

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

Uveitis 2022

“Now the Future We Foresee”

Subspecialty Day | AAO 2022

Chicago | Sept 30

Uveitis 2022

“Now the Future We Foresee”

Program Directors

Russell W Read MD PhD and Lucia Sobrin MD

In conjunction with the American Uveitis Society

McCormick Place
Chicago, Illinois
Friday, Sept. 30, 2022



Presented by:
The American Academy of Ophthalmology



AMERICAN ACADEMY
OF OPHTHALMOLOGY®
Protecting Sight. Empowering Lives.

Uveitis 2022 Planning Group

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Uveitis Subspecialty Day 2022 Planning Group

On behalf of the American Academy of Ophthalmology and the American Uveitis Society,
it is our pleasure to welcome you to Chicago and Uveitis 2022: “Now the Future We Foresee.”



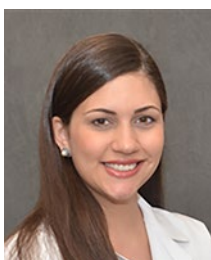
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 Allergan, Inc.: C
 Aura Biosciences: C
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 Cognition Therapeutics: C
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 Greybug: S | Iveric Bio: C
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 Luxa: C | NGM: S
 Novartis Pharma AG: C
 Opthea: C | Quark: C
 Regeneron Pharmaceuticals, Inc.: C,S
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 Stealth: S | Unity: C
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CME Credit

The Academy's CME Mission Statement

The purpose of the American Academy of Ophthalmology's Continuing Medical Education (CME) program is to present ophthalmologists with the highest quality lifelong learning opportunities that promote improvement and change in physician practices, performance, or competence, thus enabling such physicians to maintain or improve the competence and professional performance needed to provide the best possible eye care for their patients.

Uveitis Subspecialty Day Meeting 2022 Learning Objectives

This meeting will enable attendees to:

- Identify the various forms of ocular inflammatory diseases, including retinal vasculitis and anterior, intermediate, and posterior uveitis
- Construct a differential diagnosis for various forms of uveitis
- Classify the principles of diagnosis of ocular inflammatory disorders in order to initiate appropriate, disease-directed evaluations
- Identify the important and appropriate role of immunomodulatory therapy for patients with specific ocular inflammatory diseases and also for patients with steroid-dependent inflammation
- Describe the various gaps that currently exist in the management of uveitis and ocular inflammatory diseases
- Describe potential new diagnostic and treatment modalities for uveitis and ocular inflammatory diseases, including selected therapeutic agents in development

Uveitis Subspecialty Day Meeting 2022 Target Audience

The intended audience for this program includes general ophthalmologists, comprehensive ophthalmologists, uveitis specialists, other ophthalmologic subspecialists (cornea, retina, etc.), and allied health personnel who are involved in the management of patients with uveitis and ocular inflammatory diseases.

Teaching at a Live Activity

Teaching instruction courses or delivering a scientific paper or poster is not an *AMA PRA Category 1 Credit™* activity and should not be included when calculating your total *AMA PRA Category 1 Credits™*. Presenters may claim *AMA PRA Category 1 Credits™* through the American Medical Association. To obtain an application form, please contact the AMA at www.ama-assn.org.

Scientific Integrity and Disclosure of Conflicts of Interest

The American Academy of Ophthalmology is committed to ensuring that all CME information is based on the application of research findings and the implementation of evidence-based medicine. It seeks to promote balance, objectivity, and absence of commercial bias in its content. All persons in a position to control the content of this activity must disclose any and all financial interests. The Academy has mechanisms in place to resolve all conflicts of interest prior to an educational activity being delivered to the learners.

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Subspecialty Day CME Credit

The American Academy of Ophthalmology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

Friday Subspecialty Day Activity: Glaucoma, Pediatric Ophthalmology, Refractive Surgery, Retina (Day 1), and Uveitis

The Academy designates this Other (blended live and enduring material) activity for a maximum of 12 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Saturday Subspecialty Day Activity: Cornea, Oculofacial Plastic Surgery, and Retina (Day 2)

The Academy designates this Other (blended live and enduring material) activity for a maximum of 12 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Physicians registered as In Person and Virtual are eligible to claim the above CME credit.

Attendance Verification for CME Reporting

Before processing your requests for CME credit, the Academy must verify your attendance at AAO 2022 and/or Subspecialty Day. Badges are no longer mailed before the meeting. Picking up your badge onsite will verify your attendance.

How to Claim CME

Attendees can [claim credits online](#). For AAO 2022, you can claim CME credit multiple times, up to the 50-credit maximum, through Aug. 1, 2023. You can claim some in 2022 and some in 2023, or all in the same year. For 2022 Subspecialty Day, you can claim CME credit multiple times, up to the 12-credit maximum per day, through Aug. 1, 2023. You can claim some in 2022 and some in 2023, or all in the same year.

You do not need to track which sessions you attend, just the total number of hours you spend in sessions for each claim.

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CME Questions

Send your questions about CME credit reporting to cme@aao.org. For Continuing Certification questions, contact the American Board of Ophthalmology at MOC@abpo.org.

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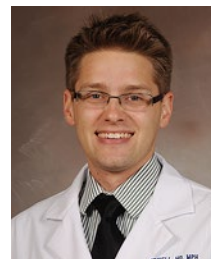
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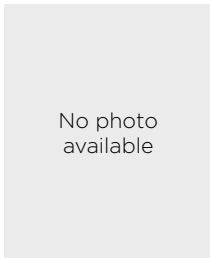
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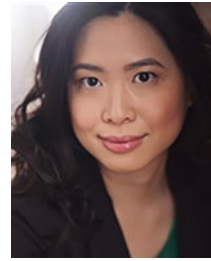
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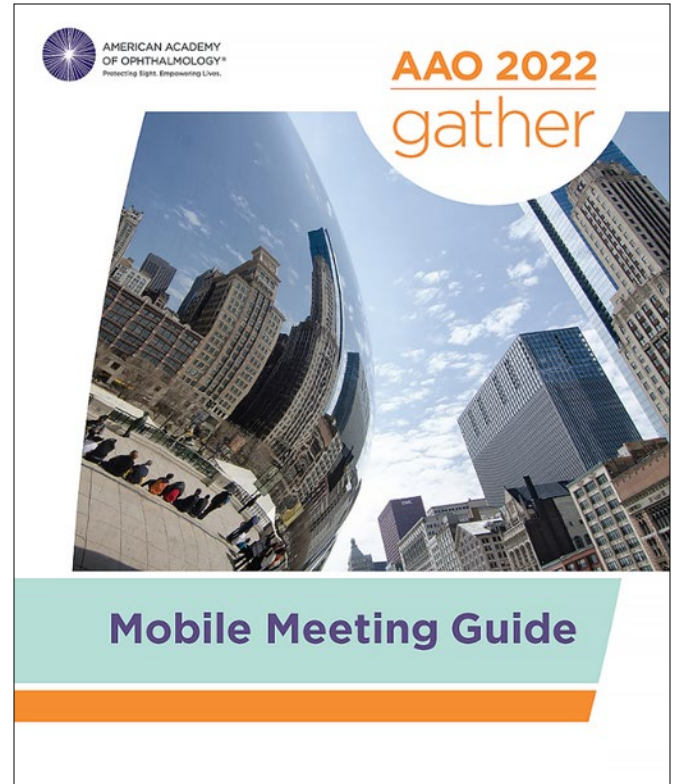


Jessica E Weinstein MD
Lexington, KY

Ask a Question Live During the Meeting Using the Mobile Meeting Guide

To ask the moderator a question during the meeting, follow the directions below.

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- Choose “Ask a Question”



Uveitis Subspecialty Day 2022

“Now the Future We Foresee”

FRIDAY, SEPT. 30, 2022

8:00 AM	Welcome and Introductions	Russell W Read MD PhD
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Section I: Basics

Moderator: Russell W Read MD PhD

Virtual Moderator Morning Sessions: Daniel A Brill MD

8:05 AM	Epidemiology of Uveitis	Eric L Crowell MD	1
8:15 AM	Approach to the Uveitis Patient	Ramana S Moorthy MD	2
8:25 AM	Don't-Miss Diagnoses	Arthi Ganesh Venkat MD	4
8:35 AM	Laboratory Testing of the Uveitis Patient	Lyndell Lim MD PhD	6
8:45 AM	Ocular Imaging in Uveitis	Marion Ronit Munk MD PhD	8
8:55 AM	Health Disparities in Uveitis	Grace A Levy-Clarke MD	10

Section II: Anterior Uveitis

Moderator: Edmund Tsui MD

Panelists: Rupesh Agrawal MBBS DMS FRCS, Christopher D Conrady MD, Chloe C Gottlieb MD, Laura J Kopplin MD PhD, Anjum F Koreishi MD, Kara C Lamattina MD, and Lana M Rifkin MD

9:05 AM	Anterior Uveitis Overview	Lana M Rifkin MD	11
9:15 AM	One Eye . . . or Two?	Laura J Kopplin MD PhD	13
9:25 AM	Case: O-h-h, Child!	Anjum F Koreishi MD	15
9:35 AM	Case: Oh, That Pterygium . . .	Christopher D Conrady MD	18
9:45 AM	Case: Don't Crack Under Pressure!	Kara C Lamattina MD	20
9:55 AM	Take-Home Points	Edmund Tsui MD	
10:00 AM	In These Unprecedented Times . . .	Janice C Law MD	22
10:05 AM	REFRESHMENT BREAK		

Section III: Intermediate Uveitis

Moderator: Ann-Marie Lobo MD

Panelists: Nicholas J Butler MD, Lisa J Faia MD, Sapna Gangaputra MD MPH, Timothy Y Lai MD FRCOphth FRCS, Paulina Liberman MD, and Francesco Pichi MD

10:35 AM	Intermediate Uveitis Overview	Sapna Gangaputra MD MPH	24
10:45 AM	Case: Totally “Tubular”	Pooja Bhat MD	26
10:55 AM	Case: Between a Fern and a Flower	Francesco Pichi MD	29
11:05 AM	Case: Just the Tip of the Iceberg . . .	Lisa J Faia MD	31
11:15 AM	Case: A Late Bloomer	Paulina Liberman MD	33
11:25 AM	Take-Home Points	Ann-Marie Lobo MD	
11:30 AM	LUNCH		

Section IV: Posterior Uveitis

Moderator: Kathryn L Pepple MD PhD

Virtual Moderator Afternoon Sessions: Lianna M Valdes

Panelists: John A Gonzales MD, Lynn M Hassman MD, Joon-Bom Kim MD, Ninani E Kombo MD, Jessica G Shantha MD, and Jessica E Weinstein MD

12:50 PM	Posterior Uveitis Overview	Lynn M Hassman MD	35
1:00 PM	Case: To Inject or Not to Inject, That Is the Question: Wet vs. Inflamed Eye	Joon-Bom Kim MD	36
1:10 PM	Case: A Case of White Dots: “Why Is That P Silent?”	Jessica E Weinstein MD	38
1:20 PM	Case: A Case of Recurrent Retinal Vessel Aneurysms	Ninani E Kombo MD	41
1:30 PM	Case: Immunosuppressed Patient	Jessica G Shantha MD	43
1:40 PM	Take-Home Points	Kathryn L Pepple MD PhD	

Section V: Panuveitis

Moderator: Wendy M Smith MD

Panelists: Karen R Armbrust MD, Emilio M Dodds MD, Shilpa M Kodati MD, Thellean K Leveque MD, Careen Yen Lowder MD PhD, Sumit Sharma MD, and Ilknur Tugal-Tutkun MD

1:45 PM	Panuveitis Overview	Emilio M Dodds MD	45
1:55 PM	Case: Syphilis or Atypical Toxoplasmosis	Sumit Sharma MD	47
2:05 PM	Case: Impersonating the Great Imitator	Thellean K Leveque MD	48
2:15 PM	Case: Is Hindsight Better Than 20/80?	Karen R Armbrust MD	50
2:25 PM	Case: It Helps to Stay Fluid	Shilpa M Kodati MD	53
2:35 PM	Take-Home Points	Wendy M Smith MD	
2:40 PM	REFRESHMENT BREAK		

Section VI: Complications and Surgery in Uveitis: To Cut or Not to Cut, That Is the Question

Moderator: Lucia Sobrin MD

3:10 PM	Perioperative Management of the Uveitis Patient	Caroline L Minkus MD	55
3:20 PM	Diagnostic Surgical Procedures in Uveitis	Phoebe Lin MD PhD	56
3:30 PM	Therapeutic Retinal Surgery in Uveitis	Kareem Moussa MD	57
3:40 PM	Cataract Surgery in Uveitis	George N Papaliodis MD	59
3:50 PM	Glaucoma in Uveitis	Debra A Goldstein MD	60

Section VII: Treatment

Moderator: Stephanie M Llop Santiago MD

4:00 PM	Treatment Paradigm for Uveitis	Armando L Oliver MD	61
4:10 PM	Corticosteroids	Thomas A Albini MD	62
4:20 PM	Immunosuppression	Eduardo Uchiyama MD	63
4:30 PM	Local Therapy	Arjun B Sood MD	64

Section VIII: Hot Topics

Moderator: Lucia Sobrin MD

4:40 PM	Association Between Use of Immunosuppression and the Incidence of Cancer	John H Kempen MD PhD	65
4:50 PM	Macular Edema Ranibizumab vs. Intravitreal Anti-inflammatory Therapy (MERIT)	Nisha Acharya MD	66
5:00 PM	Conclusion and Thank You	Lucia Sobrin MD	
5:02 PM	ADJOURN		

Epidemiology of Uveitis

Eric L Crowell MD

I. Prevalence and Incidence

A. Anatomical classification

1. Anterior
2. Intermediate
3. Posterior
4. Panuveitis

B. Age

1. Children
2. Adults
3. Elderly

C. Race and ethnicity

D. Geography

E. Infectious vs. noninfectious and differences between the developed and developing world

II. Severity and Outcomes

A. Prognostic indicators

1. Smoking
2. Prior surgery
3. Systemic diseases

B. Geography

C. Race and social determinants of health

III. Impacts

A. Daily functioning

B. Economic

Selected Readings

1. Thorne JE, Suhler E, Skup M, et al. Prevalence of noninfectious uveitis in the United States: a claims-based analysis. *JAMA Ophthalmol.* 2016; 134(11):1237-1245.
2. Gonzalez MM, Solano MM, Porco RC, et al. Epidemiology of uveitis in a US population-based study. *J Ophthalmic Inflamm Infect.* 2018; 8:6.
3. Zhang Y, Amin S, Lung KI, Seabury S, Rao N, Toy BC. Incidence, prevalence, and risk factors of infectious uveitis and scleritis in the United States: a claims-based analysis. *PLOS One.* 2020; 15(8):1-16.
4. Tallouzi MO, Moore DJ, Bucknall N, et al. Outcomes important to patients with non-infectious posterior segment-involving uveitis: a qualitative study. *BMJ Open Ophthalmol.* 2020; 5(1):e000481.
5. Groen F, Ramdas W, de Hoog J, Vingerling JR, Rothova A. Visual outcomes and ocular morbidity of patients with uveitis referred to a tertiary center during first year of follow-up. *Eye* 2016; 30:473-480.
6. Smith JA, Mackensen F, Sen HN, et al. Epidemiology and course of disease in childhood uveitis. *Ophthalmology* 2009; 116(8):1544-1551.
7. Stolk-Vos AC, Kasigar H, Nijmeijer KJ, et al. Outcomes in patients with chronic uveitis: which factors matter to patients? A qualitative study. *BMC Ophthalmol.* 2020; 20(1):125.
8. Rathinam SR, Namperumalsamy P. Global variation and pattern changes in epidemiology of uveitis. *Indian J Ophthalmol.* 2007; 55(3):173-183.

Approach to the Uveitis Patient

Ramana S Moorthy MD

I. History is everything.

A. Temporal characteristics of uveitis

1. Onset: acute or insidious
2. Course: constant, unrelenting-progressive, or periodic flareups
3. Duration: How long have you been dealing with this?
4. Consequences to vision: stable or progressive loss

B. Laterality

1. Unilateral: Consider herpes simplex virus (HSV), varicella zoster virus (VZV), cytomegalovirus (CMV), toxocariasis, toxoplasmosis
 - a. IOP elevation: herpetic disease and toxoplasmosis
 - b. Sectoral iris atrophy: VZV or HSV
 - c. Corneal scarring/edema: HSV and VZV
 - d. Unilaterality is not always helpful. Many noninfectious entities present unilaterally.
 - i. HLAB27+ anterior uveitis
 - ii. Scleritis

2. Bilateral

C. Details about visual symptoms

1. Visual loss
 - a. Acute
 - b. Chronic
2. Floaters
3. Photopsias – paracentral
4. Redness
 - a. Perilimbal
 - b. Diffuse injection
 - c. Violaceous hue
 - d. None
5. Pain
 - a. Photophobia
 - b. Dull, gnawing, nauseating
 - c. Sharp foreign body sensation
 - d. None

D. Systemic diseases

1. Infections: TB, syphilis, Lyme, others
 - a. Fevers, chills, weight loss
 - b. Other organ systems: lungs, GI tract, lymphadenitis/lymphangitis
 - c. Poor nutrition: malnourished, hyperalimentation
 - d. Immunocompromised
 - i. Iatrogenic: chemotherapy, indwelling catheters
 - ii. Acquired: HIV
2. Autoimmune diseases
 - a. Vasculitis
 - b. Arthritis: Seronegative spondyloarthropathy, RA, psoriatic
3. Cancer history
 - a. Cancer immunotherapy
 - b. Extent and type: cancer-associated retinopathy, melanoma-associated retinopathy, bilateral diffuse uveal melanocytic proliferation
4. Medications: drug-induced uveitis

E. Review of systems

1. Integumentary and mucosal
2. Pulmonary
3. GI
4. GU
5. Musculoskeletal
6. Animal exposure
7. Travel history
8. Work history
9. Lifestyle

II. Physical Examination

A. General

1. Skin
2. Lungs
3. GU, if indicated
4. Extremities and joints

B. Ocular

1. Slit-lamp exam
 - a. Conjunctival nodules
 - b. Cornea
 - c. Anterior chamber
 - d. Iris
 - e. Lens
 - f. Vitreous
2. Gonioscopy
3. Dilated fundus exam
 - a. Disc
 - b. Macula
 - c. Vessels
 - d. Periphery: Pars plana
4. Ancillary testing
 - a. OCT
 - b. Fluorescein angiography, wide field
 - c. Indocyanine green
 - d. B-scan ultrasound/ultrasound biomicroscopy

III. Summarize history and physical findings into 1 sentence.

- A. Acute or chronic
- B. Unilateral or bilateral
- C. Anatomic location: anterior, intermediate, posterior, or pan-uveitis
- D. Structural complications: cataract, glaucoma, cystoid macular edema, etc.
- E. Associated systemic features

IV. Guided Laboratory Testing

- A. Serologic testing: sarcoid, syphilis, TB and chest x-ray: Everyone
 - B. AC tap and PCR: HSV, VZV, CMV, toxoplasmosis
 - C. Focused testing based on history and exam findings
 - D. Don't forget conjunctiva – granulomas
- V. Is it infectious or noninfectious uveitis?
- A. Infectious: antimicrobials combined with steroids. Never use local or intraocular steroids alone.
 - B. Noninfectious
 - C. Masquerade syndromes

Selected Readings

1. Doan T, Pinsky BA. Current and future molecular diagnostics for ocular infectious diseases. *Curr Opin Ophthalmol*. 2016; 27:561-567.
2. Jabs DA, Busingye J. Approach to the diagnosis of the uveitides. *Am J Ophthalmol*. 2013; 156:228-236.
3. Majumder PD, Sudharshan S, Biswas J. Laboratory support in the diagnosis of uveitis. *Indian J Ophthalmol*. 2013; 61(6):269-276.
4. de Parisot A, Kodjikian L, Errera MH, et al; ULISSE Group. Randomized controlled trial evaluating a standardized strategy for uveitis etiologic diagnosis (ULISSE). *Am J Ophthalmol*. 2017; 178:176-185.

