

## UVEITIS:

### SYSTEMIC & OCULAR APPROACHES TO MANAGEMENT

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## Overview

- Definition
- Etiology
- Signs/Symptoms
- Classification/Diagnosis
- Systemic Associations
- Lab Testing
- Treatment
- Follow-up

## What is Uveitis?

- Uveitis:
  - Generic, broad term referring to any inflammation of the uvea (iris, ciliary body, and choroid)
    - More precise terms include iritis and iridocyclitis
  - The inciting event -> release of chemotactic factors/mediators that increase vascular permeability -> breakdown of the blood-aqueous barrier -> macrophages/lymphocytes/proteins = CELLS & FLARE

## Etiology

- 3 main underlying causes are:
  - reaction to trauma
  - autoimmune
    - response to autoantigens
  - response to infectious agent

## Uveitis – Signs and Symptoms

- ▣ Patient symptoms are often very similar with all of the various etiologies
  - Can be some differences
- ▣ Anterior uveitis
  - pain, redness, photophobia
- ▣ Intermediate/Posterior uveitis
  - Floaters, mildly decreased vision from CME, etc

## Symptoms

- ▣ Common patient symptoms include:
  - pain – ciliary spasm
  - red eye – ciliary flush
  - tearing
  - photophobia
  - blurred vision
  - Pupillary miosis



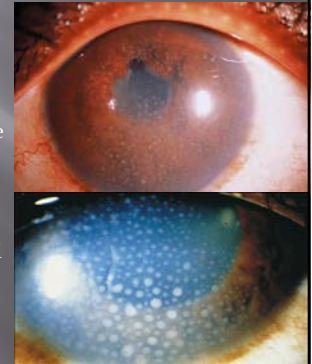
## Signs - Cells/Flare

- ▣ Critical signs are cells and flare in the anterior chamber
  - Cells are lymphocytes and macrophages and indicate active inflammation in the iris and ciliary body.
  - Flare is a result of protein leakage.



## Signs - KP's

- ▣ Keratic precipitates
  - collections of inflammatory cells deposited on the endothelial surface of the cornea from the aqueous humor
  - fresh KP's -> white and round
  - older KP's -> pigmented or faded.
  - Document size, color, distribution, and # of KP's



## Signs - Nodules

- ▣ Accumulation of cells on the iris are referred to as iris nodules. Two types exist:
  - Koeppe nodules are found on the pupillary border and Busacca nodules are on the anterior surface.
  - Nodules on the pupillary border may result in posterior synechiae between the iris and lens.



## Signs

- ▣ IOP must be monitored initially and at subsequent visits
  - usually a patient with acute uveitis will present with low pressure likely due to infiltration of the ciliary body and reduced aqueous secretion
  - the pressure may be elevated secondary to inflammation in the trabecular meshwork or by blockage of the angle by cells and debris
  - in addition treatment with corticosteroids can result in glaucoma due to the patient being a steroid responder.

## Signs

- ▣ Every patient with uveitis should have a DFE:
  - posterior inflammation (vitritis) may be overlooked in a diagnosed case of anterior uveitis
  - Macular area should be evaluated especially if there is any decrease in acuity
    - ▣ CME frequently results from anterior uveitis and should be suspected if decreased VA
    - ▣ Epiretinal membranes can form and distort the macular tissue.

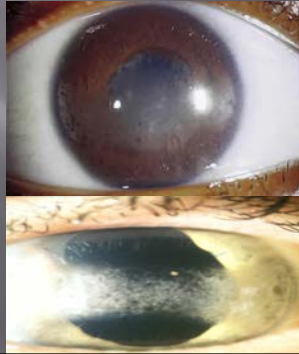
## Signs - Long-Standing Uveitis

- ▣ Cataract is a common complication of long-standing uveitis as well as chronic steroid therapy
  - most cataracts are PSC, but cortical opacities may also be seen.
- ▣ CME
- ▣ Glaucoma



## Signs - Long-Standing Uveitis

- ▣ Band keratopathy is also seen in chronic conditions such as uveitis
  - it is the deposition of calcium at the level of Bowman's and in severe cases requires chelation therapy or mechanical scraping.



## Classification

- Classification is the key to the proper diagnosis and management of the uveitic patient
- Most common classifications
  - Anterior vs. Intermediate vs. Posterior vs. Panuveitis
  - Acute vs. Chronic
  - Granulomatous vs. Non-granulomatous
  - Infectious vs. Autoimmune

## Classification of Uveitis

- 4 main questions we need answered
  - Where is the inflammation located?
  - Is disease acute or chronic?
  - Granulomatous or non-granulomatous?
  - Unilateral or bilateral?

