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Adalimumab for Pediatric Sympathetic Ophthalmia

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Introduction

Sympathetic ophthalmia (SO) is an autoimmune, bilateral, granulomatous panuveitis occurring after accidental or surgical trauma to the eye.[1] Systemic corticosteroids are first-line therapy for SO with immunomodulatory therapy employed for corticosteroid-sparing immunosuppression and chronic, refractory cases. Biologic response modifiers (BRMs) are a class of therapeutics that target specific cytokines mediating inflammation, and TNF-α antagonist BRMs have shown promise for uveitis.[2] Herein, we report the first use, to our knowledge, of adalimumab for refractory pediatric SO leading to resolution of inflammation.

Case Report

A 5-year-old Caucasian girl suffered accidental trauma to the right eye resulting in corneoscleral laceration repaired the day of trauma. Post-operative visual acuity (VA) was hand-motions. Two weeks later, increasing inflammation concerning for endophthalmitis prompted intravitreal antibiotic injection and subsequent pars plana vitrectomy with lensectomy. Vision became no light perception post-operatively.

Nine weeks after her initial injury, the patient began experiencing photophobia and redness of her uninjured, left eye. Vision was 20/20 OS. An examination under anesthesia of the left eye documented anterior and posterior segment inflammation with white peripheral chorioretinal deposits concerning for sympathetic ophthalmia. Topical prednisolone acetate 1% and oral prednisone 60mg daily was started. Enucleation of the right eye was performed 11 weeks after the initial injury with histopathologic examination consistent with sympathetic ophthalmia (Figure 1). The patient was referred to our service for further management.

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Conflicts of Interest Disclosures

None reported.

On our initial examination, VA was 20/25 OS and intraocular pressure was 36 mmHg with rare anterior chamber cell and trace flare. Ophthalmoscopic examination showed 1+ vitreous cell without choroidal lesions. The patient developed weight gain and cushingoid habitus on oral prednisone. Topical timolol 0.5% was started for elevated IOP.

Oral prednisone was tapered to 10mg daily over a 12-week period in conjunction with initiating methotrexate 10mg subcutaneous injection (SQ) weekly. Despite dose escalation of methotrexate to 25mg SQ weekly over the following nine months, the patient continued to have low-grade anterior chamber inflammation, developed posterior synechiae (figure 2), and experienced flares up to 3+ anterior chamber cell when tapering oral prednisone below 10mg daily.

Adalimumab 20 mg SQ every 2 weeks was initiated after a negative PPD reading, and within three months inflammation completely resolved with discontinuation of oral prednisone, prednisolone acetate, and timolol. After six months of stability on adalimumab, methotrexate was tapered and discontinued over six months.

After 18 months on adalimumab, VA was 20/25 OS with no evidence of recurrent inflammation, posterior synechiae, or fundus abnormalities.

Comment

Sympathetic ophthalmia is presumed to be an autoimmune, T-cell-mediated response to melanocyte self-antigens exposed during surgery or trauma. A cytokine-profiling study in an animal model resembling SO showed upregulation of TNF-α levels associated with photoreceptor damage.[3] As TNF-α potentiates T-cell-mediated immunity, TNF-α antagonist therapy may provide a targeted approach for anti-inflammatory therapy.[2]

Gupta et al reported a case of pediatric SO refractive to multiple immunosuppressants treated with intravenous infliximab, a chimeric murine/human monoclonal antibody targeting TNF-α, with prolonged control of inflammation achieved on infliximab alone.[4] Another case of an adult with SO refractory to multiple immunosuppressants achieved inflammation resolution with addition of adalimumab, a recombinant human monoclonal anti-TNF-α antibody dosed subcutaneously.[5] In a series of 131 patients with refractory uveitis, addition of adalimumab reduced immunosuppressive load by 50% in 85% of patients.[6]

This is the first report, to our knowledge, of TNF-α blocker adalimumab's use leading to resolution of inflammation in refractory pediatric SO. Addition of adalimumab led to long-term control with discontinuation of all other immunosuppressants for our patient. Although experience is limited to case reports, adalimumab could be considered for refractory SO and potentially other ocular autoimmune conditions where TNF-α is thought to play a role in its pathogenesis.

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Dr. Yeh and Joon-Bom Kim had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Role of the Sponsors

The sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

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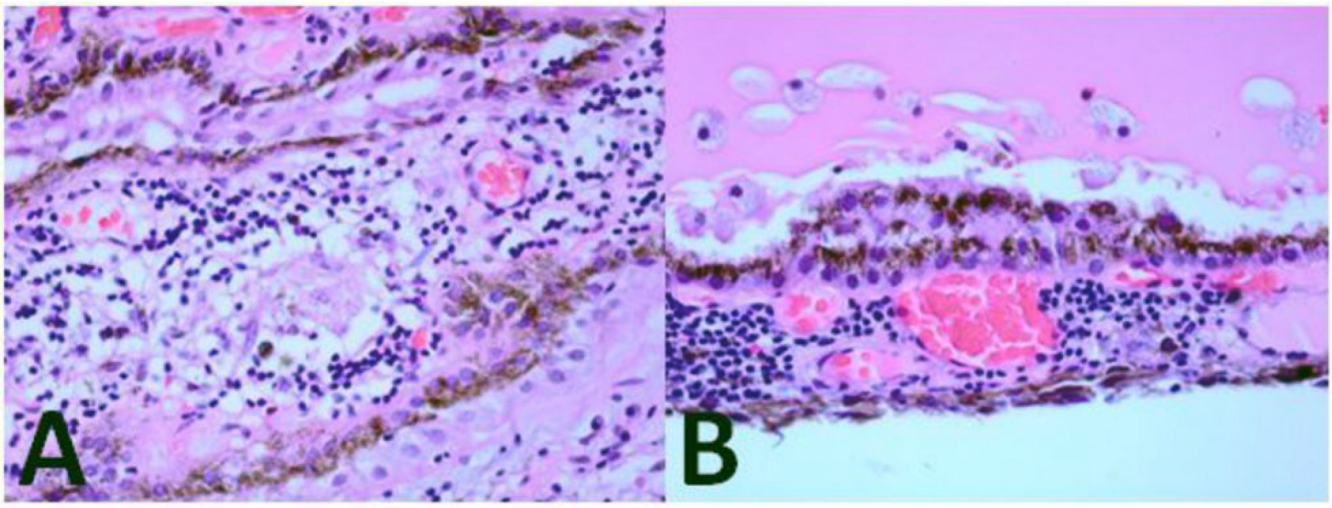

