HLA-B27–Associated Uveitis With a Chorioretinitis Manifestation

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Abstract. A 29-year-old man who had been treated for acute anterior uveitis in a local medical office and observed for 1 month presented complaining of distorted vision in his left eye for 1 week. On ophthalmic examination, the anterior segment was relatively quiet with few cells. A posterior segment examination revealed cystoid macular edema and multiple splinter retinal hemorrhages. Results of all laboratory and imaging studies were negative, except for a positive HLA-B27 haplotype. Fluorescein angiography revealed massive leakage in the mid and late phase, consistent with chorioretinitis. Periocular corticosteroid injections and oral prednisolone were administered. The patient responded to the treatment well with subsequent resolution of chorioretinitis 2 months later. Although rare, chorioretinitis can occur in the setting of uveitis associated with HLA-B27 and seems to respond well to corticosteroid treatment. [Ophthalmic Surg Lasers Imaging 2005;36:158-162.]

INTRODUCTION

Acute anterior uveitis is the most common form of intraocular inflammation and its association with the HLA-B27 haplotype has been well documented. Anterior uveitis associated with HLA-B27 has also been shown to be strongly associated with seronegative spondyloarthropathies, especially with ankylosing spondylitis in 84% to 90% of patients. Other systemic associations include Reiter's syndrome, psoriatic arthropathy, and inflammatory bowel disease. Depending on the associated systemic findings and the ocular segment involved, different uveitis entities associated with HLA-B27 may manifest differently and have dramatic differences in causing visual impairment.

Uveitis occurring in conjunction with the HLA-B27 haplotype is characterized by unilateral ocular involvement, short duration of activity, and recurrent attacks of iridocyclitis. The inflammation may occasionally become chronic, leading to the formation of cataract, glaucoma, and posterior segment manifestation such as cystoid macular edema and causing marked secondary visual impairment. Although uveitis associated with HLA-B27 has been discussed extensively in the literature, little information is available on the less common, but more serious, posterior segment forms of the disease, including vitritis, pars planitis, papillitis, and chorioretinitis. It is commonly known that the HLA-A29 haplotype is strongly associated with birdshot chorioretinopathy in more than 90% of cases. However, the manifestation of chorioretinitis in HLA-B27–positive patients has rarely been described in the literature.

We describe a case of seronegative uveitis associated with HLA-B27 with chorioretinitis, a less frequent but more serious form of the inflammation. The case was successfully treated with systemic steroids and posterior sub-Tenon steroid injections with full recovery of the visual acuity.

CASE REPORT

A 29-year-old Chinese man was referred to our outpatient clinic with acute blurred vision and metamorphopsia in the left eye for 1 week. The patient had...
a history of chronic lower back pain for 3 years. His father was being treated for ankylosing spondylitis. Prior to coming to our outpatient service, the patient was observed for 1 month in a local medical office for acute anterior uveitis of the left eye. He received topical 1% prednisolone acetate eyedrops every 2 hours, cycloplegics, and systemic oral steroids (40 mg of prednisolone daily). When the patient was first seen in our clinic, his corrected visual acuity was 20/20 in the right eye and 20/60 in the left eye. He had multiple fine corneal keratic precipitates and a relatively quiet anterior chamber with few cells in the left eye. A posterior segment examination of the left eye revealed multiple splinter hemorrhages, accompanied by marked hyperemic disc and macular edema. Examination of the right eye revealed normal findings.

The patient received a complete laboratory work-up, which included a chest and lumbar spine x-ray, rheumatoid factor tests, anti-nuclear antibodies, C-reactive protein, IgA, HLA-B27, erythrocyte sedimentation rate, rapid plasma reagin, Treponema pallidum hemagglutination tests, toxoplasmosis titers, and human immunodeficiency virus tests. Results were all negative except for a positive HLA-B27 haplotype. Fluorescein angiography revealed macular edema with diffuse dye leakage, especially in the posterior pole, and staining of the optic disc in the left eye consistent with chorioretinitis and papillitis (Fig. 1). Results of fluorescein angiography of the right eye were within normal limits.

The patient subsequently received a sub-Tenon injection of 10 mg of triamcinolone acetonide in the

**Figure 1.** Fluorescein angiography of a patient with acute anterior uveitis prior to treatment. (A) Arterial phase. (B) Arterio-venous phase. (C) Venous phase. (D) Late phase. Notice the massive leakage from the choroidal and retinal vessels, and the cystoid macular edema in the mid and late phases of the fluorescein angiogram. Notice also the blocked fluorescein of the splinter hemorrhages just inside the superior arcade in all phases.
left eye and was prescribed 30 mg of oral prednisolone daily. Three weeks later, his visual acuity in the left eye improved to 20/40. He then received another 10-mg sub-Tenon injection of triamcinolone acetonide. At 1 month after the second injection, the visual acuity in the left eye improved to 20/20. Fluorescein angiography revealed a normal fundus with complete resolution of the chorioretinitis and macular edema in the left eye (Fig. 2).

