A Rare Intervention in a Rare Disease: Simultaneous Bilateral Keratoplasty in Bilateral *Acanthamoeba* Keratitis

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Abstract

The purpose of this report is to present simultaneous bilateral penetrating keratoplasty (PK) in *Acanthamoeba* keratitis (AK). A 42-year-old male with keratoconus, wearing bilateral hybrid contact lenses, presented with pain in the left eye. He had a history of intrastromal corneal ring segment placement in the right and PK in the left eye. His best corrected visual acuity (BCVA) was 20/640 in the right eye and 20/2000 in the left. Slit-lamp examination revealed a ring-shaped infiltration on the left. Despite two months of broad-spectrum topical antibiotic therapy, microbiological examination of corneal scraping samples was repeated but revealed no evidence of microbial agents. *In vivo* confocal microscopy findings were not compatible with AK. During the follow-up, corneal infiltration and stromal melt were observed in the right eye. Corneal scraping samples from the right eye were sent for microbiological examination, but again no microbial agents were identified. Histopathological examination revealed spherical cysts consistent with AK. Corneal perforation developed in the right eye, while simultaneous wound dehiscence occurred in the left eye. Since the patient had a history of renal failure, simultaneous bilateral tectonic-therapeutic PK was performed to minimize the risks arising from general anesthesia. Postoperative BCVA was 20/50 in the right eye and 20/125 in the left eye at 6 months. Diagnostic tools can be misleading in eyes with altered anatomy. Careful examination and a timely decision to perform tectonic-therapeutic PK are vital in preventing devastating complications.

Keywords: Bilateral *Acanthamoeba* keratitis, contact lens, simultaneous bilateral penetrating keratoplasty, tectonic and therapeutic keratoplasty

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Introduction

Acanthamoeba spp. are free-living protozoans found in contaminated water and soil.[1] Early diagnosis and treatment of *Acanthamoeba* keratitis (AK) is critical to prevent full-thickness corneal perforations, which in some cases are inevitable despite aggressive treatment.[2]

Herein, we aimed to report a patient who underwent simultaneous bilateral tectonic-therapeutic penetrating keratoplasty (PK) for bilateral AK. To the best of our knowledge, simultaneous bilateral PK, which is a rare practice, has not been previously reported in bilateral AK, which is also a rare disease.

Case Report

A 42-year-old male patient with bilateral keratoconus presented with redness, pain, photophobia, and decreased vision in the left eye for 2 months. He was referred to our clinic with a diagnosis of keratitis resistant to empirical therapy. At the referring clinic, microbiological analyses of corneal scraping samples, contact lenses, and the contact lens container were performed, and no microbial agents were reported. He received broad-spectrum topical antibiotic therapy and antiviral therapy. His medical history revealed that intrastromal corneal ring segments (ICRS) were implanted in the right eye 16 years ago and he had undergone PK surgery on his left eye 13 years ago. The patient also had a history of using hybrid contact lenses in both eyes. Best corrected visual acuity (BCVA) was 20/640 in the right and 20/2000 in the left eye. Slit-lamp examination revealed a clear cornea with ICRS in the right eye, and a ring-shaped corneal infiltration with deep stromal haze and surrounding corneal edema in the central cornea accompanied by a large corneal epithelial defect (Figure 1) in the left eye. Despite two months of broad-spectrum topical antibiotic therapy, microbiological examination of corneal scraping samples was repeated, but these investigations also revealed no evidence

