Not Another Uveitis

PRESENTED BY:
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Disclosures

- The content of this presentation was prepared independently by Michael Cooper, OD without input from members of the ophthalmic community.
- Dr. Cooper is affiliated with Allergan, Alcon Surgical, BioTissue, Shire, JJVC, TearScience, Glaukos, Bausch + Lomb/Valeant, Quidel, Mentholatum, and TearLab as a consultant/speaker in the past 12 months.
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Uveitis: What is it?

- According to the CDC, approximately 10% of all cases of blindness in the United States are caused by uveitis.
- 30,000 new cases of legal blindness in the United States per year.
- 4th leading cause of blindness in U.S.
- Impact can be socioeconomic and affect QOL.

Examining a patient with Uveitis

- History
- Signs from arm’s length (wearing sunglasses in the exam room, redness, etc)
- Pupils
- BCVA
- Slit lamp with attention to corneal endothelium, optical clarity of the aqueous, anterior lens, subtle irregularities in the shape of the pupil (anything else?)
- Lacrimal Gland
- Cornea – Sensation
- IOP – High or low in the affected eye?
- Vitreous – looking for what?
- DME with attention to what?
- Macular OCT for what?
- Any value in doing a visual field? What type of field?
- Follow up even if referring out?
- When should we communicate with the PCP?
Case #1

- 32 year old Caucasian male
- Same day referral from Windham ER, patient was hit by exploding sparkler firework into his right eye.
- Swollen, painful red eye that was shut upon presentation
- Vision was unstable with excessive tearing
- Patient has had prior surgery twice for a previous paintball injury in the same eye.

Exam

- VA: 20/200 OD, 20/15 OS
- Positive Slit Lamp findings:
  - Upper and lower right lid: 2+ swelling and ecchymosis
  - Open wound on right cheek
  - 3+ cell in anterior chamber, no flare present
  - No bleb formation, conjunctiva: bulbar 1+ inferior
- Gonioscopy revealed multiple areas of iris tears and prolapse superior OD
- IOP: 11 OD, 14 OS
- Dilated Fundus Exam:
  - Commotio Retinae parafoveal
  - Multiple chorioretinal scars extending from ONH to nasal macula

“Peek a Boo” IOL

Treatment

- Cyclo 1% bid OD
- Durezol qid OD
- Generic Cosopt tid OD (pre-existing medication)
- Bacitracin ophthalmic ointment tid for abraded skin tissue

Long Road Ahead

- Took 2-3 months for the Traumatic Iridocyclitis to resolve
- It could take longer
- Luckily, pressure remained low and did not spike
- It can...
  - Be mindful of retinal pathology
  - Macula
  - Periphery
  - Acquired Optic Neuropathy

Injury Epidemiology

- Ocular injuries in children account for 20%–50% of all ocular injuries.
- Perforating eye injuries make up 21–24% of serious ocular trauma and are a significant cause of visual loss.
- It is estimated that they can be prevented in up to 90% of cases.
- There is a male predominance of 2:1-6:1
Uveitis Incidence

Total Patients: 731,898

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Incidence rate per 100,000 person-years

Adapted from Gritz et al., 2004

Uveitis Prevalence

Total Patients: 731,898

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Adapted from Gritz et al., 2004

Uveitis: Where is it?

- Inflammation of the uvea, the eye’s middle layer consisting of the iris, ciliary body and choroid.
- Iritis is the most common type of uveitis.
- It can be...
  - Anterior
  - Intermediate
  - Pars Planitis
  - Iridocyclitis
  - Posterior
  - Choroiditis
  - Panuveitis

Uveitis Signs

- Signs:
  - Redness – dilated ciliary vessels “ciliary flush”
  - Cells / flare
  - Hypopyon
  - Deposits on lens / corneal endothelium
  - Pupillary irregularities
  - Iris color changes
  - High (or low) IOP
  - Busacca/Koeppe nodules on iris

More Uveitis Signs

- Fine Keratic Precipitates (KP)
- Mutton Fat Keratic Precipitates
Uveitis Symptoms

- Symptoms
  - Onset may be rapid or gradual
  - Blurred vision (acuity may vary)
  - Floaters
  - Eye pain
  - Photophobia
  - Redness
  - Photopsia (in posterior uveitis)
  - History of trauma (intraocular foreign body, infection, sympathetic ophthalmia)
  - History of previous eye surgery (Propionibacterium acnes, haptic rub, sympathetic ophthalmia)

