MANAGING GLAUCOMA IN THE PATIENT WITH HERPETIC DISEASE

Success requires treating the underlying disorder, inflammation, and elevated IOP.

BY ADAM BREUNIG, MD, AND STEVEN V. L. BROWN, MD

CASE PRESENTATION

A 70-year-old woman was referred to our office as a glaucoma suspect in the setting of recurrent herpes simplex virus (HSV) epithelial and stromal keratitis of the right eye. The patient had no history of associated uveitis. Primary angle closure was suspected, and she underwent bilateral laser peripheral iridotomies (LPIs). Her medications at presentation included latanoprost at bedtime, a fixed combination of dorzolamide and timolol twice daily, brimonidine twice daily, trifluridine of varying frequency, frequent loteprednol tapers for intermittent corneal stromal involvement, and oral acyclovir 800 mg three times daily.

Although the LPIs succeeded in opening the angles, IOP remained in the mid-20s in the right eye. Optical coherence tomography of the retinal nerve fiber layer showed thinning of the right optic nerve compared to the left, with a corresponding nasal step on the visual field. Because the patient was overwhelmed by the drop regimen and we were concerned about corneal toxicity, we performed selective laser trabeculoplasty (SLT) in an attempt to reduce the medication burden. Unfortunately, the IOP remained unchanged.

Subsequently, the patient underwent trabeculectomy with mitomycin C in the right eye. Approximately 6 months postoperatively, she underwent a full-thickness corneal transplant in the same eye. Ten years later, she maintains a BCVA of 20/40 and an IOP in the upper teens on no glaucoma drops in the right eye. She continues to use loteprednol etabonate ophthalmic ointment 0.5% (Lotemax; Bausch + Lomb) once daily for rejection prophylaxis and takes oral acyclovir 400 mg twice daily to reduce the risk of recurrent HSV.

WHY TRY SLT?

This case illustrates the complexity of glaucoma management in the setting of herpetic eye disease. There were multiple reasons for the patient to have elevated IOP, including occludable angles with subsequent open-angle glaucoma after LPI, secondary open-angle glaucoma from chronic steroid use, and trabeculitis from herpetic eye disease. Because this patient had no prior episodes of uveitis, we felt safe performing SLT. Whether the procedure was ineffective because of possible underlying HSV is unclear. Regardless, the next step was more invasive glaucoma surgery.

HERPES, OCULAR HYPERTENSION, AND UVEITIS

Herpes simplex and herpes zoster are the two most common herpes viruses associated with elevated IOP and uveitis. They may cause a unilateral granulomatous keratouveitis with a recurrent course, associated with acute episodes of elevated IOP.[1] There are myriad possible etiologies for developing ocular hypertension (OHT) and/or secondary glaucoma from herpetic eye disease, including secondary angle closure owing to pupillary block from chronic inflammation, increased aqueous viscosity, trabeculitis, and steroid response. Previous studies of HSV and associated OHT have shown cellular changes in the trabecular meshwork suggestive of trabeculitis as a cause of elevated IOP.[1,2] Disruptions in the blood-aqueous barrier also give plasma proteins and inflammatory cells access to the anterior chamber, causing disruptions in outflow resistance (Figure 1).[2,3]

Interestingly, OHT may occur in 20% to 40% of uveitic patients, with one study finding a 13.1% rate of secondary glaucoma development requiring long-term therapy or surgery.[4] For HSV, the Herpetic Eye Disease Study (HEDS) gives guidelines on treating the underlying disorder,

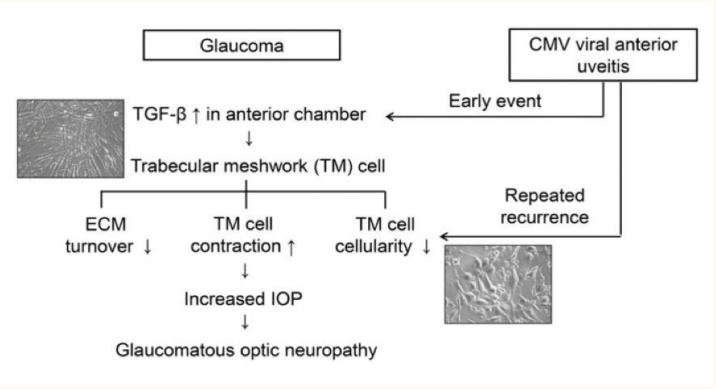

Figure 1. One possible mechanism for IOP elevation in herpetic anterior uveitis. Reprinted from Choi JA et al.[3] Creative Commons Attribution 4.0 International License: creativecommons.org/licenses/by/4.0.