## Anterior Uveitis Work-up

- ▣ After classification, 3 most common groups of uveitis include:
  1. Acute, unilateral (or bilateral), non-granulomatous anterior uveitis
    - ▣ Idiopathic, HLA-B27, Herpetic, Behcet's
  2. Chronic, bilateral (or unilateral), non-granulomatous anterior uveitis
    - ▣ JIA, Fuch's Heterochromic, Idiopathic, Herpetic
  3. Chronic, bilateral (or unilateral), granulomatous anterior uveitis
    - ▣ TB, Sarcoid, Syphilis, VKH

## Classification of Uveitis

- ▣ Secondary Questions:
  - Demographics of the patient
  - Has this happened before? If so did it respond to treatment?
- ▣ Systemic questions:
  - Lung /breathing problems?
  - Rashes / skin problems?
  - Joint problems or low back pain?
  - Urination issues?
  - Digestive problems – diarrhea? Bloody stools? Cramps?
  - Have you been out of the country recently?
  - Have you been in a wooded area? Ticks?
  - Any other systemic/autoimmune diseases?

## Anterior Uveitis Work-up

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## Duane's Ophthalmology

- Most commonly encountered uveitic causes:
  1. Traumatic
  2. Post-surgical
  3. Anterior Idiopathic
  4. HLA-B27 associated uveitis
  5. JIA associated uveitis
  6. Fuch's heterochromic iridocyclitis
  7. Posner-Schlossman syndrome
  8. Herpetic anterior uveitis
  9. Pars Planitis
  10. TB/Sarcoid/Syphilis

## I. Acute, unilateral (or bilateral), non-granulomatous anterior uveitis

- Most common group
  - Idiopathic - most common cause of anterior uveitis
  - HLA-B27 - 2<sup>nd</sup> most common cause of anterior uveitis - nearly 20 - 50% of acute anterior uveitis pts are HLA-B27+
    - Ankylosing Spondylitis
    - Reactive Arthritis (Reiter's syndrome)
    - Psoriatic Arthritis
    - Inflammatory Bowel Disease
  - Herpetic
  - Behcet's

## HLA-B27 (+) Associated Uveitis

- Acute, rapid onset of unilateral pain and intense photophobia
- Moderate to severe inflammatory reaction
  - 3-4+ cells
  - Hypopyon
  - Fibrin meshwork
  - Plasmoid aqueous
- Aggressive treatment important
  - Average tx time = 6-10 weeks

## HLA-B27 (+) conditions

- Ankylosing Spondylitis
  - Low back pain
  - Diagnosis:
    - Abnormal S-I joint X-ray
    - Increased ESR
  - Treatment:
    - Exercise
    - Oral NSAID's

## HLA-B27 (+) conditions

- Reactive Arthritis (Reiter's syndrome)
  - "Can't see, can't pee, can't climb a tree"
    - Conjunctivitis/Uveitis
    - Urethritis
    - Arthritis - lower joints
  - Dermal skin lesions
  - Diagnosis:
    - Elevated ESR
  - Treatment:
    - NSAIDS

## HLA-B27 (+) conditions

- Inflammatory Bowel Syndrome
  - Ulcerative Colitis
  - Crohn's Disease
    - Stomach problems - diarrhea, bloody stools, abdominal cramping
  - GI referral - tx with diet change and immunosuppressives
- Psoriatic Arthritis
  - Arthritis upper extremities
  - Characteristic skin lesions



## Herpetic Uveitis

- ▣ HSV
  - H/O unilateral red eye
  - Corneal scarring
  - Active corneal disease
  - IOP increase & iris atrophy
- ▣ HZO
  - Characteristic skin lesions
  - Iris atrophy

## 2. Chronic, bilateral (or unilateral), non-granulomatous anterior uveitis

- ▣ Most common cause
  - Juvenile Idiopathic Arthritis (JIA)
    - 80% of pediatric uveitis cases are associated with JIA
    - Slow, chronic onset; mild sx's, many chronic signs
    - ANA (+) triples the risk of uveitis - base f/u's on this
    - RF (-)
    - Tx: NSAID's, steroids, immunosuppressives

## JIA lab tests

- ▣ ANA - very non-specific test
  - Used to confirm an autoimmune collagen vascular disease
    - Lupus and JIA
    - Weaker associations: Sjogren's, RA, scleroderma, AS, MG
  - 15% of normals have a mildly elevated ANA (diabetics, elderly women)

## JIA lab tests

- ▣ RF
  - 80% of RA pts are seropositive
  - Most often JIA patients are RF negative
    - ANA (+) and RF (-) -> significantly increased risk of uveitis in a suspected JIA patient

## 2. Chronic, bilateral (or unilateral), non-granulomatous anterior uveitis

- ▣ More common causes
  - Fuch's Heterochromic Iridocyclitis
    - Low-grade chronic uveitis with iris heterochromia
    - Usually unilateral - cataract & glaucoma
    - Uveitic eye is usually lighter in color
  - Idiopathic
  - Herpetic

### 3. Chronic, bilateral (or unilateral), granulomatous anterior uveitis

- ▣ Most common causes
  - Sarcoid
  - Syphilis
  - TB

### Sarcoidosis

- ▣ Systemic granulomatous inflammation -> unknown etiology - Young, black, females
  - Pulmonary - 95%
  - Ocular - 25-70%
  - Skin
- ▣ Diagnosis
  - Serum
    - ACE, lysozyme, calcium
  - Chest X-ray, Gallium scan, biopsy of granulomas
- ▣ Treatment
  - Immune suppression