Uveitis Complications: The Aftermath

- Complications vary by location, intensity, recurrence, duration and how early treatment can be initiated
  - Band keratopathy
  - Anterior synechiae / narrow or closed angles
  - Posterior synechiae / pupillary block
  - Uveitic glaucoma, a sneaky variant of an already sneaky disease
  - Cataract
  - Macular edema
  - Retinal detachment
  - Vision loss
  - CNV
  - Ischemia
  - Neovascularization
  - Photoreceptor Degeneration

Etiologies: The Rivers of Logic Pt 1

- If no history of recent ocular surgery nor trauma, think of:
  - Noninfectious
    - Behçet’s, Fuch’s, granulomatosis with polyangiitis, relation to HLA-B27, JA, sarcoidosis, spondyloarthritides, sympathetic ophthalmia, tuberculosis and uveitis syndrome
  - Infectious – the minority of cases fall into this category
    - Brucellosis, leptospirosis, Lyme disease, PCOS, syphilis, toxocariasis, toxoplasmosis, tuberculosis
  - Systemic disease
    - Ankylosing spondylitis, Behçet’s, chronic granulomatous disease, encephalitis, inflammatory bowel disease, JRA, Kawasaki’s disease, AIDS, polyarteritis nodosa, psoriatic arthritis, reactive arthritis, sarcoidosis, SLE, Wini syndrome, Whipple’s disease

Brucellosis

- Bacterial Zoonotic Disease, typically laboratory acquired infection in nature and endemic in individuals tending domestic herd animals in the US, but that is changing...

- Symptoms include undulant fever, myalgia, arthralgia, night sweats, and malaise, spontaneous abortion in females, intrauterine fetal death.

- No birth defects have been reported.

- Bacteria is readily aerosolized with an infective dose of 10-100 organisms.

- Known species in human population: Brucella melitensis/abortus/suis

Case #2

- A 54 year old Hispanic female presents with grittiness, light sensitivity, and moderate discomfort in her left eye. Her medical history is pertinent for hypertension and asthma. Recently she had mentioned that she was bitten by a tick and was awaiting test results.

- What else would you like to know about this patient?
- What are the differential diagnoses?
- How do we counsel this patient on his diagnosis?
- How do we treat this patient?
- Are there any treatment pitfalls in managing this patient?

Exam

- VA acc: 20/70 (Ph 20/30) OD, 20/20 OS
- IOP: 12 OD, 17 OS
- PD: 12 OS, 17 OS
- Pupil: No APD, WNL OS, Slight sluggish and irregular OD
- Slit lamp findings:
  - 2+ conjunctival injection OD
  - 2+ cell OD
  - H-L FOC
  - Several areas of F5 OD
- Dilated fundus exam: Unremarkable
Treatment and Follow up

- Cyclo 1% bid OD (Homatropine 5% if available)
- Durezol qid OD
- Patient returned on Day 3 and looked like this...
- VA: 20/40 OD; 20/20 OS
- IOP: 13 OD; 16 OS
- Pertinent Slit Lamp:
  - 1+ cell
  - PS areas mostly broken

**Lab Results came back positive for Borrelia (Lyme)**

Collaborative Care Steps

- Reported to the State of CT for epidemiological record
- Sent letter to PCP that we treated patient from an ophthalmological and systemic perspective (I started patient on Doxycycline 100 mg 1 tab bid po for 14 days)
- Made patient aware that she may need to see infectious Dz specialist depending on clinical course to co-manage her case

Lyme Disease

- More than 22 variants caused by tick bites
- B. Miyamotoi is resistant to doxycycline, but exceedingly rare in US (n=18)
- Powassan Virus is a flavivirus, the latest to see press time- no current treatment available.
- Babesia and Anaplasma have seen tremendous incremental increase in the past 5-8 years

What I Order for Lyme

- A Lyme Titer even with a reflex may not be helpful
- Go for the Gold- The Antibodies (IgG and IgM)
- Lyme Disease: Need at least 5 IgG bands to be a positive result
- Babesiosis Reference Range:
  - Babesia microti Antibodies IgG<1:64  Babesia microti Antibodies IgM<1:20
- Anaplasmosis Reference Range:
  - A. phagocytophilum IgG<1:64  A. phagocytophilum IgM<1:20
  - A. centrale IgG<1:64  A. centrale IgM<1:20

