

# 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

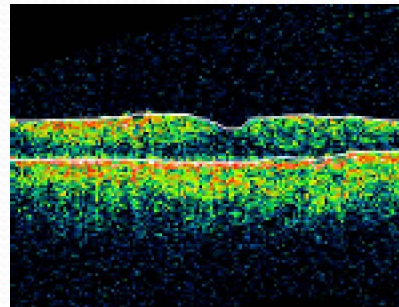
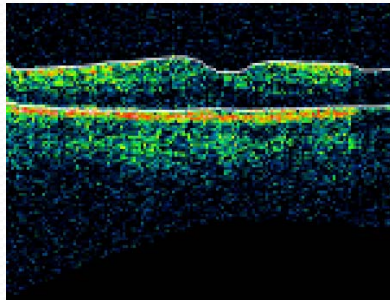
Painful or swollen joints

	OD	OS
Vision	20/50 cc	20/25 cc
IOP (mm of Hg)	15	12
Pupils	synechia	
EOM	full	full
SLE:		
conjunctiva	Normal	normal
cornea	Diffuse keratic precipitates	Clear and compact
Anterior chamber	2.5+cells and flare	Deep and quiet
Iris	Posterior synechia	normal
Lens	Hazy anterior capsule, cortical (1+ ) and nuclear sclerosis (2+)	Nuclear sclerosis (1+)
vitreous	Hazy view	normal
Fundus	Hazy view	normal

# 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

Time line	Event	Management
<p>March 14, 2008 (3 weeks later)</p>	<p>Tapering dose of Prednisolone acetate (q2h) Stopped Homatropine</p> <p>-Flare up: Redness, Pain OD</p> <p>-Vision: 20/ 50 OD</p> <p>-IOP: 17 /14</p> <p>+2 conjunctival injection</p> <p>Keratic precipitates</p> <p>AC: 2+cells +flare</p> <p>Posterior synechiae</p>	<ul style="list-style-type: none"> <li>•Dose of Prednisolone acetate increased to q1h</li> <li>•Restarted Homatropine tid OD</li> <li>•Transeptal Kenalog 40 mg</li> <li>•Continue Xibrom</li> </ul>

Time line	Event	Management
<p>March 26, 2008 (3 weeks later )</p>	<p>Pain and Redness OD: 1 day Headaches Decreased vision OD</p> <p>-Vision: <b>LP OD</b> 20/20 OS</p> <p>-IOP: <b>60 OD</b> 22 OS</p> <p>-Cornea: stromal edema 1+ anterior synechiae</p> <p>-AC: 2+ cell and flare</p> <p>-Iris: <b>Iris bombe</b></p> <p>-Fundus: OD: RPE mottling at macula Attenuated vessels</p>	<p>Emergent treatment:</p> <p>50 cc of 25% Mannitol</p> <p>500 mg Diamox</p> <p>YAG iridotomy and AC paracentesis -22 mg Hg OD</p> <p>Cytosan infusion: dose 1 gm q 2 weekly</p> <p>Cosopt (Timolol maleate/dorzolam)</p> <p>Pred forte q2h OD</p> <p>Homatropine q4 h OD</p> <p>Xibrom bid OD</p>

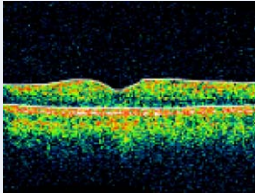
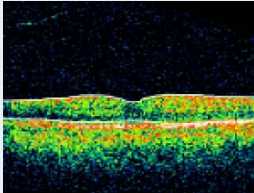


Time line	Event	Management
<p>April 01, 2008 (1 week later)</p>	<p>No pain or redness Better vision</p> <p>Vision: <b>cc 20/ 50</b></p> <p>-IOP: <b>11 /11</b></p> <p>-Pupils : round and reactive</p> <p>-AC: rare cell, well formed chamber</p> <p>-Iris: Posterior synechiae at 11 o'clock</p> <p>-Fundus: OD: Vitreous strands Pale OD RPE mottling at macula Attenuated vessels</p> <p>WBC: <b><u>6.2 k/u</u></b></p>	<p>Pred forte tapered to 6 times/day</p> <p>Cosopt continued</p> <p>Xibrom continued</p>