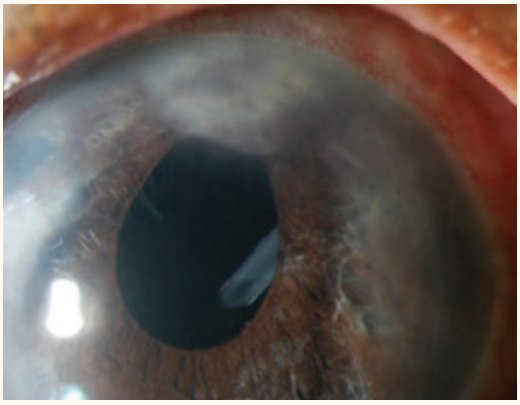

Figure 2. Sulcus placement of a glaucoma drainage device in a patient with glaucoma secondary to uveitis.

but the study does not pertain directly to glaucoma management.[5]

APPROACH TO GLAUCOMA MANAGEMENT

Medical

Glaucoma management in the setting of herpetic eye disease depends on several factors: treating the underlying disorder, treating inflammation, and treating the elevated IOP. The regimen includes oral antivirals (acyclovir, valacyclovir, or famciclovir) and topical antiviral agents (trifluridine or ganciclovir gel). Oral agents are used for stromal or endothelial involvement or when there is concern about surface toxicity from topical antivirals. Although the HEDS did not demonstrate a statistically significant benefit of oral acyclovir in treating HSV iridocyclitis, most practitioners prescribe long-term systemic antiviral therapy in an attempt to reduce recurrence risk (Table).[6]

Topical corticosteroids, cycloplegics, IOP-lowering drops, and surgery may also be needed, and it is crucial to treat inflammation adequately to reduce the risk of long-term damage to the trabecular meshwork. A common mistake is to undertreat inflammation for fear of a steroid-induced elevation of IOP, but steroid dosage and frequency do require close monitoring.

IOP-lowering drops may be less effective in the setting of uveitis, but there is no evidence supporting a first-line therapy.[7] The use of prostaglandin analogues in patients with uveitis is controversial, but a study comparing latanoprost with a fixed combination of dorzolamide and timolol revealed similar efficacy and no difference in inflammatory recurrence rates.[8] Laser trabeculoplasty may be considered for elevated IOP due to a steroid response, but the procedure is generally not recommended for patients with active uveitis because of concern about exacerbating inflammation.[9]

Surgical Intervention

If surgery is required, inflammation must be suppressed to optimize the success rate. In general, surgical success rates are lower for uveitic glaucoma than for primary open-angle glaucoma. Anti-inflammatory drops, perioperative systemic corticosteroids, and intraoperative subconjunctival or intravitreal triamcinolone may be beneficial. Risk factors for surgical failure include male sex, age younger than 45 years, nongranulomatous inflammation, and prolonged postoperative inflammation.[7]

Glaucoma drainage devices are often used for patients with uncontrolled uveitic glaucoma (Figure 2). A recent meta-analysis comparing the Ahmed Glaucoma Valve (New World Medical) and the Baerveldt implant (Johnson & Johnson Vision) in patients with refractory glaucoma, including uveitic glaucoma, concluded that the devices lower IOP comparably.[10] Trabeculectomy with mitomycin C is another option for surgical management, but it may be less effective in the long term compared to a glaucoma drainage device because of fibrotic tissue obstructing the filtering pathway.[11]

Microinvasive glaucoma surgery may one day prove beneficial for uveitic patients, given that these procedures reduce ocular tissue trauma. More long-term studies are needed to confirm their efficacy.

TABLE. CHARACTERISTICS OF ORAL ANTIVIRAL AGENTS FOR THE TREATMENT OF HSV

Acyclovir	400 mg	5 doses/day (active) 2 doses/day (suppressive)
Valacyclovir	1,000 mg	2 doses/day (active) 1 dose/day (suppressive)
Famciclovir	250 mg	3 doses/day (active) 1 dose/day (suppressive)

AT A GLANCE

- Herpes simplex and herpes zoster are the two most common herpes viruses associated with elevated IOP and uveitis.
- Glaucoma management in the setting of herpetic eye disease depends on several factors: treating the underlying disorder, treating inflammation, and treating the elevated IOP.
- In most cases, suppressive antiviral and anti-inflammatory medications, along with topical IOP-lowering drops, are successful for managing these patients. In recalcitrant cases, surgical intervention may be warranted.

CONCLUSION

Glaucoma and OHT may be associated with herpetic eye disease. In most cases, suppressive antiviral and anti-inflammatory medications, along with topical IOP-lowering drops, are successful for managing these patients. In recalcitrant cases, surgical intervention may be warranted. ■

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