Clinical Decisions in Uveitis Management
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Uveitis Take Home Pearls
- Be a detective and find the cause
- Be aggressive with treatment
- Don’t taper too soon
- Treat and follow

“The Common Eyeritis”
- 32YOWM, Red, Painful Eye OD, Photophobic, No discharge
- No previous episodes
- Ocular/Medical Hx: Unremarkable
- No other associated symptoms
- SLE: 2+ injection / 2+ cells
What is Your Treatment?

- Which steroid should you use?
- What about cycloplegics?
- When do you prescribe an oral medication?
- Would you consider lab testing?
- When to schedule follow-up?

Anatomy and Physiology

- Uveal Tract
  - Iris – anterior extension of CB
  - Ciliary Body – posterior extension of iris
    - Accommodation
    - 2 Layers of epithelium
      - Outer – RPE
      - Inner – sensory retina, produces aqueous
    - Choroid
      - Supplies nutrition for external retina
      - Function is nourishment

Uveitis Demography

- 3rd leading cause of preventable blindness in developed countries
- Prevalence of 38 per 100,000 population
- Mean age of onset is 30.7 years (+/-15)
- Approximately 85 causes of uveitis

Uveitis Demography

- Age
- Sexual predilection
- Race
- Family History
- Geographic
- Other
  - Personality
  - Trauma
  - Exposure
  - Psychological
  - Social habits
  - Travel

Classification of Uveitis

- Anatomical / structural location
- Etiology
- Acute vs. Chronic
- Non-granulomatous vs. Granulomatous
- Unilateral vs. Bilateral

Anterior Uveitis

- Causes
  - Idiopathic
  - Traumatic
  - HLA-B27
  - Herpetic
- Can be recurrent, recalcitrant, granulomatous, or non-granulomatous
Intermediate Uveitis

- 8-15% of all uveitis
- Involved pars plana, peripheral retina, vitreous
- Anterior vitreous cells
- Associated symptoms???

Posterior Uveitis

- Many systemic causes
- Many ocular diseases
- Consider infectious causes
- Common signs – retinal vasculitis

Panuveitis

- Defined as inflammation of the entire uvea
  - Anterior, intermediate, and posterior
  - Most serious of all uveitis cases

Etiology of Uveitis

- Idiopathic
- Autoimmune
- Infectious
- Infiltrative
- Traumatic
- Ischemic
- Iatrogenic
- Inherited

Is it Acute or Chronic?

- Sudden or insidious
- Systemic history
- Limited or persistent
- Response to therapy
- Recurrent
- Bilateral

Histopathology

- Granulomatous
  - Mutton fat KPs
  - Iris nodules
  - Often chronic
- Nongranulomatous
  - Fine KPs
  - Often acute
History is Key

- Patient medical history
- Consider Past, Family, and Social History
- Practical Diagnostic Approach
  - Naming
  - Meshing

Uveitis

- Classic Symptoms
  - Acute onset
  - Decreased vision
  - Redness
  - Photophobia
  - Pain
  - Excessive tearing

Clinical Signs

- VA
- Conjunctiva
- Cornea
- Anterior chamber
- Iris
- Pupil
- IOP
- Lens
- Vitreous
- Disc edema
- Macular edema
- Periphlebitis

Case Example

- Referred for second opinion
- IOP improved to 32 mm Hg
- Dx: HSV Iridocyclitis OD
- Tx:
  - Valacyclovir 500 mg TID PO
  - Loteprednol etabonate QID OD
  - Timolol BID OD

HSV Iridocyclitis

- Granulomatous vs. Non-granulomatous
- Presents with KPs, stromal edema, uveitis
- Trabeculitis
- Patchy iris defects
**Anterior Chamber Cells**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cells in Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>0.5+</td>
<td>1-5</td>
</tr>
<tr>
<td>1+</td>
<td>6-15</td>
</tr>
<tr>
<td>2+</td>
<td>16-25</td>
</tr>
<tr>
<td>3+</td>
<td>26-50</td>
</tr>
<tr>
<td>4+</td>
<td>50+</td>
</tr>
</tbody>
</table>

Abbreviation: SUN, standardization of uveitis nomenclature

**Anterior Chamber Flare**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>1+</td>
<td>Faint</td>
</tr>
<tr>
<td>2+</td>
<td>Moderate (iris / lens details clear)</td>
</tr>
<tr>
<td>3+</td>
<td>Marked (iris / lens details hazy)</td>
</tr>
<tr>
<td>4+</td>
<td>Intense (fibrin / plastic aqueous)</td>
</tr>
</tbody>
</table>