Don't-Miss Diagnoses in Uveitis

Arthi Venkat MD

I. Introduction

- A. Certain uveitides should not be missed due to high risk of morbidity and blindness.
- B. It is crucial to identify and appropriately refer and manage these conditions in a timely fashion to avoid poor outcomes.

II. Infectious Necrotizing Retinitis: Acute Retinal Necrosis/Progressive Outer Retinal Necrosis

- A. Caused by herpes simplex virus (HSV)-1, HSV-2, or varicella zoster virus (VZV)
- B. Rapidly progressive
- C. Loss of vision most often attributable to optic neuropathy or retinal detachment¹
- D. Case

1. 74-year-old female presents with dim vision in the left eye. She has a history of lymphoma on bendamustine/rituximab and received zoster vaccine live during a 2-month treatment holiday. She subsequently developed disseminated shingles approximately 1 month following the shingles vaccine, at which time her vision changes occurred.
2. VA: 20/20 OD, 20/40 OS
3. Exam: 360 degrees of retinal whitening in the left eye
4. Course: Vitreous tap was performed and VZV PCR was positive. Treatment with intravitreal foscarnet and systemic valacyclovir successfully arrested progression of retinal whitening.

III. Syphilitic Uveitis/Retinitis

- A. Readily treatable with neurosyphilis treatment/IV penicillin²
- B. Rapidly progressive in cases of immune suppression or steroid therapy without antibiotic therapy³
- C. Case
 1. 48-year-old male presents with bilateral decreased vision over 1-2 weeks. He has not seen a physician in over a decade.
 2. VA: 20/250 OD, 20/80 OS
 3. Exam: endothelial pigment and 2+ anterior chamber and vitreous cell OU; fundus exam with granular changes in macula OU
 4. OCT: retinal pigment epithelial (RPE) irregularity OU

5. Fluorescein angiography (FA): diffuse retinal vascular leakage, perifoveal leakage/staining, and disc leakage OU
6. Fundus autofluorescence: stippled hypo- and hyperautofluorescence in maculae, diffuse ill-defined hyperautofluorescence into midperiphery OU
7. Labs: syphilis IgG >8.0, RPR 1:128, HIV positive

IV. Chronic Postoperative Endophthalmitis

- A. Often misdiagnosed as chronic postsurgical inflammation⁴
- B. Case
 1. 61-year-old female presents with hypopyon after repeated unsuccessful attempts to taper topical difluprednate for treatment of inflammation following uncomplicated cataract surgery.
 2. VA: 20/20 OD, 20/25 OS
 3. Anterior chamber tap reveals atypical organism, *Aquamicrobium terrae*.
 4. Course: Repeated intravitreal antibiotics failed to clear the organism. Explantation of IOL and endoscopic vitrectomy with laser photocoagulation of retained capsular fragments were required for resolution of inflammation.

V. Endogenous Endophthalmitis

- A. Can be an indication of life-threatening illness⁵
- B. Bacterial etiologies may indicate systemic conditions.
- C. Fungal etiologies should prompt review of systems to elicit history of recent GU instrumentation or IV drug use.
- D. Case
 1. 59-year-old female presents 1-2 weeks of blurred vision and altered mental status. She has a history of metastatic small cell lung cancer on chemotherapy.
 2. VA: 20/150 OD, 20/125 OS
 3. Exam: vitreous haze OU, multifocal elevated round sub-RPE lesions of varying sizes OU, "string-of-pearls" appearance of vitreous snowballs

4. Course: Diagnostic vitrectomy done with intravitreal voriconazole, vancomycin, ceftazidime. Although vitreous fluid was culture negative, systemic workup was done with inpatient admission for altered mental status that uncovered blood cultures positive for acid-fast gram-positive bacilli, ultimately speciating to *Nocardia kropenstedii*.

VI. Necrotizing Scleritis

- A. Infectious causes: trauma, endogenous infectious keratitis with contiguous spread, recent surgery, local antimetabolite use (mitomycin C) or local radiotherapy, HSV/VZV⁶
- B. Noninfectious causes: granulomatosis with polyangiitis, rheumatoid arthritis, relapsing polychondritis, inflammatory bowel disease, and less commonly systemic lupus erythematosus (SLE)⁷

VII. Occlusive Vasculitis

- A. Infectious causes
 1. Bacterial: *Mycobacterial tuberculosis*, syphilis, *Bartonella henselae*, *Tropheryma whippelii*, endogenous/exogenous endophthalmitis
 2. Viral: HSV, VZV, CMV, HTLV-1, West Nile, dengue, Rift Valley fever
- B. Noninfectious causes
 1. Arterial: Behçet disease, SLE
 2. Venous: sarcoidosis, SLE

VIII. Neoplastic

- A. Primary vitreoretinal lymphoma: Associated with CNS lymphoma and can masquerade as multiple types of uveitides⁸
- B. Uveal lymphoma
 1. Often indolent, with extraocular involvement commonly in lymph nodes. Can resemble bird-shot chorioretinopathy and other white dot syndromes.⁹
 2. Case
 - a. 77-year-old female presents with photopsias in the right eye
 - b. VA 20/25 OD and 20/40 OS.
 - c. Exam: multifocal creamy yellow lesions at the level of outer retina/choroid OD, normal OS. No macular edema OU. Systemic imaging demonstrated lymphadenopathy consistent with low-grade lymphoma.

C. Metastatic disease masquerading as uveitis: Case

1. 82-year-old male presents with decreased vision and floaters in the right eye. He is monocular (NLP vision in the left eye from previous trauma).
2. VA: 20/60 OD, NLP OS
3. Exam: globular deposits on IOL, dense vitreous debris OD without macular edema. Normal exam aside from dry macular degeneration changes OS.
4. OCT: drusen OU, no edema
5. FA: disc leakage OD, no leakage OS
6. Course: Patient was started on topical steroid drops with initial improvement, but returned with sudden dense pigment dispersion on IOL and within vitreous strands. Ultimately diagnostic vitrectomy revealed malignant cells positive for melanoma markers.

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Laboratory Testing of the Uveitis Patient

Tackling the perennial question “What’s the ‘Uveitis panel’ that you always order in your uveitis patients?”

Lyndell Lim MD PhD

I. Introduction

One of the more common laments from ophthalmology residents is that they never know which lab tests to order when a patient presents with uveitis for the first time. So by default they tend to order everything they can think of, ranging from infections such as tuberculosis and toxoplasmosis through to autoimmune conditions such as sarcoidosis and rheumatoid arthritis. The result is a list of 20 or more tests requiring a significant blood draw and often multiple imaging investigations, resulting in a significant cost to the patient in both time and money, let alone potential morbidity associated with further investigations that may be ordered as a result of positive results from the initial gamut of investigations.

But are all of these tests really necessary?

The answer is often a resounding NO. Rather than using a “one size fits all” panel of investigations for every single presentation of uveitis, one should instead tailor the investigation list according to the patient’s presentation, using Bayes Theorem as a guide.

II. Bayes Theorem

- A. Bayes theorem is a formula that calculates conditional probabilities:

$P(A|B) = P(A) P(B|A)/P(B)$, where

$P(A|B)$ = probability of the disease being present with a positive test (ie, the positive predictive value [PPV] of the test),

$P(B|A)$ = probability that the test will be positive in the presence of disease (ie, the sensitivity of the test),

$P(A)$ = general probability of the disease (ie, disease prevalence), and

$P(B)$ = general probability of test positivity in the wider population, calculated as $(\text{test sensitivity} \times \text{disease prevalence}) + [(1 - \text{test specificity}) \times (1 - \text{prevalence})]$

- B. With these definitions, Bayes theorem could thus be rewritten as follows:

$$\text{PPV} = \frac{\text{sensitivity} \times \text{prevalence}}{[\text{sensitivity} \times \text{prevalence}] + [(1 - \text{specificity}) \times (1 - \text{prevalence})]}$$

- C. Similarly, for the negative predictive value (NPV), that is, the probability that the disease is not present when the test is negative:

$$\text{NPV} = \frac{\text{specificity} \times (1 - \text{prevalence})}{[(1 - \text{sensitivity}) \times \text{prevalence}] + [\text{specificity} \times (1 - \text{prevalence})]}$$

- D. Simply put, if you know the sensitivity and specificity of the test and the pretest likelihood of the disease in question, then Bayes theorem will give you the post-test probability of the disease being present.

- E. In addition, it is very clear from the above equation that the PPV of a test and its sensitivity are not the same, as it can be seen that the PPV is greatly influenced by the prevalence of the disease being tested for.

III. Illustrative Scenarios

The following clinical scenarios will be used to help illustrate these points.

- A. A hypothetical (excellent) test with 95% sensitivity and specificity
1. If the prevalence (pretest probability) of the disease is only 1%, then the PPV of such a test is only 0.16, which means that almost 85% of cases that test positive in this setting are actually a false positive. The NPV of the test would be 100%; that is, every negative result is a true negative.
 2. However, if the same test is applied to a population with higher prevalence, where the pretest probability is 0.5, then the PPV and NPV are both 0.95, where such a test functions equally well to rule in or out the disease in question.
 3. It should also be noted that highly specific tests, but with lower sensitivity, are particularly useful to rule-in a diagnosis when the pretest probability is >20%. (At lower probabilities, false positives will be an issue.) Conversely, highly sensitive tests with low specificity are good for ruling out disease when the result is negative.

B. Tuberculosis (TB) testing

1. Almost 25% of the population worldwide is latently infected with tuberculosis; however, there is a very high variability between different global regions, with the highest prevalences in South East Asia and Africa, and low rates in Europe and the Americas. Thus, the PPV of tuberculosis testing in South East Asia is very different from that in North America.
2. The QuantiFERON-TB Gold assay has a sensitivity of 97.9% and specificity of 98.1%.
3. The tuberculin skin test (PPD) has a sensitivity of 59%-100% and specificity of 75%-100%.
4. In North America, 0.3% of anterior uveitis is associated with TB. The PPV of the QuantiFERON test would thus be only 13.4%, with a NPV of 99.9%. Using a sensitivity of 79.5% and specificity of 87.5% for the PPD, its PPV in this scenario is only 1.9%.
5. In Asia, where 17% of posterior uveitis is associated with TB, the PPV of the QuantiFERON is 91.3%, compared with a PPV of 56.6% with the PPD.

C. Antinuclear antibody (ANA) testing for systemic lupus erythematosus (SLE)

1. ANA has a low specificity, as it can be positive in healthy controls.
2. SLE is associated with <1% of uveitis.
3. Using a reported sensitivity of 99% and specificity of 85%, with the above low prevalence rates of SLE associated with uveitis (<1%), the PPV of an ANA in a patient with any form of uveitis and no other systemic symptoms of SLE is *less than 4.5%*.
4. ANA should therefore *not* be used for routine screening of patients with uveitis.

D. Syphilis testing

1. Testing for syphilis involves treponemal tests (eg, syphilis IgG, FTA-ABS, TP-PA assay) and nontreponemal tests (eg, VDRL and RPR). Traditionally, the nontreponemal tests were used for screening, and positive results from these were confirmed with a treponemal test.
2. “Reverse screening,” where the order of the treponemal and nontreponemal tests is reversed, is now commonly used and is particularly appropriate for suspected ocular syphilis, with a reported sensitivity and specificity of 99.85% and 99.98%.
3. In populations with a low reported syphilis prevalence of only 0.12% (eg, Europe), the PPV of this testing regimen is 85.7%, which means that up to 15% of positive tests are false. In contrast, the PPV rises to 98% or higher once the population prevalence of syphilis infection reaches 1% or more.
4. Rates of syphilis have jumped sharply in recent years, and syphilis is now an epidemic in many populations worldwide. Given this sharp increase in infections and the potential catastrophic sequelae that may occur if a patient with ocular syphilis receives unopposed systemic corticosteroid or a local corticosteroid injection into or around the eye without parenteral penicillin treatment, if there is one test that should be considered routine in most presentations of uveitis, syphilis testing would be that test.

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Ocular Imaging in Uveitis

Marion R Munk MD PhD

Image Modalities in Uveitis

Multimodal imaging is of uppermost importance in the daily uveitis clinic. New technologies such as swept source OCT (SS-OCT), ultrawide (UW)-field imaging, and OCT angiography (OCT-A) have significantly added to more conventional image techniques such as conventional fluorescein and indocyanine green angiography.

SS-OCT and wide-field OCT

Because SS-OCT is twice as fast as conventional spectral domain OCT, it allows scanning of a wider field of view in a similar time frame. Using a tunable laser, the vitreous, retina, choroid, and sclerochoroidal border can be depicted. Large scan patterns allow the visualization of these structures beyond the vascular arcades and the posterior pole. The thickness maps of these large scan patterns may be used, for example, to identify perivascular thickening—a parameter that nicely correlates with leakage of respective vasculature on fluorescein angiography. These wide-field en face maps may then be used to follow therapy and disease activity.

Wide-field OCT may be helpful in further investigating peripheral lesions, such as vasoproliferative tumors or retinosis, which can be all signs of disease activity in intermediate uveitis.

Multispectral imaging

Light-emitting diodes of different wavelengths allow examination of the different layers of the retina and choroid. These wavelengths range from 520 nm (green) to 940 nm (infrared). The longer the wavelength, the deeper they penetrate the different ocular structures. This helps to identify details that otherwise may have remained undetected, and it is also useful in determining the depth of a lesion. A channel around 532 nm (green) will mainly highlight (outer) retinal lesions, while a longer channel, around 635 nm (red), will highlight choroidal lesions.

UW-field imaging

UW color fundus images and UW-field FA allow us to detect far peripheral NVE (neovascularization elsewhere) and peripheral nonperfusion. Peripheral vascular leakage assessable using UW-field FA is highly specific and sensitive for clinical activity in uveitis and is an important parameter for following disease activity and (additional) treatment need. Automated, quantitative assessment of peripheral vascular leakage may become a surrogate endpoint in the near future.

OCT-A

Another important image modality is OCT angiography. This rather new image modality allows us to reliably detect, for example, secondary CNV in multifocal choroidopathy (MFC) and punctate inner choroidopathy (PIC) patients. Up to 83% of MFC/PIC lesions are found to present flow consistent with

CNV and help nowadays to differentiate between active MFC/PIC lesions and CNV membranes. Prior the OCT-A era, CNV was found in more than 50% of cases. Characteristically, these secondary inflammatory CNVs are Type 2 macular neovascularization. The presence of subretinal fluid and sometimes also intraretinal fluid indicates exudative activity; sometimes, however, a lesion may be active without the presence of fluid. In these cases, a so-called pitchfork sign may be appreciable.

Particularly, (wide-field) SS-OCT-A may be also used to assess the choroidal involvement in uveitis. Current advancements in UW-field SS-OCT-A enable us to image the retina and choroid beyond the anterior part of the vortex vein ampullae. In birdshot choroidopathy, (wide-field) SS-OCT-A identifies the exact depth of the lesions. In early stages, areas of flow attenuation and flow deficit in the Sattler layer may be detected, while the choriocapillaries are still completely intact. In addition to Goldmann visual fields and electroretinography, wide-field SS-OCT-A may therefore be employed to guide treatment and follow potential disease progression. Granulomatous lesion involvement, such as in Vogt-Koyanagi-Harada syndrome (VKH), ocular sarcoidosis, and TB, may also be followed by respective image modality.

Area of flow deficits in the choriocapillaries and the deeper choroidal layers can be also (automatically) quantified, which can help us to assess potential lesion growth and disease progression. Areas of flow deficit quantified on OCT-A show a strong correlation with the lesion size measured in indocyanine green.

Quantitative OCT-A metrics of the choriocapillaries and choroid show promising results and may help in the near future to distinguish between active and inactive disease.

Anterior segment imaging

Significant insights via imaging are not confined to the posterior part of the eye. Laser flare photometry and anterior segment OCT-A are important tools that help in quantifying anterior segment involvement, specifically useful in following treatment response and quantifying anterior segment inflammation.

Outlook

In the future, (semi-)automated quantification of characteristic ocular inflammatory features will help us follow disease activity more precisely. Automated assessment allows for quantification of vitreous cells, vitreous flare, and peripheral nonperfusion, which may in the future serve as quantitative outcomes in clinical trials and may help us to follow our patients more precisely. It also allows for automated quantification of choroidal lesions and potential growth.

Machine learning algorithms and AI will further help in the interpretation of these image modalities in uveitis, despite the (current) limitation of large datasets to train these algorithms properly.

Diagnostic Imaging Signs in Uveitis

Multimodal imaging supports our understanding of the underlying pathology, but it also holds valuable clues to guide the correct diagnosis. OCT especially offers a lot of useful hints, including the following examples:

- **Bacillary detachment** on OCT is defined by the presence of membranous structures on the floor of a cystoid space, continuous with the ellipsoid zone (EZ) band within the attached retina. It has been described in severe systemic lupus erythematosus–associated central serous retinopathy, VKH, acute posterior multifocal placoid pigment epitheliopathy, toxoplasmosis, posterior scleritis, and MEK inhibitor–induced panuveitis and indicates the presence of a proinflammatory state.
- **SRF** on OCT associated with subretinal membranous structures, the loss of normal choroidal structure, choroidal thickening, retinal pigment epithelium (RPE) folds, and undulation of RPE is very characteristic for VKH.
- **Syphilitic posterior placoid chorioretinopathy** also presents very characteristically on OCT. Granular RPE hyperreflectivity and thickening associated with a disrupted EZ and an intact external limiting membrane are very indicative of respective disease entity.
- Focal disruption of the EZ, RPE mottling, and dense and oval dots in the outer nuclear layer are indicative of **multiple evanescent white dot syndrome**.
- **Posterior hyaloid face precipitates and superficial retinal precipitates** visible on OCT are characteristics of an infectious cause. Posterior hyaloid precipitates indicate reactive granulomatous inflammation and are often associated with herpetic retinal necrosis and toxoplasmosis retinochoroiditis.
- OCT may also help to differentiate different **infectious causes** of retinitis. Sometimes toxoplasmosis retinochoroiditis and viral necrotizing retinitis are hard to differentiate. While viral necrotizing retinitis presents as full-thickness retinitis on OCT with disruption of the retinal structures and formation of lacunae, with or without choriocapillary thickening and RPE involvement, toxoplasmosis retinochoroiditis presents with full-thickness retinitis *plus* choroidal involvement and infiltration, visible as disruption of the normal choroidal structure. Especially in immunocompromised patients with atypical presentations, these signs may help to differentiate both entities.
- **Choroidal granulomas** possess characteristic OCT features as well. On SS-OCT or enhanced depth imaging OCT, a choroidal granuloma will exhibit an increased hyperreflective transmission signal, while other hyporeflexive choroidal structures such as vessel lumen will lack this characteristic feature.

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Health Disparities in Uveitis

Grace Levy-Clarke MD

- I. Health Disparity: Overview and Definition
- II. The Epidemiologic View of Uveitis Through the Lens of Health Disparity
 - A. The social determinants of health
 - B. The measures for health outcomes
- III. Current Gaps in Uveitis Care Delivery That Foster Health Disparity
 - A. Access to care
 - B. Access to subspecialty care
- IV. Potential Mitigation Strategies to Address Health Disparity in Uveitis
 - A. Resident training
 - B. Practicing ophthalmology forums

Anterior Uveitis Overview

Lana M Rifkin MD

I. Classification

- A. Acute: sudden onset, limited duration (<3 months)
- B. Chronic: insidious onset, >3-month duration
- C. Recurrent: after period of quiescence >3 months

II. Epidemiology

- A. Most common type of uveitis
- B. Incidence of 20.3 per 100,000 person-years
- C. Rate increases with age.

