Management of Posterior Segment Uveitis

**Posterior uveitis classification**
- Focal or Multifocal
- Chorioiditis or Chorioretinitis
- Retinitis or Retinochoroiditis
- Neuroretinitis

SUN = Standardization of uveitis nomenclature 2004

**Presentation goes beyond classification**
- Vasculitis
- Vitritis
- Variable Neovascularization
- Vascular occlusions
- Variable IOP
- Variable RDs
- CME
- Vascular retinopathy

- Chorioretinal atrophy
- Optic atrophy
- Cataracts
- Glaucoma

Retinitis vs vasculitis in CMV-R

Internet photos

**The challenge of posterior uveitis**
- Encompasses a broad spectrum of diseases
- Leading cause of blindness among 20-50yo
  - Permanent VI if untreated
    - Aggressive tx is typically a NECESSITY
- It is likely a manifestation of UNDERLYING systemic disease
  - Many cases require SYSTEMIC tx
- May affect the host regardless of their immunity

**Ohio river valley & HISTO**
- 20-50 yo
- 6x more prevalent in whites than blacks

Endemic to areas bordering Ohio river valley
- (Indiana, Ohio, Illinois, Kentucky, Tennessee, and Mississippi)
- Parts of mid-Atlantic (Maryland, W. Virginia & Virginia)
- 200,000 NEW report/yr
- Many will lose vision in 1 or both eyes attributed to HISTO

**Internet photos**
Possible associations

- May develop flu-like symptoms (but not common)
  - Scars in lungs
  - Dense nodules with central calcification

Refer for possible neoplasm nodule in lung
Note: calcifications

Ocular Histoplasmosis

- Linked to *H. capsulatum* (a fungus)
  - Found in soil with high concentration of fecal material (excrements) from chickens, pigeons and bats
  - GUANO...OH MY!

Ocular Histoplasmosis Syndrome

- Inhale spores

OHS can lag behind systemic infection by many yrs

Dx & Treatment options

<table>
<thead>
<tr>
<th>Dx</th>
<th>Treatment</th>
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<tr>
<td>Clinical Dx</td>
<td>CNVM treatment</td>
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<tr>
<td>OCT/FA for CNVM</td>
<td>Antifungal used only if concomitant systemic involvement</td>
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<td>?Histo skin test</td>
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Dx

Treatment

- CNVM therapy
- Antifungal used only if concomitant systemic involvement

WDS: Is it a single disease or distinct entities?

- *Idiopathic variable multiple?* bilateral white dots
- *Viral prodrome*
- Variable symptoms
- VL, photopsia, scotoma, floaters

idioopathic chorioretinal inflammatory syndromes
White Dot Syndromes

<table>
<thead>
<tr>
<th>MEWDS</th>
<th>Birdshot</th>
<th>Serpiginous</th>
<th>AMPPE</th>
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Entities that you typically follow

AMPPE Acute Multifocal Placoid Pigment Epitheliopathy

Birdshot Chorioretinopathy

MEWDS Multiple evanescent white dot syndrome

Serpiginous Choroiditis

Steroids & Posterior Uveitis

- Commonly used to target inflammation, depending on severity one may use:
  - Topical (rarely alone)
  - Oral (common)
  - Periocular
    - Intravitreal
    - Sub tenon’s
      - Chronic cases
  - Implants (Retisert & Ozurdex)
    - Chronic NON-infectious cases

Retisert (B&L) 2005

For non-infectious chronic uveitis
Last for ~2.5 yrs
Most concerning side effects: Complications of surgery, IOP rise & cataracts

Ozurdex™

- VERY POTENT
- Short ½ life
- First drug approved for tx of ME associated with VO (June 2009)
- Biodegradable dexamethasone (0.7mg) implant injected through 22-gauge applicator
  - Last few months
- Approved in 2010 w/ 6M efficacy