### Syphilis

- ▣ Infection with spirochete *T. pallidum*
  - Primary stage - Chancre
  - Secondary stage - rash palms of hands/soles of feet
    - Most ocular involvement
  - Latent and Tertiary Stage
- ▣ Diagnosis:
  - RPR or VDRL - general non-treponemal tests
  - FTA-ABS or MHA-TP - specific treponemal tests
- ▣ Treatment:
  - Penicillin

### TB

- ▣ Infectious disease caused by *Mycobacterium tuberculosis*
  - Very rare
  - Exposure/Cough/Pulmonary involvement
  - Granulomatous ant uveitis, Choroiditis, phlyctenular keratoconjunctivitis
- ▣ Diagnosis
  - PPD - not useful in uveitis patients
  - Chest X-ray/Sputum culture
- ▣ Treatment
  - Isoniazid, Rifampicin, Ethambutol, Pyrazinamide

### Uveitis Work-up Rule of Thumb

- If a patient presents with a uveitis that is:
    - First episode
    - Unilateral
    - Non-granulomatous
    - Mild->moderately severe AND
    - Fairly good health
- = no further work-up required**

### Uveitis Work-up Rule of Thumb

- ▣ If the uveitis is:
    - Recurrent
    - Bilateral
    - Severe
    - Granulomatous OR
    - Resistant to standard treatment;
    - AND History does NOT point to a specific condition
- = Non-specific baseline eval**
- ▣ Work-up:
 

- CBC	- Lyme titer (depending on what area of the U.S.)
- ESR/CRP	- PPD/anergy panel and Chest X-ray
- ANA/RF	- RPR or VDRL and FTA-ABS or MHA-TP
- HLA-B27	- ACE

## Lab Work Costs

- ▣ CBC - \$9 - 12
- ▣ ESR - \$5 - 7
- ▣ CRP - \$18 - 24
- ▣ HLA-B27 - \$36 - 49
- ▣ ANA - \$15 - 21
- ▣ RF - \$8 - 11
- ▣ ACE - \$20 - 28
- ▣ VDRL/RPR - \$6 - 8
- ▣ FTA-ABS/MHA-TP - \$18 - 25
- ▣ Lyme titer - \$24 - 32
- ▣ Chest X-ray - \$75 - 250
- ▣ Total = \$216 - 443

## Uveitis Work-up Rule of Thumb

- ▣ If the history, symptoms, and/or signs point strongly to a certain etiology, then the work-up should be tailored accordingly
  - that is, the lab tests should be tailored for the condition suspected
    - ▣ Ex: Black female with a chronic, granulomatous uveitis - likely chest x-ray, serum ACE and/or lysozyme, PPD, gallium scan of head and neck; consider biopsy of any skin or conjunctival nodule.

## Treatment of Uveitis

- ▣ Treat the disease properly
  - Minimize complications of the disease itself
  - Minimize complications of the treatment
- ▣ 2 main drugs/drops
  - Cycloplegics
  - Topical Corticosteroids

## Treatment

- ▣ Cycloplegia:
  1. used for reduction of pain,
  2. break/prevent the formation of posterior synechiae
  3. also functions in the reduction of inflammation

## Cycloplegics

- ▣ Common cycloplegic agents include:
  - cyclopentolate 1-2% tid for mild-to-moderate,
  - homatropine 5% or
  - scopolamine 0.25% or
  - atropine 1% bid-tid for moderate-to-severe inflammation
- ▣ most common is the use of Homatropine 5% bid

## Treatment

- ▣ Steroids: necessary for the treatment of active inflammation
- ▣ Most commonly used:
  - Prednisolone acetate 1% (Pred Forte 1%)
  - Prednisolone phosphate???
  - Loteprednol etabonate 0.5% (Lotemax)
    - ▣ Drop, gel, ung



## Treatment

- Durezol (difluprednate ophthalmic emulsion) 0.05%
  - Dosing QID
  - Thought to be as potent or even more potent when compared to Pred Forte q2h
  - Minimal to no shaking of the bottle
  - No BAK



## Treatment

- Topical administration is most common though periocular injections and systemic meds are useful for posterior uveitis and difficult cases
- Dosing:
  - Pred Forte q1h or q2h
  - Durezol QID
  - Lotemax ung qhs

## Treatment

- NOTE: it is crucial to taper your steroid treatment!
  - You will have a rebound inflammation if you simply remove your patient from their steroids...
  - How long???
- Treat beyond the cell & flare
  - 5-7 days

## Rules For Managing Uveitis

1. Remember the classifications.
2. Determine if there is corneal involvement
3. Check the IOP.
4. Rule out recent surgery
5. Determine the severity.
6. Is this a chronic problem?
7. Treat strongly.