III. Presentation

- A. Symptoms: pain, redness, photophobia; floaters, decreased vision rare
- B. Unilateral or bilateral
- C. Sequential or simultaneous onset

IV. Examination

- A. VA: Not typically decreased unless corneal edema, macular edema, lenticular opacity, optic nerve edema, or vitreous haze is present.
- B. IOP: May be elevated with inflammation in herpetic disease, sarcoidosis, others
- C. External: conjunctival granulomas, enlarged lacrimal glands
- D. Cornea: loss of corneal sensation, corneal edema, dendrites, keratic precipitates (note type/distribution), band keratopathy
- E. Anterior chamber: Cells may be seen in anterior chamber (iritis) or anterior vitreous, behind the lens (iridocyclitis), hypopyon.
- F. Iris: inflamed iris vessels vs. neovascularization, transillumination defects, atrophy, nodules (Koeppe, Busacca, Berlin)
- G. Lens: cataract, IOL position
- H. Anterior vitreous: vitreous cell, haze

Table 1

Differential Diagnosis	Associated Considerations
Idiopathic	
HLA-B27 associated	ROS + lower back pain, alternating hip pain, stiffness
Sarcoidosis	Breathing trouble, heart issues, skin rash
Postinfectious	ROS + recent URI, etc.
Drug-induced	Oral antibiotics, cancer meds
TINU	Associated kidney disease
Inflammatory bowel disease	Diarrhea
JIA	ROS + joint pain
TB	
Syphilis	

Abbreviations: ROS, review of systems; TINU, tubulointerstitial nephritis and uveitis syndrome; JIA, juvenile idiopathic arthritis.

Table 2

Workup	Associated Considerations
HLA-B27	Ankylosing spondylitis, psoriasis, inflammatory bowel disease
ACE, lysozyme/muramidase, chest x-ray, ± CT	Sarcoidosis
Urine B2 microglobulin, BUN/Cr	TINU
Serum antistreptolysin O (ASO) titer	Post-streptococcal
<i>Treponema pallidum</i> Ab, FTA-Abs, RPR (do not order alone)	Syphilis
QuantiFERON-TB Gold or T spot	TB
ANA, RF (in kids only)	JIA

Abbreviations: TINU, tubulointerstitial nephritis and uveitis syndrome; JIA, juvenile idiopathic arthritis.

V. Treatment

- A. Topical steroids
 - 1. Lower potency (loteprednol, fluorometholone) unlikely to be effective
 - 2. Prednisolone
 - 3. Difluprednate
 - 4. No role for topical NSAIDs
- B. Cycloplegics
- C. Oral steroids for severe inflammation and/or associated CME, optic nerve edema
- D. Periocular/intravitreal steroids injections
- E. Steroid-sparing immunosuppressives

Selected Readings

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Case: One Eye . . . or Two?

Laura Kopplin MD PhD

CASE PRESENTATION

Fifty-four-year-old white female presenting with right eye blurred vision, redness, and photophobia

History

- Past medical history: Plantar fasciitis, acne, seasonal allergies
- Past ocular history: Myopia
- Medications: Fluticasone nasal spray, diphenhydramine, tretinoin cream
- Family history: Mother with psoriasis

Ocular Examination

- VA: 20/40 OD, 20/20 OS
- IOP: 17 mmHg OD, 13 mmHg OS
- Conjunctiva: 2+ injection OD, normal OS
- Anterior chamber: 3+ cell and 3+ flare OD, no cell or flare OS
- Iris: Posterior synechiae OD, normal OS
- Fundus: Normal fundus OU

Etiologic Testing

- Treponemal Ab: Negative
- QuantiFERON Gold: Negative
- ACE and chest x-ray: Normal
- HLA-B27: Positive

Ocular Course

- Started on prednisolone acetate 1% 6x/day and atropine 1% 2x/day OD
- Five days later developed new-onset redness, blurred vision, and photophobia OS. Found to have persistent anterior chamber 2+ cell and flare OD and new anterior chamber 2+ cell and flare and posterior synechiae OS. Transitioned to difluprednate 0.05% 4x/day OD; difluprednate 0.05% and atropine 1% 2x/day added OS.
- Review of systems: Notable for recent-onset diarrhea and hematochezia
- Positive fecal calprotectin

DIAGNOSIS & TEACHING POINTS

Clinical Course, Final Diagnosis, and Outcome

- Gastroenterology referral. Colonoscopy identified colon and rectal inflammation and confirmed on biopsy. Diagnosed with Crohn disease and HLA-B27 positive Crohn-associated bilateral anterior uveitis.
- Patient started on prednisone 40 mg daily, followed by infliximab 5 mg/kg loading doses with subsequent maintenance infusions every 6 weeks.
- Uveitis remained controlled with maintenance infliximab after taper off oral prednisone and difluprednate 0.05% drops.

Discussion of Disease

I. Epidemiology

- A. HLA-B27 is associated with 18%-32% of acute anterior uveitis.
- B. Six to 13% of people with European ancestry carry the HLA-B27 allele.
- C. ~50% of patients with HLA-B27 anterior uveitis will have an associated seronegative spondyloarthropathy (ankylosing spondylitis, reactive arthritis, psoriatic arthritis, inflammatory bowel disease).

II. Clinical Features

- A. Acute, unilateral
- B. Sudden onset
- C. Significant inflammation: fibrin, hypopyon, or high cell grade
- D. Posterior synechiae common
- E. Nongranulomatous
- F. Episodic, alternating
- G. More likely to present with bilateral disease, insidious onset, and nonanterior uveitis in patients with associated psoriatic arthritis or inflammatory bowel disease

III. Differential Diagnosis

- A. Syphilis
- B. Behçet
- C. Endophthalmitis
- D. Viral-associated anterior uveitis
- E. Drug induced (rifabutin)
- F. Idiopathic

IV. Diagnosis

- A. Lab testing for HLA-B27 allele
- B. Review of systems for joint, skin, and bowel disease

V. Etiology and Pathogenesis

- A. Uveitogenic peptide hypothesis: HLA-B27 molecule presents antigen with sequence homology to self-peptides to CD8+ T cells. Activated T cells induce uveitis due to cross-reactivity with ocular peptides.
- B. HLA-B27 misfolding hypothesis: Misfolding of HLA-B27 heavy chains triggers a protein stress response with induction of inflammatory cytokines.
- C. Innate immune recognition of aberrant HLA-B27

VI. Management

- A. Medical
 - 1. Topical corticosteroids
 - 2. Cycloplegia
 - 3. Periocular or systemic corticosteroids for severe inflammation
 - 4. Disease-modifying antirheumatic drugs
 - a. Sulfasalazine reduces recurrence risk and severity of flares in ankylosing spondylitis.
 - b. Methotrexate, mycophenolate, and azathioprine may benefit uveitis but have variable efficacy in the spondyloarthropathies and require coordination of care.
 - 5. Tumor necrosis factor inhibitors: Often preferred in setting of active spondyloarthropathy
- B. Surgical: Laser peripheral iridotomy or synechiolysis with surgical iridectomy if iris bombe develops secondary to posterior synechiae

VII. Prognosis

- A. Recurrences are more frequent early in the disease course.
- B. Small portion of patients develop chronic anterior uveitis after severe attacks or frequent recurrences.
- C. Evidence is mixed regarding whether visual outcomes and structural complications are worse in HLA-B27 uveitis compared to HLA-B27 negative anterior uveitis.

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Case: O-h-h, Child!

Anjum F Koreishi MD

CASE PRESENTATION

History of Present Illness

Ten-year-old female with history of uveitis since age 4 and joint pain since age 5, referred for management of “recurrent acute anterior uveitis.” Has been treated chronically with fluctuating doses of topical steroids, on methotrexate recently. Never had any ocular symptoms aside from blurred vision OD.

Medications

- Prednisolone acetate 1% daily OU
- Methotrexate 20 mg subcutaneous weekly
- Folic acid 1 mg daily

Family History

Unremarkable

Review of Systems

Positive for knee and ankle pain

Examination

- Uncorrected vision
 - OD: 20/50
 - OS: 20/20
- IOP
 - OD: 12
 - OS: 13
- Anterior segment
 - Cornea
 - OD: peripheral band keratopathy, endothelial dusting without keratic precipitates
 - OS: clear
 - Anterior chamber
 - OD: 1+ flare, 3+ cell
 - OS: 1+ flare, 1+ cell
 - Iris
 - OD: broken synechiae at 6:00
 - OS: normal
 - Lens
 - OD: 1+ posterior subcapsular cataract, pigment on capsule
 - OS: clear
 - Vitreous
 - OD: 1+ cell
 - OS: 0.5+ cell
- Fundus exam: OU small cups, otherwise unremarkable

DIAGNOSIS & TEACHING POINTS

Differential Diagnosis

- Juvenile idiopathic arthritis (JIA)-related chronic anterior uveitis
- JIA-related chronic anterior uveitis
- JIA-related chronic anterior uveitis
- Tubulointerstitial nephritis and uveitis (TINU) syndrome
- Sarcoidosis
- Blau syndrome
- Syphilis
- HLA-B27 related

Investigations

- ANA+ 1:640
- Negative: RF, HLA-B27, syphilis IgG, ACE, lysozyme

Final Diagnosis

The patient was diagnosed with JIA-related chronic anterior uveitis (not recurrent acute disease as initially diagnosed), with oligoarticular ANA+/RF- arthritis.

Clinical Course and Outcome

- At initial visit, topical prednisolone was increased for active inflammation. Adalimumab was started at 40 mg every other week, and methotrexate was continued.
- Eyes were quiet after tapering off topical steroids, on adalimumab every 2 weeks. Methotrexate was tapered to 7.5 mg subcutaneous.
- 8 months later developed asymptomatic 2+ cell OD with no inciting event. Topical prednisolone was restarted and methotrexate was increased.
- By 3 months later, could not taper off steroids. Adalimumab increased to 40 mg weekly.
- Over the next 2 years, recurrent flares with any missed dose, vaccination, or illness, requiring steroids.
- Infliximab 10 mg/kg every 4 weeks was started, adalimumab stopped, methotrexate continued.
- 8 months later developed 1+ cell OD; infliximab increased to 12.5 mg/kg every 4 weeks.
- 18 months later developed 0.5+ cell OD, restarted topical steroids and tapered to once daily prednisolone.
- Now quiet on daily prednisolone OD, infliximab 12.5 mg/kg every 4 weeks, subcutaneous methotrexate 22.5 mg weekly.

Teaching Points

- JIA-uveitis is a chronic and asymptomatic disease, requiring screening and frequent ophthalmic examinations, even when disease may be controlled.
- While steroids are used as initial therapy and for flares, chronic therapy with systemic immunomodulation is necessary and should be started right away.
- Following closely for progression of cataract, posterior synechiae, macular edema, and IOP spikes is important.
- Given risk of amblyopia, always refract when vision decreases.
- Given growth in children, make sure medication dosing is appropriate.

Disease Discussion

I. Definition

A. Chronic arthritis onset in a child under 16 years old

B. Subtypes

1. Oligoarticular JIA (uveitis ~30%)
2. Polyarticular JIA (uveitis ~10%)
3. Systemic JIA (uveitis ~1%)
4. Enthesitis-related arthritis (uveitis ~7%-15%)
5. Psoriatic arthritis (uveitis ~10%)

II. Epidemiology

- A. Uveitis most common in oligoarticular, ANA+, RF- disease
- B. Average age of diagnosis is 6 years old.
- C. Highest risk of uveitis is within 4 years of JIA diagnosis, most within 7 years.
- D. Family history increases risk.
- E. High-risk features: female, young age, ANA+

III. Clinical Features

- A. Asymptomatic and chronic anterior uveitis, usually bilateral
- B. Usually nongranulomatous inflammation
- C. Anterior chamber and anterior vitreous inflammation
- D. Complications include band keratopathy, posterior synechiae, peripheral anterior synechiae, cataract, macular edema, optic disc edema, glaucoma, hypotony, amblyopia.

IV. Diagnosis

- A. Systemic findings and evaluation with pediatric rheumatology
- B. Typical ocular findings and presentation
- C. Labs: ANA, RF, HLA-B27
- D. Rule out other etiologies

V. Pathogenesis

Multifactorial, likely genetic component

VI. Management

A. Screening (for patients without diagnosed uveitis)

1. Initial evaluation with ophthalmology within 6 weeks of diagnosis of JIA
2. Every 3 months
 - a. Oligoarticular, polyarticular, psoriatic, undifferentiated, *and*
 - b. ANA+, onset < 7 years old, duration ≤ 4 years
3. Every 6 months
 - a. Systemic, enthesitis-related, *or*
 - b. ANA-, onset > 7 years old, duration > 4 years

B. Treatment

1. Topical corticosteroids for initial disease or flares of disease. Prednisolone is safer than difluprednate.
2. Systemic corticosteroids for severe disease, short-term use only
3. Early institution of systemic immunomodulation
 - a. Goal: control of chronic inflammation while minimizing adverse effects
 - b. Methotrexate is generally first line.
 - c. Refractory cases
 - i. Adalimumab every 2 weeks, can advance to weekly
 - ii. Infliximab
 - iii. Tocilizumab
 - iv. Others, including rituximab, golimumab
4. Surgical intervention
 - a. Goal is to avoid surgical intervention with early and aggressive therapy.
 - b. Eyes must be quiet at least 3 months prior to surgical intervention.
 - c. Cataract surgery: Consider aphakia, consider core vitrectomy.
 - d. Glaucoma surgery: Drainage devices with best long-term control
 - e. Band keratopathy: Chelation in visually significant cases

VII. Prognosis

Good with appropriate diagnosis and management

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Case: Oh, That Pterygium . . .

Christopher D Conrady MD

CASE PRESENTATION

Sixty-seven-year-old white female presents with persistent del-
len with worsening scleral thinning

Symptoms

Blurred vision and eye pain of the left eye

Ocular History

Pterygium resection 8 months prior. No improvement with del-
len despite topical prednisolone, cyclopentolate, and 60-mg oral
steroids.

Current Medications

60-mg oral prednisone, prednisolone 6x/day, cyclopentolate 2x/
day

Ocular Examination

- VA
 - OD: 20/25
 - OS: 20/100
- IOP
 - OD: 10 mmHg
 - OS: 9 mmHg
- Anterior segment
 - OD: Unremarkable
 - OS: Elevated, yellowish nodules inferonasally with
localized, injected conjunctival vessels and underlying
scleral thinning with adjacent corneal thinning
- Anterior chamber: No cell or flare OU
- Iris
 - OD: Normal
 - OS: Posterior synechiae at 6
- Lens
 - OU: 2+ nuclear sclerotic cataract
 - OS: Pigment on lens capsule
- Vitreous segment
 - OD: No cell or haze
 - OS: No cell or haze
- Posterior segment
 - OD: Unremarkable
 - OS: Inferior exudative detachment and choroidal folds
through macula

DIAGNOSIS & TEACHING POINTS

Final Diagnosis, Clinical Course, and Outcome

- Pseudomonal scleritis
- Started on 500 mg daily of levofloxacin (Levaquin)
- Tapered prednisone
- Start moxifloxacin 4x/day
- Switch to difluprednate (Durezol) 4x/day
- Continue cyclopentolate 2x/day
- Injected subconjunctival ceftazidime
- Basic uveitis laboratory evaluation unremarkable
- Culture (+) for *Pseudomonas* sensitive to levofloxacin and
ciprofloxacin
- Resolution of nodules and exudative detachment, stabili-
zation of scleral thinning, completion of 30-day course of
levofloxacin and 3 subconjunctival ceftazidime injections,
and final visual acuity of 20/50 OS off all medications

Discussion of Disease

I. Epidemiology

- A. Infectious scleritis represents 5%-10% of all cases.
- B. Typically follows trauma or prior surgery
- C. Higher rates with the use of radiation and mitomy-
cin C
- D. Most common cause of infectious scleritis in devel-
oped countries: *Pseudomonas aeruginosa*

II. Clinical Features

- A. Unilateral
- B. Scleral thinning (necrotizing scleritis)
- C. Conjunctival inflammation
- D. Microabscesses
- E. Associated choroidal effusions or retinal detach-
ments
- F. Delayed presentation from prior trauma or surgery

III. Differential Diagnosis

- A. Other infectious causes of scleritis: *Nocardia*,
Streptococcus, *Haemophilus*, *Candida*, and *Asper-
gillus*
- B. Noninfectious causes of scleritis (~90% of cases)
- C. Episcleritis

IV. Diagnosis

- A. Rule out noninfectious causes with laboratory evaluation: ESR, CRP, rheumatoid factor, anti-nuclear antibodies, anti-DNA antibodies, HLA-B27, anti-neutrophil cytoplasmic antibodies, ACE/lysozyme.
- B. Rule out systemic infection (syphilis: FTA/RPR, tuberculosis: QuantiFERON Gold, chest x-ray).
- C. Identify offending organism to guide antimicrobial therapy.

V. Management

A. Medical

1. Systemic, topical, and subconjunctival antibiotics
2. 18% of cases are effectively treated with medical therapy alone.

B. Surgical

1. Debridement and irrigation
2. Patch grafts for scleral thinning and/or perforation
3. Amniotic membranes

VI. Prognosis

- A. Better presenting VA is associated with better long-term outcomes.
- B. Poor prognosis in many despite aggressive treatment
- C. The development of perforations and endophthalmitis

Selected Readings

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Case: Don't Crack Under Pressure!

Kara C LaMattina MD

CASE PRESENTATION

A 13-year-old asymptomatic Brazilian female is referred for evaluation of elevated IOP with low-grade anterior segment inflammation of the right eye. She had 2 prior episodes of “high pressure” in the right eye over last 2 years for which she received pressure-lowering drops.

Medications

- Prednisolone acetate 1% q.i.d. OD
- Dorzolamide-timolol b.i.d. OD
- Brimonidine b.i.d. OD

Family History

Uncle with glaucoma, no known uveitis

Review of Systems

Positive for cold sores, otherwise negative

Examination

- Vision: 20/20 OU
- IOP: 10/16
- Central corneal thickness: 565/566
- Gonio: open without peripheral anterior synechiae OU
- Anterior segment
 - OD: 8 small white keratic precipitates on inferior half of cornea, rare cell with trace flare, iris mamillations without transillumination defects
 - OS: unremarkable
- Fundus exam
 - Cup-to-disc ratio: 0.4 OD and 0.3 OS
 - Otherwise normal OU
- OCT: Relative thinning OD compared with OS though within normal limits OU

DIAGNOSIS & TEACHING POINTS

Differential Diagnosis

- Viral-associated anterior uveitis
 - Herpetic-associated
 - Herpes simplex virus (HSV)
 - Varicella zoster virus (VZV)
 - Cytomegalovirus (CMV)
 - Rubella-associated
 - Zika-associated
- Toxoplasmosis
- Idiopathic uveitis

Investigations

- HLA-B27: negative
- Syphilis IgG/IgM: negative
- QuantiFERON Gold: negative
- ACE/lysozyme: negative
- RF/ANA: negative
- Toxoplasmosis IgG/IgM: negative
- Chest x-ray: negative
- Anterior chamber (AC) paracentesis? Serology?

Final Diagnosis and Clinical Course

This was a case of hypertensive unilateral anterior uveitis secondary to presumed HSV. Given the high clinical suspicion for herpesvirus, AC tap was deferred and empiric therapy with valacyclovir was initiated at 1000 mg t.i.d. Because this was the third episode in 2 years and there were early signs of glaucomatous damage, the patient was kept on prophylactic valacyclovir at 500 mg daily for a 1-year course. She was tapered off all topical therapy during that time without recurrence. She was weaned off valacyclovir and has been without an additional flare for 6+ months.

Teaching Points

- Open-angle hypertensive anterior uveitis is generally infectious in etiology.
- While AC paracentesis for polymerase chain reaction (PCR) is very useful in the adult population, it is important to weigh the risks/benefits in the pediatric population. More important if suspicious for CMV due to toxicity of valganciclovir.
- Antivirals may impact the yield of aqueous PCR, and should not be started ahead of a planned AC paracentesis under general anesthesia.
- Prophylactic valganciclovir is safe long term and may be indicated in cases with progressive glaucomatous damage.

