteroids and/or immunosuppressive treatment. Main outcome measures were improvement in best-corrected visual acuity (BCVA), reduction of central macular thickness (CMT), control of intraocular inflammation and occurrence of adverse events. Patients were evaluated at baseline and on the posttreatment 1st, 30th, 60th, 90th and 180th days.

Results: The mean age and the mean follow-up period were 49.8 (±7.1) years and 7.1 months respectively. Six (54.5%) eyes had intermediate, 3 (27.3%) had posterior and 2 (18.2%) had panuveitis. Six (66.7%) of patients had unilateral and 3 (33.3%) had bilateral involvement. Resolution of ME was achieved in 10 of 11 eyes (91%) on the 30th day. The mean baseline CMT 523.6±109.4 µm decreased to 317±100.4 µm at 30 days ($p<0.001$), 332 ±108 µm at 90 days and then increased to 418±99.6 µm at 180 days ($p<0.05$). Comparison of BCVA values showed a significant improvement ($p<0.05$). In 2 eyes (18.1%) reinjection of the implant was needed. Increase in intraocular pressure controlled with medical treatment was the most common (45.4%) adverse event.

Conclusions: The DEX implant is an effective adjuvant therapy in patients with refractory ME secondary to uveitis already on systemic treatment or patients with asymetric or unilateral involvement.

«Optic Neuritis Complicating Herpes Zoster Uveitis»

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Introduction: Herpes Zoster (HZ) is one of the most frequent infection disease of the eye, which can may lead to severe pain ans a wide spectrum of sight-threateting complications. Optic neuritis (ON) is a very rare complication of ocular HZ.

Case report: a 52-year-old woman presented with right unilateral anterior uveitis with ocular hypertension with best corrected visual acuity (BCVA) at 6/12. Serology for HZ was positive. The patient had undergone acyclovir therapy and after 3 weeks all clinical signs were resolved and BCVA was at 6/6. Three weeks later, she experienced visual impairment at 6/8 with normal ocular exam. Visual field indicated ON. The patient received systemic corticosteroid therapy associated with acyclovir. The vision returned to normal after one month.

Conclusion: althrought rare, visual ampairment can be associated to ON complicating HZ uveitis. The patient must be warned of the risk of this complication after HZ uveitis which require specific treatment.

«Clinical Presentations, Treatment And Outcome Of Intra-Ocular Tuberculosis: Experience From Tunis, North Of Africa»

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Purpose: to describe clinical patterns and to propose a diagnostic approach to tuberculosis presumed uveitis.

Methods: retrospective, nonrandomized, study of 16 patients with a presumed diagnosis of tuberculosis uveitis from 206 till 2013. Theses patients had a minimum of 1-year follow-up after initiating anti-appropriate antimycobacterial therapy.

Results: the mean age group was 40,21 years. There were 11 women and 5 men. Contage was present in 6/16 cases. The involvement was bilateral in all cases, with a serpiginous-like choroiditis in 7/16 cases, an occlusive retinal vascularitis in 4/16 cases, a kerato-uveitis in 2/16 cases and a panuveite with pupillary secclusion in 3/16 cases. The Mantoux test was strongly positive in all cases. In 6 cases, it was about assumption of diagnosis in front of epidemiological and clinical arguments. In 6/13 cases in which it was made, Quantiferon-TB Gold in Tube (QFT-GIT) was positive.

Conclusion: Tuberculosis uveitis is characterized by a polymorphic clinical presentations. Its diagnosis is essentially clinical, by difficulties obtaining microbiological proofs and/or anatomopathological eye prelevements. The presence of the following elements allows an etiological orientation, avoiding immediate corticosteroid therapy, and requires QFT-GIT and a antitubercular therapy: 1-notion of tuberculosis contage 2- serpigineuse-like choroiditis and/or retinal occlusive vasculitis corresponding to no specific eye or systemic entity 3- exclusion for other causes of uveitis. Favorable clinical outcome after 2 months of antitubercular therapy will allows to confirm the inital presumptive diagnosis.

«Endogenous Bilateral Vitreous Abcess Following Primary Blast Traumatic Brain Injury»

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Introduction: endogenous bilateral endophthalmitis is rarely reported, 116 cases rapported on Pubmed.

Case report: A 25-year-old man presented with history of blurred vision of both eyes after intracerebral abcess following primary blast traumatic brain injury. Visual acuity was hand motion on both eyes. He had bilateral panuveitis with a prepapillary vitreous abcess with three quadrants of chorioretinal scarring and ischemic retina in both eyes and inferior peripheral retinal detachment in left eye. Review of system was unremarkable. Polymerase chain reaction (PCR) testing of the aqueous humor and the vitreous from both eyes was negative. The patient underwented pars plana vitrectomy and, due to the history of intracerebral abcess, associated with intravitreal (vancomycine +amykacine + amphotericineB) and systemic same triple antibiotheray than used before. One year later, visual acuity was hand motion on right eye and no perception light on left eye, without any episodes of recurrent inflammation.

Conclusion: this is the first report of bilateral endogenous endophthalmitis after primary blast traumatic brain injury. Prognosis for visual outcome is very severe.

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