Corneal Endotheliitis With Quantitative Polymerase Chain Reaction Positive for Human Herpesvirus 7

H
uman herpesvirus 7 (HHV-7), a common virus of the subfamily of β-herpesviruses like cytomegalovirus (CMV) and HHV-6, was isolated initially from peripheral blood cells in adults. It causes ubiquitous infection in children as well as exanthema subitum. However, HHV-7–related ocular manifestations have not been reported. We describe a patient with unilateral corneal endotheliitis with aqueous humor positive for HHV-7 DNA by real-time polymerase chain reaction (PCR).

Report of a Case. A 62-year-old man had a foreign-body sensation and decreased vision in his left eye. When the symptoms worsened despite treatment with topical antibiotics and betamethasone sodium phosphate, 0.1%, he was referred to us. At the first examination, the best-corrected visual acuity was 20/400 and the intraocular pressure was 33 mm Hg in the affected eye. Slitlamp examination showed severe corneal edema, ciliary injection, and keratic precipitates (Figure 1). The fundus, optic nerve, and fellow eye were normal.

Serologic testing results for HHV (herpes simplex virus, varicella-zoster virus, Epstein-Barr virus, CMV, HHV-6, and HHV-7) were positive. The patient had no history of systemic diseases. Based on the ocular manifestation, idiopathic corneal endotheliitis with iridocyclitis was suspected; however, topical and systemic steroids (topical betamethasone, 0.1%, 4 times daily and oral betamethasone, 1 mg/d) and ocular antihypotensive therapy (timolol maleate, 0.5%, twice daily and oral acetazolamide, 500 mg daily) were ineffective, resulting in suspicion for a viral infection. After the patient provided informed consent, an aliquot of 0.1 mL of aqueous humor was collected from the affected eye and real-time PCR analysis for HHVs (herpes simplex virus 1 or herpes simplex virus 2, varicella-zoster virus, Epstein-Barr virus, CMV, HHV-6, HHV-7, and HHV-8) was performed. Our real-time PCR procedure detected only HHV-7 DNA, which amplified the U37 gene DNA of HHV-7 (126 base pairs) using a specific primer and probe (HHV-7 DNA copies, 4.1 × 10^5/mL). Twenty aqueous humor samples from patients with cataract without keratitis who were negative controls contained no HHV-7 DNA. These findings led to the diagnosis of HHV-7–related keratitis. The medications were replaced with topical ganciclovir, 1%, an antiviral agent not only for CMV but also for HHV-7, 6 times daily with a topical steroid (betamethasone, 0.1%, 4 times daily). Slitlamp examination, visual acuity measurements, and real-time PCR were performed throughout the clinical course (days 0, 14, and 28). After ganciclovir therapy was started, corneal edema and keratic precipitates ultimately resolved (Figure 2). The intraocular pressure gradually decreased to less than 15 mm Hg without hypotensive agents. The best-corrected visual acuity recovered to 20/20 along with improved slitlamp findings. The HHV-7 copies decreased after the start of ganciclovir therapy to an undetectable level with clinical improvement, and the antiviral therapy was terminated. The number of corneal endothelial cells in the affected eye decreased to 1052/mm² during the recovery stage compared with 2432/mm² in the unaffected eye. There has been no recurrence 1 year after treatment.

Comment. To our knowledge, this is the first report of real-time PCR–confirmed corneal endotheliitis positive for HHV-7 in the aqueous humor of the affected eye, which is also the first ocular manifestation related to HHV-7. This confirmation by real-time PCR allowed confident initiation of the appropriate ganciclovir treatment and subsequent clinical improvement.

Using PCR to detect HHV-7 did not necessarily mean that HHV-7 caused the clinical manifestations of corneal endotheliitis. However, in our patient, topical antiviral therapy effective for HHV-7 improved the clinical status along with the decreasing HHV-7 load, indicating that HHV-7 was a causative agent of corneal endotheliitis.

This case of HHV-7 corneal endotheliitis manifested unilaterally in the same manner as other types of herpetic keratitis such as herpes simplex virus, varicella-zoster virus, or CMV. A previous article indicated that HHV-7 appears to be closely related to CMV and is found in similar clinical situations. We recently reported detecting CMV in about 25% of cases with corneal endo-
Endotheliitis of unknown etiology.5 The causes of the other 75% of cases of endotheliitis are unknown. Further investigation is needed to identify the HHV-7 prevalence in corneal endotheliitis.

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Figure 2. The relationship between therapeutic outcome with ganciclovir, 1%, and human herpesvirus 7 (HHV-7) copy number. A, A slitlamp photograph shows total corneal edema with keratic precipitates before ganciclovir treatment (day 0). B, The corneal edema gradually has decreased, but localized edema remains 2 weeks after ganciclovir treatment (day 14). C, The corneal edema and keratic precipitates are decreased 4 weeks after ganciclovir treatment (day 28). D, The HHV-7 copy number gradually has decreased in response to ganciclovir and by day 28 has reached an undetectable level along with improved visual acuity and slitlamp findings. BCVA indicates best-corrected visual acuity.

Systemic and local diseases can affect the content and color of the tear film. Bloody tears (hemato dacryorrhea) are a red discoloration of the tears associated with several conditions, including epistaxis, contact lens irritation, severe anemia, coagulopathies, conjunctival vascular tumors, Osler-Weber-Rendu disease, nasolacrimal sac tumors, and conjunctival melanoma.1,2 Additionally, some drugs and diagnostic dyes can also change the color of the tears. Ghassemi et al3 have recently reported black tears (melanodacryorrhea) due to necrotic uveal melanoma. In this article, we describe a patient with bilateral black tears who was found to have bilateral argyrosis of the conjunctiva.