

Adenovirus-mediated corneal endotheliitis: a case report

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Dear Editor,

Corneal endotheliitis is a common and intriguing clinical entity characterized by corneal edema, keratic precipitates, and mild to moderate anterior chamber reaction, which occupies the important pathogenic factor of corneal blindness^[1]. Robin *et al*^[2] first described a patient who suffered from intraocular inflammation and progressive corneal endotheliitis associated with herpes simplex infection. Since then, accumulating clinical evidence confirmed that its etiology was mainly attributed to the family of herpesviridae, including herpes simplex virus, varicella zoster virus, and cytomegalovirus, which initiated the direct cell damage and immune- and inflammatory-mediated lesion on endothelial cells^[1,3]. However, some other pathogenic microbes were involved in corneal endotheliitis. We previously reported several cases of uncommon fungal corneal endotheliitis^[4]. Here, we presented a case diagnosed as adenovirus-mediated endotheliitis. This study was approved by the Ethical Committee of the Third Affiliated Hospital of Guangzhou Medical University. The informed consent was obtained from the patient and his guardian. The treatments of this study followed the Declaration of Helsinki.

Case Presentation A 14-year-old male complained eye redness, watery discharge, and photophobia in both eyes 10d before, accompanied by a blurred vision for 1d in the left. His medical history did not show any systemic disease, ocular trauma, surgery, and infection in both eyes. The clinical symptoms still progressed even if a levofloxacin eye drop was administered by the local medical clinic for 7d. The visual acuity was counting fingers/50 cm in the left eye and 40/50 in the right. Intraocular pressure (IOP) was about 12-14 mm Hg

in both eyes. Preauricular lymphadenectasis appeared on both sides. The slit-lamp examination revealed serious conjunctival congestion and some small circular subepithelial infiltrates scattered in the central area of the cornea in the left eye. Stromal edema, Descemet's membrane folds, anterior chamber flare, and some keratic precipitates could be found in the lesion area, but without epithelial defect and ulcer. The endothelial layer looked blurred like the ground glass. At 4 o'clock position of the right, one subepithelial infiltrate was found but lacked stromal edema and ulcer. Conjunctival scrapings were performed for the etiologic assay of herpes simplex virus, cytomegalovirus, varicella zoster virus, and adenovirus through reverse transcription-polymerase chain reaction (RT-PCR). But they were all negative. With the clinical presumed diagnosis of adenovirus-mediated endotheliitis, topical ganciclovir ophthalmic gels were applied to the left eye 3 times a day, together with 1% dexamethasone eye drops 6 times a day, and to the right 1 time a day. The symptoms of the left eye improved, however, those of the right progressed on day 3, showing for the occurrence of stromal edema near the initial lesion. And then, 1% dexamethasone eye drops 6 times a day was added to the right eye. After 7d, the signs and subjective symptoms of both eyes improved (Figures 1 and 2). However, another episode occurred that topical ganciclovir and dexamethasone were abruptly stopped by the patient himself, rather than gradually tapered according to the doctor's advice, which resulted in the relapse of the corneal endotheliitis in the left eye 4wk later, accompanied by serious iritis. The slit-lamp examination found stromal edema, Descemet's membrane folds, anterior chamber flare, and inflammatory keratic precipitates. A fibrous membranous exudation was deposited at the surface of the lens of the pupil area, with partial posterior synechia of the iris. Adenoviral etiology was found in the aqueous humor by RT-PCR. Acyclovir 400 mg 4 times a day were used, combined with topical ganciclovir gels and 1% dexamethasone eye drops. After 7d, the corneal edema, fibrous membranous exudation, and anterior chamber flare relieved and gradually disappeared. Topical and systemic medications were tapered over the next 4wk. In the 6-month followed-up, the endotheliitis never relapsed and the cornea remained clear.

