American Uveitis Society Spring Meeting 2015

tchaired by
Tammy M. Martin, PhD  
Casey Eye Institute, OHSU & Devers Eye Institute, LRI

Rooms 708/710/712, Colorado Convention Center

2 May, 2015

Program

5.00 PM  Social Hour  (Room 703)

6.00 PM  Plenary Session: Basis for and Uses of Biologic Drugs in Uveitis

Rachel Caspi, PhD
National Eye Institute, National Institutes of Health
“Mirroring the Clinical and Immunological Complexity of Autoimmune Uveitis in Animal Models”

Eric B. Suhler, MD, MPH
Oregon Health & Science University, VA Portland Health Care System
“Biologic Warfare on Uveitis: Perspectives from the Clinic”

7.00 PM  Business Meeting

7.30 PM  Free papers

7.30 PM  Gary Holland, MD: Interaction between Killer Immunoglobulin-like Receptor (KIR) Gene-HLA Combinations and Parasite Serotypes among Hispanic Individuals at Risk for Ocular Toxoplasmosis

7.45 PM  Douglas A. Jabs, MD, MBA: Long-term Outcomes of Cytomegalovirus Retinitis in the United States in the Era of Modern Antiretroviral Therapy

8.00 PM  John A. Gonzales, MD: Quality of Life Outcomes from a Randomized Clinical Trial for Noninfectious Intermediate, Posterior, and Pan-Uveitis
8.15 PM   **Ali K. Tayyeba, MD:** Management of End Stage Corneal Disease and Chronic Uveitic Hypotony by Combining the Boston Type 1 Keratoprosthesis with Pars Plana Vitrectomy and Silicone Oil Fill

8.30 PM   **Daniel L Feiler, MD:** Treatment of Uveitic Cystoid Macular Edema with Topical Difluprednate.

8.45 PM   **Laura J. Kopplin, MD:** Peginterferon alfa-2a (PEGASYS) in the Treatment of Inflammatory Cystoid Macular Edema

9.00 PM   **Blake A. Isernhagen, MD:** Autoimmune Retinopathy: A Guide for Clinicians Based on Recommendations of an Expert Panel

9.15 PM   **Sarju S. Patel, MD:** The Utility and Limitations of Wide-Field Autofluorescence in Inflammatory Choroiditis

9.30 PM   **Friederike Mackensen, MD:** Is There a Correlation Between Multiple Sclerosis and Fuchs Uveitis
ABSTRACTS

Interaction between Killer Immunoglobulin-like Receptor (KIR) Gene-HLA Combinations and Parasite Serotypes among Hispanic Individuals at Risk for Ocular Toxoplasmosis

Authors
Gary N. Holland,1A David C. Reed,1A Christian J. Sanfilippo,1A Fei Yu,1A Jeffrey L. Jones,2 Patrick A. Coady,3 Leanne T. Labriola,4 Ann-Marie Lobo,5 Ying Qian,6 Jose G. Montoya,7 Michael E. Grigg,8 Raja Rajalingam,1B and the North American Ocular Toxoplasmosis Study Group.

Author Affiliations
A Ocular Inflammatory Disease Center, Stein Eye Institute and Department of Ophthalmology.
B Immunogenetics Laboratory, Department of Pathology and Laboratory Medicine.
1 David Geffen School of Medicine at UCLA, Los Angeles, CA.
2 Parasitic Disease Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA.
3 Dartmouth Medical School, Lebanon, NH.
4 Department of Ophthalmology, University of Southern California, Los Angeles, CA.
5 Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA.
6 Francis I. Proctor Foundation and Department of Ophthalmology, UC San Francisco, San Francisco, CA.
7 Department of Immunology and Infectious Diseases, Stanford University School of Medicine, Stanford, CA.
8 Molecular Parasitology Unit, Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD.