Time line	Event	Management
May 07, 2008 (5 weeks later)	Trouble with nocturnal vision with oncoming lights while driving  Vision: cc 20/40 OD  IOP: 14/14  Pupils : round and reactive  AC: deep and quiet  Lens: nuclear sclerosis and posterior subcapsular cataract OD  WBC: 4.3 k/ul	Cytosan withheld  Pred forte bid  Xibrom continued

Time line	Event	Management
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

Time line	Event	Management
July 7, 2008 (1 month later)	CE/IOL OD	Cytoxan reduced to 500 mg (every 3 weekly)  Solumedrol 1 gm  Xibrom  Cosopt
Aug 07, 2008 (1 month later)	Increasing fatigue  Advised to decrease Cytoxan by Oncologist	Cytoxan changed to Methotrexate 15 mg/week  Xibrom  Cosopt  Pred forte qd OD
November 25, 2008 (3.5 months later)	Vision: cc <b>20/20</b>  IOP: 8/9  AC: deep and quiet	Methotrexate 15 mg/week  Cosopt  Xibrom

Time line	Event	Management
January, 2009	Restarted chemotherapy for CLL with Rituxan, Fludarabine and Cytosan	Stopped MTX Xibrom continued Cosopt continued
Feb 03, 2009	Vision cc 20/20  OCT: <div style="display: flex; justify-content: center; align-items: center; gap: 20px;">   </div> Foveal thickness OD 248 OS 215 IOP: 8/10 OD quiet	Xibrom  Cosopt
April 28, 2009	Follow up Vision: cc 20/20 IOP: 12/10 OD quiet	Xibrom reduced to qd  Cosopt
July 28, 2009	Follow up Vision cc 20/20 IOP 12/11 OD quiet	Xibrom qd  Cosopt bid

# 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, 3<sup>rd</sup> 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

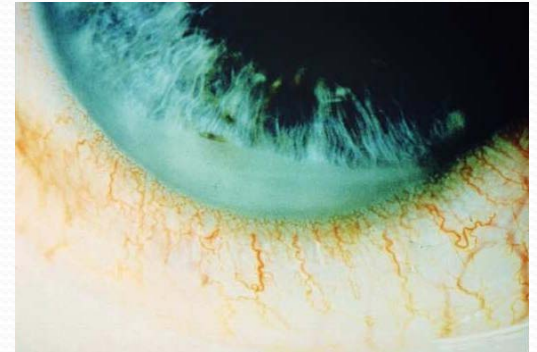
- Ulcerative colitis (5-12%) and Crohn disease (2.4%) are associated with AAU
- 50-60% cases with spondylitis in association with inflammatory bowel disease are positive for HLA-B27
- Small bony erosions and joint space narrowing
- Ankylosing spondylitis

# 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

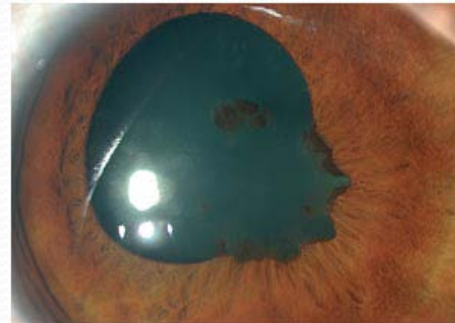
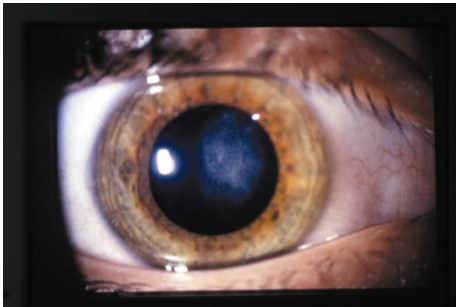
# HLA-B27 associated Acute anterior uveitis

- 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.....*