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## **Case Report**

# **Case Report: Reduced Inflammation** after Corneal Perforation in Eyes with Acanthamoeba Keratitis

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### **Abstract**

Purpose: We report two cases of Acanthamoeba keratitis and corneal perforation, which were successfully treated at our institution.

**Observations:** Case 1 had intractable *Acanthamoeba* keratitis, and treatment was prolonged. As corneal perforation was accompanied by lens prolapse, corneal transplantation was performed to patch the preserved cornea. Following the procedure. initial inflammation and subjective symptoms caused by the infection subsided, and no relapse or worsening of infection was observed. In case 2, there were findings suggestive of corneal perforation, including descemetocele rupture and anterior chamber destruction during treatment. During follow-up, reducing the number of instillations alleviated conjunctival hyperemia and pain, and the infection improved. Both patients had a favorable outcome.

Conclusion and Importance: The symptoms and clinical findings of Acanthamoeba keratitis with corneal perforation may be alleviated by following the medical procedures described in this case report.

**Keywords:** Acanthamoeba; keratitis; perforation

inflammation;

## **Abbreviations**: AK: Acanthamoeba keratitis

#### Introduction

Acanthamoeba Keratitis (AK) is an infectious disease caused by the protozoan Acanthamoeba. From early stages of the disease, patients often experience severe pain that does not correlate with the corneal findings. AK generally has a poor prognosis in terms of visual acuity; it causes blindness in one-third of the patients, while one-quarter of them require corneal transplantation [1]. Corneal perforation has been observed unusually during treatment [2]. Herein, we present two cases of patients with AK along with corneal perforation that may have alleviated the infection, leading to a favorable outcome.

#### **Case Presentations**

#### Case 1

A 59-year-old woman with no history of systemic disease visited a local ophthalmology clinic complaining of a foreign body in her eye after trauma. She complained of blurred vision and pain in eye due to the movement of the foreign body in the left eye. Slit-lamp examination revealed conjunctival hyperemia and an opacity in the center of the cornea. The initial dagnosis was bacterial keratitis, which was treated with antibacterial eye drops, 42 days after the onset. Due to absence of improvement at 102 days, a superficial keratectomy, centered on the lesion, was performed on the entire cornea using an excimer laser. The patient was instructed to wear soft contact lenses. Further, the patient was prescribed levofloxacin and 0.1% flumetholon instillation four times a day. However, the epithelial defect persisted, and

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the hyperemia, infiltrative lesions, and subjective pain worsened. Thus, she was referred to our hospital 105 days after the onset. At the first visit to our hospital, she complained of highly blurred vision and persistent and increasing eye pain. Ophthalmoscopy revealed marked corneal opacity from the center to the inferior border of the cornea, conjunctival and scleral hyperemia over the entire left eyeball, and subjective pain (Figure 1, (A) and (B)). Corneal scraping microscopy was performed, and abundant *Acanthamoeba* cysts were detected using Fungiflora Y staining. Hence, the patient was diagnosed with AK. The initial treatment plan was conservative medical treatment with ophthalmic solution and oral administration, in addition to corneal epithelial scrapings.

#### Case 2

A 63-year-old man with a history of hypertension experienced pain in his eye while performing farm work. He complained of blurred vision and persistent eye pain. The pain did not subside; thus, he was referred to our hospital after consulting a local ophthalmologist 19 days after the onset. Levofloxacin was administered five times a day, although corneal infiltration and radial corneal neuritis were observed, and Acanthamoeba was detected using corneal scraping and a polymerase chain reaction test. Subsequently, three ophthalmic solutions containing 0.2% fluconazole, 0.02% chlorhexidine, and 0.3% dibekacin sulfate were administered every 30 min, pimaricin ointment was administered six times/ day, 400 mg of itraconazole was orally administered daily, and corneal scraping was performed three times a week. Because no improvement was observed 49 days after the onset, the patient was referred to our hospital. At the first visit to our hospital, he complained of deteriorating blurred vision and increasingly intense eye pain. Ophthalmoscopy revealed corneal opacity and marked conjunctival hyperemia from the center to the inferior border of the cornea (Figure 2 (A)). The previous physician continued eye drops and followed up with the patient. The initial treatment plan was continued conservative medical treatment with ophthalmic

solution and oral administration, in addition to corneal epithelial scrapings.