Two-Tiered Testing for Lyme Disease

- First Test
  - Enzyme Immunoassay (EIA): OD
  - Immunofluorescence Antibody (IFA)
- Second Test
  - IgG ELISA
  - IgG Western Block

Lyme Treatment

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<th>Drug</th>
<th>Dosage for adults</th>
<th>Dosage for children</th>
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<tr>
<td>Doxycycline</td>
<td>100 mg twice per day*</td>
<td>50-80 mg/kg twice per day*</td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>500 mg twice per day</td>
<td>500-800 mg per day in 3 divided doses (maximum, 1 gram per day)</td>
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<tr>
<td>Penicillin G</td>
<td>25-50 million units per day</td>
<td>5 million units per day in 3 divided doses (maximum, 1 gram per day)</td>
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* Dosages should be based on patients with impaired renal function.
**Babesiosis Treatment**

- Atovaquone 750 mg 1 tab bid po PLUS Azithromycin
- On the first day, give a total dose in the range of 250-1000 mg orally; on subsequent days, give a total daily dose in the range of 250-1000 mg.
- OR
- Clindamycin 600 mg orally 3 times a day, 300-600 mg intravenously 4 times a day
- PLUS Quinine 600 mg orally 1 tab bid po (this combination is the standard of care for severe III patients).
- Treatment Time: 7-10 days

**New Drug Candidates:** Psidomycin and FR900098

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**Anaplasmosis Treatment**

- Doxycycline is the first line treatment for adults and children of all ages:
- Adults: 100 mg every 12 hours
- Children under 45 kg (100 lbs): 2.2 mg/kg body weight given twice a day
- Treatment Time: 7-14 days

In B. burgdorferi infected children younger than 8 years:
- Doxycycline should be continued until the patient is afebrile for 3 days, with the remainder of the 14-day course completed with an alternative agent active against B. burgdorferi (eg, amoxicillin or cefuroxime axetil) to minimize the risk of dental discoloration.
- Patients who fail to respond clinically to doxycycline monotherapy after 72 hours should be evaluated for an alternative diagnosis or the possibility of Babesiosis infection.

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**Lyme Maps**

- **33** American Dog Tick (R. sanguineus)
- Rocky Mountain Spotted Fever, Tularemia

- **34** Blacklegged Tick (I. scapularis)
- Lyme, Babesiosis, Anaplasmosis, Powassan

- **35** Brown Dog Tick (R. sanguineus)

- **36** Gulf Coast Tick (D. variabilis)

[Image of maps showing tick distributions across the United States]
10/22/2018

Lyme Maps

Ehrlichiosis, Tularemia, STARI

Lyme Maps

Rocky Mountain Spotted Fever, Colorado Tick Fever, Tularemia

Lyme Maps

Lyme, Anaplasmosis

Watch for These Patterns

- Alternating unilateral (B27 associated)
- Explosive onset and rapid resolution (Behcet’s, B27 associated)

History and Sympathetic Ophthalmia

- Rare, bilateral, granulomatous uveitis due to trauma (more common) or surgery (less common) to one eye.
- Thought to be secondary to the development of an autoimmune reaction to ocular antigens that are exposed during the traumatic or surgical event. The primary mediators are thought to be a initial wave of CD4+ helper T cells and the later wave of CD8+ cytotoxic T cells.
- Injury to onset is 5 days to 66 years, although most is within first year.
- Inflammation is granulomatous. The choroid is diffusely thickened with lymphocytes, nests of epithelioid cells and multinucleated giant cells, and Dalen-Fuchs nodules.

Etiologies: The Rivers of Logic Pt 2

- Drug induced side effects
  - Allopurinol
  - Prostaglandins
  - Rituximab
  - Steroids
- White dot syndromes – occasionally, uveitis is confined to the eye and there is no underlying systemic condition, the etiology remains unknown. This characteristic presentation may be attributable to one of the following diagnoses
  - MPPE, Behcet, multicystic choroiditis and panuveitis, MENGES, punctate inner choroiditis, serpiginous choroiditis, acute anterior uveitis, outer retinopathy.
Etiologies: The Rivers of Logic Pt 3

- Masquerade syndromes – conditions where intraocular cells are present, but are not due to immune-mediated entities.
- Neoplastic:
  - Leukemia
  - Malignant melanoma
  - Lymphoma
  - Reticulum cell sarcoma
- Non-neoplastic:
  - Intraocular foreign body
  - Juvenile xanthogranuloma
  - Retinal detachment
  - Exvivo pigmentation

Social History: Bonus Case #3 from Kenya!