Abbreviation: SUN, standardization of uveitis nomenclature

**Anterior Synechiae**

- Occurs in both acute and chronic uveitis
- Watch for angle closure
- Commonly found in:
  - Deeply pigmented eyes
  - Granulomatous disease
  - Traumatized eyes

**Posterior Synechiae**

- Chronic anterior uveitis
- At location of Koepppe nodules
- Found in granulomatous and non-granulomatous forms
- Does not occur in pars planitis

**Grading of Vitreous Haze**

- Grade 0 - Good view of NFL
- Grade 1 - Clear disc and vessels but hazy NFL
- Grade 2 - Disc and vessel hazy
- Grade 3 - Only disc visible
- Grade 4 - Disc not visible
Ancillary Testing

- Fluorescein angiography
- Indocyanine green angiography
- Optical coherence tomography
- Ultrasound

Complications of Uveitis

- Evolution into chronic uveitis
- Macular edema
- Ocular hypertension
- Glaucoma
- Cataract

Case Example

- 44yo Asian American c/o blurred VA, redness, tearing, peri-orbital edema starting 2-3 days prior
- Med Hx: Uncontrolled DM (Dx in 1998)
- Vasc: OD 20/60 PH 20/30
  OS 20/80 PH 20/40
- IOP: 21 / 18

When Should Lab Tests Be Ordered?

- Bilateral cases
- Hyperacute cases
- Atypical age group
- Worsens with tapering
- Recurrent uveitis
- VA worsens
- Recalcitrant cases
- Immunosuppressed
Uveitis:
Common Systemic Associations

• Most common cause
  – Idiopathic: 38-70%

• Other systemic causes
  – HLA-B27 related disease
  – Sarcoidosis
  – Systemic Lupus Erythematosus
  – Rheumatoid Arthritis
  – Behcets Disease

Lab Testing

• Minimum lab testing
  – CBC with differential
  – Erythrocyte sedimentation rate (ESR)
  – Angiotensin converting enzyme (ACE)
  – Venereal disease research laboratory (VDRL)
  – Fluorescent treponemal antibody absorption (FTA-ABS)
  – Lyme titers in endemic areas
  – HLA-B27
  – Antinuclear antibody (ANA)
  – Urinalysis
  – Chest X-ray
  – PPD

Considerations

• Joint pain
• Breathing problems?
• Retrobulbar eye pain?
• Skin lesions?
• Retinal scars?

Complete Blood Count (CBC)

• Order with differential
• Used to evaluate general health status
• Helps differentiate infection vs. inflammation
• Additionally, a CBC can detect a white blood cell malignancy such as leukemia or lymphoma

Erythrocyte Sedimentation Rate (ESR)

• Westergren ESR is best
• Order STAT
• Normal values
  – 0-13 mm/hr (males)
  – 0-20 mm/hr (females)
• > 50 mm/hr is suggestive of temporal arteritis
• If elevated, start oral prednisone 60 – 100 mg / day
• Temporal artery biopsy to confirm within one week
C-Reactive Protein

- Ordered in conjunction with ESR
- Checks inflammatory component of enzymes secreted from the liver
- Consider ESR & CRP in autoimmune conditions
- For GCA, 99% sensitivity with ESR and CRP

Angiotensin Converting Enzyme (ACE)

- Produced by a variety of cells including granulomatous cells
- Serum ACE levels reflect the total amount of granulomatous tissue in the body
- Screen for sarcoidosis
  - 75% sensitive
  - 95% specific
- False positives include:
  - TB
  - Lymphomas
  - Leprosy
- Consider serum lysozyme / calcium assay

Sarcoidosis

- Often young, African American females
- Granuloma forming disease
- Enlarged lymph nodes
- Shortness of breath
- Fatigue
- Diagnostic Testing
  - Chest X-ray
  - Elevated ACE
  - PPD: TB vs. Sarcoid
  - Biopsy of nodule

Purified Protein Derivative (PPD)

- Skin test to screen for tuberculosis
- Intradermal injection of 0.1ml of soluble antigen from a given TB organism in forearm
  - Positive test: 5 – 15 induration in 2-3 days
- Specificity increased with chest x-ray
- False positives include prior exposure to TB

Screening Tests for Syphilis

- Venereal Disease Research Lab (VDRL)
  - VDRL may become non-reactive in latent syphilis or after successful treatment
  - False positives may occur in:
    - Pregnancy
    - Infectious mononucleosis
    - Systemic lupus erythematosus
- Rapid Plasma Reagin (RPR)
  - Alternative to VDRL

