Successful Treatment of Refractory Sympathetic Ophthalmia in a Child With Infliximab

Sympathetic ophthalmia (SO) is a bilateral granulomatous panuveitis following accidental or surgical trauma to 1 eye. Systemic corticosteroid therapy is first-line therapy, but immunosuppressive agents are commonly required for longer-term treatment. There is scant literature on the treatment of SO in children and none using modern therapy with biological response modifiers. We report a case of SO in a child treated successfully with infliximab after having failed therapy with methotrexate, cyclosporine, mycophenolate mofetil, and daclizumab.

Report of a Case. A 7-year-old boy was struck in the right eye by a toy arrow. The injury was repaired the same day with pars plana vitrectomy and lensectomy, corneal wound and retinal detachment repair, and intraocular foreign body removal. Seven days later, repeated vitrectomy was needed for endophthalmitis with subsequent visual acuity of no light perception. Enucleation of the damaged eye was not elected at the time. Six weeks after the injury, the patient visited his referring ophthalmologist with bilateral eye pain. Examination revealed visual acuity of 20/20 OS and 4/110 cells in the anterior chamber, with reported normal retinal examination results. He began treatment with oral prednisone, 60 mg/d; topical prednisolone acetate in the left eye hourly; neomycin sulfate, polymyxin B sulfate, and dexamethasone (Maxitrol) ointment in the left eye at bedtime; and scopolamine hydrobromide in the left eye twice daily. He was referred to our uveitis clinic, where he was seen 9 days later. At his initial visit to our clinic, visual acuity was no light perception OD and 20/50 OS. The right anterior segment was grossly malformed with no posterior view, while the left eye examination revealed 1+ cells in the anterior chamber. Posterior segment examination of the left eye revealed 1+ vitreal cells and haze, a normal optic nerve, and a whitish, pale retinal appearance diffusely throughout the posterior pole, with numerous midperipheral elevated, edematous choroidal infiltrates consistent with Dalen-Fuchs nodules. Fluorescein angiography demonstrated serous macular detachment and active chorioretinitis (Figure 1A and B).

Figure 1. Fluorescein angiograms at presentation depicting active chorioretinitis coalescing into central serous retinal detachment. A, Early phase. B, Late phase. C, Late phase 2 weeks after initiation of therapy.
The patient was treated with pulse intravenous methylprednisolone sodium succinate (Solu-Medrol), 650 mg/d (30 mg/kg), for 3 days followed by oral prednisone, 50 mg/d, cyclosporine, 60 mg twice daily (3.2 mg/kg), and methotrexate, 12.5 mg every week. The patient's family elected expeditious enucleation of the right eye, with histopathologic examination of the enucleated eye showing prominent choroidal granulomatous inflammation consistent with SO (Figure 2). The aforementioned regimen led to initial improvement, with all chorioretinal lesions gaining an atrophic appearance (Figure 1C and Figure 3). However, on steroid tapering to 40 mg of prednisone daily over 4 weeks, a recurrence of panuveitis required a repeated course of pulse methylprednisolone followed by oral prednisone, 50 mg/d, cyclosporine, 80 mg twice daily (6.5 mg/kg), and methotrexate, 12.5 mg every week. A second attempt to taper corticosteroids led to a third flare 4 months later, which occurred a week after treatment with oral prednisone was discontinued. This required a third round of pulse intravenous methylprednisolone followed by oral prednisone, 60 mg/d, cyclosporine, 100 mg twice daily, and substitution of mycophenolate mofetil, 600 mg twice daily, for methotrexate. His cyclosporine dose subsequently was reduced to 75 mg twice daily owing to elevation of the creatinine level. A third attempt to taper his prednisone dosage to 15 mg/d over the next 2 months led to another recurrence, requiring an oral steroid increase to 30 mg/d and initiation of treatment with intravenous daclizumab, 2 mg/kg every 2 weeks, with continuation of treatment with mycophenolate and cyclosporine; however, inflammation recurred 3 months later when the patient reached a prednisone dosage of 7.5 mg/d. At this time, treatment with daclizumab was stopped and treatment with infliximab was started at a dosage of 10 mg/kg every 4 weeks, with the prednisone dosage increased to 30 mg/d and the dosages of mycophenolate and cyclosporine maintained.