- Social history
- Race, ethnicity
- Geographic residence
- Diet
- Animal exposure
- Travel
- Social behavior
- Sexual habits

Case #4

- A 60 year old African American female presents with a history of previous bouts of anterior uveitis in both eyes. Her medical history is pertinent for diabetes mellitus, hypertension, and sarcoidosis. With regard to her ocular history, every time she has a uveitic episode, her intraocular pressure becomes elevated.

Sarcoidosis Stats

- Incidence in US of systemic sarcoidosis ranges from 5-40 per 100,000 population
- Prevalence is 10 times greater for African Americans when compared to Caucasians (non-Hispanic)
- Slight female preponderance, with most symptomatic patients being between 20-50 years old

Review of Systems

- General health
- Skin
- Neurologic
- Ears, nose, throat
- Respiratory
- Gastrointestinal
- Bones and joints
- Vascular
- Genitourinary

Diagnostic Testing

- Negative tuberculin skin test in a BCG-vaccinated patient or in a patient having had a positive tuberculin skin test previously
- Elevated serum ACE levels and/or elevated serum lysozyme
- Chest x-ray revealing bilateral hilar lymphadenopathy (BHL) – still #1 method for diagnosis (90%)
- Abnormal liver enzyme tests
- Chest CT scan in patients with a negative chest x-ray result

Lucky #7…

7 Signs of Intraocular Sarcoidosis
- Mutton-fat keratic precipitates (KPs)/small granulomatous KPs and/or iris nodules
  (Koeppe/Busacca)
- Trabecular meshwork (TM) nodules and/or tent-shaped peripheral anterior synechiae (PAS)
- Vitreous opacities displaying snowballs/"strings of pearls"
- Multiple choroidal peripheral lesions (active and/or atrophic)
- Nodular and/or segmental peripheral iritis (-/-; candlewax drippings) and/or retinal macroaneurism in an inflamed eye
- Optic disc nodules/granulomas and/or solitary choroidal nodule
- Bilaterality

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Exam
- VA: 20/60 OD; 20/80 OS (PNH OU)
- Pupils: WNL, No APD OU
- Positive Slit Lamp findings:
  - 1+ cell OU
  - 1-2 fresh mutton fat KP’s intercentral, several residual brown colored KP’s present inf
  - No PS, but there was pigmented areas on lens capsule present
  - Several iris nodules at pupil margin
- IOP: 12 OD; 17 OS
- Dilated Fundus Exam:
  - Vit Snowballs inf (several “pearls”), no heme

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Treatment and Follow up
- Atropine 1% bid OU
- Pred Acetate 1% q1h OU
- Patient returned on Day 7:
  - VA: 20/50 OD; 20/80 OS
  - IOP: 13 OD; 15 OS
  - Positive Slit Lamp:
    - 1+ cell OU
    - 1-2 fresh mutton fat KP’s intercentral, several residual brown colored KP’s present inf
  - No iris nodules at pupil margin
- Dilated Fundus Exam:
  - Vit Snowballs inf (several “pearls”) still present, no heme

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Collaborative Care and F/U Steps
- Sent letter to PCP that we treated patient from an ophthalmological perspective and that we ordered bloodwork to compare normative levels
- Made appointment for patient to see Pulmonology
- Made patient aware that she may need therapy (MTX, Steroids) or other classes (INF-alpha inhibitors) depending on clinical course
- Potential surgical intervention with intravitreal injections, cataract surgery (2* to chronic inflammation, vitrectomy and/or steroids), MIGS/Trab/Drainage devices
- Followed patient on a step ladder approach (1 day, 1 wk, 2 wk, 1 mo, 3 mo, 6 mo)

*Be wary of Steroid induced Glaucoma, Pulmonary fibrosis, deafness, acquired optic atrophy

Slit Lamp Examination: Conj and Cornea
- Conjunctival nodules (sarcoidosis)
- Keratitic precipitates: granulomatous versus nongranulomatous
- Interstitial keratitis (syphilis, Cogan’s syndrome)
- Stromal edema and/or fibrils (HSV)

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Anterior Chamber Grade SUN System

