

# Herpes Simplex Virus Keratitis

BY MICHAEL L. NORDLUND, MD, PhD; TERRY KIM, MD; AND FRANCIS S. MAH, MD

## CASE PRESENTATION

A 60-year-old male presents with a significant nuclear sclerotic cataract. His examination is otherwise unremarkable except for a 4-mm nummular scar with inactive vesicles in the inferotemporal quadrant. Notably, the patient has a positive history of herpes simplex virus (HSV) keratitis that occurred 5 years ago (his only episode). How would you treat this patient?

### MICHAEL L. NORDLUND, MD, PhD

The question is, what is the appropriate prophylaxis against recurrent HSV in this patient? There are two objectives in HSV prophylaxis in this case. The first is to prevent a reactivation of the latent HSV, which would result in recurrent infection and intraepithelial keratitis. The second objective is to prevent a reactivation of the immune processes associated with HSV immune stromal keratitis. Both of these manifestations of HSV infection can be exacerbated by any source of inflammation or stress, including cataract surgery. Additionally, the use of topical steroids after cataract surgery suppresses the immune function of the ocular surface and anterior segment, which can further facilitate the transition of latent HSV to its active phase.

Prophylactic doses of oral antivirals disrupt HSV replication, and their reduction of both the frequency and duration of the HSV's recurrence is well documented.<sup>1</sup> Common oral antiviral prophylactic doses are acyclovir 400 mg b.i.d., valacyclovir 500 mg q.d., or famciclovir 250 mg b.i.d., but dosing must be adjusted in patients with reduced renal function. Although topical antivirals reduce HSV replication on the ocular surface, they penetrate the cornea poorly and thus are inadequate in prophylaxis.

To my knowledge, there is no definitive paper that provides guidance on when oral antivirals should be started and how long they should be used postoperatively. My standard approach is to start oral acyclovir

400 mg b.i.d. at the time of cataract surgery, and I ask the patient to continue the drug for 1 month while he is on a tapering dose of a topical steroid. In patients with evidence of previous HSV infection in or approaching the visual axis, I am more aggressive and will often recommend prophylactic acyclovir long term, even in the absence of surgery.

Topical steroids are the treatment of choice for both the management and prophylaxis of the recurrent inflammatory processes in HSV immune stromal keratitis. As mentioned earlier, I use a declining regimen of topical steroids (typically prednisolone acetate 1%) for 1 month after cataract surgery. In patients with HSV immune stromal keratitis that is in remission at the time of cataract surgery, I use the same tapering dose but watch the patient closely for evidence of recurrent inflammation. Occasionally, such individuals will require a slower tapering. Patients who are already on topical steroids to control HSV immune stromal keratitis at the time of surgery require more aggressive treatment. I typically dose them with increased topical steroids 1 week preoperatively and frequent topical steroids postoperatively. Thus, in this patient, I would start acyclovir 400 mg orally b.i.d. at the time of surgery and continue it for 1 month postoperatively as he tapered his topical prednisolone acetate.

### TERRY KIM, MD

Based on the clinical findings in this case, my recommendations regarding antiviral prophylaxis include starting the patient on oral acyclovir at 400 mg b.i.d. (or the equivalent dose of valacyclovir or famciclovir) along with topical prednisolone acetate 1% q.i.d. for at least 2 weeks prior to cataract surgery. I would then taper the topical corticosteroid appropriately after cataract surgery and continue the oral acyclovir for at least 6 (and preferably 12) months, as long as the patient's renal function is normal.

My rationale for this prophylactic medication regimen lies in the patient's clinical history and examination and is supported by some of the conclusions of the Herpetic Eye Disease Study (HEDS) group. The combination of his doc-

umented history of HSV keratitis and an obvious nummular corneal scar with associated vascularization (albeit inactive) warrants topical and oral therapy. The HEDS showed that topical corticosteroids are safe and effective in reducing the persistence and progression of HSV stromal keratitis when used in combination with an antiviral agent (ie, topical trifluorothymidine or oral acyclovir).<sup>2</sup>

The study also showed that oral acyclovir can decrease the frequency of recurrent HSV keratitis, especially in patients with a history of stromal disease.<sup>3</sup> Furthermore, the HEDS and other studies have demonstrated that long-term suppressive therapy with an oral antiviral agent (ie, acyclovir 400 mg b.i.d. for 12 months) greatly reduces the recurrence of HSV epithelial and stromal keratitis and showed that long-term antiviral prophylaxis was most beneficial for patients with a history of HSV stromal keratitis.<sup>1,4</sup> Because various factors have been associated with the reactivation of HSV (ie, surgery, trauma, physical/emotional stress, fever, UV exposure, etc.), the benefits of instituting an antiviral prophylactic regimen and continuing it long term in this patient would certainly outweigh the limited risks associated with these medications.

**FRANCIS S. MAH, MD**

This case is interesting because the current peer-reviewed literature is lacking. There has not been a randomized, masked clinical trial to help answer the question of what to do upon encountering a history of HSV keratitis prior to otherwise routine cataract surgery. There are five postoperative complications that we clearly must try to prevent in this patient: (1) a recurrence of HSV epithelial keratitis; (2) HSV uveitis; (3) HSV stromal keratitis; (4) HSV endotheliitis; and (5) HSV trabeculitis. The first two complications in the list are the most likely to occur.

Given the landmark HEDS, it would be most prudent to start the patient on acyclovir 400 mg b.i.d. 2 or 3 days before surgery. I would commence therapy early, because stress alone could cause a recurrence of HSV keratitis, and I want the level of the drug to be high enough to produce effective prophylaxis. Alternatives to acyclovir include valacyclovir 500 mg b.i.d. or famciclovir 250 mg b.i.d. I would continue the oral prophylaxis for 1 month or at least until the epithelium had healed, the normal postoperative inflammation had resolved, and/or the topical anti-inflammatory medications (steroid and/or NSAID) were discontinued, because these medications can facilitate a recurrence. Although the HEDS indicated that topical trifluridine would be an efficacious alternative, I would avoid this topical agent in lieu of the oral medications, because the former can be toxic to the epithelial surface.

Regarding the possibilities of HSV-related uveitis, stro-

mal keratitis, endotheliitis, and trabeculitis, I would increase my postoperative dosing of prednisolone acetate 1% to every 2 hours for the first couple of days. If everything seemed in order, I would taper the drug during the following 4 weeks.

Finally, I would use an aqueous suppressant such as a beta-blocker, calcium channel blocker, or alpha-agonist immediately following surgery as prophylaxis against the possibility of a pressure spike from trabeculitis. If the IOP were normal, I would discontinue the glaucoma drug. I would avoid the use of a prostaglandin analog due to the potential risk of stimulating a recurrence of HSV keratitis and the possibility of predisposing the patient to cystoid macular edema.<sup>5-8</sup> ■

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