Abstract
Purpose: To investigate relationships between ocular toxoplasmosis and the following factors among T. gondii-infected Hispanics: killer immunoglobulin-like receptor (KIR) genes; HLA types; KIR/HLA combinations; and parasite serotypes. We also sought evidence of KIR/HLA combination-serotype interactions.

Methods: We evaluated 88 T. gondii-infected Hispanic adults who did (n=37) or did not (n=51) have toxoplasmic retinochoroiditis. Serotypes were determined with an ELISA that identified host antibodies against 8 peptides associated with genotype-specific alleles. Odds ratios (ORs) for ocular involvement among those with non-Type II infections vs. those with Type II infections were calculated for subgroups with and without various KIR/HLA combinations. The Breslow-Day test for homogeneity of ORs between 2 groups was used to identify interactions between KIR/HLA combinations and serotype.

Results: Ocular involvement was not significantly associated with serotype or any KIR gene in crude analyses. Ocular involvement was associated with the following factors: HLA types A68 (p=0.0002), B39 (p=0.011), B65 (p=0.038), and C06 (p=0.011); HLA Group C1 (p=0.0006); and KIR/HLA combination KIR2DL2/2DL3/HLA-C1 (p=0.0006). There appeared to be interactions between serotype and at least 6 of 10 KIR/HLA combinations chosen prospectively for testing. Regarding risk of ocular involvement with non-Type II infections, each of 4 KIR/HLA combinations was associated with increased risk of ocular involvement, while absence of each of the same combinations was associated with decreased risk. The reverse was observed for 2 KIR/HLA combinations.
**Conclusion:** Host factors can influence risk of ocular involvement among *T. gondii*-infected individuals, even without evidence of immune dysfunction. Parasite virulence likely depends on interactions of host and parasite-derived gene products, as demonstrated in animal models. Study of these interactions may provide insight into ocular disease pathogenesis.

This research is NOT a clinical trial.

**Disclosure(s)**
None

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Research to Prevent Blindness, Inc, New York, NY (Dr. Holland); Centers for Disease Control and Prevention, Atlanta, GA (Drs. Holland, Jones); the Skirball Foundation, New York, NY (Dr. Holland), the Alta California Eye Research Foundation, San Francisco, CA (Dr. Sanfilippo), and the Intramural Research Program of the National Institutes of Health, NIAID (Dr. Grigg). Dr. Grigg is a Scholar of the Canadian Institute for Advanced Research (CIFAR) Integrated Microbial Biodiversity Program.
Long-term Outcomes of Cytomegalovirus Retinitis in the United States in the Era of Modern Antiretroviral Therapy

Authors
Jabs, Douglas; Ahuja Alka; Van Natta, Mark; Lyon, Alice; Yeh, Steven; Danis, Ron

Author Affiliations
From the Departments of Ophthalmology and Medicine, the Icahn School of Medicine at Mount Sinai; the Center for Clinical Trials, the Department of Epidemiology, The Johns Hopkins University Bloomberg School of Public Health; the Department of Ophthalmology, the Northwestern University Feinberg School of Medicine; the Department of Ophthalmology, the Emory University School of Medicine; and the Department of Ophthalmology, the University of Wisconsin, Madison.

Abstract
PURPOSE: To describe the long-term outcomes of patients with cytomegalovirus (CMV) retinitis and the acquired immunodeficiency syndrome (AIDS) in the era of modern combination antiretroviral therapy (ART).

METHODS: Prospective, observational, United States cohort of 479 patients with AIDS and CMV retinitis diagnosed in the era of modern ART. Patients were categorized as immune recovered, defined as a CD4+ T cell count >100 cells/µL for >3 months, or not. Outcomes included mortality, visual impairment (visual acuity worse than 20/40), blindness (visual acuity 20/200 or worse), and loss of visual field on quantitative Goldmann perimetry.

