Glaucoma-associated Ocular Surface Allergy and Toxicity

A Step Ladder Approach to Management

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CASE STUDY

A 78 year old Hispanic male veteran presented to the Miami VA eye clinic with complaints of “burning” in both eyes for the past 2 months. His symptoms were assessed as severe by a standardized 5-item Dry Eye Questionnaire (DEQ-5 = 17). He reported minimal relief of his symptoms using over-the-counter artificial tears 4–6 times daily. His past ocular history was significant for primary open angle glaucoma, treated with timolol BID, brimonidine BID, and travoprost QHS in both eyes. On examination, best corrected visual acuity was 20/30 OU and intraocular pressures were well controlled (18 OD, 16 OS) in comparison to his historic values (Tmax 32 OD, 26 OS). Examination of the anterior segment revealed normal lid margins, 1+ injection of the bulbar conjunctiva, trace papillae over the tarsal conjunctiva, and moderate punctate epithelial erosions over the inferior cornea OU. The posterior segment was remarkable only for glaucomatous cupping of the optic nerve head (cup-to-disc ratio of 0.6 OD, 0.8 OS). Ancillary testing revealed normal tear break-up time (TBUT 9s OD, 8s OS), moderate aqueous tear deficiency by anesthetized Schirmer testing (4mm OD, 5mm OS at 5min), and increased tear osmolarity (316 mOsms/L OD, 328 mOsms/L OS).

How would you address this patient’s chief complaint?

DISCUSSION POINTS

It is important to recognize ocular surface disease (OSD) as a common comorbidity complicating the management of glaucoma. Patients on medical treatment for glaucoma are 1.7 times more likely to report severe symptoms of OSD. Recognizing and addressing glaucoma-associated OSD can have important implications for treatment compliance, visual functioning, and overall quality of life.

The first and most important step in the evaluation of a patient with glaucoma-associated OSD is discriminating allergic from toxic etiologies. True allergic reactions to glaucoma medication are relatively uncommon. Hallmarks of an allergic response to glaucoma medication include contact dermatitis (Figure 1A), conjunctival chemosis or follicles, and rarely a vernal-like keratoconjunctivitis (Figure 1B). For patients with any of these stigmata of ocular allergy, the treatment is to identify and stop the offending medication, most commonly brimonidine.

Glaucoma-associated ocular surface toxicity is extremely common, and often overlooked by the clinician singularly focused on the management of glaucoma. Patients may have a normal exam or manifest subtle findings of OSD, such as conjunctival or corneal staining, tear film instability, or aqueous tear deficiency. The number of drops a patient is on, the daily load of preservatives, and the use of certain classes of glaucoma medication (viz. beta blockers and prostaglandin analogs) are recognized risk factors for the development of ocular surface toxicity.
Benzalkonium chloride (BAK) is the most commonly used preservative in commercially available glaucoma drops. While this cationic detergent has favorable bactericidal properties and promotes drug penetration into the eye, its chemical properties may also cause toxicity to the ocular surface. At the concentrations typically found in glaucoma medications (0.004-0.02%), BAK has been shown to disrupt lipid layering and alter the cytokine profile of the tear film, while exerting cytotoxic effects on conjunctival goblet cells, corneal epithelial cells, and corneal nerves. Therefore, efforts to reduce a patient’s daily exposure to BAK may significantly improve the signs and symptoms of glaucoma-associated OSD.

We advocate a “step ladder” approach to the management of this condition with objective and standardized follow-up (Figure 2). Typically, the first intervention we advise is the use of preservative-free artificial tears, keeping in mind that most bottled artificial tears also contain preservatives and use of these products may exacerbate glaucoma-associated ocular surface toxicity. The next step in management is to address BAK-induced inflammation on the ocular surface; sometimes simply a short course of topical corticosteroids can quiet the inflammation, but in many cases cyclosporine 0.05% ophthalmic emulsion (Restasis®) is more effective in achieving long-term remission of OSD signs and symptoms. For patients with recalcitrant symptoms despite these measures, it may be necessary to switch to preservative-free timolol (Timoptic Ocudose®) or tafluprost (Zioptan®), or non-BAK containing glaucoma medications, such as Alphagan® P (preserved with Purite®) and Travatan-Z® (preserved with sofZia®). Bear in mind that these medications are significantly more expensive than their BAK-containing counterparts and may not be covered by some insurance plans. In some cases, it may be more cost-effective to consider laser trabeculoplasty or surgical intervention to lower the patient’s IOP with less exposure to BAK-containing medications. However, in the majority of cases, we have found that patient’s symptoms can be controlled with more conservative interventions.

CASE STUDY: WRAP-UP

Our examination did not reveal any stigmata of allergy to glaucoma medication. The patient was diagnosed with glaucoma-associated ocular surface toxicity and switched to preservative-free artificial tears 4-6 times daily. He returned for follow-up 2 months later with persistent complaints of corneal dysesthesia, and at this point the decision was made to start prednisolone BID for one month and cyclosporine 0.05% BID. Three months later, his symptoms had improved (DES-5 = 9), his papillary conjunctivitis had resolved, and his tear film parameters had normalized (TBUT 10s OU, Schirmer’s 5mm OD, 6mm OS, tear osmolarity 310 mOSms/L OD, 308 mOsms/L OS).

CONCLUSION

Managing OSD in patients with glaucoma is similar to any other ocular disease, and is best approached with a standardized and objective method of diagnosis and management. True allergy to glaucoma medications is rare, but should be addressed by discontinuing glaucoma medications in this subset of patients. In cases of glaucoma-associated ocular surface toxicity, efforts to address BAK-induced inflammation and reduce the patient’s daily exposure to preservatives may significantly improve the signs and symptoms of OSD. We advocate a “step ladder” approach to management, beginning with preservative-free artificial tears, topical corticosteroids, and cyclosporine 0.05% (Restasis®), before
considering non-BAK preserved glaucoma medications, laser trabeculoplasty, or surgical IOP-lowering therapy.

REFERENCES


FIGURE LEGENDS

Figure 1: Stigmata of ocular surface allergy to glaucoma medications. A. Contact dermatitis. B. Vernal-like keratoconjunctivitis.

Figure 2: A “step ladder” approach to the management of glaucoma-associated ocular surface toxicity.