Disease Discussion

- I. Epidemiology
 - A. HSV accounts for 5%-10% of anterior uveitis.
 - B. Prevalence increases with age.
- II. Clinical Features
 - A. Unilateral (rarely bilateral)
 - B. Small-large keratic precipitates, often extending beyond Arlt triangle
 - C. Sectoral or patchy iris atrophy
 - D. Increased IOP
 - E. Decreased corneal sensation
 - F. ± keratitis (epithelial or stromal)
- III. Differential Diagnosis
 - A. Other viral uveitides
 1. Herpesviridae (VZV, CMV)
 2. Rubella
 3. Zika
 - B. HLA-B27-associated uveitis
 - C. Syphilitic uveitis
 - D. Toxoplasmosis
 - E. Idiopathic
 - F. Masquerade syndrome
- IV. Diagnosis may be made based on:
 - A. Clinical findings
 - B. Response to empiric antiviral treatment
 - C. Testing of intraocular fluid
 1. HSV/VZV/CMV PCR
 2. Rubella PCR (if available)
 3. Metagenomic deep sequencing

V. Pathogenesis

- A. Reactivation of Herpesviridae
- B. Immune-mediated response to Herpesviridae

VI. Management

- A. Oral antivirals (acyclovir, valganciclovir, famciclovir) ± prophylaxis
- B. Topical steroids
- C. IOP-lowering agents

VII. Prognosis

Good with appropriate diagnosis and management

Selected Readings

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In These Unprecedented Times . . .

2022 Uveitis Subspecialty Day

Janice C Law MD

Action Requested: Support Ophthalmology's Advocacy Efforts

Please respond to your Academy colleagues and be part of the community that contributes to OPHTHPAC®, the Surgical Scope Fund, and your State Eye PAC. Be part of the community that ensures ophthalmology has a strong voice in advocating for patients.

Where and How to Invest

During AAO 2022 in Chicago, invest in OPHTHPAC and Surgical Scope Fund at either of our two convention center booths (in the Grand Concourse and Lakeside Center) or [online](#). You may also invest via phone by texting **MDEYE** to **41444** for OPHTHPAC and texting **SCOPE** to **51555** for the Surgical Scope Fund.

We also encourage you to support our congressional champions by making a personal investment to their re-election campaign via [OPHTHPAC Direct](#), a unique and award-winning program that lets *you decide* who receives your political support.

Surgical Scope Fund contributions are completely confidential and may be made with corporate checks or credit cards. PAC contributions may be subject to reporting requirements.

Why Invest?

Academy Surgical Scope Fund contributions are used to support the infrastructure necessary in state legislative/regulatory battles and for public education. OPHTHPAC investments are necessary at the federal level to help elect officials who will support the interests of our profession and our patients. Similarly, state Eye PAC contributions help elect officials who will support the interests of our patients at the state level. Contributions to EACH of these three funds are necessary and help us protect sight and empower lives.

Protecting quality patient eye care and high surgical standards is a “must” for everybody. Our mission of “protecting sight and empowering lives” requires robust funding of both OPHTHPAC and the Surgical Scope Fund. Each of us has a responsibility to ensure that these funds are strong so that ophthalmology continues to thrive and patients receive optimal care.

OPHTHPAC for Federal Advocacy

OPHTHPAC is the Academy's award-winning nonpartisan political action committee, representing ophthalmology on Capitol Hill. OPHTHPAC works to build invaluable relationships with our federal lawmakers to garner their support on issues such as:

- Improving the Medicare payment system, so ophthalmologists are fairly compensated for their services

- Securing payment equity for postoperative visits, which will increase global surgical payments
- Stopping optometry from obtaining surgical laser privileges in the veterans' health-care system
- Reducing prior authorization and step therapy burdens

Academy member support of OPHTHPAC makes all this possible. Your support provides OPHTHPAC with the resources needed to engage and educate Congress on our issues, helping advance ophthalmology's federal priorities. Your support also ensures that we have a voice in helping shape the policies and regulations governing the care we provide. Academy member support of OPHTHPAC is the driving factor behind our advocacy push, and in this critical election year, we ask that you get engaged to help strengthen our efforts.

At the Academy's annual Mid-Year Forum, the Academy and the American Uveitis Society (AUS) ensure a strong presence of uveitis specialists to support ophthalmology's priorities. As part of this year's meeting, the AUS supported participation of fellowship trainees via the Academy's Advocacy Ambassador Program. During Congressional Advocacy Day, they visited members of Congress and their key health-care staff—either in person or virtually—to discuss ophthalmology priorities. The AUS remains a crucial partner with the Academy in its ongoing federal and state advocacy initiatives.

Surgical Scope Fund for State Advocacy

The Surgical Scope Fund (SSF) provides grants to state ophthalmology societies in support of their efforts to protect patient safety from dangerous optometric surgery proposals. Since its inception, the Surgery by Surgeons campaign and the SSF, in partnership with state ophthalmology societies, have helped 43 state/territorial ophthalmology societies reject optometric scope of practice expansions into surgery.

If you have already made a SSF contribution, please go to safesurgerycoalition.org to see the impact of your gift.

Dollars from the SSF are critical to build complete cutting-edge political campaigns, including media (TV, radio, and social media), educating and building relationships with legislators, and educating the voting public to contact their legislators. This helps to preserve high surgical standards by defeating optometry's surgical initiatives.

Each of these endeavors is very expensive, and no one state has the critical resources to battle big optometry on their own. Ophthalmologists must join together and donate to the SSF to fight for patient safety.

The Academy's Secretariat for State Affairs thanks the AUS for joining state ophthalmology societies in contributing to the SSF. These ophthalmic organizations complete the necessary SSF support structure for the protection of our patients' sight.

Surgical Scope Fund	OPHTHPAC®	State Eye PAC
To protect patient safety by defeating optometric surgical scope-of-practice initiatives that threaten quality surgical care	Support for candidates for U.S. Congress	Support for candidates for state House, Senate, and governor
Political grassroots activities, government relations, PR and media campaigns	Campaign contributions, legislative education	Campaign contributions, legislative education
No funds may be used for campaign contributions or PACs.		
Contributions: Unlimited	Contributions: Personal contributions are limited to \$5,000.	Contribution limits vary based on state regulations.
Individual, practice, corporate, and organization	Corporate contributions are confidential.	
Contributions are 100% confidential.	Personal contributions of \$199 or less and all corporate contributions are confidential. Personal contributions of \$200 and above are on the public record.	Contributions are on the public record depending upon state statutes.

State Eye PAC

The presence of a strong State Eye PAC providing financial support for campaign contributions and legislative education to elect ophthalmology-friendly candidates to the state legislature is critical as scope-of-practice battles and many regulatory issues are fought on the state level.

Support Your Colleagues Who Are Working on Your Behalf

Two Academy committees made up of your ophthalmology colleagues are working hard on your behalf. The OPHTHPAC Committee continues to identify Congressional Advocates in each state to maintain close relationships with federal legislators to advance ophthalmology and patient causes. The Surgical Scope Fund Committee is raising funds used to protect Surgery by Surgeons during scope battles at the state level.

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Intermediate Uveitis Overview

Sapna Gangaputra MD MPH

I. Intermediate Uveitis

A. Epidemiology

1. Least common of the uveitides (~15% of cases)
2. Prevalence estimate in the U.S.: 1 in 100,000
3. Bimodal age distribution: pediatric population <16 and ages 20-40¹
4. Bilateral in 80% of cases, but can be asymmetric

B. Clinical features

1. Symptoms: floaters, blurred vision
2. Clinical exam findings: vitreous cell and haze, "snowballs," pars plana exudates/snowbanks, retinal vascular sheathing, cystoid macular edema (CME)

C. Differential diagnosis

1. Pars planitis: idiopathic intermediate uveitis characterized by inflammation of the pars plana
2. HLA B27-associated intermediate uveitis
3. Sarcoid-associated uveitis
4. Multiple sclerosis-associated uveitis
5. Infections: syphilis, TB, Lyme, herpes

D. Imaging modalities

1. Ultrawide-field fluorescein angiography²
2. OCT
3. Ultrasound/ultrasound biomicroscopy: cyclitic membranes

E. Diagnostic testing

1. Infectious workup: syphilis serologies, QuantiFERON-TB Gold, Lyme antibodies, *Bartonella*
2. Noninfectious testing: serum ACE/lysozyme, urine B2 microglobulin, chest x-ray, MRI of brain/spine

F. Ocular complications³

1. CME: most common cause of vision loss
2. Retinal vasculitis: periphlebitis
3. Epiretinal membrane
4. Retinal neovascularization
5. Cataract
6. Glaucoma
7. Other complications: peripheral retinoschisis, retinal detachment, vasoproliferative tumor, papillitis

II. Medical Management

A. Corticosteroids

1. Topical difluprednate for mild inflammation and CME
2. Local: periocular, intravitreal
3. Systemic: 1 mg/kg up to 60 mg daily starting dose

B. Steroid-sparing immunosuppressive therapy

1. Antimetabolites: methotrexate, mycophenolate mofetil, azathioprine
2. Biologics: adalimumab, infliximab

C. Considerations in pregnancy/lactation⁴

III. Surgical Management

A. Laser photocoagulation: peripheral retinal ablation

B. Pars plana vitrectomy⁵

IV. Prognosis

- A. 60% of cases may have a prolonged course; low incidence of remission.⁶
- B. Overall prognosis is generally good, with >85% of patients retaining median visual acuity of 20/40 over time.⁷
- C. Factors associated with vision loss include macular scarring, CME, retinal detachment, hypotony, and optic neuropathy.

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Case: Totally “Tubular”

Pooja Bhat MD

CASE PRESENTATION

History

- History of present illness: 15-year-old female presents with persistent redness, pain, light sensitivity, and blurry vision in one eye followed by, a few days later, similar complaints in the other eye ×2 weeks
- Past medical history: none
- Ocular history: mild myopia
- Medications: none
- Review of systems: Endorses waxing and waning tension headaches for several months, self-treating with ibuprofen and acetaminophen, headaches particularly worse prior to the onset of eye symptoms
- Visual acuity
- OD: 20/30
- OS: 20/30
- No afferent pupillary defect
- Slit lamp exam: 2+ anterior chamber cell OU, posterior synechiae OU
- Fundus exam: 2+ anterior vitreous cell OU with 1+ vitreous haze OU, mild hyperemia of optic disc OU with nasal fullness, inferonasal small punched out chorioretinal scar OD

Differential Diagnosis

- Infectious: syphilis, Bartonella, TB
- Noninfectious: Vogt-Koyanagi-Harada (forme fruste), HLA-B27 related disease, tubulointerstitial nephritis and uveitis (TINU) syndrome, idiopathic
- Other causes of sudden-onset, bilateral, sequential-onset uveitis: post-infectious autoimmune, drug-induced

Workup

- OCT with preserved foveal contour OU but color map with thickening around fovea bilaterally
- Fluorescein angiography with significant retinal vasculitis in both eyes with uptake of dye by both optic discs
- CBC, CMP, QuantiFERON-TB Gold, FTA-ABS, ACE, lysozyme, x-ray chest 2 views: all normal or negative; urine B2 microglobulin elevated at 411
- Rheumatologic evaluation with no evidence of systemic autoimmune disease, additional workup
 - C3, C4, UA: normal
 - ANA screen: negative
 - CRP: elevated
 - HLA-B27: negative
- Pediatric nephrology evaluation with trending of urine B2 microglobulin values

DIAGNOSIS & TEACHING POINTS

Diagnosis

TINU-associated anterior and intermediate uveitis with retinal vasculitis OU

Clinical Course and Outcome

- Treated with systemic corticosteroids with taper.
- Given significant retinal vasculitis, antimetabolite and biologic combination recommended and patient on methotrexate subcutaneous weekly + adalimumab (Humira) subcutaneous every other week.
- Systemic steroids tapered and stopped, inflammation controlled, and retinal vasculitis resolved on combination systemic immunomodulatory therapy.
- Urine B2 microglobulin trended and eventually normalized while on steroid-sparing therapy.

Discussion

- TINU can have a variable presentation and may not always present with a bilateral anterior uveitis.
- Elicit specific history of potentially nephrotoxic agents, especially if the pattern of uveitis presentation, patient age, etc. fits TINU, such as antibiotics and NSAIDs for sinus/ear infections, colds, childhood migraines, and headaches with NSAID use.
- TINU is a diagnosis of exclusion, and it is important to rule out other etiologies for the uveitis.
- Optic disc hyperemia and edema can be seen in children and young adults related to their ocular inflammation and may not be a separate process. Additional discussion with parents about monitoring the nerve as the inflammation resolves and considering neuroimaging if there is persistent nerve head edema or worsening is important.
- Obtaining FAs in children (either PO or IV dye) with vitreous haze, disc hyperemia/edema, and macular thickening/CME can help clearly define extent of anatomic involvement of inflammation and disease burden by the discovery of retinal vasculitis, which may not be overtly apparent on exam, with resultant institution of appropriate and more aggressive therapy.

I. TINU

A. Epidemiology¹⁻⁵

1. Accounts for up to 2% of patients seen in uveitis centers and nearly 32% of children and adolescents under 20 years old with characteristic sudden-onset bilateral anterior uveitis
2. Initially reported to be more common in females; however, gender differences are now thought to be weaker.
3. Median age of onset is 15 to 17 years, with earlier age of onset among males.
4. Stronger association with HLA-DRB1*0102 allele

B. Clinical features⁶⁻¹⁴

1. Ocular and renal symptoms can present asynchronously.
2. Uveitis follows nephritis in most cases (65%) with average delay of 3 months, but could present up to 14 months later.
3. Ocular disease may precede nephritis in 20% of patients, and they may be present concurrently in 15%.
4. Bilateral disease is found in 80% of cases, with median time to second eye involvement of about 1 week in the initially unilateral cases.
5. Most common presentation is a nongranulomatous anterior uveitis of sudden onset with redness, pain, and light sensitivity.
6. Other clinical findings include vitritis, optic disc swelling, posterior and panuveitis in about 20% of patients.

C. Diagnostic testing and criteria^{1,5}

1. Abnormal renal function testing (elevated blood urea nitrogen and/or serum creatinine or progressive reduction in glomerular filtration rate)
2. Elevated urine B2 microglobulin
3. Abnormal urinalysis
4. Definitive diagnosis based on renal biopsy showing interstitial edema with infiltration of inflammatory cells and tubular damage with tubular edema. Conversely, there is preservation of the glomerular matrix, blood vessels, and mesangial cells.
5. Mandeville diagnostic criteria based on presence or absence of 3 components and further categorization as definite, probable, or possible (see Table 1)

Table 1.

Definite diagnostic	Typical (bilateral anterior) uveitis <i>and</i> interstitial nephritis (renal biopsy <i>or</i> TIN clinical criteria)
Probable diagnostic	Atypical uveitis <i>and</i> positive renal biopsy <i>or</i> typical uveitis <i>and</i> incomplete TIN criteria
Possible diagnostic	Atypical uveitis <i>and</i> incomplete TIN clinical criteria

1. Abnormal serum renal function
Increased serum creatinine or decreased creatinine clearance.
2. Abnormal urinalysis
Increased urinary β 2-microglobulin, low-grade proteinuria, presence of urinary eosinophils, pyuria or haematuria without infection, urinary white cell casts or normoglycaemic glycosuria.
3. Systemic illness lasting ≥ 2 weeks
 - i. *Signs and symptoms:* Fever, weight loss, anorexia, malaise, fatigue, rash, abdominal or flank pain, arthralgia or myalgia.
 - ii. *Laboratory findings:* Anaemia, eosinophilia, abnormal liver function or erythrocyte sedimentation rate >40 mm/hour.

Figure 1

1. Abnormal serum renal function: increased serum creatinine or decreased creatinine clearance
 2. Abnormal urinalysis: increased urinary β 2-microglobulin, low-grade proteinuria, presence of urinary eosinophils, pyuria, or hematuria without infection, urinary white cell casts or normoglycemic glycosuria
 3. Systemic illness lasting ≥ 2 weeks
 - a. Signs and symptoms: fever, weight loss, anorexia, malaise, fatigue, rash, abdominal or flank pain, arthralgia or myalgia
 - b. Laboratory findings: anemia, eosinophilia, abnormal liver function or ESR >40 mm/hr
- D. Differential diagnosis
1. TINU is a diagnosis of exclusion.
 2. Consider conditions that can cause renal and ocular inflammation, including sarcoidosis, Sjögren syndrome, systemic lupus erythematosus, granulomatosis with polyangiitis, Behçet disease, tuberculosis, and syphilis.

II. Treatment and Prognosis^{3,8,15,16}

- A. Renal disease and uveitis typically have independent courses and severities.
- B. Uveitis becomes chronic with recurrence of inflammation in up to 50% of patients after stopping systemic corticosteroids without immunomodulatory therapy.
- C. Renal disease and outcome are favorable, with response to systemic corticosteroids and recovery of renal function.
- D. Prognosis of uveitis and renal disease is favorable. Ocular complications occur in 20% of patients, including posterior synechiae, disc edema, CME, or chorioretinal scarring.

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Case: Between a Fern and a Flower

Francesco Pichi MD

CASE PRESENTATION

- 32-year-old Arabic woman
- Past medical history: “heaviness” in both legs; history of seizures on levetiracetam (Keppra)
- Started having blurry vision with redness and pain for 2 weeks in both eyes
- Pain in the right eye accompanied by movement
- BCVA: 20/150 OU
- Anterior segment exams showed 3+ anterior chamber cells; fundus examination showed 2+ vitreous haze and macular edema
- Fluorescein angiography with macular petaloid leakage and fern-like leakage in the mid to far periphery of the left eye

Differential Diagnosis

- Infectious: syphilis, tuberculosis
- Noninfectious: pars planitis, multiple sclerosis (MS)–associated intermediate uveitis, sarcoidosis, systemic lupus erythematosus (SLE) with vasculitis

Workup

- CBC, ESR, CRP, syphilis IgG, QuantiFERON-TB Gold, ACE, lysozyme
- MRI brain and spine with/without contrast: multiple periventricular and deep white matter and 1 cerebellar lesions with typical MS features, 1-2 tiny enhancing lesions evidence of an enhancing lesion at the level of C5
- Refused spinal tap
- Rheumatologic evaluation with no evidence of systemic autoimmune disease
- Neurological evaluation: relapsing remitting multiple sclerosis

DIAGNOSIS & TEACHING POINTS

Diagnosis

Intermediate uveitis secondary to MS

Clinical Course and Outcome

- IV methylprednisolone followed by 1 mg/kg oral prednisolone
- Started on interferon beta-1a (Avonex) but self-discontinued it

- Underwent multiple bridge treatment with intravitreal injection of dexamethasone implant (Ozurdex) in the left eye
- Follow-up ocular examinations revealed a progressive decrease of the anterior segment inflammation, resolution of the intraretinal fluid, and persisting mild vitritis in the left eye
- Follow-up MRI brain showed small multiple new enhancing and nonenhancing lesions (a new enhancing lesion in the right frontal lobe, a new nonenhancing lesion in the right inferior frontal lobe, a new punctate lesion in the right supramarginal gyrus, and a punctate enhancing focus in the right centrum semiovale); MRI t-spine showed a nonenhancing T2 hyperintense lesion and a larger lesion at T7-T8.
- Due to her poor compliance with treatment and her desire to become pregnant, patient was started on cladribine (Mavenclad) and all steroids were stopped.
- At last follow-up BCVA was 20/30 in both eyes, with retina vessels cuffing in both eyes, and trace vitritis and mild focal vasculitis on fluorescein angiography.

Disease Discussion

Intermediate uveitis secondary to MS

I. Clinical Manifestation

- A. MS is a clinical diagnosis.
- B. The typical patient is a young adult (age between 15 and 50) with 2 or more distinct episodes of CNS dysfunction with at least partial resolution (relapses and remission).
- C. Intermediate uveitis is the most frequent form of MS-associated uveitis.
 1. It can be accompanied by retina vasculitis that seems to affect exclusively veins (periphlebitis).
 2. In the chronic form, sheathing appears as dense, white linear stripes following the course of venous trees.
 3. Another sign of intermediate uveitis accompanying MS is snowbank and secondary changes such as cystoid macular edema and (more rarely) occlusive vasculitis with proliferation.