RESULTS: Patients without immune recovery had a mortality of 44.4/100 person-years (PY), and a median survival of 13.5 months after the diagnosis of CMV retinitis, whereas those with immune recovery had a mortality of 2.7/100 PY, and an estimated median survival of 27.0 years. The rates of bilateral visual impairment and blindness were 0.9/100 PY and 0.4/100 PY, respectively, and did not differ by immune recovery status. Rates of visual field loss were 7% of the normal field/year for those without immune recovery and 1%/year for those with immune recovery.

CONCLUSIONS: Among persons with AIDS and CMV retinitis, long-term survival is possible, if there is immune recovery. If there is no immune recovery, the mortality rate is substantial and similar to the pre-modern ART era. Although low, the rates of bilateral visual impairment and blindness are greater than those seen in an HIV-uninfected population.

This research is NOT a clinical trial.

Disclosure(s)
None

Support
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Quality of Life Outcomes from a Randomized Clinical Trial for Noninfectious Intermediate, Posterior, and Pan-Uveitis

Authors
Gonzales, John A., MD 1,5 Rathinam, Sivakumar R., MD, PhD 2, Babu, Manohar, MD 3, Thundikandy, Radhika, MD 2, Kanakath, Anuradha, MD 3, Browne, Erica N., MS 1, Acharya, Nisha R., MD, MS 1,4,5

Author Affiliations
Institutions: 1 F.I. Proctor Foundation, University of California, San Francisco; 2 Aravind Eye Care System, Madurai, India; 3 Aravind Eye Care System, Coimbatore, India; 4 Department of Epidemiology & Biostatistics, University of California, San Francisco; 5 Department of Ophthalmology, University of California, San Francisco

Abstract
Purpose: To evaluate quality of life (QOL) changes in patients treated with methotrexate (MTX) or mycophenolate mofetil (MMF) for non-infectious intermediate, posterior, or pan-uveitis.

Methods: This is a secondary analysis from a clinical trial of 80 patients enrolled in a randomized observer-masked trial to compare the effectiveness of MTX vs. MMF. Patients received systemic corticosteroids which were tapered according to SUN guidelines. Patients were enrolled at Aravind Eye Hospital in India and followed monthly for 6 months. The main outcome was the proportion of patients achieving corticosteroid-sparing control of inflammation. QOL measurements were collected at baseline and at the final study visit using the Indian Vision Function Questionnaire (IND-VFQ33) and the Short Form Health Survey (SF-36). T-tests were used to compare changes in scores and Fishers exact test was used to compare proportions.

Results: 67 patients with complete follow-up were included in the analysis. Overall, the IND-VFQ33 composite score improved by an average of 9.7 points (95% confidence interval (CI): 5.6, 13.9, p<0.001). There was no statistically significant difference in improvement by treatment group (p=0.86). The VFQ composite score improved for 97% of treatment successes compared to 68% of treatment failures (p=0.001). In general, there was no significant change in the SF-36 physical component summary score (p=0.58), but there was a slight decrease in the mental component summary score (mean change -1.8 points, 95% CI: -3.8, 0.1 p=0.07). This was mainly due to a decrease in the vitality domain (mean change -3.2 points, 95% CI: -5.3, -1.2, p=0.002).

Conclusions: Vision-related QOL improved with immunosuppressant treatment. There was consistent improvement in those who were a treatment success and results were mixed for treatment failures. There was no change in the physical component of general health, but there was a significant decrease in vitality in both treatment groups.

This research IS a clinical trial and is registered at www.clinicaltrials.gov.

Disclosure(s)
None

Support
Funding for this trial was provided by That Man May See and The South Asia Research Fund.
Management of End Stage Corneal Disease and Chronic Uveitic Hypotony by Combining the Boston Type 1 Keratoprosthesis with Pars Plana Vitrectomy and Silicone Oil Fill

Authors
Tayyeba K. Ali, MD,1 Guillermo Amescua, MD,1 Allister Gibbons, MD,1 Victor L. Perez, MD1, Janet L. Davis, MD,1

Author Affiliations
1 Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine; Miami, FL.