Non-infectious

<table>
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<tr>
<th>Immune-related</th>
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<tr>
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<tr>
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<td>Pars planitis</td>
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<tr>
<td>Bechet’s</td>
<td>Sympathetic ophthalmitis</td>
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The infectious posterior uveitis

<table>
<thead>
<tr>
<th>Nematode</th>
<th>Bacteria</th>
<th>Protozoa</th>
<th>Fungi</th>
<th>Viral</th>
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<tr>
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<td>Syphilis</td>
<td>Toxoplasmosis</td>
<td>Histo</td>
<td>CMV</td>
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<tr>
<td>Toxocariasis</td>
<td>Lyme</td>
<td>Candida</td>
<td>ARN</td>
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<td>TB</td>
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<td>PORN</td>
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Depending upon presentation, specific hx can be elicited and additional labs may be necessary

When managing posterior uveitis... KEY is to avoid John Wayne's shotgun approach to investigation!

Narrow the possible culprits by recognizing the clinical syndrome: medical hx, SocHx, recent contact, geographic & demographic

And then consider ordering all these

- General
  - Erythrocyte sedimentation rate (ESR)
  - C-reactive protein (CRP)
  - VDRL/FTA-ABS
  - Chest X-ray (CXR)
  - Angiotensin converting enzyme (ACE)
  - ANA (antinuclear antibody)
  - CBC (complete blood count)
  - Meningeal test: Purified Protein Derivative (PPD)
  - Lyme titer (depending on area)

- Specific
  - HLA typing
  - Toxo Elisa titers
  - Western blot
  - RF (rheumatoid factor)
  - CSF (cerebrospinal fluid)
  - DNA polymerase chain reaction

Lack of convenient biopsy may hinder Dx

Ocular Toxoplasmosis

Some studies suggest that half of all fundus infections/inflammations are due to toxoplasmosis

Management

- Enlist the assistance of an infectious disease physician in the management of the patient
- Attempt to educate the community regarding expectant mother avoidance of cat litter and undercooked meat
- Educate patient regarding inactive scars and follow at routine intervals
- An active attack usually is self-limited, lasting up to 4 months
- Active lesions/laboratory tests:
  - serum antitoxoplasma antibody at 1:1 dilution
  - ELISA
  - FTA-ABS
  - PPD with anergy panel
  - Chest x-ray
  - Toxocara ELISA
  - HIV test if patient is at high risk

Toxoplasmosis retinochoroiditis tx

- Uveitis: PF + cycloplegic
- The classic TRIPLE therapy (4-6 wk course)
  1. Daraprim (Pyrimethamine): Two 50mg tablets (100mg) loading dose, followed by 50mg QD (may be divided BID)
     - Range is 75-100mg loading dose, followed by 25-50mg
     - BM suppression & liver toxicity
  2. Steroid PO 0.5mg-1mg/kg/day (40-80mg QD)
  3. Sulfadiazine: 2g loading dose, followed by 1g QID
     - Initial loading dose ranges from 2-4mg
     - BM suppression & hypersensitivity s/e

MUST ADD: Folic acid 3-5mg 2-3x/week to the above regimen
The Paradox:
To treat or not to treat...That is the question!

- **Condition is self-limited & meds may be toxic**
  - Resolution ~4wks
- **Treatment recommendations**
  - Depends on location, size or complications
  - Active for >1M
  - Lesion in HIV pt
  - Regardless of location or presentation
  - Macular/ON involvement or threaten
  - Moderate-severe vitritis associated VL
  - Tx is also consider for LARGE active lesions (>1DD)
  - MONOCULAR

Small peripheral lesions (outside the posterior arcades) – TYPICALLY observed

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**Contemporary tx**

- Bactrim DS (Co-trimoxazole) 800/160
  - Double strength (DS) QD
  - 800mg sulfamethoxydazole + 160mg trimethoprim
  - Use for 4-6wks
- **ASK PT ABOUT SULFA ALLERGIES...**
  - May use regular strength as BID
  - Cheaper & safer profile than CLASSIC tx

1990 Am Uveitis Soc had NO consensus of most appropriate tx
Treatment does NOT eliminate tissue cyst, thus cannot PREVENT recurrence.

