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CE Credit - Case Report(s) & Topic Review

HLA-B27 Associated Acute Fibrinous Anterior Uveitis

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This case describes the clinical course of a patient with severe acute anterior uveitis with fibrin formation in the anterior chamber. Rheumatological as well as infectious testing revealed HLA-B27 involvement to be likely. HLA-B27 associated uveitis tends to show a greater inflammatory reaction including fibrin production. A discussion of HLA-B27 and possible pathogenicity is discussed.

INTRODUCTION

CASE REPORT

A 26-year-old white female presented for possible eye infection in the right eye. Additional complaints included of redness, irritation, photophobia, blurred vision, and burning of the right e ye which had progressively worsened over a two week period. The patient did not have any symptoms of discharge and denied overnight contact lens wear. Ocular history included previous treatment for contact-lens associated red eye (CLARE) in the left eye 13 months prior to the visit. Family medical history was positive for autoimmune disease (relative unknown). The patient denied joint or muscle pain, back pain or stiffness, recent illness or injury, bowel or urinary symptoms, or any other inflammatory symptoms. Social history was positive for occasional alcohol use and was otherwise unremarkable.

Aided visual acuities were 20/400 OD and 20/20 OS. With pinhole, visual acuity improved to 20/100 in the right eye. Manifest refraction did not improve visual acuity. The right pupil appeared fixed at 4.0mm; there was however a direct and consensual response in the left eye, hence no relative afferent pupillary defect. Confrontation fields were full to finger count in both eyes. Extraocular muscles were unrestricted in all gazes with the patient reporting pain in the right eye in all gazes. Physical evaluation revealed preauricular nodes which were not palpable with no tenderness. The eyelids, brow, nasal bridge, forehead, and cheek of the patient showed no signs of erythema or lesion bilaterally. Slit lamp examination of the right conjunctiva showed 2+ bulbar injection with trace palpebral injection. Corneal epithelium was clear and intact in the right eye. The corneal stroma of the right eye showed trace and diffuse edema. The corneal endothelium had 3+ fine keratic precipitates and a fibrin strand that was attached and extending posteriorly to the anterior lens capsule in the right eye. The conjunctiva and cornea of the left eye was normal. The anterior chamber in the right eye was deep with 4+ cell and flare, and fibrin was seen throughout the anterior chamber most prominently reaching from the corneal endothelium to the anterior lens capsule. The anterior lens capsule of the right eye had 3+ cells and fibrin deposits. The iris of the right demonstrated posterior iris synechiea from 12:00 to 11:00 covering 11 clock hours, and the iris appeared mildly hyperemic. The lens of the right eye was difficult to view and appeared grossly normal. Ocular structures of the left eye were unremarkable including the anterior chamber, iris, lens and cornea. Fluorescein staining was not observed in either eye. Goldmann applanation tonometry measured 18 mmHg OD and 15 mmHg OS at 2:44PM. Fundus examination of the posterior segment of the right eye was difficult due to poor dilation of the iris inhibited by the iris synechia and poor view of the lens, vitreous, retina, and optic nerve due to the hazy anterior lens capsule. The fundus appearance that could be viewed in both eyes was normal.

The differential diagnoses considered included

- Acute anterior iritis
- Panuveitis
- Herpes Simplex Viral uveitis
- Posterior uveitis
- Infectious keratouveitis
- Acute anterior iritis presents with recent onset photophobia, blurred vision, redness, and excessive tearing. Clinical findings include circumlimbal flush, corneal edema, and inflammatory cells in the aqueous humor.
- Panuveitis describes diffuse inflammation of the anterior and posterior chamber that presents clinically very similar to anterior iritis with the exception of floaters which may be more prominent in panuveitis.[1]
- Herpes simplex often presents with some level of corneal involvement. Herpes simplex uveitis can present clinically in the absence of corneal disease with granulomatous keratic precipitates on the corneal endothelium, inflammatory cells in the anterior chamber, and possible elevated intraocular pressure.[i]
- Posterior uveitis generally presents with symptoms similar to panuveitis. Clinically posterior uveitis would have inflammatory cells in the anterior and posterior chamber, cells in the vitreous causing a hazy appearance to the vitreous, and retinal or choroidal inflammatory findings.[i]
- Infectious Keratouveitis often presents with symptoms of eye irritation or pain, photophobia, mucous

discharge, diffuse redness, and blurred vision. Clinical findings may include conjunctival injection, superficial punctate staining of the corneal epithelium with sodium fluorescein, corneal edema, and inflammatory cells in the anterior chamber.