Abstract
PURPOSE:
To review the outcomes of Boston type 1 keratoprosthesis (B-KPro) implantation in combination with pars plana vitrectomy and silicone oil for the treatment of end stage bullous keratopathy and uveitic hypotony.

METHODS:
This was a retrospective chart review. Six eyes of 5 patients underwent B-KPro implantation, pars plana vitrectomy, and silicone oil placement. All preoperative characteristics, including visual acuity and intraocular pressure, intraoperative events, and postoperative outcomes were analyzed.

RESULTS:
Mean patient age was 63.9 years (range 40.9-86.4 years). Mean pre-operative BCVA was logMAR 2.73 (range 2.60 to 3.00). Initially, a gain of visual acuity was seen in half the sample with mean BCVA logMAR 1.90 (Range 0.90 to 3.00). At final follow-up (mean 25.8 months and range 12 to 52 months), mean visual acuity was logMAR 2.23 (range 1.20 to 3.00) and no eye lost vision. Two eyes (33%) had previously undergone corneal transplantation, one of which was an endothelial keratoplasty (DSAEK). The other 4 eyes had a B-Kpro as their first corneal procedure. No intraoperative complications occurred, though one patient had a concomitant retinal detachment (RD) repair for pre-existing RD. B-KPro retention rate was one hundred percent. One patient developed a retroprosthetic membrane (RPM); no patients experienced complications such as melt, endophthalmitis, or extrusion. The one patient who had an RPM had a psuedophakic B-Kpro, which may have contributed to persistence of RPM. There were no uveitic flares and hypotony was controlled, though further intervention, including repeat SO fill in one patient, was required over the extended follow-up of these patients.

CONCLUSIONS:
B-KPro implantation in combination with pars plana vitrectomy and intraocular silicone oil fill is a safe, though end-stage, procedure that maintains control of uveitis, can improve vision in some chronically hypotonous eyes, and may delay or prevent phthisis.

This research is NOT a clinical trial.

Disclosure(s)
None

Support
None
Treatment of Uveitic Cystoid Macular Edema with Topical Difluprednate.

Authors
Feiler, Daniel L; Srivastava, Sunil K; Lowder, Careen Y

Author Affiliations
Cleveland Clinic, Cole Eye Institute

Abstract
Purpose: Cystoid macular edema (CME) is a common cause of vision loss in patients with uveitis. Evidence for optimal treatment strategies is lacking. The potency, limited systemic absorption, and non-invasive nature of topical difluprednate make it an attractive treatment option when compared to traditional or novel treatments. We retrospectively reviewed the efficacy of difluprednate ophthalmic emulsion 0.05% in the treatment of CME in patients with uveitis.

Methods: Twenty two eyes of 18 patients with uveitic CME treated with topical difluprednate four times daily for 3 weeks and tapered over 1 month were reviewed for best-corrected Snellen visual acuity (VA), central foveal thickness (CFT) on optical coherence tomography (OCT), and intraocular pressure (IOP). A mixed model was fit with each measure as the outcome, and visit time as the primary predictor, with patient and eye as random effects. Analyses were performed using SAS software (version 9.3; Cary, NC). A significance level of 0.05 was assumed for all tests.

Results: Twenty two (100%) eyes had a decrease in CFT at follow-up. Mean CFT decreased by 121 μm (P<0.001) at 30 days±15 days (21 eyes), and 137 μm (p<0.001) at 60 days±15 days (12 eyes). Six of 21 (28%) eyes had complete resolution of IRF at 30 days±15 days, while 8 of 12 (66%) had complete resolution of IRF at 60 days±15 days. LogMAR VA improved by a mean of 0.160 (P=0.013) and VA improved by at least 1 line in 9 of 12 eyes (75%) (P=0.013) at 60 days±15 days. Mean increase in IOP was 2.0 mmHg at 30 days±15 days (P=0.040) and 2.2 mmHg at 60 days±15 days (P=0.086). No significant ocular or systemic adverse effects were observed.