of microbial agents. *In vivo* confocal microscopy (IVCM) was performed with the suspicion of AK. Although the typical cyst appearance could not be distinguished on IVCM, topical 0.02% chlorhexidine gluconate (4 times daily) was initiated due to the lack of response to prolonged antibiotic and antiviral therapies. Broad-spectrum topical antibiotic therapy (fortified vancomycin 50 mg/mL, ceftazidime 50 mg/mL, fluconazole 2 mg/mL) was continued simultaneously, as the possibility of a mixed infection could not be excluded. During follow-up, decreased vision in the right eye and severe pain were added to the clinical picture. On slit-lamp examination, superficial punctate infiltrates and stromal haze were observed in the central cornea. Corneal scraping samples from the right eye were sent for microbiological examination, and all yielded negative results. Biomicroscopic findings progressed rapidly and within days, an epithelial defect and mild stromal melting appeared (Figure 1) with constant severe pain in the right eye. IVCM was repeated for both eyes and showed rare round or ovoid hyperreflective cysts without a hyporeflective halo and severe loss of keratocytes. At the same time, the liberated stromal tissue in the stromal melt area was dissected from the right eye and sent for histopathological assessment. Histopathological examination revealed defective corneal epithelium, polymorphic inflammatory cells in an edematous stroma, neovascularization, and spherical cysts with the typical double ring sign consistent with AK (Figure 2). Topical 0.1% propamidine isethionate (Brolene®; Sanofi, UK), which does not have a commercial form in our country, was obtained and added to treatment. Within the first month of presentation, bilateral stromal melting developed despite comprehensive and intensive therapy. On day 41 of hospitalization, a full-thickness corneal perforation developed in the cornea corresponding to the ICRS, exposing the rings in the right eye. Simultaneous non-traumatic wound dehiscence occurred at the recipient-graft junction in the left eye. Therefore, emergency tectonic and therapeutic PK was planned for both eyes. Since the patient had a recent history of acute renal failure, simultaneous bilateral PK was performed in the same session to minimize the risks arising from general anesthesia. Donor corneal buttons for both eyes were obtained from the same donor, thus reducing the risk of graft rejection in the recipient eyes. Postoperative BCVA was 20/50 in the right eye and 20/125 in the left eye with clear grafts bilaterally and no recurrence during 6 months of follow-up (Figure 3).

Informed consent for all procedures and this report was obtained from the patient.

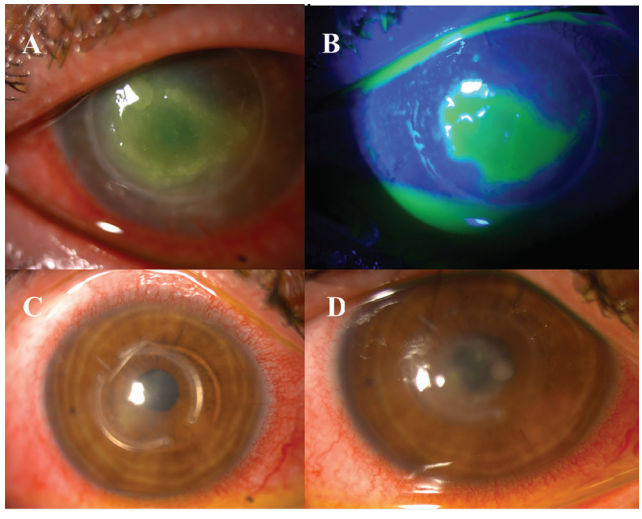

Figure 1. A, B) Anterior segment photographs of the left eye at presentation showing a large corneal epithelial defect in the central cornea with ring-shaped corneal infiltration and deep stromal haze. C, D) Anterior segment photographs of the right eye demonstrating the rapid progression of stromal invasion during follow-up

Discussion

Acanthamoeba, a free-living protozoan, can cause severe ocular morbidity and permanent blindness. Contact lens wear is a well-known risk factor for keratitis. Clinical manifestations of AK range from superficial punctuate keratopathy to full-