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**Toxoplasmosis Ocular Treatment REVIEW**

- No clinical trial has demonstrated that one antibiotic is superior to another
  - Gilbert 2002 (review of current research in toxo)
- Note when using steroids
  - Prior to initiating therapy CBC and TB test are needed
- **Do not Rx oral steroid w/o antibiotics**
  - Sabates 1991
  - When tapering corticosteroids, REMEMBER that antimicrobial agent are continued until corticosteroids are STOPPED!

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**Ocular Toxocariasis**

- **Medical Treatment Options**
  - Corticosteroids (systemic/periocular)
    - Moderate-severe or visual threatening presentations
    - 0.5mg-1mg/kg QD for wks-month with taper

Treatment is designed to minimize host defense system
Antihelmantics

- If used, it is in **Combo** with steroids if:
  - Ocular dz not responding to steroids alone
  - Systemic disease is present
  - Variable choices X 7-10d
  - Thiabendazole (Mintezole)
  - Albendazole (Albenza)
  - Diethylcarbamazine citrate (Hetrazan)
  - Mebendazole

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**How to determine proper dosage?**

- Determine weight of patient (in Kg)
- Determine total amount of med per day based on mg/Kg/day
- Determine frequency of dosing
- Determine amount of med to administer at each dosing

**Example:**  
**Erythromycin for 60 lb child**

- Available concentration 200 mg or 400 mg
- Recommended dose is 30-40 mg/kg/day

SO……..

- 60 lb = 27 kg
- 60/2.2

- Dosage = mg (recommended)/kg/day
- 30 mg X 27 kg = 810 mg/day
- Dosing interval (what's available)
- 810 mg / 4 doses = 202.5 mg
- Rx: 200 mg QID

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**Rx Writing**

- In children there is a 3X greater risk of medication error & related injury
- Use hourly dosing rather than number of times per day
  - Q 6 hours in lieu of QID
- Decide on proper administration
- Be careful with similar names
  - TobraDex and Tobrex

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**Toxocariasis**

- Human infestations by *worm’s larva migrans*
  - Dog nematode (*T. canis*)
  - Cat nematode (*T. cati*)
- Infestation
  - Ingestion of the ova
  - Eating contaminated foods
  - Close contact with larvae

**Young kids are most susceptible**
PUPPY’s feces
May remain in soil

Unilateral Granuloma posterior pole
(+ VITRITIS

Ocular Toxocariasis

- Surgical Intervention
  - Vitrectomy &/or RD surgery:
    - If TRD or ERM present
    - Considered if extensive fibrosis present
  - Photocoagulation
    - May be used for mobile larvae but at what risk?
  - Don’t forget to recommend animal de-worming

The future treatment

- The genome of BOTH toxocara have been sequenced
  - May pave the way for future treatment & prevention

Ocular Syphilis

- Direct invasion of Treponema pallidum
  - Spirochete (gram negative bacteria)
- Congenital form
- Acquired form

Acquired: Early stages

- Primary
  - At inoculation site
    - Chancre: Round, firm & painless ULCER
    - Few wks after inoculation
- Secondary
  - Systemic treponemal spread
    - RASH (maculopapular) Rough, red & diffuse
    - Palms of hands and soles of the feet
    - Ocular manifestations
Ocular manifestations

- conjunctivitis/(epi) scleritis
- interstitial keratitis
  - **BILATERAL**
- uveitis
- iris Roseolae (**rare**)
- cataract/secondary glaucoma
- posterior uveitis
- pupillary abnormalities/optic neuropathies
  - Tonic Argyll Robertson pupil

Acquired: Late stages

- Latent (hidden)
  - Can last yrs
  - (+) blood tests without si/s
- Tertiary (3rd stage): 1-10yrs after exposure
  - Neurosyphilis (10% of cases)
    - Paresis & meningitis
    - Neuro-ophtalmic Si/s
  - Cardiovascular syphilis
    - Affects coronary or aorta
    - Gumma
    - Soft non-cancerous growth
    - Benign
  - T-cell response to the bacteria

DIVERSE PRESENTATION

- Posterior findings (50% bilateral)
  - Retinitis
  - Focal or Diffuse multifocal chorioretinitis
    - Inactive: Salt & pepper Fundus (DDx)
  - But normal ERG
  - Vitritis
  - CME
  - Peri-vasculitis
  - Vein occlusion
  - Optic neuropathy
  - Neovascularization

What questions should you consider asking?