Conclusions: These results suggest that topical difluprednate is a well-tolerated and effective treatment for uveitic CME with decreased OCT CFT, mild improvement in VA, and mild elevation of IOP in the studied patients. Further evaluation of topical difluprednate for uveitic CME in controlled randomized studies is warranted.

This research is NOT a clinical trial.

Disclosure(s)
Daniel Feiler (none), Sunil Srivastava (Alcon, Allergan, Bausch and Lomb), Careen Lowder (None)

Support
None
Peginterferon alfa-2a (PEGASYS) in the Treatment of Inflammatory Cystoid Macular Edema

Authors
Kopplin, Laura J. [1]; Stiefel, Hillary C. [1]; Vegunta, Sravanthi [2]; Albini, Thomas A. [2]; Suhler, Eric B. [1,3]

Author Affiliations
[1] Casey Eye Institute, Portland, OR
[2] Bascom Palmer Eye Institute, Miami, FL

Abstract
Purpose: To assess the utility of peginterferon alfa-2a (PEGASYS) in the treatment of refractory inflammatory cystoid macular edema (CME).

Methods: We conducted a retrospective chart review of four patients with recalcitrant inflammatory CME treated with peginterferon alfa-2a at the Portland VA Health Care System and Bascom Palmer Eye Institute.

Results: Three patients had CME secondary to chronic bilateral idiopathic anterior and intermediate uveitis and one patient had primary idiopathic CME without a known history of uveitis. All patients failed multiple treatment regimens with local and/or systemic therapies prior to initiation of treatment with peginterferon alfa-2a. Peginterferon alfa-2a therapy resulted in improvement in central macular thickness (CMT) in all patients (average CMT was 475 μm pre-treatment [range 304-752], 279 μm post-treatment [range 204-373], Wilcoxon signed-rank test p<0.05) and resolution of cystic intraretinal fluid in all cases. Visual acuity improved in the majority of patients; one patient had significant preexisting photoreceptor atrophy limiting visual recovery. Fatigue and flu-like symptoms occurred in three patients and resulted in two patients electing to discontinue therapy with resultant recurrence of CME.

Conclusions: Peginterferon alfa-2a is an effective treatment for refractory inflammatory CME, although side effects may limit patient tolerability.

This research is NOT a clinical trial.

Disclosure(s)
None relevant to this presentation

Support
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Autoimmune Retinopathy: A Guide for Clinicians Based on Recommendations of an Expert Panel

Authors
Blake A. Isernhagen, MD1, Hassan A. Aziz, MD1, Lucia Sobrin, MD2, Steven K. Lundy, PhD3, John R. Heckenlively, MD3, Debra A. Goldstein, MD4, Thiran Jayasundera, MD3, Janet L. Davis, MD1

Author Affiliations
1 Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami, Miller School of Medicine, Miami, FL; 2 Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA; 3 Department of Ophthalmology, Kellogg Eye Center, University of Michigan Medical School, Ann Arbor, MI; 4 Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, IL

Abstract
Purpose: To provide clinicians with guidance in diagnosing and interpreting ancillary testing, proposing different modalities of treatment depending on the disease severity, and organizing the follow-up care of patients with non-paraneoplastic autoimmune retinopathy (np-AIR).

Methods: Physicians and immunologists with experience in the diagnosis of np-AIR convened at the Bascom Palmer Eye Institute. The panel reviewed available literature and case presentations of presumptive np-AIR collected from tertiary uveitis practices. After round table discussions, a writing group agreed to summarize the opinions of the group regarding identification of cases, selection of ancillary tests and evaluation of proposed treatments based on the current state of knowledge and the current management practices in tertiary care subspecialty clinics.