#### Results

#### Case 1

As the initial treatment, 0.02% chlorhexidine ophthalmic solution was administered every 30 min, tobramycin was administered six times/day, pimaricin ointment was applied six times/day, 400 mg of itraconazole was orally administered daily, and corneal epithelial scrapings were performed three times a week. However, although a mild improvement was observed, extensive corneal epithelial defects, infiltrative lesions that extended to the corneal stroma, and scleral and conjunctival hyperemia persisted. A low-viscosity hypopyon was observed 175 days after symptom onset (Figure 1, (C) and (D)), and 182 days after the onset, a broad Descemet's membrane aneurysm was observed (Figure 1, (E) and (F)). A persistent epithelial defect occurred, and corneal perforation associated with stromal lysis was observed 183 days after the onset (Figure 1, (G) and (H)). However, the lens nucleus was not affected by the corneal perforation (Figure 1 (I)). The patient visited our hospital outpatient department three times a week before the perforation. The intraocular inflammation was thought to be caused by the lens cortex melting and anterior lens capsule rupturing. She was hospitalized and corneal transplantation using cryopreserved donor cornea was performed to patch and close the preserved cornea 186 days after the onset (Figure 1 (J)). Subsequently, conjunctival hyperemia and pain improved along with the infection, and she was successfully discharged from the hospital, 21 days after the transplantation. The patient's recovery without complications, and regeneration of almost the entire epithelium was confirmed 259 days after the onset (Figure 1, (K) and (L)). The patient remained in good health at the last follow-up, 287 days after onset. The inflammation had completely resolved. She is waiting for radical penetrating keratoplasty, scheduled after more than 1 year after remission of corneal neovascularization.

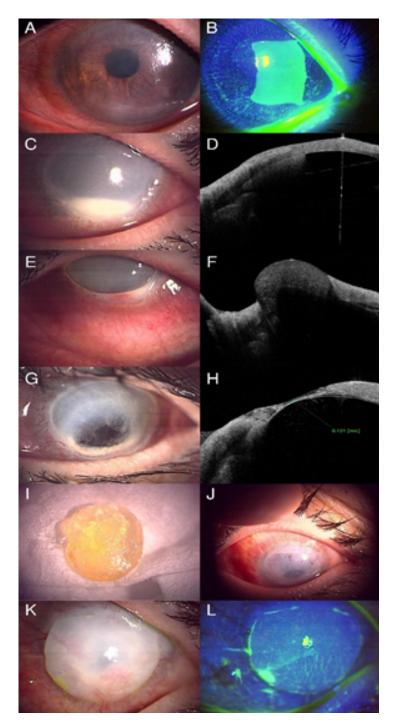
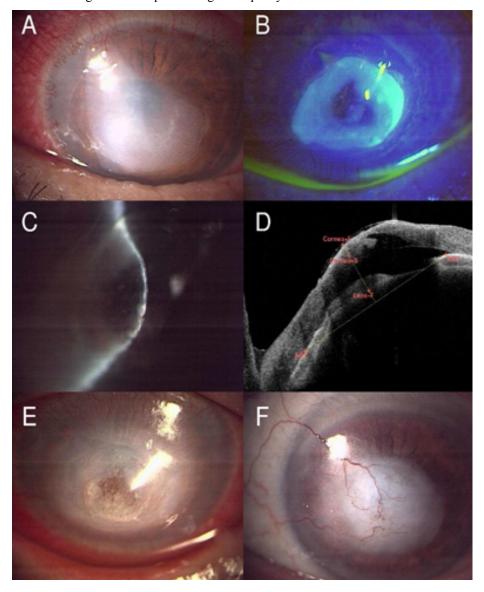