- Elicit sexual history
  - Sexually active?
  - Multiple partners?
- Ask about **specific rashes**
- Ask about ulcers
- Hx of HIV
- IV drug user

Reviewing tests & importance to ODs

- If suspect Syphilitic posterior uveitis
  - Use a non-treponemal test (i.e. VDRL) to screen for the disease
    - Obtain quantitative measurement of antb production, which can be used later to determine if tx is affective
  - Use the treponemal test (FTA-ABS) to confirm the (+) screening test
    - can also help determine the presence of the ANY stage (including LATENT stage)

Possible cause?

- Cat Scratch Disease
- Lyme Disease
- Syphilis
- Viral
- Toxoplasmosis
- **NOT AION**
- MORE...

He adds the fact that he was hunting recently & thought he got poison IVY...likely culprit?

Doxycycline 100mg PO BID
Lyme disease

- Most common arthropod-borne disease
  - Endemic to N.A., Europe & northern Asia
  - 1st report in Lyme, Connecticut (1975)
  - Like syphilis, it is a spirochete illness (*Borrelia burgdorferi*)
  - Ticks are the carriers
  - White tail Deer is the most common host
  - Prevalence in summer months

Systemic clinical manifestations...

- **Stage 1: RASH (Erythema migrans)**
  - Flue like symptoms: Fever, headache, aches/fatigue, joint pain
- **Stage 2**
  - Neurological manifestations
    - Bell’s palsy & peripheral neuropathy & optic neuropathy
- **Stage 3**
  - Associated eye signs
    - Posterior uveitis
    - Carditis (heart inflammation)
    - Arthritis - chronic/relapse (rheumatologic)
    - Knee

Variable ocular manifestations

- Just like syphilis
  - Anterior segment uveitis
  - IK
  - Conjunctivitis/scleritis
  - Optic neuritis
  - Chorioretinitis
    - Pars planitis
    - Vitritis
    - Pigmentary changes
    - Vasculitis

Dx criteria

- **Classic skin rash + Hx of exposure within the month**
  - Hx of a bite
  - Visit in endemic area
  - If no rash, then Hx of exposure + an organ involvement
  - Serological testing + rash
    - ELISA titers & Western blot for *B. burgdorferi* (IgG and IgM)
    - Be careful with endemic areas

International Lyme & Associated Diseases Society

- www.ilads.org
  - Fosters care for Lyme disease pts through physician training
    - Emphasis on “how to properly diagnose the disease”
    - Current treatment
      - Set up today’s guidelines in 2006
    - Advancements in research
**Lyme disease treatment 14d course**

- 1st line treatment
  - Doxycycline 100mg PO BID or Tetracycline 500mg QID
  - Amoxicillin 500mg PO TID or PNC 500mg QID
- Allergies to 1st line treatment
  - Erythromycin 250mg PO QID
  - Cefuroxime axetil 500mg PO BID
- Neurological involvement
  - PNC G intravenous...JUST like ______!

Most effective treatment for ocular manifestation is unclear

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**Sarcoidosis**

- Noncaseating (degeneration) granulomatous inflammatory MULTI-systemic disease
  - Chronic with remission/exacerbation
- Prevalence: 10-20 cases/100,000
  - In US it is commonly observed in 20-50 y.o. **black** FEMALES (F:M 3:2)
  - Progressive/relapse

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**Multi-Systemic Disease**

- Lungs (95%)
  - May be the cause of death
- Ocular system
  - 25-60% have ocular manifestations
- Lymph nodes
- CNS
- Salivary glands
- Liver/spleen/heart

What is **Sark & oid**?