Fluorescent Treponemal Antibody Absorption (FTA-ABS)

- Detects specific antibodies against T pallidum
- Confirms diagnosis of syphilis
  - More specific than VDRL
- More sensitive in primary syphilis
- Test may remain positive for life
- Reactive:
  - Primary syphilis 95%
  - Secondary 100%
  - Late latent 100%
  - Tertiary 96%
  - False positives may occur in pregnancy and SLE
**Syphilis**

- STD caused by T pallidum / great imitator / any tissue and organ
- Sexually active / multiple partners
- Systemic Sx – Depends on stage – primary painless ulcer / secondary skin rash palms, soles, trunk / tertiary neurosyphilis
- All types of ocular inflammation
- Labs
  - VDRL / RPR
  - FTA – ABS
  - ESR elevated
- Tx – penicillin therapy
- Good prognosis if treated early

**Lyme Titer**

- Ordered based on suspicion
- Erythema migrans is the only manifestation of Lyme disease in the United States for which clinical diagnosis should be made in the absence of laboratory confirmation
- A patient with a significantly characteristic symptom with the appropriate history of possible exposure should be started on antibiotics after appropriate laboratory studies have been drawn

**Tx for Lyme Disease**

- Early infection or nonspecific symptoms with positive Lyme titers in the adult may be treated with oral doxycycline (100 mg twice daily for 14 days) or amoxicillin (500 mg three times a day for 14 days)
- Severe infection in adults with definitive ocular, neuroophthalmic, neurological, or cardiac involvement may be treated with penicillin G (24 million units, intravenous, daily in four divided doses for 21 days) or intravenous ceftriaxone (2 g/day in two divided doses for 21 days).

**Human Leukocyte Antigen**

- Positive in several conditions
  - Ankylosing spondylitis
  - Reiter's syndrome
  - Inflammatory bowel disease
  - Psoriatic arthritis
  - Behcet's disease
- HLA-B27 typing may yield false positives
- Most useful for patients with acute, unilateral anterior uveitis

**HLA-B27**

- Ankylosing spondylitis
  - Affects males 20-40yo
  - Sacroiliac joint- lower back pain
  - HLA-B27 – 88%

- Inflammatory bowel disease
  - Bloody stool, abdominal pain
  - Weight loss
  - HLA-B27 – 60%

- Reactive Arthritis
  - Triad: Urethritis, Arthritis, Uveitis
  - More commonly affects men in 30-40yo
  - HLA-B27 – 88%

- Psoriatic arthritis
  - Skin lesions precede joint inflammation
  - Red, painful, swollen joints
  - Worse in the am
  - HLA-B27 – 70%
Behcet Disease

- Often Japanese or Middle eastern men 20-40yo
- Triad: Sores on mouth & genitals, uveitis
- Arthritis, skin problems, inflammation of spine
- Diagnosis
  - Positive Behcetine (pathergy) test
  - Recurrent mouth and genital sores
  - Rule out disease with similar presentation

Antinuclear Antibody (ANA)

- In autoimmune diseases, plasma cells produce antibodies directed against the body's tissues
- Positive values (titers < 1:20) are associated with connective tissue diseases
  - Systemic lupus erythematosus
  - Tuberculosis
  - Chronic hepatitis
  - Lymphoma
  - Sjogrens
  - Scleraderma
- Helpful in children to r/o JRA

Systemic Lupus Erythematosus

- African American women 20-40yo
- Rash, arthritis, fever
- Malaise, fatigue, hair loss, chest pain
- Vasculitis, kidney disease
- Diagnostic testing
  - ANA
  - CBC - decreased complement levels
  - ESR
  - Chest X-ray, Kidney biopsy

Rheumatoid Factor (RF)

- Differentiates RA from other chronic arthritides
- Positive values (titers > 1:80) occur in approximately 70% of patients with rheumatoid arthritis
- Positive in only 5% of patients with JRA
- Can be positive in the following
  - Sjogren's
  - SLE
  - Syphilis
  - Chronic infections
  - Sarcoidosis
  - Liver disease

Rheumatoid Arthritis

- Middle aged women
- Arthritis affecting both sides equally
- Morning stiffness
- Inflammation of joints and tissue
- Diagnostic Testing
  - Positive rheumatoid factor
  - Anti-CCP present
  - Elevated CBC
  - Joint X-ray