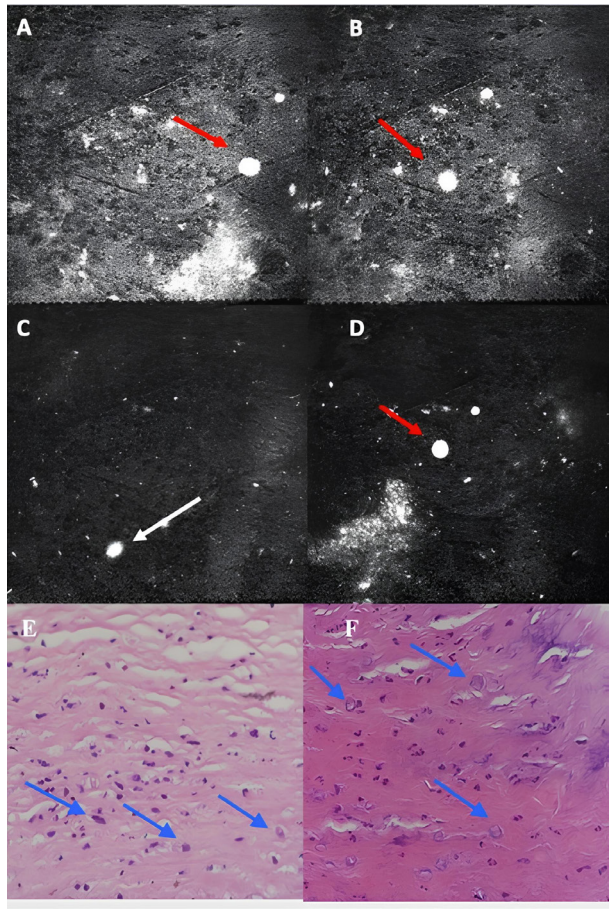

Figure 2. Representative *in vivo* confocal microscopy images of the patient's right eye (A, B) and left eye (C, D). Red arrows indicate round or ovoid hyperreflective cysts without a hyporeflective halo in the stroma. The white arrow indicates the amoeba form. E, F) Histopathological examination revealed defective corneal epithelium, polymorphic inflammatory cells in edematous stroma, neovascularization, and spherical cysts (blue arrows) with the typical double ring sign consistent with *Acanthamoeba* keratitis (hematoxylin and eosin x100, diastase-Periodic acid-Schiff x200)

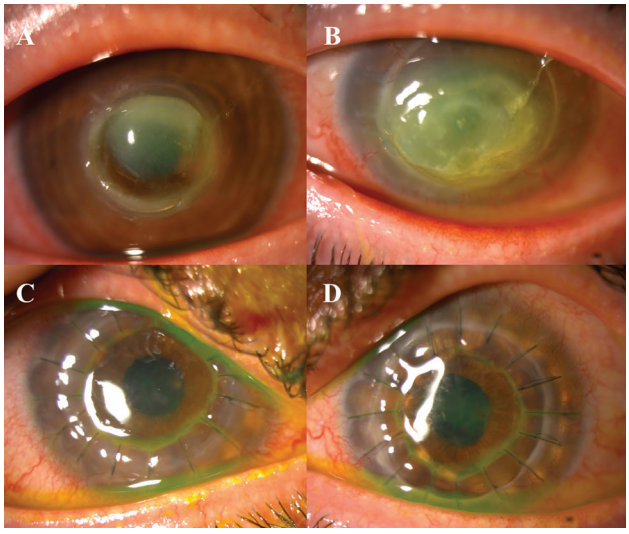

Figure 3. Preoperative anterior segment photographs of the right (A) and left (B) eye showing severe corneal melting and non-traumatic perforation. Ten weeks after simultaneous bilateral penetrating keratoplasty, anterior segment photographs showed clear grafts in both the right (C) and left (D) eye

thickness corneal perforations.[3,4] Although the importance of early diagnosis in AK is already emphasized, it involves number of challenges. In addition to manifesting with atypical findings, *Acanthamoeba* can mimic other keratitis agents.[5] This causes delay in treatment and may rarely lead to secondary complications.

Although involvement is usually unilateral, bilateral AK can also be seen in rare cases. The use of contact lenses stands out as a prominent risk factor in these cases.[6,7] Wilhelmus et al.[7] reported bilateral AK in 5 of 45 patients who used contact lenses bilaterally. Similarly, in the present case report, the patient had a history of using bilateral hybrid contact lenses.

A high index of suspicion is crucial for the timely diagnosis of AK, and early intervention improves outcomes. Treatment response and visual prognosis are excellent in the early stages, when signs such as superficial punctate keratopathy and subepithelial infiltrates predominate.[8] In our previous case report, we described Y-shaped linear epitheliopathy with negative fluorescent staining as an early sign of AK. With this early and exceptional finding of AK, that patient received timely treatment and had an excellent prognosis with a final BCVA of 20/20.[9] However, the prognosis is guarded in cases with deep stromal invasion and ring-shaped corneal infiltration. In its natural course, the infection quickly penetrates deeply into the stroma. Therefore, PK is almost always inevitable in advanced stages with progression to full-thickness corneal involvement.[8] Herein, the diagnosis of the patient was delayed, and therefore tectonic and therapeutic PK became imperative. The inconsistency between the diagnostic methods and the patient's clinical presentation is thought to play a major role in this situation.