II. Etiology and Pathogenesis

- A. Optic neuritis is the most common ocular manifestation of MS.
- B. The higher frequency of intermediate uveitis in patients with MS is thought to be based on immunogenic predisposition (HLA-DR15).

III. Diagnosis

- A. MRI of the brain and spinal cord is the test of choice.
 - 1. Discrete region of demyelination in the periventricular white matter region
 - 2. Need to be differentiated from CNS lesions due to ischemia, SLE, Behçet, sarcoidosis
- B. CSF analysis for oligoclonal bands is the confirmatory study.
- C. Fluorescein angiography of active retinal vasculitis demonstrates delayed uptake and leakage from affected vessels, even in areas without clinically detectable vessel changes. Venous sclerosis may show either late staining or normal appearance on angiography.

IV. Differential Diagnosis

All CNS inflammatory and infectious diseases such as SLE, Behçet disease, syphilis, neuro-borreliosis, Vogt-Koyanagi-Harada syndrome

V. Medical Management

- A. Close collaboration between ophthalmologist and neurologist is paramount.
- B. Whether intermediate uveitis should be considered as a new event of MS or as an association is debatable.
- C. Treatment of MS should be early and aggressive.
 - 1. Agents to decrease the frequency of relapses are interferon beta drugs (Avonex, Rebif, Betaseron), glatiramer acetate (Copaxone), natalizumab (Tysabri), mitoxantrone, and fingolimod (Gilenya).
 - 2. Anti-CD20 agents (ocrelizumab and ofatumumab) are gaining popularity in reducing the number and severity of relapses.
 - 3. In the presence of anterior chamber cells, topical steroids are useful.
 - 4. In asymmetric diseases and/or complicating macular edema, depot injections are used.
 - 5. Alternatively, systemic corticosteroids can be given.
 - 6. There is increasing evidence that interferon is very effective in the treatment of uveitis associated with MS, especially the accompanying macular edema.
- D. Prognosis
 - 1. The prognosis of uveitis associated with MS is generally good.
 - 2. Visual outcome in MS patients is heavily influenced by the occurrence of optic neuritis, which may lead to irreversible visual loss.

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Case: Just the Tip of the Iceberg . . .

Lisa J Faia MD

CASE PRESENTATION

History of Present Illness

- Ten-year-old Hispanic female presented with a significant decrease in vision OD for 1 month and blurred vision OS. She denied any trauma to her eyes.
- Past medical history: GA 40 weeks, uncomplicated pregnancy
- Ocular history: None
- Medications: None
- Review of systems: Negative
- Visual acuity
 - OD: HM
 - OS: 20/25
- IOP
 - OD: 20 mmHg
 - OS: 20 mmHg
- Slit-lamp examination: trace posterior subcapsular cataract (PSC) OD
- Posterior examination
 - Vitreous
 - OD: 3+ cell/3+ haze, vitreous hemorrhage, no view of the posterior pole; B-scan: no retinal detachment
 - OS: 1+ cell/1+ haze, snowballs, mild vitreous hemorrhage, snowbanking
 - OCT
 - OD: no view
 - OS: no edema
 - Fluorescein angiography
 - OD: no view
 - OS: leakage of optic nerve and venules

Differential Diagnosis

- Pars planitis
- Trauma
- Familial exudative vitreoretinopathy
- Retinoblastoma
- Juvenile x-linked retinoschisis
- Juvenile sarcoidosis
- Toxoplasmosis
- Lyme
- Syphilis
- Tuberculosis
- Regressed ROP

Workup

- Negative: RF, QuantiFERON-TB, Lyme, HLA-B27, antiphospholipid antibody, hepatitis panel, Toxoplasma IgM/IgG, ANA, HIV, RPR, and lysozyme; ACE slightly elevated
- Originally sent in by pediatric ophthalmologist to rule out retinal detachment and for pars plana vitrectomy (PPV) OD for vitreous hemorrhage to avoid possible amblyopia

DIAGNOSIS & TEACHING POINTS

Final Diagnosis

Pars planitis

Clinical Course and Outcome

- Previously started on topical steroids with little help
- Added oral steroids and discussed immunosuppression
- Elevated IOP on subsequent examination
 - OD: 40 mmHg
 - OS: 25 mmHg
- Started on Cosopt b.i.d. OU and prednisolone drops reduced
- Patient was started on methotrexate.
- Two months after presentation and after being on methotrexate for 1 month
 - OD: HM
 - OS: 20/20
- Patient underwent:
 - OD: 23-gauge PPV/EL/cryotherapy/subtenon triamcinolone 20 mg
 - OS: Cryotherapy for NV/subtenon triamcinolone 20 mg
- Five months after surgical intervention
 - OD: 20/80
 - OS: 20/20
- One year after surgical intervention – patient had CE OD; VA OD ultimately improved to 20/20.
- Three years after retinal intervention
 - OD: 20/20
 - OS: 20/30 with mild PSC
 - Able to reduce dose of methotrexate from 25 mg/week to 17.5 mg/week without flare

Disease Discussion

Pars Planitis

I. Introduction

Subset of idiopathic intermediate uveitis where there is snowbank or snowball formation in the absence of infectious or systemic disease

II. Epidemiology

- A. Predominantly affects children and adolescents; accounts for 5%-30% of uveitis cases
- B. Majority are bilateral, though may be asymmetric.
- C. More severe forms with earlier onset of the disease

III. Clinical Features

A. Symptoms

- 1. Usually minimal without pain or photophobia
- 2. Floaters
- 3. Blurred VA

B. Signs

- 1. Possible mild AC reaction
- 2. Hallmark large gray-white or yellow exudative aggregates, called snowballs, are present in the vitreous cavity.
- 3. Hallmark white collagen bands at the pars plana, called snowbanks, are seen chronically in some patients, even during periods of quiescence.

IV. Ancillary Testing

- A. Comprehensive slit lamp and dilated examination with scleral depression to look for snowbanking
- B. Fluorescein angiography (FA) to assess cystoid macular edema (CME) and leakage
- C. OCT to assess for CME

V. Laboratory Testing

- A. Rule out infectious causes: Lyme disease, toxocariasis, Whipple disease, tuberculosis, syphilis, human T cell leukemia virus type 1, Epstein-Barr virus, and cat scratch disease
- B. Rule out systemic causes: sarcoidosis, Behçet disease, MS, retinoblastoma, familial juvenile systemic granulomatous, or intraocular leukemia/lymphoma

VI. Management

A. Medical

- 1. Local steroids: topical, periocular, intraocular
- 2. Oral steroid: to be limited in the pediatric population

3. Systemic immunomodulation

- a. Conventional: methotrexate, mycophenolate mofetil, azathioprine, and cyclosporine
- b. Biologic: infliximab and adalimumab

B. Surgical

- 1. PPV is typically used to treat the complications of pars planitis.
- 2. Also shown to be effective in patients with active inflammation and CME refractory to medical treatment

VII. Complications

- A. May be from the disease itself or treatment
- B. Cataract, band keratopathy, CME, epiretinal membrane, retinal neovascularization, vitreous hemorrhage, visually obscuring vitreous opacities, retinoschisis, and retinal detachments
- C. The longer the disease remains uncontrolled, the more likely it is for the above complications to occur.

VIII. Prognosis

- A. Generally good
- B. Worse prognosis is associated with earlier age of onset, severity of inflammation, duration of inflammation, and male gender.
- C. Fifty-nine percent with prolonged course with exacerbations and 31% with chronic smoldering course
- D. VA loss is associated with CME, retinal detachment, cataract, and band keratopathy.

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Case: A Late Bloomer

Paulina Liberman MD

CASE PRESENTATION

- History of present illness: 66-year-old Hispanic woman presents with floaters of 2 months duration.
- Past medical history: Primary biliary cholangitis leading to cirrhosis. Admitted 3 months prior to presentation for 5 days for ascites management and prophylactic endoscopic variceal band ligation.
- Ocular history: None
- Medications: rifaximin, midodrine, spironolactone, propranolol, ursodeoxycholic acid, lactulose
- Review of systems: mood changes, occasional episodes of disorientation, and inappropriate behavior
- Social history: Nurse. No intravenous drug use (IVDU).
- Visual acuity
 - OD: 20/40
 - OS: 20/25
- No afferent pupillary defect
- Slit-lamp exam: trace anterior chamber cell OD; no cell OS
- Fundus exam
 - OD: 1+ vitreous haze, with white spherical aggregates in the inferior vitreous and a white lesion in the retina at 7 o'clock
 - OS: trace cell in the vitreous and no chorioretinal lesions

Differential Diagnosis

- Infectious: fungal endophthalmitis (high suspicion for *Candida spp*), syphilis, tuberculosis
- Noninfectious: primary vitreoretinal lymphoma, sarcoidosis
- Workup
 - CBC, FTA ABS, VDRL, HIV, Hep C, QuantiFERON-TB Gold: All negative
 - Chest x-ray and MRI of brain with/without contrast: Normal
 - Pars plana vitrectomy (PPV) and vitreous biopsy and culture: Culture was positive for *Candida albicans*.
 - Systemic workup for candidemia blood cultures, beta-d glucan assay, echocardiography, and abdominal ultrasound: All negative

DIAGNOSIS & TEACHING POINTS

Diagnosis

Candida albicans endogenous endophthalmitis

Clinical Course and Outcome

- Treated with PPV and voriconazole injection (100 µg/0.1 mL)
- Vitreous haze resolved and has remained clear at 1 year follow-up. BCVA is 20/20 OD and 20/25 OS.

Disease Discussion

I. Endogenous Fungal Endophthalmitis (EFE)

A. Epidemiology

1. *Candida* is the most common cause of endogenous fungal endophthalmitis. *Candida albicans* is the predominant species of EFE.
2. In patients with candidemia screened for *Candida*, EFE incidence is ~2.3%.¹

B. Clinical features

1. Symptoms: floaters, blurred vision
2. Clinical exam findings^{2,3}
 - a. Nonspecific: vitreous cell and haze, intraretinal hemorrhages, Roth spots, cotton wool spots
 - b. Typical findings associated with *Candida* EFE: multiple creamy-white or fluffy, well circumscribed retinal lesions, early lesions: “puff ball” abscesses. Vitreous: “string of pearls.”
3. Classic risk factors for endogenous fungal endophthalmitis⁴
 - a. Prolonged hospital stay
 - b. Indwelling intravenous catheters (OR 8.35)⁴
 - c. Prolonged or broad-spectrum antibiotic use
 - d. Neutropenia
 - e. IVDU (OR 4.76)⁴

- f. Other: sepsis, malignancy, hepatitis B, hepatitis C, pneumonia, UTI, prolonged corticosteroid use
- g. Some of these (eg, neutropenia) have not been found to be risk factors in subsequent systematic reviews.¹

C. Imaging modalities

1. Ultrawide-field fundus photography
2. OCT
 - a. “Raincloud” sign: hyper-reflective preretinal aggregates causing a shadowing effect, sign of vitreous involvement. Also, 2 patterns are described: intraretinal pattern and chorioretinal pattern.⁶
 - b. Another classification: subretinal macular, inner retinal, full-thickness retina with macular edema, and sub-internal limiting membrane types, according to invasion depth⁷
3. Ultrasound: When poor view to fundus. Helpful to evaluate endophthalmitic lesions.

D. Diagnostic testing

1. Infectious workup for differential diagnosis: syphilis serologies, QuantiFERON-TB Gold, chest x-ray
2. Noninfectious testing for differential diagnosis: MRI of brain
3. If patient has positive blood cultures and classic eye findings, there is no need for intravitreal culture.
4. Use of vitreous β -D glucan (cell wall constituent of *Candida* and several other fungi) and vitreous polymerase chain reaction testing: Lack of standardized methodology but promising

E. Screening for endogenous endophthalmitis

1. In the setting of candidemia, routine screening in the absence of symptoms is a low-value practice (AAO Statement 2021).⁷
2. Infectious Diseases Society of America Clinical Practice Guideline for the Management of Candidiasis (2016) promotes routine screening of patients with *Candida* septicemia.⁸

II. Medical Management

A. Antifungals

1. Systemic: Azole class (voriconazole), or non-azoles (amphotericin B). Azole resistance is a problem in systemic candidemia. Most eyes respond well to systemic therapy only, but local therapy should be considered if significant vitreous involvement.^{8,9}
2. Local (intravitreal): voriconazole (100 μ g/0.1 mL) or amphotericin B (5-10 μ g/0.1 mL)

III. Surgical Management

Pars plana vitrectomy has a triple role: diagnostic, treatment of infection, and management of complications secondary to infection.

IV. Prognosis

- A. Endogenous fungal endophthalmitis has better visual outcome than exogenous or post-traumatic. In endogenous *Candida* endophthalmitis, BCVA <20/200 in 37%.¹⁰
- B. Risk factors for severe visual loss: central lesion, poor initial visual acuity

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Posterior Uveitis Overview

Lynn M Hassman MD

The Secret Sits

We dance round in a ring and suppose,
But the Secret sits in the middle and knows.
—Robert Frost

Learning Objectives

- Recognize the signs and symptoms of posterior uveitis
- Use multimodal imaging to establish the diagnostic category
- Identify infectious and autoimmune causes
- Determine the treatment options for posterior uveitis

I. Definition of Posterior Uveitis

A. Broad categories

1. Vasculitis
2. Retinitis
3. Chorioretinitis
 - a. Multifocal choroiditis
 - b. Placoid choroidopathies
4. Neuroretinitis

B. Symptoms suggest the diagnosis.

1. Photopsias
2. Scotomas
3. Nyctalopia
4. Floaters

C. Signs dictate further image analysis.

1. Vascular sheathing
2. Hemorrhages
3. Retinal whitening
4. Spots
5. Subretinal fluid

II. The Posterior Uveitis Toolkit for Diagnosing and Managing These Cases

A. A broad differential

1. Infectious
2. Inflammatory
3. Malignant

B. Multimodal imaging/pattern recognition

1. (Diagnosis and disease activity)
2. *OCT

3. *Fundus autofluorescence

4. Fluorescein angiography

5. Indocyanine green angiography

6. Ultrasound

7. (OCT angiography, if ya got it)

C. Questions about systemic disease

1. Key review of systems: brain, lungs, skin, mouth/GI, joints, B-symptoms
2. Personal/family history of autoimmune disease, cancer
3. Exposures: health-care, travel, cats, ticks, drugs

D. Focused testing

1. Labs
2. Imaging

E. Treatments for noninfectious posterior uveitis

1. Local and systemic steroids (not eye drops!)
2. Steroid-sparing immune suppression

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Case: To Inject or Not to Inject, That Is the Question: Wet vs. Inflamed Eye

Joon-Bom Kim MD

CASE PRESENTATION

- 32-year-old African-American man with ~10-year history of chronic bilateral panuveitis
- Symptoms
 - Blurred vision with distortion OD, stable poor vision OS
 - Mild stable photosensitivity
 - No pain OU
- Ocular history: Patient had fluocinolone implants (Retisert) in both eyes 6 years ago and subsequent glaucoma and cataract surgeries in both eyes 5 years ago. Three years prior to presentation, patient developed a foveal macular scar of unclear etiology in left eye, resulting in poor central vision.
- Medical history: liver biopsy-proven systemic sarcoidosis
- Medications: prednisone 2.5 mg daily, azathioprine 250 mg daily, infliximab 5 mg/kg every 8 weeks

Ocular Examination

- VA with correction
 - OD: 20/80
 - OS: 20/400 OS
- IOP
 - OD: 15
 - OS: 13
- Anterior segment
 - Pigmented keratic precipitates OU
 - No cell OU
 - Posterior chamber IOL OU
- Posterior segment
 - Rare vitreous cells OU
 - No vitreous haze OU
- Fundus examination
 - OD: hypopigmented lesion without hemorrhage in fovea, multiple pigmented chorioretinal scars in periphery
 - OS: large macular scar without hemorrhage

OCT

- OD: subfoveal subretinal hyporeflective lesion without intraretinal or subretinal fluid
- OS: large subretinal scar

Fluorescein Angiography

- OD: hyperfluorescence of foveal lesion
- OS: staining of macular scar

OCT Angiography

- OD: large choroidal neovascular membrane (CNVM) network in the fovea

Differential Diagnosis

- Inflammatory sarcoid granuloma
- Infectious choroidal granuloma
- Idiopathic CNVM
- Myopic CNVM

Workup

- Treponemal antibody: nonreactive
- QuantiFERON-TB Gold: negative
- Complete blood count with differential: within normal limits

DIAGNOSIS & TEACHING POINTS

This was a case of foveal granuloma in a patient with systemic sarcoidosis with ocular involvement complicated by CNVM. OCT showed an elevated subfoveal hyporeflective lesion, and fluorescein angiography demonstrated hyperfluorescence in the fovea, which could be seen in both due to staining of inflammatory choroiditis lesion or leakage of choroidal neovascular membrane. OCT angiography offered helpful guidance for the appropriate treatment. This patient was treated with the combination of oral steroids, escalation of immunomodulating therapy, and anti-VEGF injection.

Discussion

I. Introduction

- A. Sarcoidosis is a multiorgan inflammatory disease of unknown cause with pathological hallmark of noncaseating granuloma and is a commonly encountered cause of uveitis.
- B. Ocular sarcoidosis has various manifestations, and posterior segment findings include vitritis, choroiditis, retinal vasculitis, and optic nerve/choroidal granuloma.

II. Epidemiology

- A. Incidence and prevalence of sarcoidosis vary markedly with geographic location.
- B. Annual incidence ranges from 3 to 80 per 100,000 person years in the United States. The disease is more common in African-Americans in the U.S. and in northern Europe.

III. Clinical Symptoms and Signs

- A. Patients typically present with pain or redness if anterior segment inflammation is present but can also present with painless floaters or loss of vision if only posterior segment inflammation is present.
- B. Anterior chamber cells, keratic precipitates, vitritis, vascular sheathing, and choroidal granuloma may be seen.

IV. Differential Diagnosis

- A. Ocular tuberculosis
- B. Syphilis
- C. Noninfectious multifocal choroiditis with panuveitis

V. Diagnosis

- A. Histopathology of tissue demonstrating noncaseating granuloma
- B. Clinical history and ocular examination
- C. Multimodal retinal imaging to monitor posterior segment inflammation

VI. Management

- A. Local or systemic corticosteroids for acute inflammation of the disease
- B. Anti-VEGF for CNVM associated with choroiditis and chorioretinal scars
- C. Systemic immunosuppressive therapy in patients with recurrent or chronic disease

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Case: A Case of White Dots: “Why is that P silent?”

Jessica E Weinstein MD

CASE PRESENTATION

- 32-year-old woman presents with blind spot in her right eye for 1 month
- Review of symptoms: positive for headaches, otherwise negative

Past Medical History

First-time episode of psychosis 3 months prior where she was hospitalized and diagnosed with bipolar type 1; on mood stabilizer/anti-psychotic now. No prior history of mental illness.

Social History

Sexually active with husband, no illicit drug use, no pets, no recent travel, no history of international travel, born in the United States.

