Case conference

Manisha Mehta, M.D
On Feb 26, 2008, a 63 year old white male was referred for

• Red and painful right eye with decreased vision
• Anterior uveitis not responding to topical steroids
• With increasing posterior synechial formation

**Past history:**

• HLA-B27 positive recurrent anterior uveitis
  Affecting the right eye 2-3 times/year
  Responding to steroids and cycloplegics for the past 10 years

• Macular edema OD
Medical history:

• Psoriatic arthritis and skin lesions treated with narrow beam UV radiation

• Chronic lymphoid leukemia for one year on treatment with Rituxan and Fludarabine

• Family history:
  Father: Cancer
  Grandfather: Diabetes
  Aunt: Arthritis

• Medications:
  IVIG (for treatment of peripheral neuropathy 2 years before CLL)
  Aspirin
Review of systems:

Fatigue

Poor appetite

Severe / recurrent nose bleeds

Skin rashes

Stiff joints

Painful or swollen joints
<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
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<tbody>
<tr>
<td>Vision</td>
<td>20/50 cc</td>
<td>20/25 cc</td>
</tr>
<tr>
<td>IOP (mm of Hg)</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Pupils</td>
<td>synechiae</td>
<td></td>
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<tr>
<td>EOM</td>
<td>full</td>
<td>full</td>
</tr>
<tr>
<td>SLE: conjunctiva</td>
<td>Normal</td>
<td>normal</td>
</tr>
<tr>
<td>cornea</td>
<td>Diffuse keratic precipitates</td>
<td>Clear and compact</td>
</tr>
<tr>
<td>Anterior chamber</td>
<td>2.5+cells and flare</td>
<td>Deep and quiet</td>
</tr>
<tr>
<td>Iris</td>
<td>Posterior synechiae</td>
<td>normal</td>
</tr>
<tr>
<td>Lens</td>
<td>Hazy anterior capsule, cortical (1+) and nuclear sclerosis (2+)</td>
<td>Nuclear sclerosis (1+)</td>
</tr>
<tr>
<td>vitreous</td>
<td>Hazy view</td>
<td>normal</td>
</tr>
<tr>
<td>Fundus</td>
<td>Hazy view</td>
<td>normal</td>
</tr>
</tbody>
</table>
Management:

Investigations:
OCT:

Foveal thickness               OD: 274                           OS: 229

Medications:
Posterior synechiae broken with a ‘dynamite cocktail’ (adrenalin, atropine and cocaine)
Transeptal Kenalog (40 mg) and IV Solumedrol (1 gm)
Plan to start Humira (anti TNF alpha) after discussion with Oncologists

Enconopred Plus (Prednisolone Acetate 1%) q 1 hour OD
Xibrom (Bromfenac Sodium) bid OD
Homatropine tid-qid OD
<table>
<thead>
<tr>
<th>Time line</th>
<th>Event</th>
<th>Management</th>
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</thead>
<tbody>
<tr>
<td>March 14, 2008 (3 weeks later)</td>
<td>Tapering dose of Prednisolone acetate (q2h) Stopped Homatropine -Flare up: Redness, Pain OD -Vision: 20/ 50 OD -IOP: 17 /14 +2 conjunctival injection Keratic precipitates AC: 2+cells +flare Posterior synechiae</td>
<td>• Dose of Prednisolone acetate increased to q1h • Restarted Homatropine tid OD • Transeptal Kenalog 40 mg • Continue Xibrom</td>
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| March 26, 2008 (3 weeks later)    | Pain and Redness OD: 1 day Headaches Decreased vision OD              | Emergent treatment:  
|                                   | -Vision: LP OD 20/20 OS                                               | 50 cc of 25% Mannitol  
|                                   | -IOP: 60 OD 22 OS                                                    | 500 mg Diamox  
|                                   | -Cornea: stromal edema 1+ anterior synechiae                         | YAG iridotomy and AC paracentesis  
|                                   | -AC: 2+ cell and flare                                               | -22 mg Hg OD  
|                                   | -Iris: Iris bombe                                                    | Cytoxan infusion: dose 1 gm q 2 weekly  
|                                   | -Fundus: OD: RPE mottling at macula Attenuated vessels               | Cosopt (Timolol maleate/dorzolam)  
|                                   |                                                                       | Pred forte q2h OD  
|                                   |                                                                       | Homatropine q4 h OD  
|                                   |                                                                       | Xibrom bid OD  