*Flesh-like skin lesions*

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**Ocular involvement varies in severity**

- Anterior
  - Uveitis
    - Chronic, mutton fat (granulomatous), iris nodules
    - Lid nodules
    - Lacrimal gland infiltration
    - Band keratopathy
    - Orbital granuloma
    - proptosis
- Neurological involvement
  - Optic nerve edema (direct infiltration or compression)

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**Most common cause of fungal infection**

**CANDIDA**

- Endogenous endophthalmitis
  - IV drug users (heroin addict)
  - AIDS pts or other debilitating dzs (DM, alcoholism, cancer, transplantation)
  - Other intra-ocular hematogenous spread
    - recent major surgery (abdominal), bacterial sepsis, indwelling intravenous catheters/placement of central venous device
- Exogenous endophthalmitis
  - Organism enter eye s/p ocular trauma or surgery

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**The paradox**

- Although immunosuppression is a risk factor for fungal infections, candidal endophthalmitis is NOT common in AIDS pts
  - Immune response is necessary
Candida endophthalmitis

- Chorioretinitis
  - Creamy whitish chorioretinal spot
    - Single or multiple
    - Isolated or confluent
  - Progress to scars
- Vitreous involvement
  - More pronounce in advance stage of the dz
  - vitreal pearl
  - “puff ball”

How is the DIAGNOSIS confirmed?

CLINICAL APPEARANCE AND A (+) FUNGAL CULTURE
BLOOD CULTURES
VITREAL BIOPSY
But this is challenging

Treatment
Back to the case

Medications:
- 100 mg **Diflucan** Qd X 1 month
- HAART regiment
- CMV-R tx
  - Valganciclovir (Valcyte) PO 900mg BID X 3 wks
  - Intravitreal foscarnet/ganciclovir intravitreal injection combination

Which of the following is a common complications of CMV-R?

A. Optic atrophy
B. Retinal detachment
C. Severe vitritis
D. Neovascularization

Inactive CMV-R

Pt was asymptomatic and NEVER treated before for CMV-R but had been taking HAART cocktail X 2 yrs
WHAT HAPPENED?

Viral load undetectable & CBC was relatively high

Cat Scratch Disease

- Infection Bartonella henselae (1985)
- Gram (-) bacteria
- Cat’s scratch is principal RESERVOIRE.
  - Watch Out! It’s the Attack of the Rawr Kitten!
Clinical Picture 1-3 weeks after inoculation

- Lymphadenopathy
- Flu like prodome (fever)
- Regional swollen lymph

Parinaud’s Oculoglandular Syndrome
Conjunctivitis + PAN + fever

Ocular manifestations

- Parinaud’s oculoglandular syndrome
- Vitritis/uveitis
- Focal Chororetinitis
  - With or with associated optic nerve swelling
- Neuroretinitis

Diagnostic Criteria

- Bartonella titers
- Lymph node biopsy of bacilli
- Known cat contact
- Regional lymphadenopathy

Treatment Options:
Bartonella susceptible to a # of antimicrobial

- Macrolide
  - Azithromycin 250mg PO
  - Erythromycin 500mg QD
- Bactrim QD
- Ciprofloxacin 20-30 mg/kg BID
- Rifampin 600-900mg PO QD
- Doxycycline 100-200mg BID
  - Can’t use in pt < 8yo

Review of Posterior Uveitis

- May affect immunocompromise & immunocompetent pts
- Make correct diagnosis in timely fashion
  - Management requires proper lab workup
  - Treat aggressively
  - Primary goal is to prevent damage & reduce complications
- Co-management approach may be a necessity
  - Rheumatologist, infectious dz, PCP...
  - Referral for further treatment:
    - If posterior uveitis unresponsive to topical/oral treatment
    - Tx of underlying disease