Persistent epithelial defect after penetrating keratoplasty caused by adenoviral infectious keratitis

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SUMMARY

A causal role of herpes simplex infection in persistent epithelial defect following penetrating keratoplasty (PKP) has been documented in the past. Instead, not much information is available on the role of adenovirus infection in delayed epithelization following PKP. Here, we describe a case of persistent epithelial defect due to adenoviral infection keratitis confirmed by PCR analysis. Adenovirus keratitis can be an unusual cause of delayed epithelization after PKP.

KEY WORDS: Adenovirus, Persistent epithelial defect, Penetrating keratoplasty, PCR (polymerase chain reaction)

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INTRODUCTION

Epithelial defects frequently occur in the donor cornea in the early and, less commonly, in the late postoperative period after penetrating keratoplasty (PKP). Epithelial defects in the early postoperative period may result from exposure before death, trauma during tissue retrieval, loss of the donor epithelium during storage or the accidental, or purposeful removal of graft epithelium during surgery. Contributing factors for postoperative epithelial defects include ocular surface disorders, such as aqueous deficiency dry eye, exposure secondary to eyelid abnormality, ocular cicatrizing disorders, limbal stem cell deficiency and donor-recipient misalignment resulting in dry areas (Mannis *et al.,* 1997). When epithelial defects do not heal within the first 10 to 14 days with conventional treatment they are called persistent epithelial defects (PED) and they are considered one of the most common early postoperative complications after PKP (Mannis *et al.,* 2006).

Early postoperative epithelial defects usually respond promptly to supplemental lubrication, punctum plugs, serum eye drops, bandage contact lens and less often may require a tarsorrhaphy. Nonresponsive epithelial defects may also result from herpes simplex virus (HSV) infection, even in patients without a clinical history of HSV (Beyer *et al.,* 1990; Remeijer *et al.,* 1997).

We describe a case of persistent epithelial defect after an uncomplicated PKP for keratoconus in a young patient (with no limbal or conjunctival epithelial abnormalities) in which PCR analysis of conjunctival scraping demonstrated the presence of adenoviral infection.

CASE REPORT

A 42 year-old male with keratoconus presented with visually limiting irregular astigmatism in his right eye with a best-corrected visual acuity of 2.0 LogMAR and with pinhole visual acuity of 0.4 LogMAR. An uncomplicated penetrating keratoplasty (PKP) was performed with an 8.50 mm or-

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gan-cultured donor cornea secured into a 8.25 mm recipient opening with a single 16 bite running 10-0 nylon suture. On the first postoperative day the graft demonstrated mild diffuse stromal edema and a 6 mm diameter oval shape epithelial defect in the central cornea with moderate perikeratic injection. These findings were consistent with the first post operative day of uncomplicated PKP. Standard systemic (methylprednisolone 80 mg/die IV) and topical medication (Tobradex x 3/die, Oftacilox x 3/die and Atropine 1%) were started.

In the following days the epithelial defect did not resolve. At day five after surgery it started to increase in its dimension with worsening of corneal edema and perikeratic injection. Culture of both explanted host cornea and corneo-scleral ring of donor cornea were negative for bacteria and fungi. Fellow eye showed no alteration at this time. At day eight after surgery the epithelial defect in-