Two weeks after starting treatment with infliximab, the patient's inflammation was well controlled. We were able to successfully taper the prednisone dosage to 5 mg/d within 5 months of starting treatment with infliximab, with subsequent discontinuation of treatment with cyclosporine, prednisone, and mycophenolate 13, 17, and 24 months, respectively, after starting treatment with infliximab. At the last follow-up 26 months after starting treatment with infliximab, his visual acuity was 20/30–1/1 with continued quiescence.

Comment. To our knowledge, this is the first reported case of the use of infliximab, or any biological response modifier, in pediatric SO. Infliximab has been shown in previous studies to be an effective immunosuppressant for the treatment of refractory uveitis in adults and children. Elevated ocular and systemic levels of tumor necrosis factor have been found in patients and the retinas of enucleated eyes with SO and tumor necrosis factor may contribute to photoreceptor damage leading to vision loss in SO.

Our patient had been refractory to combination therapy with methotrexate and cyclosporine as well as combination therapy with mycophenolate, cyclosporine and daclizumab. Initiation of infliximab therapy led to a durable remission for more than 2 years and allowed a good visual outcome. Therefore, we suggest that infliximab therapy should be considered in cases of pediatric SO that are refractory to conventional therapy.

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Photographic Monitoring of Herpes Simplex Virus Keratitis During Anti-inflammatory Treatment

In the course of the Herpetic Eye Disease Study, we validated digital photomicrography and computer-assisted image analysis for evaluating the severity of stromal keratitis and endotheliitis due to herpes simplex virus. We have now conducted a nested prospective cohort study to investigate how corneal imaging can track the geometric metamorphosis of herpetic keratitis among 62 patients during the systematic administration of a topical corticosteroid and antiviral agent.

Methods. Individuals with herpes simplex virus stromal keratitis or endotheliitis gave informed consent under protocols approved by institutional review boards and were assigned to a Herpetic Eye Disease Study treatment regimen of prednisolone sodium phosphate, 1%, tapered from 8 times per day to once daily over 5 weeks and trifluridine, 1%, 4 times per day for 3 weeks and then twice daily. Standardized corneal photographs were obtained at baseline, and 62 patients had repeated photography taken a mode of 35 days (range, 32-38 days) later. Diapositives archived at the Herpetic Eye Disease Study Photography Reading Center were later scanned, converted to gray-scale equivalents, and calibrated to linear and luminance scales. Interactive image processing by one of us (B.M.M.), who was masked to slitlamp biomicroscopic measurements, estimated paired morphometric, cartographic, and densitometric values for area (in millimeters squared), shape factor (\(4\pi \times \text{area} / \text{perimeter}^2\)), location (polar coordinates on a corneal template), and relative intensity (average pixel-based gray level) of corneal inflammation and opacification at baseline and at 5 weeks.

Results. The area of corneal opacification contracted significantly \((P < .001)\) during 5 weeks of topical treatment with prednisolone and trifluridine. Inflammatory signs resolved with the prescribed treatment schedule in 43 eyes, while 19 eyes had lingering corneal infiltration also confirmed that a greater intensity of stromal inflammation and edema were more likely \((P < .001)\) to end up with a denser opacity. On completing 5 weeks of treatment, eyes having visual acuity worse than 20/100 on a modified Bailey-Lovie chart averaged a whiter opacity than those with better visual outcome \((P = .03)\).

Comment. Slitlamp photography is able to monitor dynamic alterations of corneal disease. In managing herpes simplex virus keratouveitis and endotheliitis, the examiner strives to adjudicate treatment responses during dosage adjustment of corticosteroids and antivirals. We found that digitized photographs can supplement the clinical follow-up of patients with herpetic keratitis and could potentially contribute to therapeutic decision making. Photoanalysis demonstrated how the disciform contour of stromal inflammation and edema fades and shrinks with treatment while retaining an ellipsoidal shape centered at its initial topographic position. Image processing also confirmed that a greater intensity of stromal inflammation predisposes to a whiter corneal opacity that in turn contributes to poorer vision.

New modalities in documenting conditions of the anterior segment are leading to improved representation and quantitative interpretation of ocular disorders. The integration of bioimaging and other ophthalmic metadata into a comprehensive electronic record offers the prospect of enriching patient management and facilitating teleconsultation in corneal practice.

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