Ocular Exam

- VA
 - OD: 20/50
 - OS: 20/30
- IOP
 - OD: 15 mmHg
 - OS: 18 mmHg
- PERRL with no afferent pupillary defect
- Anterior segment exam without keratic precipitates, anterior chamber cell, or flare
- Fundus exam
 - OD: clear media, 1+ disc edema and hyperemia, multiple creamy colored placoid lesions in the posterior pole and near periphery, vessels normal course and caliber
 - OS: with clear media, 0.25 cup-to-disc ratio with nasal peripapillary lesion with mixed pigmentation and focal subretinal fibrosis, macula flat, vessels normal course and caliber

Diagnostic Testing

- OCT
 - OD: with multiple areas of retinal pigment epithelium (RPE) and ellipsoid zone loss and trace subretinal fluid involving the fovea
 - OS: peripapillary area of RPE thickening and ellipsoid zone loss, but not involving the fovea
- Fundus autofluorescence (FAF)
 - OD: creamy placoid lesions on fundus exam corresponded with areas of hyper-autofluorescence (AF) or mixed hyper- and hypo-AF

- OS: peripapillary temporal lesion with mixed hyper- and hypo-AF centrally while the border was primarily hypo-AF
- Fluorescein angiogram
 - OD: all the lesions in the posterior pole and periphery blocked early and stained late, late staining of the disc, no vascular staining of leakage
 - OS: peripapillary lesion with center blocking early and staining late, borders just staining throughout the study, no late staining of the disc, no vascular staining or leakage
 - The staining of the borders through the study imply that part of the lesion OS is older or inactive.
- Indocyanine green angiography
 - OD: early and late phase images with multiple hypocyanescent plaques corresponding to lesions seen on clinical exam. No additional lesions noted.
 - OS: hypocyanescent peripapillary lesion that became less hypocyanescent as the study progressed

Workup

- Syphilis antibody testing, negative; RPR, negative
- QuantiFERON Gold, negative
- ACE/lysozyme, negative
- Chest x-ray, normal
- Brain MRI with no evidence of cerebral vasculitis. Incidental Chiari I malformation

DIAGNOSIS & TEACHING POINTS

Final Diagnosis, Clinical Course, and Outcome

An initial diagnosis of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) was made, and the patient was started on 60 mg daily of prednisone (1 mg/kg) and then tapered by 10 mg each week. Most lesions resolved OD with some minor residual scarring in the macula, notable on exam, FAF and OCT. The peripapillary lesion OS had improved outer retinal findings on OCT. VA improved to 20/20 OD and 20/25 OS. Lesions did not recur or progress after completion of oral prednisone taper. Given these findings and no recurrent disease, APMPPE was considered to be the final diagnosis, rather than serpinginous or ampiginous/relentless placoid.

Discussion of Disease

APMPPE is a transient autoimmune condition causing multifocal ischemic lesions at the level of the choriocapillaris, leading to outer retinal and RPE changes. Visual outcomes can vary depending on the location of the lesions and their proximity to the fovea. Main exam features are multiple creamy yellow-white plaques at the level of the choriocapillaris, RPE, and outer retina. Distribution is limited to the posterior pole and near periphery. Extension beyond this should raise suspicion for a case of relentless placoid.

I. Epidemiology

- A. No gender predilection
- B. Typically affects those 30 years or younger

II. Clinical Features

- A. Usually bilateral, but can be unilateral
- B. Classically associated with a viral prodrome, but has also been reported following vaccinations, with new medication administration, or without clear inciting event
- C. VA loss can range mild to profound depending on number, location, and severity of lesions.
- D. Anterior chamber may have no or very low grade inflammation.
- E. Vitreous inflammation is typically mild.
- F. Neurologic symptoms including headache, if present, are concerning for associated CNS vasculitis and should prompt additional evaluation with MRI/MRA.

III. Differential Diagnosis

- A. APMPPE
- B. Serpiginous
- C. Relentless placoid/ampiginous
- D. Tuberculosis-associated serpiginoid posterior uveitis
- E. Syphilitic posterior placoid
- F. Sarcoid
- G. Multifocal choroiditis

IV. Diagnosis

- A. Fluorescein angiography findings of “block early, stain late” for placoid lesions. FAF demonstrates hyper-AF of active lesions. Hypo-AF implies an older lesion or inactivity/scarring.
- B. OCT of acute placoid lesions shows disruption of outer retina and ellipsoid zone with hyperreflective material at the level of the RPE. There may also be subretinal fluid.

- C. OCT angiography will show areas of choriocapillaris flow voids that are larger than the outer retinal changes seen on OCT. This highlights that APMPPE is primarily a disease of the choriocapillaris.
- D. Laboratory testing should include QuantiFERON Gold and syphilis antibody testing.
- E. MRI should be performed in any patient with headache or manifestations of CNS vasculitis.

V. Etiology and Pathogenesis

- A. Unknown cause
- B. Patients are usually healthy with no other systemic disorder.
- C. Associated with inciting event, multiple cases of APMPPE after vaccination and various infections such as adenovirus, influenza, Coxsackie, etc.
- D. Can be associated with a CNS vasculitis that occurs acutely, though sometimes can manifest 2-3 months later; multiple reports of stroke and CNS findings

VI. Management

- A. Steroids
 - 1. Decision to observe vs. treat with oral prednisone can be based on degree of macular involvement, foveal involvement, or severity of vision loss. In the case of severe disease, oral prednisone can help prevent permanent scarring and vision loss.
 - 2. For those patients with CNS vasculitis, admission for methylprednisolone (ie, starting with 1 g daily for 3 days) is needed and should be comanaged with neurology and possibly rheumatology.
- B. Complications
 - 1. Subretinal scarring
 - 2. Choroidal neovascular membrane
 - 3. CNS vasculitis

VII. Prognosis

- A. Patients generally improve over weeks to months.
- B. If lesions involve fovea, visual recovery is varied.
- C. In the case of chronic or recurrent disease, consider another diagnosis such as relentless placoid/ampiginous, serpiginous, or posterior placoid choroiditis.

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Case: A Case of Recurrent Retinal Vessel Aneurysms

Ninani C Kombo MD

CASE PRESENTATION

A 21-year-old female presented to our uveitis service for new vision loss in her right eye. Central vision loss began 2 months earlier. She described a few flashes in the center of her vision, but no pain, redness, or floaters. She had a prior history of an incidentally discovered central scotoma identified at a contact lens fitting 5 years prior. At that time, she was not treated with immune suppression. She was otherwise healthy, no past medical history. Endorsed a short viral illness 6-7 months prior to the contact lens visit. She had never lived outside the USA and had not traveled outside the state, and her roommate had a cat.

Ocular Examination

- VA
 - OD: 20/30
 - OS: CF @ 1 ft
- IOP
 - OD: 12 mmHg
 - OS: 13 mmHg
- Pupils: round, brisk reaction, no relative afferent pupillary defect, anterior segment without abnormalities
- Dilated fundus exam
 - Vitreous clear OU
 - Cup:disc 0.1 swelling 360 OU, peripapillary exudates
 - OD
 - Macula with exudates
 - Vessels: dilation of vessels inferotemporally
 - OS
 - Macula: large scar, exudates
 - Vessels: dilated segments of vessels superiorly and inferiorly
 - Periphery unremarkable OU

Workup: Imaging

- Color fundus photos
 - OD: disc edema with exudates inferior to the disc, inferior arcade aneurysms
 - OS: disc edema with exudates surrounding disc and macula, aneurysms
- OCT macula
 - OD: normal contour
 - OS: exudates, loss of foveal contour, intraretinal fluid
- Fluorescein angiography
 - OD: aneurysms along inferotemporal arcade
 - OS: transmission defect centrally corresponding to exudate and circumferential early hyperfluorescence and leakage surrounding the exudate and among retinal vessels

Workup: Laboratory

- Negative/normal: Lyme, FTA-ABS with reflex RPR, Bartonella, toxoplasmosis IgG/IgM, ANA, ESR, CRP, QuantiFERON, ACE, HLAB27, antiphospholipid antibodies
- c-ANCA screen positive, repeat negative
- Chest x-ray and CT sinuses without any abnormalities

DIAGNOSIS & TEACHING POINTS

Clinical Course, Treatment, and Outcome

At the initial presentation to an ophthalmologist, patient was observed. Six months later she presented with a decrease in vision in the right eye. She was treated with 60 mg of prednisone with a slow taper over 2 months and then observed for 3 years. She then presented with a decrease in vision in her right eye. Bevacizumab was injected and 40 mg of prednisone was initiated and tapered over 6 months. Two years later, she developed a decrease in vision in the right eye. Intravitreal dexamethasone implant was injected into the right eye, 60 mg of prednisone was initiated, and infliximab infusions were started for maintenance. Vision was 20/20 in the right eye and 20/400 in the left eye at follow-up in May of 2022.

Discussion

I. Introduction

In 1983, Kincaid and Schatz described 2 patients with bilateral retinal vasculitis, retinitis, and neuroretinitis. In 1995, Chang et al described the largest series to date of patients who met criteria for new retinal syndrome and proposed the term “idiopathic retinitis, vasculitis, aneurysms, and neuroretinitis (IRVAN).”

II. Epidemiology

IRVAN usually affects young (30-40 years of age) healthy individuals and has a slight female predominance. There are case reports suggesting associations with p-ANCA, antiphospholipid syndrome, and fungal sinusitis.

III. Clinical Symptoms and Signs

There are no systemic abnormalities, systemic workup is usually negative, and presentation is variable, ranging from asymptomatic to decreased vision in 1 or both eyes.

IV. Differential Diagnosis

This includes vascular, infectious, and autoimmune entities that cause retinal vasculitis, vascular occlusion, and exudation: Acquired retinal macroaneurysms, branch retinal vein occlusion, sickle cell retinopathy, TB, syphilis, *Bartonella*, sarcoidosis, polyarteritis nodosa, and granulomatosis with polyangiitis. Case reports suggest a possible association with p-ANCA and antiphospholipid syndrome.

V. Imaging: Multimodal

Fundus photography can show hemorrhages, exudates, and aneurysmal dilations. Fundus autofluorescence can highlight hemorrhages and aneurysmal dilations. OCT angiography can demonstrate macular aneurysms and high blood flow signals well. Fluorescein angiography can demonstrate optic nerve leakage, vessel leakage, aneurysms, and areas of hypoperfusion. Macula OCT can be used to look for scarring, choroidal neovascularization, and intraretinal or subretinal fluid.

VI. Diagnosis

A. Major criteria

1. Retinal vasculitis
2. Aneurysmal dilation at arterial bifurcations
3. Neuroretinitis

B. Minor criteria:

1. Peripheral capillary nonperfusion
2. Retinal neovascularization
3. Macular exudation

VII. Management

- A. There is no consensus on treatment.
- B. Observation is proposed for mild cases.
- C. Often, a combination of treatments is employed.
 1. Pan retinal photocoagulation
 2. Cryotherapy
 3. Anti-VEGF
 4. Intravitreal steroids
 5. Immunosuppression
 - a. Oral steroids
 - b. Systemic immunomodulators
 6. Vitrectomy when indicated

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Case 4: Immunosuppressed Patient

Jessica G Shantha MD

CASE PRESENTATION

- 54-year-old female
- Symptoms: increased floaters in the right eye with a shade in the superior field of vision
- Ocular history: negative
- Medical history: COPD, type 2 diabetes, rheumatoid arthritis
- Current medications: adalimumab 40 mg every 2 weeks, prednisone 5 mg daily, leflunomide 20 mg daily, ASA 81 mg daily

Ocular Examination

- VA
 - OD: 20/20-1
 - OS: 20/20
- IOP (with Tono-Pen)
 - OD: 17
 - OS: 20
- 1+ anterior vitreous cell OD without haze, no vitreous cell OS
- Tortuous sclerotic arterioles along the inferotemporal arcade with areas of retinal whitening temporally OD, normal posterior segment exam OS
- OCT
 - OD: vitreous cell
 - OS: normal
- Fluorescein angiography
 - OD: leakage within area of retinitis
 - OS: normal

DIAGNOSIS & TEACHING POINTS

Unilateral Retinitis With Retinal Vasculitis (Arterioles)

- Infectious
 - Viral associated: herpetic
 - Herpes simplex virus (HSV)
 - Varicella zoster virus (VZV)
 - Cytomegalovirus (CMV)
 - Toxoplasmosis
 - Syphilitic uveitis
 - Tuberculosis
- Systemic inflammatory disease
 - Systemic lupus erythematosus
 - Sarcoidosis
 - Behçet disease
- Undifferentiated

Workup

Anterior chamber paracentesis was sent for HSV/VZV/CMV/toxoplasmosis, and polymerase chain reaction (PCR) was performed. Additional laboratory testing was sent: syphilis antibody, QuantiFERON-TB Gold, and HIV testing. The anterior chamber paracentesis was positive for CMV and negative for HSV, VZV, and toxoplasmosis. Syphilis antibody, QuantiFERON Gold, and HIV testing were negative.

Final Diagnosis, Clinical Course, and Outcome

This was a case of CMV retinitis in an immunosuppressed patient. The mechanism of immunosuppression was systemic therapy with adalimumab and leflunomide. At initial presentation, an anterior chamber paracentesis was performed with an intravitreal injection of foscarnet in the right eye. Adalimumab was held for a few weeks, and she was started on valganciclovir 900 mg 2x/day. Her ocular disease resolved, and she was restarted back on adalimumab.

Teaching Points

- CMV retinitis should be considered in the differential diagnosis in presentations of unilateral and bilateral retinitis and vasculitis.
- CMV is a member of the herpesvirus family and usually causes disease in patients who are immunosuppressed.
 - AIDS
 - Transplant patients (receiving systemic immunosuppression)
 - Systemic immunosuppression for systemic autoimmune conditions
 - Infections can present after a periocular or intraocular corticosteroid injection.
- While clinical suspicion and ocular examination can be enough to make a diagnosis, PCR testing of intraocular fluid can confirm the diagnosis.
- Systemic therapy should be initiated to treat active infection and prevent contralateral eye involvement.

Discussion

I. Epidemiology

- A. Overall, there has been a reduction in CMV retinitis by 80% in Western countries due to antiretroviral therapy (ART) in AIDS patients.
- B. CMV retinitis can be seen in patients with immunosuppression for other reasons, such as systemic immunosuppression (example: adalimumab) as well as transplant patients.
- C. Local immunosuppression of the ocular environment can occur via local corticosteroid injections.

II. Clinical Features

A. Zones of involvement

1. Zone 1: Area within 500 μm of the optic nerve or within 3000 μm of the center of the macula
2. Zone 2: Extends from zone 1 to the clinical equator of the eye
3. Zone 3: Extends from zone 2 to the ora serrata

B. Fulminant: white fluffy lesions near retinal vessels with hemorrhage

C. Indolent: peripheral granular opacities with occasional hemorrhage

D. Frosted branch angiitis: retinal vascular sheathing

E. Complications

1. Immune recovery uveitis
2. Rhegmatogenous retinal detachment

III. Pathology

A. Full-thickness retinal necrosis

IV. Diagnosis

A. Clinical diagnosis is made by suggestive clinical exam features.

B. Definitive diagnosis can be made by anterior chamber or vitreous tap for PCR testing for CMV.

V. Management

A. Systemic antivirals are the first-line treatment for CMV retinitis.

1. Systemic therapy decreases overall morbidity in patients who have other systemic manifestations of a CMV infection.
2. Systemic therapy prevents contralateral eye involvement.
3. Treatment of choice is either intravenous ganciclovir or oral valganciclovir. (Oral therapy has been shown to have same efficacy as intravenous therapy.)
4. Other systemic options include foscarnet and cidofovir. These intravenous medications are limited due to side effects.
5. Newer antivirals such as letermovir or maribavir may be used in unique situations, but evidence is limited for the treatment of CMV retinitis.

B. Intravitreal therapy

1. Ganciclovir and foscarnet can be given intravitreally.
2. Advantages of local therapy:
 - a. Direct treatment to the infection site
 - b. Good option for patients unable to tolerate the side effects of systemic therapy
3. A combination approach can be used with both systemic and local treatment.

C. ART: ART should be initiated in patients with AIDS to promote immune system recovery.

D. Prophylaxis

1. Valganciclovir and letermovir have been used for CMV prophylaxis and are indicated in patients with AIDS whose immune system has not adequately recovered.
2. CMV drug resistance can develop, with risk factors including ongoing CMV replication, duration of exposure to antiviral medications, and host immunosuppression/immune system dysregulation. Mutations occur in genes UL97 and UL54, which encode a viral kinase and DNA polymerase, respectively.

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Panuveitis Overview

Now the Future We Foresee

Emilio M Dodds MD

I. Definition

The Standardization of Uveitis Nomenclature (SUN) Working Group categorizes uveitis anatomically according to the primary site in which inflammation is detected clinically. Panuveitis is inflammation of the anterior chamber, vitreous humor, and retina/choroid, all involved without predominance in any one site.

II. Types of Panuveitis

A. Classic panuveitis

1. Infectious origin: TB and syphilis
2. Systemic disease associated: Behçet disease, sarcoidosis, and Vogt-Koyanagi-Harada (VKH)
3. Eye limited: sympathetic ophthalmia

B. Other panuveitis: idiopathic, drug induced, masquerades

III. Diagnosis

A. TB

Diagnosis is difficult since interferon-gamma release assays (IGRAs), PPD skin test, chest x-ray or chest CT, and polymerase chain reaction have exhibited variable performance in TB detection. Often, a presumptive diagnosis of ocular TB is made empirically based on corroborating ophthalmological features, exclusion of differential diagnoses, and physician expertise in local epidemiology.

B. Syphilis

Treponemal tests are qualitative assays performed on serum to detect antibodies against a variety of *T. pallidum* antigens (reactive or nonreactive). Nontreponemal tests are performed on serially diluted serum to detect total antibodies directed against antigens that are released from damaged host cells and the bacteria (reported in titers). The reverse algorithm nowadays uses a treponemal assay first, followed by a nontreponemal assay for reactive samples.

C. Behçet disease

Clinical diagnosis: Diagnostic System for Behçet Disease (International Study Group for Behçet Disease): Recurrent oral aphthous ulcers (at least 3 or more times per year) plus 2 of the following criteria:

1. Recurrent genital ulcers
2. Ocular inflammation
3. Skin lesions
4. Positive cutaneous pathergy test

D. Sarcoidosis

1. Intraocular clinical signs suggestive of ocular sarcoidosis
 - a. Mutton-fat keratic precipitates and iris nodules
 - b. Trabecular meshwork nodules and/or tent-shaped peripheral anterior synechia
 - c. Snowballs/string of pearls vitreous opacities
 - d. Multiple chorioretinal peripheral lesions
 - e. Nodular and/or segmental periphlebitis (\pm candle wax drippings) and/or macroaneurysm in an inflamed eye
 - f. Optic disc nodule(s)/granuloma(s) and/or solitary choroidal nodule
 - g. Bilaterality
2. Systemic investigation results in suspected ocular sarcoidosis
 - a. Bilateral hilar lymphadenopathy by chest x-ray and/or CT scan
 - b. Negative PPD or IGRAs
 - c. Elevated serum ACE/lysozyme
 - d. Elevated CD4/CD8 ratio (>3.5) in bronchoalveolar lavage fluid
 - e. Abnormal accumulation of gallium-67 scintigraphy or PET imaging
 - f. Lymphopenia
 - g. Parenchymal lung changes consistent with sarcoidosis, as determined by pulmonologists or radiologists

E. VKH

1. Early-stage criteria (Diagnosis requires a. or b. *and* c.)
 - a. Evidence of Harada disease: serous detachment and multiloculated appearance on fluorescein angiography or septae on OCT
 - b. Panuveitis with ≥ 2 of the following neurologic symptoms or signs:
 - i. headache *or*
 - ii. tinnitus *or*
 - iii. dysacusis *or*
 - iv. meningismus *or*
 - v. cerebrospinal fluid pleocytosis
 - c. No history of penetrating ocular trauma or vitreoretinal surgery
 - d. Exclusions
 - i. positive serology for syphilis using a treponemal test
 - ii. evidence for sarcoidosis (either bilateral hilar adenopathy on chest imaging or tissue biopsy demonstrating noncaseating granulomata)
2. Late-stage criteria
 - a. History of early-stage VKH disease *and* (b. *and/or* c.)
 - b. Sunset glow fundus *or*
 - c. Uveitis *and* ≥ 1 of the following cutaneous findings
 - i. vitiligo
 - ii. poliosis
 - iii. alopecia
 - d. Exclusions: Same

F. Sympathetic ophthalmia:

Clinical diagnosis of a panuveitis that develops from 5 days to 66 years after penetrating ocular trauma or intraocular surgery. Posterior findings typically show vitritis, papillitis, multifocal chorioiditis, Dalen-Fuchs nodules, multiple exudative retinal detachments, and macular edema.