**DISCUSSION**

The incidence of acute anterior uveitis associated with HLA-B27 depends mainly on the prevalence of the allele in the general population. The frequency of the HLA-B27 haplotype in patients with acute anterior uveitis varies among different countries (eg, 83.8% in Finland, 55.7% in England, and 18.8% in Japan). In the Chinese population, the incidence was reported to be as high as 80.9%. Acute anterior uveitis associated with HLA-B27 thus accounts for most of the endogenous uveitis in the Chinese population. With the high incidence of uveitis associated with HLA-B27 in the Chinese population, the more severe form of the disease with posterior segment involvement was seldom recognized.

Although the real prevalence of posterior segment manifestation in patients with uveitis associated with HLA-B27 is unknown, available studies in general indicate a low prevalence. A Finnish study found a mean annual incidence of posterior uveitis associated with HLA-B27 of less than 0.3 per 100,000 population. Other studies by Rothova et al. found no posterior uveitis in 153 patients with uveitis who had seronegative spondyloarthropathies or uveitis associated with HLA-B27.
Mapstone and Woodrew reported only 2 cases with posterior uveal involvement in a group of 51 patients with anterior uveitis associated with HLA-B27. In a study of 117 patients with anterior uveitis associated with HLA-B27, Chung et al. found no manifestation of chorioretinal lesions. Rodriguez et al. reported the highest prevalence (17.4%), but stated this may reflect the complicated nature of cases referred to the tertiary care center at the Massachusetts Eye & Ear Infirmary. They went further and concluded that the belief that uveitis associated with HLA-B27 is confined to the anterior segment is inaccurate.

Depending on the type of spondyloarthropathy and the segment of the eye involved, uveitis associated with HLA-B27 can manifest with different severity. Various reports have been made on the association of HLA-B27 with inflammatory bowel disease. Bayen et al. reported an incidence of 50% to 60%. Patients with inflammatory bowel disease often present with uveitis that is chronic and bilateral, involving both the anterior and posterior segments. Posterior pole involvement such as vitritis and retinal vasculitis have all been described in patients with inflammatory bowel disease. However, in patients with uveitis associated with HLA-B27 other than those with inflammatory bowel disease, the inflammation rarely involves the posterior segment, leading to significant visual impairment.

Among the posterior manifestations of uveitis associated with HLA-B27, vitritis is the most common. It was reported in 63% of patients by Bayen et al. and 93% of patients by Rodriguez et al. Retinal vasculitis has also been described in patients with uveitis associated with HLA-B27. Our patient complained of gradual onset of metamorphopsia 5 weeks after the attack of anterior uveitis. Fluorescein angiography revealed findings characteristic of diffuse chorioretinitis. A complete laboratory work-up was then done to rule out other possibilities for the posterior segment inflammation. As Rodriguez et al. reported that the severity and duration of macular edema was a major prognostic factor for poor visual outcome in patients with uveitis associated with HLA-B27, we decided to treat this patient aggressively.

Unlike anterior uveitis, which generally has good response to topical steroid therapy, posterior uveitis often requires more aggressive treatment, including periocular steroid therapy and systemic prednisolone. In a clinical investigation by Dafflon et al., posterior sub-

Tenon steroid injection was found to be an effective therapy for inflammation of the posterior segment. After a diagnosis of chorioretinitis with macular edema was confirmed, our patient was immediately treated with two successive courses of sub-Tenon steroid injection. The patient also received oral prednisolone treatment throughout the course of the disease. The patient responded to the treatment well with a final visual acuity of 20/20 in the left eye 2 months after treatment.

It has been postulated that the HLA-B27 molecule may actually act as part of an antigen-presenting process that predisposes individuals with the HLA-B27 haplotype to certain autoimmune diseases, such as ankylosing spondylitis, Reiter's syndrome, and uveitis. In patients with acute anterior uveitis associated with HLA-B27, inflammation in the anterior chamber of the eye is largely limited by anterior chamber-associated immune deviation, which is mainly regulated by the level of the anti-inflammatory growth factors. However, when the inflammatory reactions in the anterior segment are not controlled, there might be a spillover of the inflammatory material into the posterior segment, extending the inflammation posteriorly. It is possible that the inflammatory exudates may cause secondary vitritis and chorioretinitis. Unlike the exceptionally high association between HLA-A29 and birdshot chorioretinopathy, HLA-B27 is probably not the only key to the pathogenesis of chorioretinitis in patients with uveitis associated with HLA-B27, but it nevertheless may play a role in the disease expression.

Our case demonstrated that uveitis associated with HLA-B27 may not be confined to the anterior segment alone and that chorioretinitis may be a late manifestation of the disease. It is important to recognize the posterior segment manifestation of the disease because this form may have increased risks of complications and less favorable visual prognosis. In populations with a high prevalence of uveitis associated with HLA-B27 such as the Finnish and the Chinese, the importance of recognizing the posterior segment form of the disease cannot be overemphasized. Kotaniemi et al. recently examined the different etiologies of uveitis as a cause of visual loss through a retrospective study based on the data from the Finnish Register of Visual Impairment. The study concluded that there can be severe, sight-threatening posterior segment manifestations in patients with uveitis associated with HLA-B27 and it is important to look for etiologies in patients with uve-
itis. Finally, in contrast to patients with anterior uveitis associated with HLA-B27, an aggressive treatment including systemic and periocular corticosteroid treatment should be established immediately in patients with posterior uveitis associated with HLA-B27 to prevent visual handicap and blindness.

REFERENCES