The patient was diagnosed with acute anterior iritis. Without a clear view of the posterior chamber, vitreous, and fundus this was a working diagnosis. The occasional view of the peripheral retina seemed to show a retina free of inflammation and with increasing clarity of the retina toward the vitreous base made posterior involvement seem less likely. The presence of fibrin in the anterior chamber in the presence of significant anterior chamber inflammatory reaction suggested acute anterior iritis with likely autoimmune association. The patient was started on difluprednate 0.05% ophthalmic emulsion, one drop in the right eye four times a day while awake; and atropine 1% ophthalmic solution one drop in the right eye twice a day. She was scheduled for follow-up in 36 hours. In addition, lab testing was considered to investigate possible causative or associated conditions but was refused by the patient due to financial concerns. Primary care was contacted in person to discuss concern for possible autoimmune or infectious causes. Therefore, lab testing was not ordered per patient request at the initial visit.

FOLLOW-UP #1

The patient returned to clinic 2 days later for follow-up. The patient reported a decrease in pain and photophobia with an improvement in vision with slight to no improvement in redness. The patient reported good compliance to the medication schedule as prescribed. Best corrected visual acuity improved to 20/60 in the right eye and remained 20/20 in the left eye. Pinhole acuity in the right eye was 20/60. Slit lamp examination of the right eye showed normal lids and lashes, the conjunctiva showed 2+ injection, the cornea showed trace central stromal edema with 2+ fine keratic precipitates on the endothelium. The anterior chamber was graded to have 2+ cells and flare. The anterior chamber appeared deep. The iris was irregularly dilated with a posterior iris synechia from 7:00 to 9:00. The anterior lens capsule showed 2+ fibrin scattered across the central area of the lens capsule with clumps of pigment remaining from the broken synechia. Goldmann applanation tonometry measured 18 mmHg OD and 15 mmHg OS at 2:48PM. With increased pupil dilation the slit lamp view of the peripheral lens showed a clear lens in the right eye with no cells or pigment in the peripheral posterior chamber. The vitreous near the vitreous base was clear. The view of the posterior pole of the right eye remained hazy but grossly normal. The peripheral retina of the right eye remained difficult to view in places and appeared to be flat, without tears, inflammation, or vascular changes.

Improvement in visual acuity, decrease in fibrin and cells in the anterior chamber, and breaking of a large portion of the synechia suggested that the patient was responding well to the treatment. The working diagnosis of acute anterior iritis continued to be consistent with clinical findings. Inability to view the central vitreous and the posterior pole prevented exclusion of further uveitic involvement. The response to treatment showed improvement consistent with the working diagnosis. Concern remained for possible infectious causes and the need to investigate auto immune or rheumatological causes. Labs were again discussed with the patient. Even with the improvement in symptoms and clinical findings the need for lab testing remained. The following labs were ordered: Rheumatoid Arthritis Factor (RF), HLA-B27 by reflex, ANA w/reflex, C-reactive Protein (CRP), Erythrocyte sedimentation rate (ESR), complete blood count (CBC), Treponema Pallidum Antibody Reflex (RPR), and Herpes Simplex Virus by polymerase chain reaction (HSV by PCR). The patient was instructed to continue medications as previously prescribed. The patient was scheduled for follow-up in 5 days to reassess and discuss the results of the lab tests. The patient agreed to return for lab testing the next day.

FOLLOW-UP #2

The patient returned for follow-up 5 days later for follow-up, evaluation, and review of lab results. She reported a significant decrease in pain, photophobia, and redness, and no improvement in vision. She reported good compliance to the medication schedule as prescribed. She had returned to the lab as requested and the lab results were as follows:

Best corrected visual acuity remained 20/60 in the right eye and 20/20 in the left eye. Pinhole acuity in the right eye improved to 20/40. Slit lamp showed no further conjunctival injection, and the cornea was clear with trace fine keratic precipitates seen on the endothelium. The anterior chamber of the right eye showed 2+ cell and flare and appeared deep. The iris of the right eye was dilated with no synechiae present. The anterior lens capsule of the right eye showed 1+ fibrin with pigment deposits from the broken synechia. Goldmann applanation tonometry measured 15 mmHg OD and 15 mmHg OS at 9:57AM. With pupil dilation of the right eye and less fibrin on the anterior lens capsule, a view of the fundus was obtained. The posterior chamber and vitreous were clear without cells or pigment. The posterior pole was normal upon examination as was the peripheral retina.