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<tr>
<td>2</td>
<td>Moderate (iris and lens clear)</td>
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<tr>
<td>3</td>
<td>Marked (iris and lens hazy)</td>
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<tr>
<td>4</td>
<td>Intense (iris and hazy)</td>
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<td>3+</td>
<td>26-50</td>
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<tr>
<td>4+</td>
<td>50+ (Gel)</td>
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**Keratic Precipitate Differentiators**

Type of KP  
Small stellate, even distribution no gravitation  
Small gravitational or inferior random distribution  
Small/medium size, focal spherical distribution under stromal keratitis  
Medium/large gravitational distribution (mutton-fat)  
Very few (2-5) small/medium/large size, inferior peripheral (iridocorneal angle)

Clinical entity to suspect:  
Fuchs’ uveitis [Figure 6]  
CMV uveitis [Figure 7]  
h.simplex/zoster keratouveitis [Figure 8]  
sarcoidosis, tuberculosis, toxoplasmosis [Figure 9]

Posner-Schlossmann syndrome

*Image courtesy of Middle Eastern African Journal of Ophthalmology*

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**Sit on it or not: When Do You Do Bloodwork?**

- After the first event
- After the second event
- It’s complicated. I make a judgment call based on presentation!
- I never ever order bloodwork for Uveitis.

**Uveitis workup**

- Hematology  
- CBC with differential  
- ESR and CRP  
- Serology
- Rheumatology  
- ANA  
- RF  
- ACE with Reflex Chest X-ray  
- P-ANCA and C-ANCA

What about an MRI?

**Uveitis workup cont’d**

- Serology  
- TB testing (PPD with Reflex Chest X-ray)  
- TT, TST  
- FTA ABS + VDRL (Diagnosis)
- Herpes  
- Ticks: Antibody Panel (Borrelia, Babesia, and Anaplasma)  
- Bartonella

- Immunology / Genetic testing  
- HLA-B27 (Reiter’s Syndrome, Ankylosing Spondylitis, Colitis, etc)  
- Commonly associated with acute unilateral anterior uveitis, male predilection, frequent recurrence, often nongranulomatous
- HLA-B51 (Behcet’s Disease)
- HLA-A29 (Birdshot Chorioretinopathy)

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**Short List Cheat Sheet**

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<tr>
<td>Toxocara</td>
<td>Toxocara</td>
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<td>Posterior uveitis</td>
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<td>Leukemia</td>
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*Age <5*

- JIA  
- Sarcoidosis  
- Toxocara  
- Posterior uveitis  
- Trauma

*Age 5-15*

- JIA  
- Sarcoidosis  
- Pars Planitis  
- Posterior uveitis  
- Trauma

*Age 16-25*

- Pars planitis  
- Ankylosing spondylitis  
- Idiopathic anterior uveitis  
- Toxoplasmosis  
- Sarcoidosis  
- Acute retinal necrosis

*Age 25-45*

- Posterior uveitis  
- Idiopathic anterior uveitis  
- Toxoplasmosis  
- Behcet’s disease  
- Sarcoidosis  
- Intermediate/paracentral

*Age 45-55*

- Post-surgical (P. acnes)  
- Idiopathic anterior uveitis  
- Toxoplasmosis  
- Behcet’s disease  
- Sarcoidosis  
- Intermediateretinal vasculitis  
- Acute retinal necrosis

*Age 55+

- Post-surgical (P. acnes)  
- Idiopathic anterior uveitis  
- Toxoplasmosis  
- Behcet’s disease  
- Sarcoidosis  
- Intermediate/paracentral  
- Acute retinal necrosis  
- Masquerade Syndrome

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**Patient Demographics**

*Image courtesy of Middle Eastern African Journal of Ophthalmology*
Anterior Uveitis

- Frequently referred to as Iritis
- Hypopyon
- Common categories
  - Granulomatous
  - Non-granulomatous
- Etiologies – in approximately 50% of all cases, no associated condition / syndrome is identified.
  - Infectious
    - Herpetic keratitis, CMV Retinitis
    - Ebola (Occur 20% if you survive…)
  - Noninfectious
    - Autoimmune

Busacca vs. Koeppe

- Busacca's nodules on the surface of iris
- Koeppe's nodules at inner layer of iris

Agregates of epithelioid cells & mononuclear cells

Intermediate Uveitis

- Vitritis – presence of inflammatory cells in the vitreous cavity
- Pars Planitis – may see deposition of inflammatory material on the pars plana
- Iridocyclitis – presents as anterior uveitis plus vitritis
  - Snowballs
  - Snowbanks