Results: Recommendations were made regarding the utility and interpretation of the patient’s past medical history and symptoms, clinical exam findings, and ancillary testing to help diagnosis and distinguish np-AIR from paraneoplastic retinopathy and retinal degenerations. Ancillary testing includes electroretinography, fundus autofluorescence, optical coherence tomography, fluorescein angiography, evaluation for anti-retinal antibodies, and screening for systemic malignancy. In slowly progressive suspected np-AIR the treatment is usually immunosuppression. In rapidly progressive disease, intravenous corticosteroids, plasmapharesis, and intravenous immunoglobulins are sometimes used. There is no proven therapy. The disappearance of antibodies by western-blot after 6 months of treatment suggests that sufficient treatment has been given, but determining the benefits of treatment remains difficult because visual function rarely improves.

Conclusions: The observations and recommendations from the panel help clinicians diagnose and treat patients with np-AIR. It also serves as a platform for further research in this field.

This research is NOT a clinical trial.

Disclosure(s)
NONE

Support
NONE
The Utility and Limitations of Wide-Field Autofluorescence in Inflammatory Choroiditis

Authors
Patel, Sarju S

Author Affiliations
Weill Cornell Medical College

Abstract
PURPOSE: To report on the usefulness of wide-field fundus autofluorescence (FAF) in the clinical evaluation and management of inflammatory choroiditis

METHODS: Retrospective case-series

RESULTS: FAF imaging was evaluated in 15 cases of inflammatory choroiditis, including both pan- and posterior uveitis entities. Findings on FAF were present in 14 of 15 cases. However, these findings were not found to be useful in the clinical management of these patients beyond findings on other imaging modalities (optical coherence tomography, angiography, and color fundus photography) in 10 of 15 cases, which included all patients with VKH syndrome and birdshot chorioretinopathy. FAF was helpful in patients with idiopathic choroiditis and variants of acute zonal occult outer retinopathy, with subtle findings correlating with visual field defects and subjective visual changes, which dictated changes in clinical management.

CONCLUSIONS: While FAF findings are present in most cases of choroiditis, FAF is clinically useful in a subset of patients where changes can correlate with visual field defects and help dictate the management of the patient.

This research is NOT a clinical trial.

Disclosure(s)
None

Support
None
Is There a Correlation Between Multiple Sclerosis and Fuchs Uveitis?

Authors
Mackensen, Friederike; Kansupada, Kashyap; Zamir, Ehud

Author Affiliations
Interdisciplinary Uveitis Center University of Heidelberg, Germany
Charlotte Eye Ear Nose & Throat Associates, P.A., USA
Royal Victorian Eye and Ear Hospital Melbourne, Australia

Abstract
Purpose: Members of the American Uveitis Society discussed their observation that patients with Multiple Sclerosis (MS) may present with Fuchs Uveitis (FUS) which seemed to be more often bilateral. FUS is supposed to be caused by rubella infection and in MS a viral pathogenesis has been discussed as well. A correlation was hypothesized.

Methods: Retrospective database review of one center. All patients with FUS, all patients with MS and those with both diagnoses were searched for and evaluated for anatomic localization, laterality and in those patients with both diagnoses also for visual accuity, complications and details of uveitis presentation. Additional patients with both diagnoses from other centers were added.

Results: In the database 289 patients were listed with FUS, 194 with MS and 4 with both diagnoses. Thus, 2% of MS patients had FUS and 1.4% of FUS patients had MS. Additionally, 5 more patients with both diagnoses were added, so we had a case series of 9 patients with MS and FUS. Bilateral uveitis was seen in 11% of FUS and 33% of FUS/MS. All FUS/MS had stellate keratic precipitates and 7 cataract, 6 had heterochromia, 3 of 3 tested had rubella antibodies in aqueous humor and 2 had secondary glaucoma with 1 requiring surgery. Median age at diagnoses was 31 and 28 for MS and FUS, respectively, and 67% were female.

Conclusion: MS occurs in approximately 0.2% of the population, FUS in 0.05%. Therefore the coincidence of FUS and MS seems to be slightly higher than to be expected. If this is due to a higher susceptibility to rubella through MS or even a pathogenetic link to rubella in MS remains speculative.

This research is NOT a clinical trial.

Disclosure(s)
None

Support
None