Continued improvement in the visual acuity of the right eye, decrease in cells and fibrin in the anterior chamber, and significant improvement of symptoms in the right eye suggested the treatment was appropriate. The patient was instructed to discontinue atropine as the posterior synechia was broken. Difluprednate was continued as prescribed. Lab testing confirmed that patient was HLA-B27 positive suggesting a diagnosis of HLA-B27 associated uveitis. CRP was elevated, making the condition more likely to be acute and inflammatory in nature. HSV IgG testing suggested previous exposure to HSV both type I and type II, and IgM testing showed no acute component to the immunological reaction. The lab findings were discussed with the patient's primary care physician (PCP) and the patient was scheduled

for follow-up eye examination in one week and a two week follow-up with the PCP for a rheumatological consult.

FOLLOW-UP #3

The patient returned to clinic one week later for follow-up reporting no redness, pain, photophobia, and blurry vision. The patient reported good compliance to the medication schedule as prescribed. Corrected visual acuity improved to 20/30 in the right eye and remained 20/20 in the left eye. Pinhole acuity in the right eye was 20/25. Pupils were equally round and reactive to light. Slit lamp examination of the right eye showed normal lids, lashes, and conjunctiva. The right cornea was clear throughout all layers. The anterior chamber of the right eye was deep and showed no cells or flare, the iris was flat without atrophy or transillumination defect. The right anterior lens capsule was clear centrally with pigment deposited near the pupil margin. Slit lamp examination of the left eye was unremarkable. Goldmann applanation tonometry measured 15 mmHg OD and 15 mmHg OS at 10:38 AM. Fundus examination of the posterior chamber was clear without cells in both eyes. The vitreous showed no cells or pigment in either eye. The posterior pole was normal upon examination as was the peripheral retina in both eyes.

The patient was instructed to taper difluprednate 0.05% to one drop in the right eye three times a day for 5 days, then two times a day for 5 days, then once a day for 5 days and instructed to return for follow-up in 2 weeks.

FOLLOW-UP #4

On follow-up the patient reported no redness, pain, photophobia, and blurry vision as well as good compliance to the medication schedule as prescribed. Corrected visual acuity improved to 20/20 in the right eye and remained 20/20 in the left eye. Pupils were equally round and reactive to light. Slit lamp examination of the right eye showed normal lids, lashes, and conjunctiva. The right cornea was clear throughout all layers. The anterior chamber was deep and showed no cells or flare, the iris was flat in the right eye. The right anterior lens capsule was clear centrally with pigment deposited near the pupil margin. Slit lamp examination of the left eye was normal. Goldmann applanation tonometry measured 15 mmHg OD and 15 mmHg OS at 9:39 AM.

The consult to primary care noted a positive HLA-B27 lab test, uveitis, and a positive family history of auto immune disease. A physical exam revealed a small node in the clavicular area and was otherwise normal. A recommendation was made to monitor the condition until the uveitis resolved and repeat lab testing at follow-up in eight weeks.

The patient was instructed to stop difluprednate 0.05% and to watch for return of symptoms and return to clinic as soon as symptoms arise. Compliance with plan for follow-up was stressed.

On the eight-week follow-up with primary care the absence of further symptoms of rheumatological disease was seen as empirical reason to continue monitoring her condition without further work-up.

DISCUSSION

Human Leukocyte Antigen B27 (HLA-B27) is a family of alleles from the major histocompatibility complex type 1.[1] HLA-B27 has shown to have close association with inflammatory diseases such as uveitis, ankylosing spondylitis, and reactive arthritis. More than simply an etiological factor, HLA-B27 is thought to be a marker of immunological abnormality.[2] While the pathogenicity of HLA-B27 is unknown, Wakefield *et al* suggested that the expressed disease is a consequence of self-reactive T lymphocytes that are activated against a peptide only found in the joint or uvea that mimics a microbial peptide,[3,4] suggesting that the HLA-B27 immunological response is activated by previous microbial infection. This theory is supported by experimental animal studies showing that HLA-B27 positive animals raised in a germ-free environment do not develop symptoms similar to spondyloarthropathies until introduced to commensal microbes.[3]

HLA-B27 associated acute anterior uveitis typically presents as a unilateral, non-granulomatous acute anterior uveitis with a significant anterior chamber inflammatory reaction. The anterior chamber can have significant cellular and protein extravasated into the aqueous humor resulting in possible hypopyon or fibrin formation.[3] There tends to be a higher likelihood of previous history with HLA-B27 associated acute anterior uveitis.[3] HLA-B27 associated acute anterior uveitis can have a bilateral presentation, posterior segment inflammation, vitritis, or cystoid macular edema; while the prevalence of these findings is unknown, the literature suggests such these findings are less common.[3,4] There seems to be a male predominance; men being affected as much as three times greater than women.[4] There is a well-established association with systemic disease and HLA-B27 associated acute anterior uveitis with ankylosing spondylitis being the most common.[5] Further association is also seen with reactive arthritis, psoriatic arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, and juvenile idiopathic arthritis.[2,5]