Posterior Uveitis

- Choriocapillaris and retinal inflammation - choroiditis
- Noninfectious etiologies
  - Autoimmune
- Infectious etiologies
  - Toxoplasmosis
  - Toxocariasis
  - HIV / CMV Retinopathy
Pan-uveitis

- Inflammation is present in all segments of the uvea
- Noninfectious
- Autoimmune
- Infectious
- Endophthalmitis

Treatments

- Topical
  - Antibiotics
  - "Steroids"
  - NSAIDs
  - Glaucoma
  - Cycloplegic agents
  - Injectables (Depot)
    - Subtenon's Triamcinolone

- Oral
  - Antibiotics
  - "Steroids"
  - NSAIDs
  - Methotrexate
  - Metformin
  - Tramadol
  - Infectious Disease Management (multiple medications, brief overview)
Case #5

A 24 year old Caucasian male presents with a complaint of a bilateral red eyes. He mentions his eyes are painful, watery, and having excessively blurry vision. He has been experiencing these symptoms for the past few months, but has held it out due to a lack of insurance. His systemic history was unremarkable at initial presentation.

- What else would you like to know about this patient?
- What are the differential diagnoses?
- How do we counsel this patient on his diagnosis?
- How do we treat this patient?
- Are there any treatment pitfalls in managing this patient?

History Part 2: "Take a Crack at It"

- No recent illnesses, but was in basement apartment with some level of mold infestation
- He was experiencing some headaches, but attributed them to his nightshift hours at the gas station
- He had a strong receding hairline with silvery white tufts
- Patient was seen by my MD colleague in the practice who couldn't sort it out, so he sent him to me for a 2nd opinion. He had ordered the customary Uveitis bloodwork prior to presentation of which was all completely normal
- I ordered it again along with a chest X-ray and stool sample, all normal again.

Exam

- VA: 20/40 OD, 20/30 OS
- Positive Slit Lamp findings:
  - 4+ cell OD >> OS, no flare present
  - 2+ mutton fat KP present 360 OU
  - Multiple areas of Ps 360 OU
  - IOP: 17 OD, 17 OS
- Dilated Fundus Exam:
  - Unremarkable

Treatment and Follow Up (Initially)

- Atropine 1% bid OD
- Pred Acetate 1% q1h OD
- Generic Acular (Ketorolac) tid OU

- Seen daily until significant reduction of signs and improved visual quality
- Most signs and symptoms were minimized by the end of week #2
- Patient was moved to a 2-week schedule where steroids were reduced to bid then qid schedule
- VA improved to 20/20+ OD and 20/30 with rare cell OU

*Then, he was lost to follow up for 9 months until his sister (a pharmacist) called me 1 day to tell me the patient took off his side mirror of his car…

Long and Winding Road Ahead

- When he returned, his vision was significantly reduced
  - VA: 20/200 OD; 20/10 OS
  - IOP: 48 OD; 54 OS
  - He was still taking steroids daily as he mentioned for edema and intermittent pain relief
  - No dendrites present, but 2+ mutton fat KP's again
  - Be mindful of retinal pathology
    - Macula: CME OD>OS, tractional appearance, no CNVM net present
    - Periphery: Vit Snowballs inf with early snowbanking present
    - Acquired Optic Neuropathy not in this case yet
His IOP was lowered in office with Timolol. Patient came back for regular follow ups on a weekly to biweekly basis to monitor for over 3 months.

Then he disappeared again!

Collaborative Care Steps

- His IOP was lowered in office with Timolol. Patient came back for regular follow ups on a weekly to biweekly basis to monitor for over 3 months.

To Be VKH or Not To Be?

- Vogt-Koyanagi-Harada syndrome is an uncommon multisystem inflammatory disorder characterized by:
  - panuveitis with serous retinal detachments
  - neurologic and cutaneous manifestations: such as headache, hearing loss, vitiligo and poliosis.