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| April 01, 2008 (1 week later) | No pain or redness  
Better vision  
Vision: \textit{cc 20/50}  
-IOP: \textbf{11}/11  
-Pupils: round and reactive  
-AC: rare cell, well formed chamber  
-Iris: Posterior synechiae at 11 o’clock  
-Fundus: OD: Vitreous strands  
Pale OD  
RPE mottling at macula  
Attenuated vessels  
WBC: \textbf{6.2 k/ul} | Pred forte tapered to 6 times/day  
Cosopt continued  
Xibrom continued |
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<tr>
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<tr>
<td>May 07, 2008 (5 weeks later)</td>
<td>Trouble with nocturnal vision with oncoming lights while driving</td>
<td>Cytoxan withheld</td>
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<tr>
<td></td>
<td>Vision: cc 20/40 OD</td>
<td>Pred forte bid</td>
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<tr>
<td></td>
<td>IOP: 14/14</td>
<td>Xibrom continued</td>
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<tr>
<td></td>
<td>Pupils: round and reactive</td>
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<td></td>
<td>AC: deep and quiet</td>
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<td></td>
<td>Lens: nuclear sclerosis and posterior subcapsular cataract OD</td>
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<td></td>
<td>WBC: 4.3 k/ul</td>
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</table>
| May 15, 2008 (1 week later) | Fatigue  
Vision: 20/40 cc  
AC: PI open, posterior synechiae  
IOP: 14  
WBC: 5.6 k/ul | Cytoxan resumed at lower dose 750 mg  
Pred forte qd  
Cosopt bid |
| May 30, 2008 (2 weeks later) | Fatigue and tiredness  
Vision: 20/30  
AC: 1+ flare  
WBC: 2.9 k/ul | Cytoxan withheld  
Solumedrol infusion + |
| June 05, 2008 (1 week later) | No new redness or pain  
Vision: cc 20/30  
IOP 16/14  
WBC: 5.0 k/ul | Cytoxan (750 mg, q 2 weekly)  
Solumedrol  
Pred forte qd  
Xibrom  
Cosopt |
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<tr>
<td>July 7, 2008 (1 month later)</td>
<td>CE/IOL OD</td>
<td>Cytoxan reduced to 500 mg (every 3 weekly)</td>
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<tr>
<td></td>
<td></td>
<td>Solumedrol 1 gm</td>
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<td></td>
<td></td>
<td>Xibrom</td>
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<td></td>
<td></td>
<td>Cosopt</td>
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<tr>
<td>Aug 07, 2008 (1 month later)</td>
<td>Increasing fatigue</td>
<td>Cytoxan changed to Methotrexate 15 mg/week</td>
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<td>Advised to decrease Cytoxan by Oncologist</td>
<td>Xibrom</td>
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<td></td>
<td></td>
<td>Cosopt</td>
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<tr>
<td></td>
<td></td>
<td>Pred forte qd OD</td>
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<tr>
<td>November 25, 2008 (3.5 months later)</td>
<td>Vision: cc 20/20</td>
<td>Methotrexate 15 mg/week</td>
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<tr>
<td></td>
<td>IOP: 8/9</td>
<td>Xibrom</td>
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<tr>
<td></td>
<td>AC: deep and quiet</td>
<td>Cospot</td>
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<tr>
<td></td>
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<td>Xibrom</td>
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<tr>
<td>January, 2009</td>
<td>Restarted chemotherapy for CLL with Rituxan, Fludarabine and Cytoxan</td>
<td>Stopped MTX Xibrom continued Cosopt continued</td>
</tr>
<tr>
<td>Feb 03, 2009</td>
<td>Vision cc 20/20&lt;br&gt;OCT: Foveal thickness&lt;br&gt;IOP: 8/10&lt;br&gt;OD quiet</td>
<td>Xibrom&lt;br&gt;Cosopt</td>
</tr>
<tr>
<td>April 28, 2009</td>
<td>Follow up Vision: cc 20/20&lt;br&gt;IOP: 12/10&lt;br&gt;OD quiet</td>
<td>Xibrom reduced to qd&lt;br&gt;Cosopt</td>
</tr>
<tr>
<td>July 28, 2009</td>
<td>Follow up Vision cc 20/20&lt;br&gt;IOP 12/11&lt;br&gt;OD quiet</td>
<td>Xibrom qd&lt;br&gt;Cosopt bid</td>
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HLA-B27 syndromes

