of goblet cells of the tissues in rabbit and mouse models. 3,4 For that rebamipide led to an increased number of goblet cells of the epithelium of a human. The results also verify in vitro evidence that use of rebamipide alone for 3 months resulted in a marked increase of goblet cells of the rat conjunctiva. 5,6

A limitation of this study is its short follow-up time. A previous article demonstrated that topical rebamipide could be safely used for 4 weeks in patients with dry eye syndrome and that its effectiveness would last for at least 2 weeks after the end of treatment. 2 Careful observation is mandatory to ensure the safety of topical rebamipide. Also, the conjunctiva of the fellow eye was not available in this study. Further studies are needed to verify the goblet cells in the conjunctival tissues of human eyes that have not undergone surgery.

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Herein, we report the first use, to our knowledge, of adalimumab for refractory pediatric SO leading to resolution of inflammation.

Report of a Case | A young girl had accidental trauma to the right eye resulting in corneoscleral laceration, which was repaired the day of trauma. Postoperative visual acuity was hand motions OD. Two weeks later, increasing inflammation concerning for endophthalmitis prompted intravitreal antibiotic injection and subsequent pars plana vitrectomy with lensectomy. Visual acuity became no light perception OD postoperatively.

Nine weeks after her initial injury, the patient began experiencing photophobia and redness of her uninjured left eye. Visual acuity was 20/20 OS. Examination of the left eye under anesthesia showed anterior and posterior segment inflammation with white peripheral chorioretinal deposits concerning for SO. Treatment with topical prednisolone acetate, 1%, and oral prednisone, 60 mg/d, was started. Enucleation of the right eye was performed 11 weeks after the initial injury, with histopathologic findings consistent with SO (Figure 1). The patient was referred to our service for further management.

On our initial examination, visual acuity was 20/25 OS and intraocular pressure was 36 mm Hg OD 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 with oral prednisone. Treatment with topical timolol maleate, 0.5%, was started for elevated intraocular pressure.

Oral prednisone was tapered to 10 mg/d over a 12-week period in conjunction with initiating subcutaneous injection of 10 mg of methotrexate sodium weekly. Despite dose escalation of methotrexate sodium to 25 mg by subcutaneous injection weekly over the following 9 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 10 mg/d.

Subcutaneous injection of 20 mg of adalimumab every 2 weeks was initiated after a negative purified protein derivative reading, and within 3 months inflammation completely resolved with discontinuation of oral prednisone, prednisolone, and timolol. After 6 months of stability while receiving adalimumab, methotrexate was tapered and discontinued over 6 months.

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

Discussion | 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. As TNF-α potentiates T-cell–mediated immunity, TNF-α antagonist therapy may provide a targeted approach for anti-inflammatory therapy.

Gupta et al reported a case of pediatric SO refractory to multiple immunosuppressants that was treated with intravenous infliximab, a chimeric murine/human monoclonal antibody targeting TNF-α, with prolonged control of inflammation achieved with infliximab alone. An adult case of SO refractory to multiple immunosuppressants achieved inflammation resolution with addition of adalimumab, a recombinant human monoclonal anti-TNF-α antibody given subcutaneously. In a series of 131 patients with refractory uveitis, addition of adalimumab reduced immunosuppressive load by 50% in 85% of patients.

The enucleated right eye contained a diffuse chronic inflammatory infiltrate in the choroid including epithelioid histiocytes forming noncaseating granulomas (A), and it also contained Dalen-Fuchs nodules (B) (hematoxylin-eosin, original magnification ×100).
To our knowledge, this is the first report of the use of TNF-α blocker adalimumab 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 in which TNF-α is thought to play a role in pathogenesis.

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OBSERVATION

Tethered Vitreous Seeds Following Intravitreal Melphalan for Retinoblastoma

Placing a needle into an eye with retinoblastoma, whether for diagnostic or therapeutic purposes, has historically been avoided owing to concerns of extraocular spread along the needle tract.1,2 In the past 3 years, intravitreal injections of melphalan have been used worldwide, with excellent results for vitreous seeding and an exceedingly low risk of extraocular extension.3-4 The treatment course involves repetitive puncture sites with approximately 6 to 8 weekly injections and often a concomitant paracentesis by some groups.3,5 Techniques have been adopted to enhance safety, including reduction of intraocular pressure and cryotherapy of the injection site.5 Despite low documented risk of extraocular extension,4 we describe 2 instances in which active vitreous seeds were drawn toward the ocular surface. While disease did not exit the eye, it did tether to the injection site and eventually regressed with a continuation of treatment.

Report of Cases | Case 1. A young boy with bilateral retinoblastoma was previously treated with plaque and transpupillary thermotherapy. His right eye (Reese-Ellsworth group 5B, International Classification of Retinoblastoma group D) was treated with 8 ophthalmic artery chemosurgery infusions, cryotherapy, and laser. Despite this heavy treatment a large vitreous seed persisted, hovering over the macula. Intravitreal injections of melphalan, 30 μg/0.07 mL, were initiated. In brief, the injection was performed as follows. Digital massage reduced the intraocular pressure to less than 10 mm Hg and then the eye was prepared and draped in a sterile manner. Using a 33-gauge needle, 30 μg of melphalan was injected 3.5 mm posterior to the limbus. As the needle was withdrawn, the site was sealed and sterilized with cryotherapy. Sterile water was dropped over the eye to submerge it for 3 minutes. Moxifloxacin hydrochloride was instilled and indirect ophthalmoscopy confirmed patent vasculature.

Following 2 injections of melphalan, the vitreous seed was found tethered to the injection site at the pars plana (Figure and Video). Taking advantage of its location, the seed was treated with cryotherapy and an additional 3 injections of melphalan. At 1 month, the seed regressed into a linear collection of pigment; at 1 year, the seed diminished further into a pigmented linear fragment (Figure).

Case 2. A young boy with bilateral retinoblastoma previously treated with 6 cycles of systemic chemotherapy and enucleation of the right eye was referred for active disease and vitreous seeding in his remaining left eye (Reese-Ellsworth group 5B, International Classification of Retinoblastoma group D). After 3 intravitreal melphalan injections, the seed was found tethered to the pars plana with intervening, bridging strands of vitreous. Following an additional 5 injections and no cryotherapy, the seed regressed to a calcified fragment. At 6 months’ follow-up, the vitreous seed remains inactive.