Guidelines from American Uveitis Society in 1978:
- No history of ocular trauma or surgery, and at least three of the following four signs:
  - bilateral chronic iridocyclitis
  - posterior uveitis with any of the following:
    - multifocal granulomas in the vitreous, extramacular serous retinal detachments,
    - disc hyperemia or edema, or hemorrhage in the disc
  - “smellfingers” fundus, such as yellow-orange appearance of the fundus due to depigmentation of the RPE and choroid
  - neurologic signs, including tinnitus, neck stiffness, cranial nerve or central nervous system symptoms or cerebrospinal fluid (CSF) pleocytosis or 4) cutaneous findings, including vitiligo, poliosis or vitiligo

Stages

- **Stage 1: Prodromal.** This stage, also called the meningitic stage, lasts for a few days to a few weeks and often mimics a viral infection. Patients present with fever and neurologic features, including meningeval involvement (headache, confusion, stiff neck, lethargy, unconsciousness, cranial nerve or central nervous system symptoms or cerebrospinal fluid [CSF] pleocytosis). These patients often present late in this stage and when found definitively most patients report a hypersensitivity of their scalp and skin to touch.
- **Stage 2: Acute uveitic.** The second stage occurs within three to five days of the prodromal stage and lasts for several weeks. Patients often do not present to their ophthalmologist until this stage, when they experience acute ocular pain and red eyes associated with bilateral blurring of vision secondary to uveitis.
  - anterior segment involvement: chronic bilateral granulomatous iridocyclitis with multiform keratic precipitates, iris nodules and shallow anterior chambers due to ciliary edema and suprachoroidal fluid collection.
  - posterior synchysis, pupillary membrane, glaucoma and cataract are common.

VKH Stats

- In the United States, the incidence of VKH is approximately 1.5 to 6 per 1 million patients.
- More common in Japan.
- Women make up 55% of patients.
- Ages 20 to 50.
- Greater risk in Asians, Middle Easterners, Native Americans and Hispanics.
- Less common in Caucasian and African population groups.

Harada syndrome is an uncommon multisystem inflammatory disorder characterized by bilateral and often bilateral uveitis.

- **Stage 3: Convalescent.** The convalescent stage follows the acute uveitic stage gradually, usually a few months later, and may last months or years. Findings include vitiligo, alopecia and poliosis. These skin changes generally persist despite therapy. There is also uveal depigmentation, resulting in a “sunless glow” within two to six months.

- **Stage 4: Chronic recurrent.** This stage may interrupt the convalescent stage. Studies report recurrence rates of 43 percent within the first three months and 52 percent within the first six months, often associated with rapid tapering of corticosteroids. Recurrence mainly involves anterior uveitis. In this stage, complications of VKH such as glaucoma, cataract, subretinal neovascular membrane and subretinal fibrosis may develop.

Pouring Over the Literature

- My sharp intern and I decided to dig deeper looking beyond the usual and customary HLA identifiers.
- We decided to order the original bloodwork again along with HLA-DR4 and HLA-Dw53.
- After now 3 rounds of bloodwork, HLA-DR4 came back positive.
Back to Our Patient

- Does he fill these criteria?
  - Somewhat

- What do we do next?
  - Steroids are off limits (oral or implants as Ozurdex, Illuvien), so we shift to alternative therapies...
  - MTX - started with tablets (ineffective), moved on to MTX injectables (started with 1 mL and titrated dose to 1.75 mL)
  - Started weekly and shifted to 4-6 week follow-up
  - Where to inject? In the buttocks or thigh muscle.
  - Had patient start Folic Acid 1 mg/day to stave off megaloblastic anemia + B12 deficiency

What Happened?

- He achieved a more stable appearance, but not perfect
- VA was range OU
- Residual low grade cell OD>OS
- Residual intraretinal scarring OD
- No vitreous findings OU
- IOP contained mostly to mid teens
- 2+ PSC OU

Case #6

- A 38 year old Asian male presents with a painful, red left eye. He has an unremarkable systemic history at initial presentation. His associated symptoms include blurred/fluctuating vision. Finally, his past ocular history illustrates a similar event almost one year ago with the same signs and symptoms.

- What else would you like to know about this patient?
- What are the differential diagnoses?
- How do we counsel this patient on his diagnosis?
- How do we treat this patient?
- Are there any treatment pitfalls in managing this patient?

Posner Schlossman Syndrome (Glaucomatolytic Crisis)

- Unilateral
- Recurrent
- Mild discomfort or blurring of vision
- Increased IOP with open angles
- Mild anterior chamber reaction or fine white keratic precipitates (KP)
- Crises lasting from several hours to weeks
- Normal IOP and no signs of uveitis between attacks
- Normal visual fields and optic discs