Figure 1. Enucleated Specimen

The enucleated right eye contained (A) a diffuse chronic inflammatory infiltrate in the choroid including epitheliod histiocytes forming non-caseating granulomas and (B) Dalen-Fuchs nodules (hematoxylin and eosin, 100×).

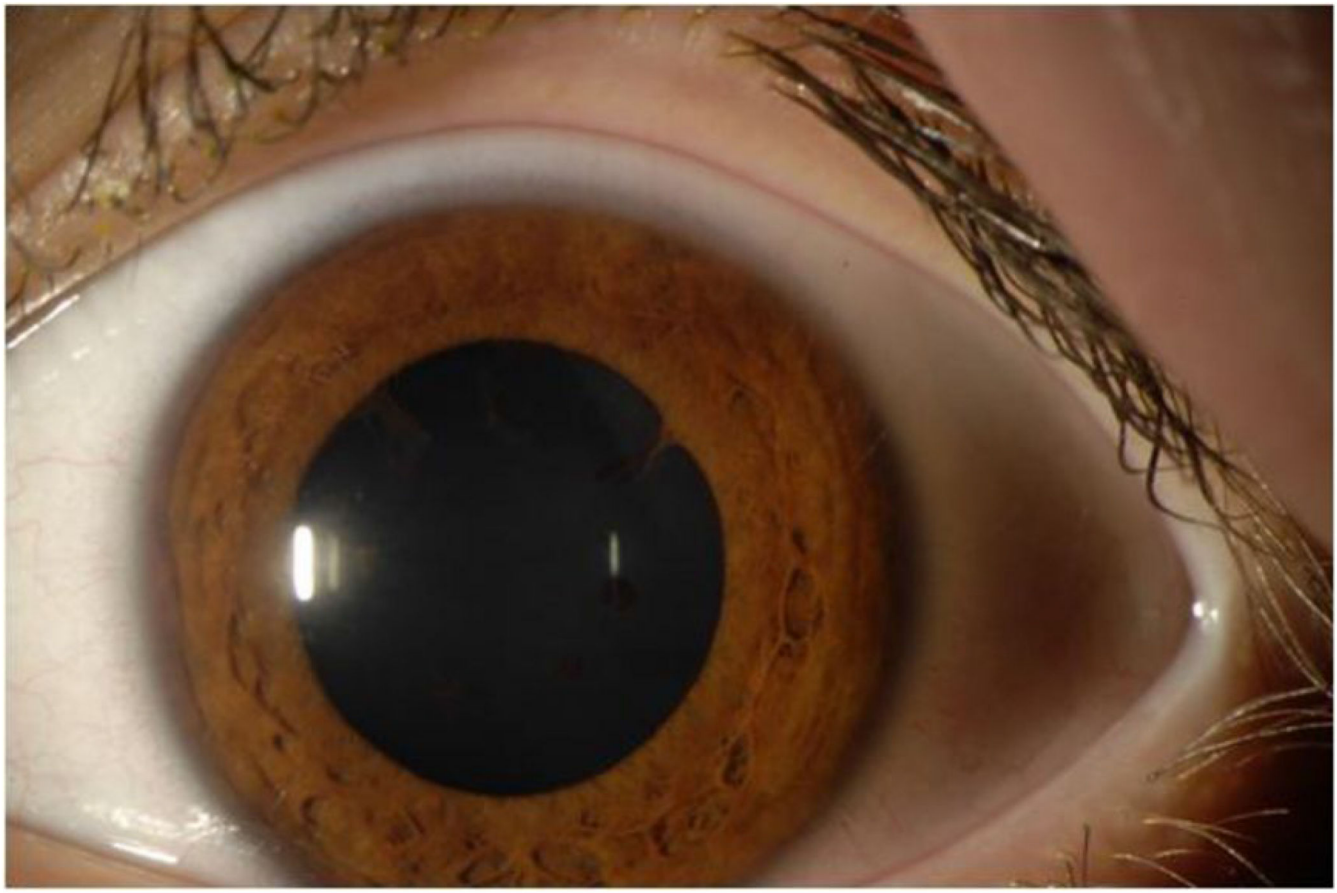

Figure 2. Anterior Segment Photograph

A chronic, low-grade inflammation including flare and posterior synechiae persisted in the left eye when oral prednisone was tapered.