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Case: Syphilis or Atypical Toxoplasmosis

Sumit Sharma MD

I. Overview

- A. Syphilis can manifest in a variety of forms in the eye, from anterior uveitis to, more commonly, posterior uveitis.
- B. It is often called the “great imitator,” as it can present in a variety of forms mimicking other diseases
- C. Testing should be done in most patients with uveitis to rule out syphilis, as it is one of the few “curable” forms of uveitis, often with rapid improvements in vision.

II. Epidemiology

- A. Syphilis rates reached their lowest levels ever in 2000; however, they have steadily increased in the United States since that time.
- B. Rates in men are much higher than rates in women: 16.9 cases per 100,000 males vs. 2.3 cases per 100,000 females in 2017 in the U.S.
- C. Rates are highest amongst men who have sex with men, representing 57.9% of cases.

III. Diagnosis

- A. Diagnosis is based on 1 of 2 types of tests: treponemal and nontreponemal.
- B. Nontreponemal tests (VDRL or RPR) are not specific for syphilis, can produce false positive results, and are insufficient for diagnosis.
- C. Treponemal tests (fluorescent treponemal antibody-absorption [FTA-Abs], *Treponema pallidum* particle agglutination [TP-PA], enzyme immunoassay [EIA], immunoglobulin G [IgG]) detect antibodies specific for syphilis.
- D. Treponemal tests remain positive for life.
- E. The reverse testing algorithm—treponemal test for screening followed by a nontreponemal test for confirmation—is now favored and recommended by the CDC for screening.
- F. Titers of nontreponemal tests can be used to assess treatment response.

IV. Clinical Presentation

- A. Can present as any form of uveitis involving any part of the eye alone or in combination
- B. Many of the forms of presentation will be reviewed.

V. Treatment

- A. Treat as neurosyphilis in coordination with infectious disease specialist
- B. Aqueous penicillin G 18-24 million units daily administered as 3-4 million units IV every 4 hours for 10-14 days. Patients with a penicillin allergy should undergo skin testing and if positive should get desensitization.
- C. Lumbar puncture with testing of CSF for VDRL
- D. All patients with newly diagnosed syphilis should receive an HIV test.
- E. Watch for the Jarisch-Herxheimer reaction and treat with steroids as needed
 - 1. Topical steroids for anterior chamber reaction
 - 2. Oral steroids for all other types
- F. Sex partners should be investigated.
- G. Reporting to local health department is mandatory in the U.S.

Case 2: Impersonating the Great Imitator

Thellea K Leveque MD

CASE PRESENTATION

67-year-old monocular male referred for second opinion of possible syphilis panuveitis in the right eye

History

- History of present illness
 - Subacute onset of right eye floaters, red eye, and decreased vision. Found to have mild keratic precipitates (KP) and anterior chamber (AC) cell, improved with topical prednisolone 1%, but then developed vitritis/vitreous haze and numerous small yellow sub-retinal lesions.
 - Workup positive for syphilis IgG and positive RPR at 1:4. Patient was treated for neurosyphilis + syphilis panuveitis with 14D IV penicillin.
 - Uveitis continued to worsen, and patient was sent to us for additional diagnosis/management.
- Past ocular history
 - Retinal detachment left eye, status post pars plana vitrectomy and attempted retinal repair
 - No light perception vision
- Past medical history
 - History of neurosyphilis, treated 10 years prior with chronic peripheral neuropathy/poor balance
 - Psoriasis
 - Osteoarthritis
 - Cured hepatitis C infection
 - Borderline diabetes
 - History of resected lip cancer
 - Cirrhosis; tobacco and alcohol abuse
- Family and social history
 - Retired millwright
 - Heavy alcohol use, quit 2 days ago
 - Quit smoking a month ago: previous 10-15 pack/year history
 - Denies intravenous drug use
- Current medications: topical prednisolone 1% 4 times daily right eye
- Review of systems: positive for joint pains, poor balance (uses cane), no recent skin rash, all others negative

Ocular Examination

- VA
 - OD: 20/60
 - OS: NLP
- IOP with applanation
 - OD: 18 mmHg
 - OS: 38 mmHg

- Anterior chamber
 - OD: 1+ injection, few medium KPs inferior, 2+ cell/flare, 3+ vitreous haze, multiple yellow choroidal lesions
 - OS: trace injection, cloudy edematous cornea with neovascularization, shallow AC, 360 posterior synechiae, seclused pupil, no view to posterior pole
- Workup
 - + Syphilis IgG + RPR 1:4
 - IGRA mycobacterium tuberculosis (QuantiFERON): negative
 - Chest x-ray: normal
 - CBC: normal
 - CMP liver function test: mild elevation
- Imaging right eye
 - OCT
 - Wide-field pseudocolor fundus photo
 - Fundus autofluorescence
 - Fluorescein angiography
 - Indocyanine green angiography

DIAGNOSIS & TEACHING POINTS

- I. The Serofast Reaction in Neurosyphilis—positive syphilis testing was unrelated to this patient's uveitis.
 - A. Treponemal tests such as syphilis IgG, treponema pallidum particle agglutination (TP-PA), and fluorescent treponemal antibody test absorption test (FTA-ABS) usually remain positive for life even after successful syphilis treatment.
 - B. Nontreponemal rapid plasma reagin (RPR) titers usually decline after successful therapy. A 2- to 4-fold decrease in titers is considered to be a therapeutic response.
 - C. In some successfully treated patients (up to 15% of early treated syphilis and greater in late syphilis), nontreponemal antibodies can persist for the patient's lifetime. Failure to decline is called a serological nonresponse. Initial decline and persistent low-level titers is called a serofast reaction.

II. Sympathetic Ophthalmia (SO)—The True Diagnosis

A. Disease entity and history

1. Bilateral granulomatous uveitis typically occurring following penetrating ocular trauma or ocular surgery in 1 eye. The eye with the original insult is called the “exciting eye” and the contralateral eye is called the “sympathizing eye.”
2. First recognized by Hippocrates c. 400 BCE. Full clinical description by W Mackenzie in 1840. Histopathologic description by E Fuchs in 1905 and separately by A Dalen in 1904. In 1910, A Elschnig proposed etiology of inflammatory response against uveal antigens.

B. Pathophysiology and epidemiology

1. Autoimmune T-cell mediated reaction against normally sequestered ocular antigens exposed to the systemic immune system through traumatic or surgical disruption of the blood retinal barrier
2. Possible genetic predisposition: HLA-A11, DRB1*04-DQA1*03
3. Overlap in risk of SO and Vogt-Koyanagi-Harada syndrome (VKH): HLA-DR4, -DQw3, and -DRw53.
4. Incidence 0.2%-0.5% after penetrating ocular injury; 0.01% after intraocular surgery. Cases reported of nonpenetrating procedures such as irradiation for ocular melanoma, cyclophotocoagulation, and infectious or chemical keratitis.

C. Presentation/diagnosis

1. Time to development usually 3 months to 1 year after the exciting event, though has been reported up to 50 years.
2. Always bilateral
3. Granulomatous panuveitis with cell and flare, mutton-fat keratic precipitates, vitritis. Acute phase may have multifocal exudative retinal detachments. About 1/3 develop multiple grouped grayish-white or yellow subretinal or choroidal lesions (Dalen-Fuchs nodules) throughout the posterior pole and midequatorial regions. May have papillitis or choroidal granulomas. Rarely tinnitus, headache, dysacusis, or sensorineural hearing loss.
4. Diagnosis based on index of suspicion, clinical features, multimodal imaging, and ruling out infection and other causes of granulomatous disease.

D. Management

1. Prevention of SO after penetrating injury: Controversy on enucleation of a blind eye with no visual potential within 2 weeks of injury to prevent disease

2. No proven benefit to removing exciting eye after SO has developed
3. Disease typically requires aggressive medical treatment with systemic corticosteroids and immunosuppressive therapy.
4. Adjunctive topical corticosteroids and cycloplegics
5. Adjunctive periocular or intravitreal corticosteroid injection

E. Prognosis

1. Disease can be aggressive and severe. Increased risk for functional impairment due to bilaterality.
2. Approximately 1/4 patients may present with 20/200 or worse in sympathizing eye.
3. Further loss to 20/200 or worse occurred in 10% of sympathizing eyes per year.
4. Exudative detachment and intraocular inflammation are significantly associated with poorer vision.

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Case: Is Hindsight Better Than 20/80?

Karen R Armbrust MD

CASE PRESENTATION

- 28-year-old African female
- Presents with acute onset of poor vision right eye and chronic poor vision left eye
- History of granulomatous uveitis left eye 10 years ago and granulomatous uveitis both eyes 7 years ago, treated with topical corticosteroids
- Treated with eye drops and injections 1-2 years ago
- No eye care for the past year
- Unremarkable medical history

Ocular Examination/Imaging

- BCVA
 - OD: 20/400
 - OS: 20/100
- IOP
 - OD: 14 mmHg
 - OS: 13 mmHg
- Pupils: irregular and poorly reactive OU, no relative afferent pupillary defect
- Cornea: iridocorneal adhesions and stromal haze OU
- Anterior chamber
 - OD: 2+ cell and 1+ flare
 - OS: 0.5+ cell and 1+ flare
- Iris: broad-based posterior synechiae OU
- Vitreous
 - OD: 2+ anterior vitreous cell
 - OS: 0.5+ anterior vitreous cell
 - OU: no haze
- Fundus examination
 - OD: peripapillary scarring with adjacent elevated yellow macular lesion, associated subretinal hemorrhage, exudates in inferior macula and along inferotemporal arcade vessels, peripheral pigmented chorioretinal scars
 - OS: peripapillary scarring extending to temporal macula, vascular sheathing and peripheral chorioretinal scars
- Fundus autofluorescence
 - Hypoautofluorescence OU at chorioretinal scars
 - Hyperautofluorescence OD corresponding to the area of active inflammation
- Fluorescein angiography
 - OD: early blockage and late staining of macular lesion, with leakage along superior and temporal edge of lesion. Small vessel leakage along inferotemporal arcade.
 - OS: staining at borders of scar, no leakage

Workup

- QuantiFERON-TB Gold testing 4 years ago was positive (>10.00 IU/mL)
 - Treated for TB in a neighboring state 2 years ago
 - Self-stopped treatment after 3 months
- Chest x-ray normal
- RPR, *Treponema pallidum* antibody, HIV: All negative

DIAGNOSIS & TEACHING POINTS

Final Diagnosis

TB-associated bilateral panuveitis with choroidal neovascular membrane right eye

Clinical Course and Outcome

Treatment

- Completed 4-drug anti-TB treatment
- Topical prednisolone acetate
- Started oral prednisone 1 week after starting TB treatment
- Monthly intravitreal anti-VEGF injections OD
- Stopped treatment after 6 months for pregnancy
- 2 years later
 - Uveitis remained quiescent on topical corticosteroids alone
 - Final BCVA: 20/80 OD and 20/70 OS

Discussion of TB-Associated Uveitis

I. Epidemiology

- A. TB prevalence varies widely by geographic location.
- B. Only 10% of TB-infected individuals develop clinical TB.
- C. The prevalence of TB uveitis is difficult to establish given its diagnostic difficulty, but reported rates of TB as the etiology for uveitis range from 0.5% to 11.4%.
- D. TB uveitis is uncommon in nonendemic areas, but consider TB risk factors:
 1. Emigration from a TB-endemic region
 2. High-risk population or work closely with a high-risk population
 3. Immunocompromised status

II. Clinical Features

- A. Many types of ocular inflammation may occur in TB uveitis.
- B. Clinical signs suggestive of TB uveitis specified in the Collaborative Ocular Tuberculosis Study (COTS)⁴:
 1. Anterior uveitis (granulomatous or nongranulomatous), iris nodules, and ciliary body granuloma
 2. Intermediate uveitis (granulomatous or nongranulomatous with exudates in the pars plana, with or without snowballs)
 3. Posterior and panuveitis, choroidal tubercle, choroidal granuloma, subretinal abscess, and serpiginous-like choroiditis
 4. Retinitis, retinal vasculitis, neuroretinitis, optic neuritis, endogenous endophthalmitis, panophthalmitis, and scleritis
- C. Standardization of Uveitis Nomenclature (SUN) criteria for a TB-compatible uveitic syndrome⁷
 1. Anterior uveitis with iris nodules
 2. Serpiginous-like tubercular choroiditis
 3. Choroidal nodule (tuberculoma)
 4. Occlusive retinal vasculitis
 5. Multifocal choroiditis in patients with active systemic TB

III. Differential Diagnosis of TB Panuveitis

- A. Ocular sarcoidosis
- B. Syphilitic uveitis
- C. Multifocal choroiditis and panuveitis
- D. Vogt-Koyanagi-Harada disease
- E. Sympathetic ophthalmia

IV. Diagnosis

- A. Definitive diagnosis of TB uveitis requires ocular tissue sampling.
 1. Smear/culture/polymerase chain reaction testing is available.
 2. Organism paucity in intraocular fluids is common in TB uveitis.
 3. False negative rates tend to limit the utility of ocular TB testing.

- B. TB uveitis is often a presumptive diagnosis based on ocular features and evidence of prior TB infection.
 1. Tuberculin skin test (purified protein derivative [PPD])
 2. Interferon gamma release assay (Quantiferon-TB Gold, T spot)
 3. Chest x-ray
 4. Chest CT
- C. A successful therapeutic trial with antituberculosis treatment may support a diagnosis of presumptive TB uveitis.

V. Etiology and Pathogenesis

- A. TB uveitis is caused by *Mycobacterium tuberculosis*.
 1. Hematogenous spread is typical.
 2. *M. tuberculosis* bacilli may remain dormant in the eye for many years prior to disease activation.
- B. Immune-mediated hypersensitivity may also play a role in TB uveitis.

VI. Management

- A. Antituberculosis treatment (ATT)
 1. The Collaborative Ocular Tuberculosis Study (COTS) provides guidelines for initiating ATT.^{5,6}
 2. ATT is a multiple drug regimen to prevent drug-resistant TB.
 - a. ATT is preferably managed by an infectious disease specialist.
 - b. Drug choice may be tailored to regional patterns of drug resistance.
 - c. Specific guidelines for TB uveitis treatment duration are not yet established.
- B. Systemic corticosteroids may be beneficial but should be administered with concurrent ATT.
- C. Topical corticosteroids treat anterior chamber inflammation.
- D. Anti-VEGF treats cases with choroidal neovascularization.

VII. Prognosis

- A. Visual outcome in TB uveitis varies depending on the site of ocular inflammation.
- B. Prompt diagnosis and appropriate management in TB uveitis may lead to visual improvement and/or prevent permanent vision loss.

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Case: It Helps to Stay Fluid

Shilpa Kodati MD

CASE PRESENTATION

- 59-year-old African male presents with a 4-week history of bilateral light sensitivity and blurred vision
- Denies prior episodes of uveitis or significant past ocular history
- Review of systems remarkable for tinnitus and hearing loss

Ocular Examination

- VA: CF at 3 ft OU
- IOP: 17/16 mmHg
- Anterior chamber: 1+ cell OU
- Anterior vitreous cell: 1+ cell OU
- Fundus
 - Disc edema OU
 - Large exudative detachments OU
 - Choroidal detachments OU

Workup

- Imaging
 - Spectral domain OCT macula: subretinal fluid, large multiseptate cystic spaces with bacillary layer detachments OU
 - Ultrawide-field fluorescein angiography: early pinpoint hyperfluorescence, pooling in areas of subretinal fluid and disc leakage
 - Indocyanine green angiography: early and midphase hypocyanescence
- Laboratory
 - Syphilis IgG: negative
 - QuantiFERON: negative
 - ACE and lysozyme: negative
 - Chest x-ray: normal

DIAGNOSIS & TEACHING POINTS

Final Diagnosis

Vogt-Koyanagi-Harada (VKH) disease

Clinical Course and Outcome

- Started on 3-day course of IV pulsed methylprednisolone (1 g) followed by high-dose oral prednisone
- Mycophenolate mofetil initiated early in disease course
- VA gradually improved, with resolution of choroidal effusions, exudative detachment, and intraretinal fluid and

reconstitution of ellipsoid zone OU. At 9-month follow-up, VA was 20/20 OU.

Discussion of Disease

I. Introduction

VKH is an autoimmune multisystem disease consisting of a bilateral granulomatous panuveitis and associated neurological, auditory, and intergumentary symptoms

II. Epidemiology

- A. More common in certain darkly pigmented ethnic groups including those of Asian, Hispanic, Native American, and Middle Eastern ancestry
- B. The incidence varies geographically.
- C. Accounts for up to 4% of uveitis referrals in the United States

III. Clinical Features

- A. There are 4 classical stages of VKH, and presenting features vary depending on disease stage.
 1. Prodromal: Variable symptoms including fever, headache, nausea, tinnitus, dysacusis, meningismus, photophobia, and skin hypersensitivity
 2. Acute uveitis: Bilateral granulomatous panuveitis characterized by optic disc edema, multifocal serous retinal detachments, and choroidal thickening
 3. Convalescent: Resolution of subretinal fluid. Sunset-glow appearance of the fundus may arise due to decrease in choroidal depigmentation. Peripheral punched-out chorioretinal lesions may develop.
 4. Chronic recurrent: Granulomatous anterior uveitis and choroidal thickening
- B. Integumentary changes (vitiligo, alopecia, poliosis) can occur weeks to months after ocular symptoms arise.
- C. Sugiura sign (perilimbal vitiligo) may be present in Asian patients.

IV. Differential Diagnosis

- A. Infectious
 1. Syphilis
 2. Tuberculosis

B. Noninfectious

1. Sympathetic ophthalmia
2. Posterior scleritis
3. Sarcoidosis
4. Immune checkpoint inhibitor-associated uveitis
5. Uveal effusion syndrome

C. Neoplastic/paraneoplastic

1. Vitreoretinal lymphoma
2. Choroidal lymphoma
3. Bilateral diffuse uveal melanocytic proliferation (BDUMP)

V. Diagnosis

- A. The diagnosis is made based on characteristic fundus exam and imaging findings.
- B. Revised diagnostic criteria (2001) include bilateral ocular involvement, absence of penetrating ocular trauma, and no evidence of other ocular or systemic diseases. Criteria classify VKH into “complete” (ocular disease and neurological/auditory findings *and* integumentary findings), “incomplete” (ocular disease and neurological/auditory findings *or* integumentary findings), or “probable” (isolated ocular disease).

C. Imaging

1. Spectral domain OCT: subretinal fluid, cystoid spaces often with a multiseptate configuration and bacillary layer detachment (split in the photoreceptor layer at level of the inner segment myoid), and subretinal hyper-reflective material. Enhanced-depth OCT reveals choroidal thickening. In the later stages, subretinal fibrosis may be evident on OCT.
2. Fluorescein angiography findings in the acute uveitic stage: disc leakage, early multiple pinpoint hyperfluorescent foci at the level of the retinal pigment epithelium (“starry-sky appearance”), and late-phase pooling of dye in the subretinal space
3. Indocyanine green angiography: early hypercyanescence of choroidal stromal vessels, hypocyanescence spots on early to intermediate phase (due to choroidal granulomas), and intermediate to late peripapillary hypercyanescence

D. Lumbar puncture

1. May be performed in atypical cases with significant neurological symptoms and less characteristic ocular findings
2. CSF typically shows lymphocytic pleocytosis.

VI. Etiology and Pathogenesis

- A. A T-cell mediated autoimmune process directed at melanocyte derived self-antigens has been implicated.
- B. The disease is associated with the HLA alleles DR1 and DR4.

VII. Management

- A. Early and high-dose corticosteroids (1-1.5 mg/kg/day) are indicated, and the disease is usually highly steroid responsive. In severe cases, 3 days of 1-g pulsed intravenous methylprednisone followed by high-dose oral corticosteroids are given. A slow taper of corticosteroids is typically followed.
- B. Systemic immunomodulatory treatment is often initiated early in the disease course to minimize risk of recurrences.
- C. Adjuvant local therapy with sustained-release steroid implants can be given.
- D. OCT is used to monitor for resolution of exudative detachment, choroidal thickening, and ellipsoid zone reconstitution.