Presence of fibrin in the anterior chamber of the discussed patient suggested a severe inflammatory reaction. Such severe reactions can be associated with auto-immune disease, infectious processes, or postoperative complications.[1] A negative surgical history made infectious causes unlikely; with a previous occurrence of similar symptoms with a different diagnosis suspicion arose that this occurrence could be a re-occurrence. Lab testing confirmed the presence of HLA-B27. In the absence of infectious causes the patient was diagnosed with HLA-B27 associated acute anterior uveitis. Upon initial examination there was significant concern for intermediate or panuveitis due to the severity of the anterior chamber reaction and the inability to visualize the posterior segment, vitreous, and most of the retina prevented definitive diagnosis of anterior uveitis. Clinical suspicion of anterior uveitis, rather than intermediate or panuveitis, was in part due to the appearance of the

peripheral retina with Binocular indirect ophthalmoscopy showing a grossly normal and healthy appearing retina with a hazy view. The presence of posterior synechia suggested that topical cycloplegic agent would serve the purposes of resolving the synechia and reducing inflammation into the anterior chamber. Topical cycloplegic agent combined with topical corticosteroid aggressively administered is the standard of care in treatment of anterior uveitis.[3]

This patient had no known systemic disease at the time of diagnosis. Having had similar symptoms just 12 months before this episode may represent a re-occurrence, a common finding in HLA-B27 associated acute anterior uveitis; in one study, reoccurrence was present in 50% of the study population.[6] The relapsing nature of the condition was discussed with the patient and prompt follow-up with onset of symptoms was encouraged. The literature suggests the most common systemic finding associated with HLA-B27 associated acute anterior uveitis is ankylosing spondylitis.[3] The described patient was seen for Rheumatology consult but did not have radiographic evaluation of the sacroiliac joint. Ankylosing spondylitis cannot be diagnosed or ruled out without such evidence. This matter was discussed and the patient felt comfortable continuing to manage their condition with primary care. In the presence of systemic disease, rheumatological treatment may need to include systemic corticosteroids or immunosuppressive therapy to control the systemic inflammation.[7]

CONCLUSION

The case discussed shows the important role of case history, clinical findings, laboratory findings, and referral in the management of HLA-B27 associated acute anterior uveitis. The need for long term follow-up in the discussed patient is based on the possibility of further re-occurrence or systemic involvement. HLA-B27 associated acute anterior uveitis is successfully managed with aggressive topical corticosteroid and cycloplegic agents. Patient education is important in informing patients of the significant potential for recurrence and the possibility of systemic involvement. Laboratory testing is important in suspected HLA-B27 associated acute anterior uveitis to examine possible infectious, inflammatory, and auto immune causes.

REFERENCES

1. Ehlers JP, Shah CP. *The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease*. Lippincott Williams & Wilkins; 2008.

2. Singleton EM, Hutson SE. Anterior Uveitis, Inflammatory Bowel Disease, and Ankylosing Spondylitis in a HLA-B27-positive Woman. *Southern Medical Journal*. 2006;99(5):531-533. doi:10.1097/01.smj.0000215747.80424.2d

3. Wakefield D, Chang JH, Amjadi S, Maconochie Z, El-Asrar AA, Mccluskey P. What Is New HLA-B27 Acute Anterior Uveitis? *Ocular Immunology and Inflammation*. 2011;19(2):139-144.

4. Hill HF, Hill AG, Bodmer JG. Clinical diagnosis of ankylosing spondylitis in women and relation to presence of HLA-B27. *Annals of the Rheumatic Diseases*. 1976;35(3):267-270. doi:10.1136/ard.35.3.267

5. Martin TM, Rosenbaum JT. An Update on the Genetics of HLA B27.associated Acute Anterior Uveitis. *Ocular Immunology and Inflammation*. 2011;19(2):108-114.

6. Agnani S, Choi D, Martin TM, et al. Gender and laterality affect recurrences of acute anterior uveitis. *British Journal of Ophthalmology*. 2010;94(12):1643-1647. doi:10.1136/bjo.2009.172312

7. Dodds EM, Lowder CY, Meisler DM. Posterior segment inflammation in HLA-B27+ acute anterior uveitis: clinical characteristics. *Ocular Immunology and Inflammation*. 1999;7(2):85-92. doi:10.1076/ocii.7.2.85.4015