• HLA molecules are genetically encoded by the major histocompatibility complex (MHC) found on chromosome 6

• Role in immunity and in self-recognition in all nucleated cells and tissues

• Mechanisms of HLA-B27 associated inflammatory response:
  - Molecular mimicry
  - Arthritogenic peptide
  - Innate etiology unrelated to HLA
  - Marker closely linked to unidentified true immune gene responsible for inflammatory response.
HLA-B27 associated Acute Anterior Uveitis:

• Male predominance
• Age: 20-40 yrs
• Associated with seronegative arthritic syndromes
  - Ankylosing spondylitis
  - Reactive arthritis
  - Psoriatic arthritis
  - Inflammatory bowel disease
Ankylosing Spondylitis

Chronic progressive disease with 88% cases positive for HLA-B27
Chance of eye disease: 1:4
Young males, 3rd decade
Sacroiliac joints: lower back pain and stiffness after inactivity
Other systems involved: lungs (pulmonary apical fibrosis)
                     heart (aortitis and aortic insufficiency)
Reactive Arthritis (Reiter syndrome)

• 18-40 years

• Acute nonpurulent arthritis secondary to an infection elsewhere

• Enteric (diarrhoea) or urogenital infections (dysuria) in HLA-B27 positive individuals

• 60-85% individuals with reactive arthritis are HLA-B27 positive

• Organisms:
  Shigella flexneri, Salmonella species, Yersinia enterocolitica, Campylobacter jejuni, Chlamydia trachomatis, Chlamydia pneumoniae, Clostridium difficile, Ureaplasma urealyticum
Reactive Arthritis

- Non specific urethritis,
- Conjunctivitis (mucopurulent and papillary)
- Arthritis (knees, ankles, feet, wrists)

Minor diagnostic criteria: plantar fasciitis, Achilles tendonitis, nail bed pitting, palate ulcers and tongue ulcers

Major diagnostic criteria: keratoderma blennorrhagicum, circinate balanitis
Inflammatory bowel disease

- Ulcerative colitis (5-12%) and Crohn disease (2.4%) are associated with AAU

- 50-60% cases with spondylitis in association with inflammatory bowel disease are positive for HLA-B27

- Small bony erosions and joint space narrowing

- Ankylosing spondylitis
Psoriatic Arthritis

• HLA-B27 is associated with the pustular form of psoriasis

• 60-70% of cases with spondylitis associated psoriasis are HLA-B27 positive

• 3-4 th decade

• Mild intermittent arthritis (sausage shaped digits) except arthritis mutilans

• Psoriatic skin lesions: look like eczema and seborrheic dermatitis
HLA-B27 associated Acute anterior uveitis

- Non granulomatous unilateral disease (pain, redness, photophobia)

- Corneal: fine KP, fibrin on endothelium, corneal edema, band keratopathy

- AC: fibrinous exudate in AC, cells and flare, iris bombe, hypopyon

- Rare posterior segment involvement

- Cystoid macular edema, disc edema, pars plana exudates, choroiditis
HLA-B27 associated Acute anterior uveitis

- Tendency to recur

- Complications: cataract, glaucoma, hypotony, CME, synechiae formation

- Poorer prognosis than HLA-B27 negative AAU
Treatment

• Steroids: Topical, periocular, intravitreal and oral

• Cycloplegics

• Immunosuppressive therapy:
  - refractory cases
  - steroid induced adverse effects, steroid dependant cases
  - vision threatening inflammation

  - Azathioprine, Cyclophosphamide, Chlorambucil, Methotrexate, Cyclosporin

• Immunomodulation therapy: Infliximab (antiTNF-alpha), Etanercept (anti TNF alpha and beta)

• Sulfasalazine (in reactive arthritis)

• HLA-B27 derived peptide (B27PD) oral tolerance therapy

• Rheumatology consult
Thank you.....