Pregnancy induced Non-Infectious Uveitis

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- 30 y/o WF, G4P3, 12 wk pregnant
  - Referred w/Dx: chronic anterior uveitis OS on Tobradex, Vigamox, and cyclopentolate gtts
  - CC: photophobia and ache OS, gtts don’t seem to help

- No GI upset, joint aches, rash, back pain, or other s/s

- PMHx of previous episodes of anterior uveitis during 1st tri of pregnancy
Exam

• VA: 20/20 OD and 20/30-OS
• IOP: 12, 13

• SLE: mild injection OS w/ciliary flush
• AC: 1+ cell
• Iris: anterior synechiae
• Fundus exam: WNL

• Switch gtts to pred forte QID and cyclopentolate, lab work
7/9/10

- Exam unchanged
- Lab results:
  - **HLA - B27 positive**
  - ANA neg
  - RF neg
  - FTA-ABS neg
  - RPR neg
  - Lyme neg
  - ACE neg
  - cANCA neg
  - pANCA neg
  - ESR neg
  - CRP neg
  - HIV neg

- VA Improved to 20/20 over 1 mo and gtts were tapered
- Pregnancy carried to term and normal delivery
- No recurrence of uveitis… until…
9/29/11

- OS photophobia and conj injection
- 7 wks pregnant (G5,P4)
- VA: 20/20, 20/60
- Conj: Mild injection
- AC: 1-2+ cell
- Iris: anterior synechiae
- Lens: pigment on capsule
- Fundus: mild edema and tortuosity of the vessels OS, ERM, macular star
- Pred forte QID and atropine daily
10/11-11/11

- Exam gradually improved to 20/20 OS
- AC inflammation, disc edema, and macular star gradually resolved

- B. henselae titer: Neg
- B. quintana titer: Neg
- Repeat of previous labs all negative except HLA-B27

- By 15\textsuperscript{th} week of pregnancy, all symptoms had resolved
HLA-B27 Uveitis

- Class I surface antigen that presents other antigens to T suppressor cells
- Encoded by the B locus of the major histocompatibility complex (MHC)
- Located on short arm of chromosome 6

- 5% of general population
- Up to 50% of Acute Anterior Uveitis patients
  - 50% of these individuals also have a spondyloarthropathy
Spondyloarthropathies

- Psoriatic Arthritis
- Ankylosing Spondylitis
- Reactive Arthritis (formerly known as Reiter’s Syndrome)
- Inflammatory Bowel Disease
  - Crohn’s Disease
  - Ulcerative Colitis

- HLA-B27 has not been reported to flare or be suppressed through with pregnancy!
MHC class I vs class II

- As a quick review:

- Class I MHC molecules (HLA -A, -B, -C)
  - Serve as antigen-presenting platform for CD8 T lymphocytes

- Class II MHC molecules (HLA-DR, -DP, -DQ)
  - Serve as antigen-presenting platform for CD4 T lymphocytes
Immune regulation during pregnancy

• Remediation of most autoimmune diseases such as:
  • Rheumatoid Arthritis
  • Multiple sclerosis
  • Uveitis (Idiopathic)
  • Vogt Koyanagi Harada (VKH)
  • Behcet’s Disease
  • Punctate Inner Choroidopathy (PIC)

• All reported to flare-up in first 4 months of pregnancy followed by a period of inactivity and a flare post-partum
Review of T-cell development

- Th1 (IL-2, INF-γ, TNF-β, IL-12) – Pro-inflammatory
- Th2 (IL-4, IL-5, IL-6, IL-10, IL-13) – secreted by fetoplacental unit
Immune regulation

• Normally the immune system remains balanced between Th1 and Th2 responses
Why would pregnancy change this?

- Th1, Th2, and (TGF-beta) shift during normal pregnancy and in the postpartum period resulting in a change of autoimmune disease

- Shift from Th1 to Th2 immune deviation – recall that the fetoplacental unit secretes Th2!

- Th2 downregulates the Th1 response (important for avoidance of fetal rejection)

- This mechanism can be used to describe the decrease in autoimmune responses during pregnancy such as uveitis.
But wait...

- HLA-B27 is an MHC class I molecule
  - Shouldn’t it activate CD8 T lymphocytes?

- How does HLA-B27 affect the immune response?
- 2 theories:
  - Antigen-specific – direct bacterial antigen response stimulates CD8 T lymphocytes to activate direct microbe killing
  - Molecular mimicry – bacterial antigens that mirror amino acid structures in HLA-B27 sequence that triggers CD4 T lymphocyte reaction

- CD4 response has been shown in many AAU animal models for HLA-B27 uveitis
Upon review:

- Rheumatoid Arthritis (Th1 upregulation)
- Multiple sclerosis (Th1 upregulation)
- Vogt Koyanagi Harada (VKH) (Th1 upregulation)
- Behcet’s Disease (Th1 upregulation or a mix of Th1/Th2)
- Punctate Inner Choroidopathy (PIC) (Th1 upregulation)
Conclusion

• Unclear how HLA-B27 really alters immune system

• Our case demonstrates what appears to be a distinct association between HLA – B27 uveitis and pregnancy, however, there is no strong association in the literature linking HLA-B27 uveitis flare-up and pregnancy.

• Further cases?

• Could this case represent an idiopathic uveitis with a coincidental HLA-B27 patient?