VIII. Prognosis

- A. Prognosis is generally considered favorable with treatment.
- B. Number of complications, higher age at onset, longer disease duration, and higher number of recurrences are poor prognostic factors.
- C. Effective treatment reduces the risk of vision loss due to CNV and subretinal fibrosis.

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Perioperative Management of the Uveitis Patient

Caroline L Minkus MD

I. Prepare the Patient

- A. Make sure uveitis is appropriately classified and managed.
 - 1. Infectious vs. noninfectious
 - 2. Anatomical location of inflammation
 - 3. At least 3 months of quiescence
- B. Perioperative medication management
Increase systemic medication if needed.
 - 1. Antivirals/antibiotics
 - 2. Supplemental steroids
 - 3. Timing relative to medications (eg, infusions, intravitreal injections)
- C. Set expectations.
 - 1. May not be straightforward surgery
 - 2. May require multiple procedures or stages
 - 3. Establish the goals of the procedure.
 - a. What improvements may the patient notice? (IOL selection)
 - b. What are we checking for in clinic?
 - 4. Postoperative course: anticipated medication regimen postoperatively
 - a. Prolonged course of topical therapy
 - b. Possible additional injections
 - c. Systemic medication management

II. Prepare Yourself/Surgical Team

- A. Preoperative imaging
 - 1. Measure twice, cut once.
 - 2. Additional imaging to help anticipate potential complications and set expectations
 - a. OCT
 - b. Fluorescein angiography
 - c. Ultrasound biomicroscopy
- B. Preoperative appointment 1-2 weeks before surgery date
 - 1. Final preop check on inflammation
 - 2. Supplemental medications/injections
- C. Plan ahead for surgery.
 - 1. Identify potential anatomical concerns.
 - 2. Make sure you have necessary equipment (eg, iris hooks, trypan blue, extra Visco).
 - a. If you think you might use it, make sure it's available.
 - b. Know your team and OR setting.
 - 3. Discuss with your surgery team.
 - a. Additional anesthesia concerns: block, general, potentially prolonged case
 - b. Surgical preferences established
 - c. Team prepared for potential changes in plan

III. Postoperative Management

- A. Patient expectations
- B. Slow taper
 - 1. Longer, slower taper than in standard cases
 - 2. May require additional medications as in preop
- C. Follow-up

Diagnostic Surgical Procedures in Uveitis

Phoebe Lin MD PhD

Introduction

The main indications for diagnostic surgical procedures in the uveitis clinic are occult infection or malignancy. These techniques are typically employed when other attempts at diagnosis have failed or are expected to fail, or when the burden of diagnosis is too high to attempt less sensitive forms of diagnostic procedures.

Background Observations

Thus, the main principles involved in diagnostic surgical procedures, including diagnostic anterior chamber washout, diagnostic vitrectomy, and diagnostic chorioretinal biopsy, are to (1) assess the risk/benefit ratio with the patient, (2) maximize sensitivity of your testing, and (3) minimize complications. In this presentation, I will go over the preoperative discussion and planning, the data on risk and benefit of these procedures, and intraoperative and postoperative tips for maximizing the outcome for the patient.

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1. Mruthyunjaya P, Jumper JM, McCallum R, Patel DJ, Cox TA, Jaffe GJ. Diagnostic yield of vitrectomy in eyes with suspected posterior segment infection or malignancy. *Ophthalmology* 2002; 109(6): 1123-1129.
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Therapeutic Retinal Surgery in Uveitis

Kareem Moussa MD

- I. Review of Basic Principles of Uveitis Management
 - A. Uveitis is a medical disease that requires treatment with either local or systemic therapy.
 - B. Surgery is sometimes needed for management of complications of uveitis.
 - C. Optimal medical management of uveitis reduces risk of development of complications of uveitis.
- II. Principles of Perioperative Management of Uveitis
 - A. Patients with noninfectious uveitis are at risk of flaring from surgical manipulation of ocular tissues.
 - B. Perioperative steroid should be strongly considered.
 1. High-dose oral prednisone (up to 1 mg/kg) starting 3 days before surgery and tapered postoperatively according to exam
 2. Intraoperative IV methylprednisolone
 3. Local steroid 1 week before surgery is an alternative to systemic steroid.
 4. Generally, patients with infectious uveitis do not require perioperative steroid. Instead, treatment dose of antiviral should be considered (for example, valacyclovir in those with a history of varicella zoster virus acute retinal necrosis).
- III. Representative Examples of Retina Surgery as a Therapeutic Option for Uveitis Management
 - A. Surgical implantation of fluocinolone acetonide implant for chronic treatment of unilateral posterior uveitis with cystoid macular edema (CME):

The fluocinolone acetonide implant should be considered in patients with chronic noninfectious intermediate, posterior, or panuveitis. Cataract formation and IOP elevation are common complications.
 - B. Removal of IOL, lens capsule, and pars plana vitrectomy for *Cutibacterium acnes*-associated endophthalmitis
 1. Persistent anterior uveitis following cataract surgery, refractory to treatment with local steroid, in particular when a plaque is visible on the lens capsule, should prompt consideration of *C. acnes*-associated chronic endophthalmitis.
 2. Pars plana vitrectomy, removal of the IOL, and removal of the lens capsule maximize success.
 - C. Rhegmatogenous retinal detachment in infectious retinitis
 1. Evidence is inconclusive regarding the use of prophylactic laser in preventing retinal detachment in acute retinal necrosis (ARN) patients.
 2. Consider combined pars plana vitrectomy and scleral buckle for patients with ARN-associated rhegmatogenous detachment.
 3. Intravitreal antiviral injections can be administered in eyes with silicone oil tamponade.
 - D. Vasoproliferative tumor in intermediate uveitis with epiretinal membrane
 1. The 3 most common causes of secondary vasoproliferative tumor are intermediate uveitis, Coats disease, and retinitis pigmentosa.
 2. Vasoproliferative tumors may result in exudation, serous retinal detachment, hemorrhage, and epiretinal membrane.
 3. Vasoproliferative tumors can be treated with cryotherapy and often require perioperative steroid. Pars plana vitrectomy and epiretinal membrane removal should be considered for visually significant epiretinal membrane.
 - E. Uveitis-glaucoma-hyphema (UGH) syndrome requiring IOL removal
 1. UGH syndrome should be considered in patients with refractory uveitis and/or complications of uveitis such as CME.
 2. A careful exam should be performed in all patients with uveitis; a 1-piece IOL in the sulcus with iris transillumination defects is highly suggestive of UGH syndrome.
 3. Removal of the IOL is curative. Pars plana vitrectomy and removal of the IOL by a retina surgeon may be required if lens stability is uncertain.

Selected Readings

1. Bavinger JC, Anthony CL, Lindeke-Myers AT, et al. Risk factors for retinal detachment in acute retinal necrosis. *Ophthalmol Retina*. Epub ahead of print 2022 Feb 1;S2468-6530(22)00038-0.
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Cataract Surgery in Patients With Uveitis

George N Papaliodis MD

I. Introduction

- A. Review challenges posed by cataract surgery in those with uveitis
- B. Review published articles with case series documenting increased risk of surgical complications
- C. Discuss management strategies that may improve outcomes

II. Management of Small Pupil

- A. Pharmacologic agents
 - 1. Epinephrine 0.025% with lidocaine 0.95% (Epi-Shugarcaine)
 - 2. Phenylephrine 1% with ketorolac 0.3% (Omidria)
- C. Mechanical dilation
 - 1. Bimanual pupil stretching (Kuglen hooks)
 - 2. Pupil ring
 - 3. Iris hooks

III. Perioperative Management of Uveitis

- A. Quiescent disease for 3 months prior to elective procedures
- B. Intravenous pulse of methylprednisolone intraoperatively

IV. Conclusion

Glaucoma in Uveitis

Uveitic Glaucoma: Pearls and Pitfalls

Debra Goldstein MD

I. Introduction

- A. Approximately 20% of uveitis patients in the United States develop glaucoma.
- B. Over 50% of uveitic eyes develop elevated IOP at some point in their course.

II. Causes

- A. There are myriad causes of elevated IOP in eyes with uveitis.
- B. Don't automatically attribute to steroid response.

III. Gonioscopy

- A. Underutilized: deep chamber \neq open angle
- B. Gonioscopy to assess angle in all uveitis patients

IV. Steroid Response

- A. More common in children
- B. May develop any time from weeks to years after starting steroids
- C. Measure IOP at every visit

V. Inflammation

- A. Don't undertreat inflammation because of IOP elevation; treat inflammation and IOP.
- B. Some types of uveitic ocular hypertension may benefit from an increase in steroids
 - 1. Herpetic anterior uveitis
 - 2. Glaucomatocyclitis crisis
- C. Better control of inflammation may result in lower risk of glaucoma
 - 1. Less cell and debris clogging trabecular meshwork
 - 2. Reduced likelihood of developing PAS

VI. Treatment

- A. Prostaglandin analogs may often be safely used in patients with uveitis.
- B. Selective laser trabeculoplasty may "buy time" in eyes with posterior uveitis and a steroid response.
- C. Variable results with minimally invasive glaucoma surgery in uveitic eyes
- D. In general, tube shunts preferred to trabeculectomy in eyes with uveitis

Treatment Paradigm for Uveitis

Armando L Oliver MD

Most uveitides are of autoimmune origin.

Most uveitides are of autoimmune origin and will benefit from local or systemic corticosteroids and immunosuppressors. However, approximately 10% of cases will have an underlying infectious etiology. Therefore, all patients should undergo a targeted infectious disease workup appropriate for the specific uveitis. Infectious uveitis can often be cured, precluding the long-term need for therapy. Conversely, once the most common infectious uveitis entities have been ruled out, the chances of infectious etiology are relatively low. Hence, systemic corticosteroid and immunosuppressor therapy should be considered without further delay.

Generally, all uveitis patients should be worked up for syphilis with a treponemal-specific test such as FTA-Abs or TP-PA. Lyme disease should be considered in most cases for patients who live in endemic areas or who have potentially been exposed. Specific signs or conditions may prompt the presence of an infectious etiology; for instance, focal retinitis should raise concerns for either toxoplasmosis or a viral etiology. Similarly, a patient with unilateral iridocyclitis who presents with either concomitant keratitis, granulomatous features, elevated IOP, or transillumination defects should be worked up for herpesviridae. Although rare in developed countries, tuberculosis should be ruled out in patients with multifocal choroiditis or serpiginous choroiditis appearance. It is noteworthy that optimally most uveitis patients should be screened for tuberculosis before starting systemic therapy.

Treatment Goals: Make It Quiet, Keep It Quiet, and Try to Induce a Remission!

Uveitis treatment goals can be divided into 3 steps: making it quiet, keeping it quiet, and the induction of remission. First, the patient's uveitis should be made quiet. Why? One cannot keep quiet what has not first been made quiet. Therefore, treatment should be aggressive at the initial stage as, in general terms, it takes more medication to make an eye quiet than to keep it quiet. At this stage, it is not uncommon to use hourly topical corticosteroids, local steroid injections, and high-dose systemic steroid therapy.

The second goal is to keep the uveitis quiet while minimizing ocular complications from the disease and systemic complications from therapy. Optimally, systemic prednisone dosages at this stage should not exceed 7.5 mg/day. Former paradigms called for the stepladder approach in which systemic immunosuppressors were used exclusively for patients who failed a steroid monotherapy taper. However, nowadays there is evidence suggesting that patients with Behçet disease uveitis, birdshot retinochoroidopathy, juvenile idiopathic arthritis (JIA)-associated uveitis, mucous membrane pemphigoid, multifocal choroiditis with panuveitis, necrotizing scleritis, serpiginous choroidopathy, sympathetic ophthalmia, and Vogt-Koyanagi-Harada (VKH) disease will have a better prognosis when immunosuppressors are started soon after the diagnosis is confirmed.

The ultimate goal of therapy is to induce long-term drug-free remission. Generally, chronic uveitis entities should be kept quiet for 2 years before tapering systemic medications to test for remission. Some drugs, such as alkylating agents, are known to induce remissions in most patients; however, their side effects limit their scope of use. Ultimately, as our knowledge of immunogenetics advances, targeted immunological therapies may be developed. Hopefully, these therapies will eventually help us cure these diseases and improve our patients' quality of life.

Thomas A Albini MD

NOTES

Immunosuppression

Eduardo Uchiyama MD

I. Introduction

Steroid-sparing agents should be considered if:

- A. The disease worsens or does not respond after 2-4 weeks on high-dose steroids.
- B. The disease is not completely controlled after 4 weeks of high-dose steroids.
- C. The disease suppression requires chronic prednisone doses of >10 mg daily.
- D. The type of uveitis requires immediate therapy with another agent.
- E. Prohibitory side effects develop from steroid therapy.
- F. Required doses of systemic steroids are highly likely to result in complications.

II. Risk/Benefit Ratio

- A. Posterior uveitis and panuveitis are associated with poor long-term outcomes if only steroids are utilized.
- B. Steroid-sparing agents used in uveitis: Most agents are used off-label when treating uveitis conditions.

1. Antimetabolites

- a. Indications, follow-up, and side effects
- b. Methotrexate
- c. Mycophenolate
- d. Azathioprine

2. Calcineurin inhibitors

- a. Indications, follow-up, and side effects
- b. Cyclosporine
- c. Tacrolimus

3. Tumor necrosis factor (TNF) inhibitors

- a. Indications, follow-up, and side effects
- b. Adalimumab
- c. Infliximab
- d. Other TNF inhibitors

4. Tocilizumab (anti-IL-6): Indications, follow-up, and side effects

5. Rituximab (monoclonal antibody targeted against CD20): Indications, follow-up, and side effects

6. Alkylating agents

- a. Indications, follow-up, and side effects
- b. Cyclophosphamide
- c. Chlorambucil

7. Other agents

III. Case Example and Summary

Local Therapy

Arjun B Sood MD

I. Local Therapy

- A. Indications and considerations
 - 1. Unilateral vs. bilateral disease
 - 2. Systemic disease
 - 3. Pregnancy
 - 4. Medication side effects with prior systemic therapy and patient preference
- B. Local steroid option
 - 1. Topical
 - 2. Periocular/posterior subtenon
 - 3. Intravitreal injection/implant
 - 4. Suprachoroidal
- C. Nonsteroid local therapy
 - 1. Antimicrobial
 - 2. Anti-VEGF
 - 3. Methotrexate
 - 4. Sirolimus

II. Topical Therapy

- A. Most commonly, use prednisolone acetate 1% and difluprednate 0.05%. Useful for treating anterior chamber cell and cystoid macular edema (CME).
- B. Cycloplegia: relieve pain and prevent synechiae
- C. NSAIDs: Useful in management of uveitic CME

III. Periocular/Posterior Subtenon Triamcinolone Acetonide (40 mg/1 mL Kenalog; PSTK)

IV. Intravitreal Injection/Implant

- A. Preservative-free triamcinolone acetonide suspension (4 mg/0.1 mL Triesence)
- B. Dexamethasone 0.7-mg intravitreal implant (Ozurdex): HURON study compared efficacy of dexamethasone implant compared to sham. At Week 8, 47% of patients in 0.7-mg implant group showed a vitreous haze score of 0, compared to 12% in the sham group.
- C. POINT Trial compared efficacy and safety of PSTK, intravitreal triamcinolone acetonide, and dexamethasone implant. All treatment arms showed reduction in macular edema, but intravitreal steroids were superior to periocular in improving vision and macular edema.

V. Fluocinolone Acetonide (FA) Implants

- A. 0.59-mg FA (Retisert): Multicenter Uveitis Steroid Treatment (MUST) Trial compared effectiveness and safety of Retisert implant vs. systemic therapy with oral corticosteroids and immunosuppressive therapy for intermediate, posterior, and panuveitis. VA improvement was comparable between systemic and FA implant arms. Rates of cataract surgery and glaucoma surgery were higher in the implant group.
- B. 0.18-mg FA (Yutiq): Two multicenter Phase 3 sham-controlled RCTs demonstrated reduced recurrence in patients with noninfectious intermediate, posterior, and panuveitis at 6 months (28% recurrence with the FA implant vs. 91% recurrence with sham) and 12 months (38% recurrence with FA implant vs. 98% recurrence with sham).

VI. Suprachoroidal Triamcinolone Acetonide (4-mg CLS-TA Xipere)

PEACHTREE Study: Phase 3 RCT comparing suprachoroidal CLS-TA vs. sham. Forty-seven percent of patients in CLS-TA gained >15 ETDRS letters, compared to 15% in sham.

VII. Nonsteroid Local Treatments

- A. Antimicrobial for viral, bacterial, fungal, and parasitic infections
- B. Anti-VEGF: Useful for treatment of macular edema, retinal neovascularization, and CNV
- C. Methotrexate
- D. Sirolimus: Nonsteroidal immunoregulator that inhibits mTOR signaling. Phase 3 LUMINA study is assessing efficacy and safety of intravitreal sirolimus 440 µg for treatment of noninfectious uveitis of posterior segment.

Association Between Use of Immunosuppression and the Incidence of Cancer

John H Kempen MD

NOTES

Macular Edema Ranibizumab vs. Intravitreal Anti-inflammatory Therapy (MERIT)

Nisha Acharya MD

NOTES

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EO	Owner of Company Ownership or controlling interest in a company, other than stock.
SO	Stock Options Stock options in a private or public company.
PS	Equity/Stock Holder - Private Corp (not listed on the stock exchange) Equity ownership or stock in privately owned firms, excluding mutual funds.
US	Equity/Stock Holder - Public Corp (listed on the stock exchange) Equity ownership or stock in publicly traded firms, excluding mutual funds.
I	Independent Contractor Contracted work, including contracted research.

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Kareem Moussa MD

None

Marion Ronit Munk MD PhD

Acucela: C
 Allergan: L
 Bayer: C,S
 Gensight Therapeutics: C
 Helbling: C
 Isarna Therapeutics: C
 Lumithera: C
 Novartis: C,L
 OcuTerra: C
 RetinAI: C
 Roche: C
 Zeiss: C,L

Armando L Oliver MD

Allergan: L
 Mallinckrodt Pharmaceuticals: L

George N Papaliodis MD

Teladoc Health: C
 UpToDate.com: P

Kathryn L Pepple MD PhD

None

Francesco Pichi MD

None

Russell W Read MD PhD

None

Lana M Rifkin MD

Bausch + Lomb: C
 Eyepoint: C

Jessica G Shantha MD

None

Sumit Sharma MD

AbbVie: C
 Alimera Sciences, Inc.: C
 Bausch + Lomb: C
 Clearside: C
 Eyepoint: C,S
 Genentech/Roche: C,S
 Gilead Sciences: S
 Ionis: S
 Regeneron Pharmaceuticals, Inc.: C,S
 Regenxbio: C
 Santen, Inc.: S

Wendy M Smith MD

None

Lucia Sobrin MD

None

Arjun B Sood MD

Carl Zeiss Meditec: C
 Eyepoint: L

Edmund Tsui MD

Cylite Pty, Ltd.: S
 EyePoint Pharmaceuticals: C
 Kowa Company, Ltd.: C,S
 National Eye Institute: S
 Pfizer, Inc.: S

Ilknur Tugal-Tutkun MD

AbbVie: C,L
 Novartis Pharma AG: C

Eduardo Uchiyama MD

Alimera Sciences, Inc.: C,L
 Allergan, Inc.: C
 Bausch + Lomb: C,L
 Eyepoint: C,L
 Genentech: C
 GSK: C
 Novartis Pharma AG: C,L
 Regeneron Pharmaceuticals, Inc.: C,L

Lianna M Valdes, MD

Has not disclosed to date

Arthi Ganesh Venkat MD

Apellis: C

Jessica E Weinstein MD

None

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