Sjögren's Is More than Dry Eye

[Image of human body with text: "Sjögren's Is More than Dry Eye"]

**Sjogrens Syndrome**

- Chronic autoimmune disease in which WBC attack moisture producing glands
- Diagnosis
  - (+) ANA
  - (+) RF
  - (+) SS-A (Ro)
  - (+) SS-B (La)
  - ESR
  - Immunoglobins

**Plaquenil (hydroxychloroquine sulfate)**

- Indicated for the treatment of discoid and systemic lupus erythematosus, rheumatoid arthritis, and malaria
- Primary risk factors
  - Duration > 5 years
  - Cumulative dose >1000g
  - Age
  - Systemic – High BMI, liver, kidney dysfunction
  - Ocular – retina or macular changes

**Urinalysis**

- Can disclose evidence of diseases, even some that have not caused significant signs or symptoms
- Commonly a part of routine health screening
  - Urinary tract or kidney infection
  - Evaluate causes of kidney failure
  - Screen for progression of some chronic conditions such as diabetes mellitus and high blood pressure
- Useful in the diagnosis of tubulointerstitial nephritis

**Recent Clinical Findings for Sjögren's**

<table>
<thead>
<tr>
<th>Current Screening</th>
<th>New SS Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined serology sensitivity &amp; specificity is around 40-60%</td>
<td>Combined serology sensitivity &amp; specificity is 87% and 82.5% respectively</td>
</tr>
<tr>
<td>None of the serology test diagnose SS early</td>
<td>Approximately 50% of the early &amp; new cases are identified (Ro and La Negative)</td>
</tr>
<tr>
<td>Misses approximately 25-35 % cases</td>
<td>finns additional cases</td>
</tr>
<tr>
<td>All serology tests identify are non-organ specific auto-antibodies and could occur in other autoimmune diseases</td>
<td>comprises of both organ/non-organ specific auto-antibodies</td>
</tr>
</tbody>
</table>

**New SS Panel**

- CA6
- SP-1
- PSP

**Plaquenil Examinations**

- Complete dilated examination
- Central visual field testing 10-2
- Fundus photography for co-existing retinal disease
- Spectral domain OCT, FAF, mfERG (if available)

**Radiology**

- Chest
  - Sarcoidosis
  - TB
- SI Joint
  - Ankylosing spondylitis
  - Reiter’s
  - Ulcerative colitis
- Large Joints
  - JRA
  - Reiter’s
  - Bechet’s
Biopsy

- Conjunctival and lacrimal gland – sarcoid
- Aqueous samples – Viral retinitis
- Vitreous biopsy – infectious endophthalmitis
- Retinal/choroid
  - Dx not established
  - No response to therapy
  - Further deterioration despite therapy
  - Exclusion of malignancy or infection

Plan for Treatment

- Protect vision
- Reduce scarring
- Reduce pain
- Decrease inflammation
- Find the cause

Treatments for Uveitis

- Steroids
  - Topical
  - Local
  - Systemic
- Cycloplegics
- Analgesics
- Immunosuppressants
- Calcineurin inhibitors
- Biological blockers
- Glaucoma medications

Steroid Pulse Therapy

- QID to Q 1 Hour for 7 to 10 Days
- Zero Tolerance for AC Cells
- Avoids Surface Toxicity
- Quick & Dirty
- Hit It Hard and Fast: Aggressive
- Treat and Follow

Don’t Forget the Cycloplegics

- Comfort
- Break synchiae
- Stabilize blood-aqueous barrier

Non-Therapeutic Treatments

- Hot compress
- Sunglasses / Hats
- Stay indoors
- Low lighting
- Plus for near
- Patching
Importance to Treat and Follow

- Mild – 4 to 7 days
- Moderate – 2 to 4 days
- Severe – 1 to 2 days
- Once resolved - q1-6 months

Current and Future Treatments for Uveitis

- Retisert – fluocinolone intravitreal implant
- Ozurdex – dexamethasome intravitreal implant
- Iluvien – fluocinolone intravitreal implant
- Humira - Adalimumab injection / TNF inhibitor
- Luveniq – voclosporin orally / calcineurin inhibitor
- Dexamethasone anterior segment iontophoresis

Case Example

- 62 yowm, cataract sx three weeks prior
- VAsc OD: 20/25
- IOP OD: 15 mmHg
- SLE: Mild K edema / 1+ cells / IOL centered

Take Home Pearls

- Be Aggressive with treatment
- Don’t taper too soon
- Be a detective and find the cause
- Treat and follow