DISCUSSION

Human adenovirus is mainly associated with epidemic keratoconjunctivitis, which characterized by eye redness, pseudomembrane formation, subepithelial infiltrates,

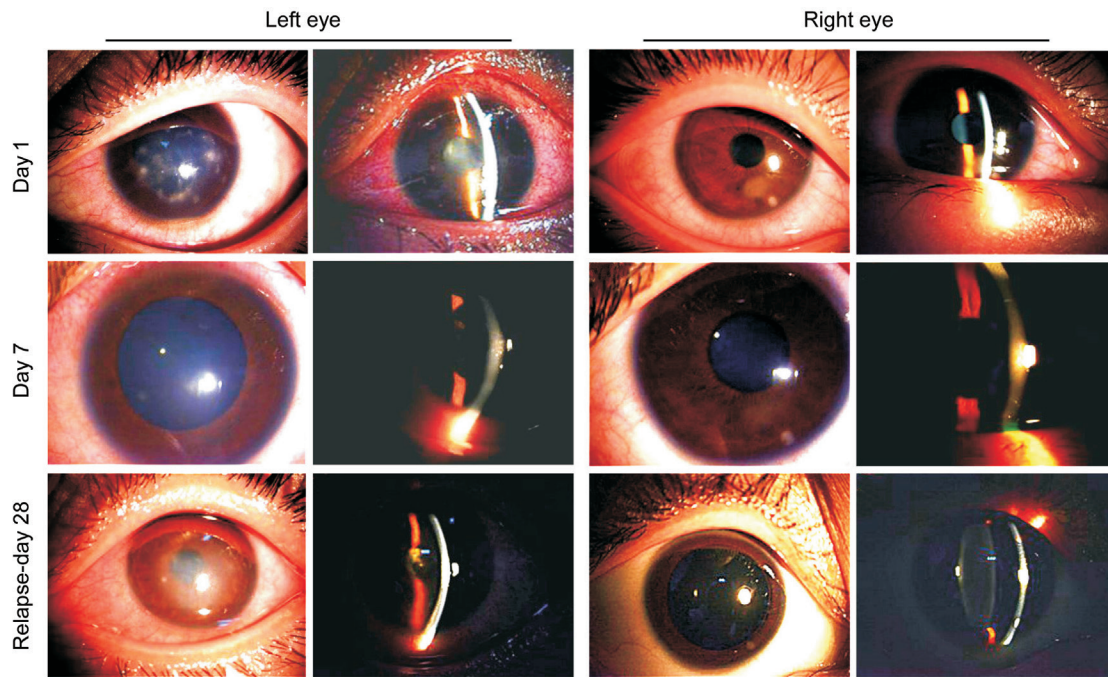


Figure 1 The slit-lamp examination revealed conjunctival congestion, subepithelial infiltrates, stromal edema, Descemet's membrane fold, anterior chamber flare, and keratic precipitates in the left eye on day 1. The endothelial layer looked blurred. In the right one, a subepithelial infiltrate was found at 4 o'clock position. The signs and subjective symptoms improved on day 7. On day 28, corneal endotheliitis relapsed in the left eye, accompanied by serious iritis, characterized by stromal edema, endothelial fold, anterior chamber flare, keratic precipitates, fibrous membranous exudation, and partial posterior synechia of the iris.