The use of diagnostic tools is as important in the diagnosis of AK as the evaluation of clinical findings and risk factors. Microbiological evaluation of corneal scrape samples together with culture and polymerase chain reaction tests can identify *Acanthamoeba*.[2,8] Furthermore, IVCM is highly beneficial in demonstrating hyperreflective spherical cysts with the typical double ring sign, which is considered a specific finding of AK.[10] Occasionally, IVCM may fail to diagnose *Acanthamoeba*, as in this case report. Although IVCM was performed with the suspicion of AK at the time of admission, no compatible finding was detected. Rare cysts without a hyperreflective halo were seen when IVCM was repeated. However, histopathological examination confirmed cysts with double ring-sign, allowing the diagnosis of *Acanthamoeba* to be made. IVCM may have been misleading in this patient because of his history of ICRS in one eye and PK in the other eye. This highlights the limitation of IVCM in eyes where normal anatomy has been altered by anterior surface surgery. Therefore, it is important to act with a multidisciplinary approach when in doubt, to insist on investigations even if reliable diagnostic methods indicate otherwise, and to benefit from conventional methods such as direct light microscopy.

Another unique feature of this case of bilateral AK is that simultaneous bilateral PK was performed at the end of extended follow-up and interventions. Because of the already well-known perioperative and postoperative complications of PK, surgeons are often hesitant to perform bilateral surgery in the same session. However, the application of simultaneous bilateral PK for different indications has been reported in the literature, albeit rarely. Md Noh and Then[11] reported simultaneous bilateral PK due to spontaneous corneal perforation in a patient with Stevens-Johnson syndrome. Bhandari[12] described simultaneous bilateral PK in a patient with pseudophakic bullous keratopathy in one eye and corneal graft rejection in the other eye. In the present case, tectonic and therapeutic PK was performed in both eyes to preserve globe integrity. Since general anesthesia poses the risk of complicating preexisting acute renal failure, bilateral PK was performed in the same session instead of sequential surgery.

Despite the disadvantages and possible risks of simultaneous bilateral PK, it may be unavoidable and even favorable in certain situations. In addition to minimizing the risks associated with general anesthesia, as in the present case, the use of donor corneal buttons from the same donor may also minimize the potential immune response and consequently the risk of graft rejection in the recipient.[13] Tuft et al.[13] reported an interesting result in patients who underwent bilateral sequential PK. They showed that performing PK in the contralateral eye increased the risk of graft rejection in the eye that underwent PK first.[13] Thus, in the present case the donor corneal buttons were taken from the same donor, which seems to have been advantageous for this patient.

In conclusion, a high index of suspicion is crucial for early diagnosis and accurate management of AK. Although diagnostic tools such as IVCM are useful in AK, it can be misleading in eyes where normal anatomy has been altered by surgery. In these

cases, inconsistency between the results of diagnostic methods and the patient's clinical picture may delay the diagnosis and necessitate PK. To the best of our knowledge, this is the first report of simultaneous bilateral PK performed in bilateral AK, both of which are rare.

Ethics

Informed Consent: Obtained.

Declarations

Authorship Contributions

Surgical and Medical Practices: Ö.B.S., S.E., B.Y., C.Ş., Concept: İ.K., Ö.B.S., Design: Ö.B.S., Data Collection or Processing: N.F.E., C.Ş., S.E., Analysis or Interpretation: N.F.E., Ö.B.S., Literature Search: İ.K., Writing: İ.K.

Conflict of Interest: Sait Eğrilmez, MD, is an Associate Editor of the Turkish Journal of Ophthalmology. He was not involved in the peer review of this article and had no access to information regarding its peer review. The other authors have no disclosures.

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