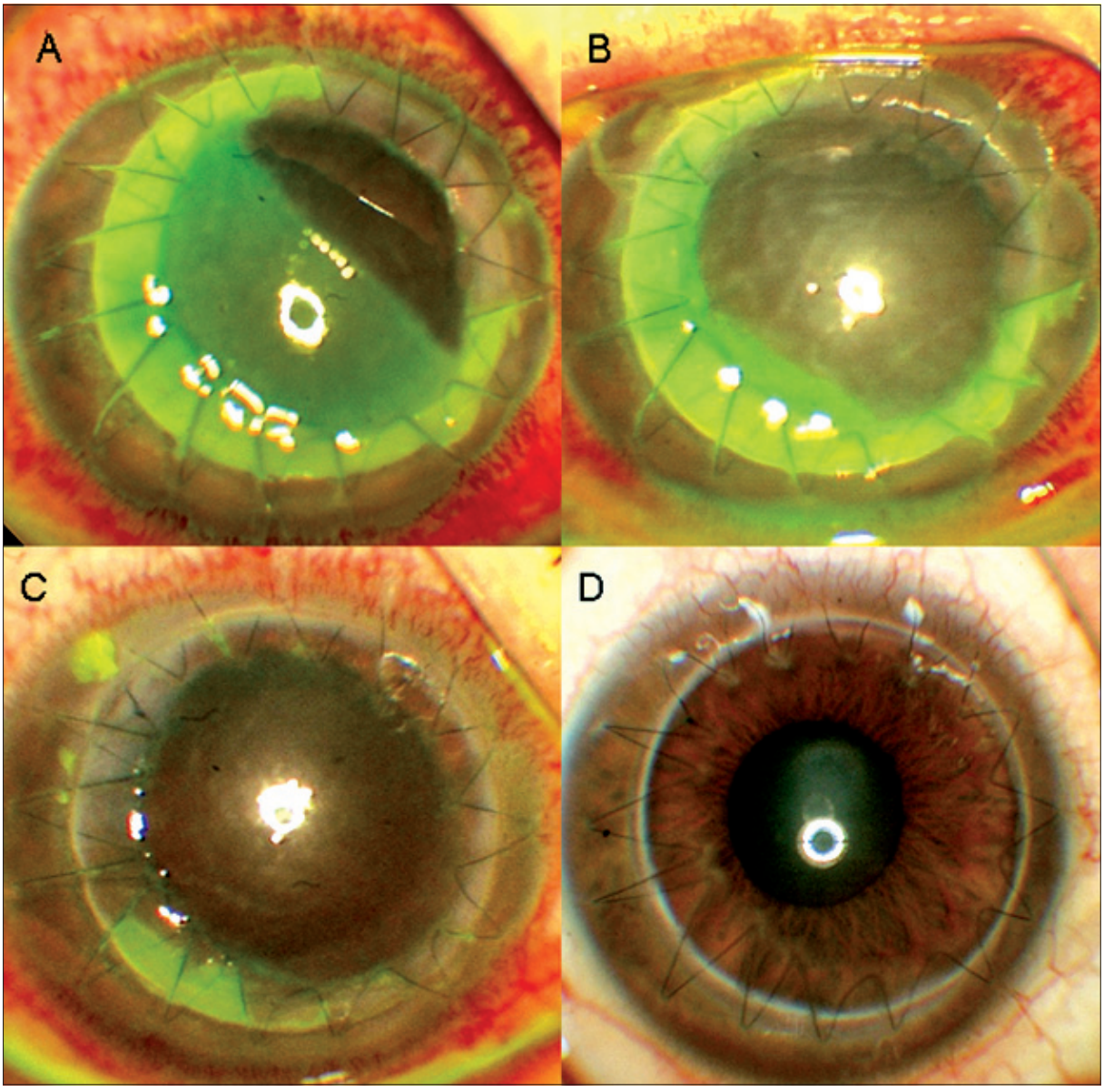

FIGURE 1 - *Fluorescein staining of the epithelial defect at 8 days after surgery (top left), at 2 weeks (top right), at 3 weeks (bottom left) and at the end of third week (bottom right).*

volved almost completely the graft (Fig. 1) and infection keratitis was suspected. Because the epithelial defect did not respond to standard treatment after PKP, HSV keratitis was considered, even if the patient had no previous history of HSV infection. The fellow eye showed mild conjunctival injection. No follicular response was detectable or subepithelial infiltrates in either eye. Furthermore no preauricular lymphadenopathy was present.

Corneal and conjunctival scraping was performed in the edge of the epithelial defect with a disposable Kimura spatula. Conjunctival scraping was performed also in the fellow eye. The collected material was immediately sent to the laboratory for HSV1&2 PCR and bacterial and fungal culture. Due to a consistent number of epidemic kerato-conjunctivitis diagnosed in our clinic during the same period, an adenovirus PCR was also requested for both eyes.

Adenovirus DNA was searched for by nested PCR using the Adenovirus Oligomix Alert kit (Nanogen Advanced diagnostics Srl., Turin, Italy). The primers target a region corresponding to the major capsid protein gene (hexon) as described (Saitoh-Inagawa *et al.,* 1996). The amplified products were run on a 2% agarose gel stained with ethidium bromide and visualized under ultraviolet light.

HSV1&2 were detected by a qualitative Real-Time PCR using the HSV typing kit (Cepheid, Sunnyvale, CA, USA). The primers included in the mix target the glycoprotein D gene of HSV1 as well as the glycoprotein G gene of HSV2. An internal control allows a control for PCR inhibition. HSV1 and HSV2 viruses isolated from Vero cells were used as positive control, while the PCR mix containing sterile water was used as negative control.

The presence of bacteria and fungi was checked by seeding a bacterial swab on 4 different culture media (CNA, PVX, Saburaud and McConkey medium, respectively).

Amplification of HSV1&2 as well as bacterial and fungal cultures gave negative results. By contrast, adenovirus amplification was positive in both eyes.

A bandage contact lens was then placed and artificial tears added to initial therapy. The epithelial defect healing process started the following week and it resolved completely at the end of the third week after surgery (Figure 1). Best Corrected Visual Acuity at week 4 was 0.5 LogMAR (-8 sphere -4 cylx95) and 0.3 LogMAR at 2 months after surgery.

After PKP large epithelial defects frequently occur in the donor cornea in the early and, less commonly, in the late postoperative period. If they are not properly diagnosed and treated, eventual graft failure may occur.

Graft re-epithelialization after penetrating keratoplasty usually takes no longer then one week after surgery. It is important to obtain rapid and complete corneal epithelial healing during the first week because PED is a risk factor for inflammation, infection, corneal scaring and graft failure. Non healing postoperative epithelial defects have been described in case of HSV infection in patients without a clinical history of herpes infection. A recent report described adenoviral-related epithelial defects as a late complication in a patient that had had a common conjunctival infection 2 years following LASIK procedure. The patient's eyes showed a compromised stability of the overlying epithelium at the flap margin that caused a frank epithelial loss (Lee *et al.,* 2007).

To our knowledge, this is the first time that adenoviral infection has been demonstrated in association with a persistent epithelial defect in the first period after PKP. Although this unique case does not allow a causal link to be established between adenoviral infection and epithelial healing delay, it is known that adenovirus can disrupt the tight junction between epithelial cells then delaying the epithelial healing process (Walters *et al.,* 2002).

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