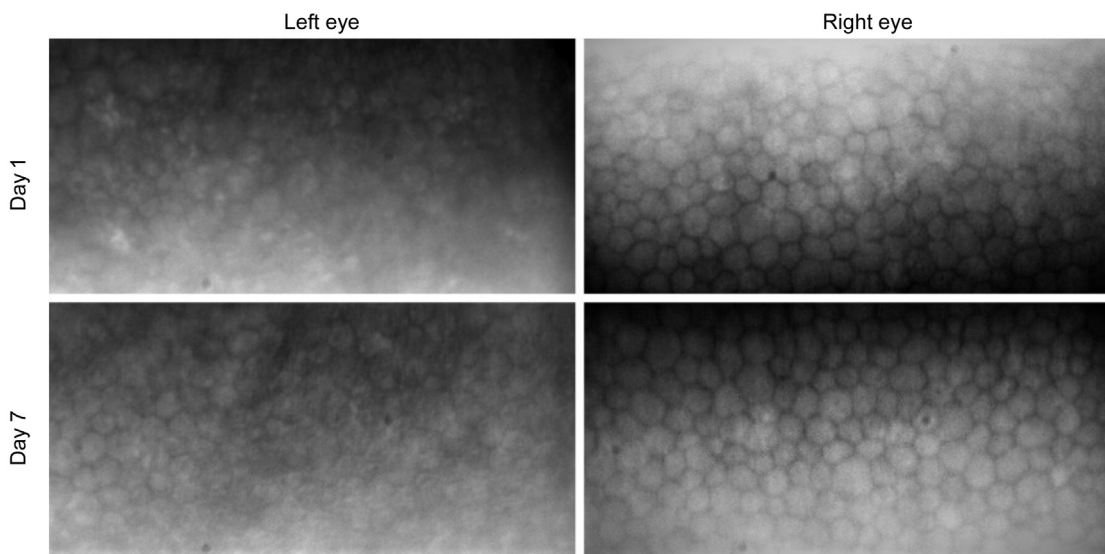


Figure 2 Specular microscope found that the endothelial layer looked blurred and the outlines of endothelial cells were obscure in the left eye on day 1. By day 7 after treatment, clear outline of cells occurred.

preauricular lymphadenectasis, and affected people of all ages and regions^[5]. There are few published reports on human adenovirus-mediated endotheliitis. Pflugfelder and Roussel^[6] had previously presented a case of endothelial dysfunction associated with adenoviral epidemic keratoconjunctivitis. Bilateral disciform keratitis or stromal edema were also found in the patients who suffered from adenoviral conjunctivitis 3wk before^[7-8]. For this case, the reasons for the initial diagnosis of adenovirus-mediated endotheliitis were as follows: first, the

clinical signs showed initial epidemic keratoconjunctivitis and subsequent corneal endotheliitis, characterized by eye redness, subepithelial infiltrates, preauricular lymphadenectasis, stromal edema, Descemet's membrane folds, anterior chamber flare, and inflammatory keratic precipitates. Second, corneal endothelial lesions were near or around the subepithelial infiltrates and their onsets were consistent with the development of an adaptive immune response, which suggested that they were associated with direct adenoviral damage and/or

adenovirus-mediated immune response. Third, a remarkable response to antiviral agents and corticosteroid was a shred of further supportive evidence for the diagnosis of adenovirus-mediated endotheliitis. Adenoviral etiology was found in the aqueous humor by RT-PCR during the relapse period, which further confirmed the initial presumed adenovirus-mediated endotheliitis.

The direct damage and immune response induced by the pathogens are the basic pathological mechanism of corneal endotheliitis. It appears that adenovirus is capable of damaging the affected cells and activating an immune response, which can cause corneal endotheliitis similar to that caused by herpesviridae or other viruses. Adaptive immunity to adenovirus hexon mediates complement-mediated lysis of adenovirus-infected cells and antibody-dependent cell-mediated cytotoxicity. However, another puzzle that needs to be further clarified is whether any variations happened to adenoviral etiology, which caused some change of its biological characteristics, prompted it to invade into the endothelial layer. Furthermore, it is worth notifying that it is possible to dig into any other novel or variant pathogens involved in the corneal endotheliitis, not only herpesviridae.

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Authors' contributions: Wang SY is the main clinician managing the patient. Li B is a member of the ophthalmologic team and drafted the manuscript. Tian Y is responsible for the

pathogenic test. Li DH is the lead consultant in the care of the patient. All authors read and approved the final manuscript.

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Conflicts of Interest: Wang SY, None; Li B, None; Li DH, None; Tian Y, None.

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