Figure 1: Case 1. (A) Anterior segment image at the first visit (105 days after the onset). (B) Anterior segment image with fluorescein staining 105 days after the onset. (C) Anterior segment image 175 days after the onset showing a hypopyon. (D) Vertical section anterior segment optical coherence tomography (AS-OCT) (CASIA 2, Tomey Corporation, Nagoya, Japan) image 175 days after the onset. (E) Anterior segment image 182 days after the onset showing a broad Descemet's membrane aneurysm. (F) Vertical section AS-OCT image 182 days after the onset. (G) Anterior segment image 183 days after the onset showing corneal perforation associated with stroma lysis. (H) Vertical section AS-OCT image 183 days after the onset. (I) The lens nucleus has escaped from the corneal perforation 183 days after the onset. (J) Anterior segment image two days after corneal transplantation using cryopreserved donor cornea (188 days after the onset). (K) Anterior segment image 73 days after corneal transplantation (259 days after the onset). (L) Anterior segment image with fluorescein staining 259 days after the onset.

#### Case 2

Despite treatment, findings of corneal perforation, such as the appearance of descemetocele and disappearance of the anterior chamber, were observed 97 days after the onset (Figure 2, (B), (C), and (D)). The number of instillations was reduced to three times a day, considering the possibility of drug-induced epithelial disorders, and follow-up was performed to detect the appearance of endophthalmitis. The patient visited our hospital outpatient department three times a week before the perforation. Seven days after the perforation, eye pain and conjunctival hyperemia improved significantly, and the signs of infection improved (Figure 2 (E)). After improvement, the patient visited our hospital outpatient department once a week or once in two weeks. Corneal transplantation was considered to address the corneal opacity; however, the patient did not wish to undergo the procedure. Progress remained good at the last follow-up on day 298 after onset, with the inflammation subsiding without relapse (Figure 2 (F)). The inflammation has completely resolved and this patient is also waiting for radical penetrating keratoplasty.



**Figure 2**: Case 2. **(A)** Anterior segment image at the first visit (49 days after the onset). **(B)** Anterior segment image with fluorescein staining 97 days after the onset. **(C)** Anterior segment image 97 days after the onset showing a Descemet's membrane aneurysm and corneal perforation. **(D)** Vertical section anterior segment optical coherence tomography image 97 days after the onset. **(E)** Anterior segment image seven days after perforation (104 days after the onset). **(F)** Anterior segment image 298 days after the onset.

#### **Discussion**

AK is an infectious disease characterized by pain and poor vision. Long-term treatment is required; in some patients, corneal transplantation is ultimately required [1,2]. Notably, corneal perforation is a serious complication of infectious keratitis. However, in some patients, the corneal infection subsides following perforation. We consider two mechanisms behind the suppression of infection. First is the excretion of infectious foci and inflammatory substances. Scraping of the corneal epithelium promotes removal of pathogens and penetration of local medication, and similar changes are thought to occur within the cornea [3]. Second, some anti-inflammatory or antibacterial substances present in the aqueous humor may alleviate disease symptoms. Notably, substances such as transforming growth factor-b2, vascular action intestinal polypeptide, calcitonin gene-related peptide, a-melanocyte stimulating hormone, and macrophage migration inhibitory factor, that are present in the anterior chamber reduce intraocular inflammation by suppressing T-/natural killer cell proliferation and the TH1 pathway of immune response [4]. In addition, the aqueous humor contains defensin, which has an antibacterial effect against pathogens [5-9]. We suspect that infection subsided when on leakage of these substances from the anterior chamber in both patients.

In Case 1, the infection could not be controlled despite aggressive treatment. It is possible that administration of steroidal eve-drops and soft contact lens use following excimer laser-assisted subepithelial keratectomy performed by the previous physician contributed to worsening of the infection [10-12] The subjective pain decreased markedly but did not disappear, and although the inflammation subsided, the epithelial defect and conjunctival hyperemia persisted. The epithelial defect and corneal perforation were accompanied by loss of the lens, which may be attributed to intense inflammation in the anterior chamber. Furthermore, the inflammation in the anterior chamber may have caused melting of the lens cortex. Additionally, rupture of the lens capsule may have caused melting cortex to accumulate in the anterior chamber, leading to appearance of low-viscosity hypopyon. However, after corneal perforation and transplantation, inflammation improved, and the pain was controlled. Subsequently, no recurrence of inflammation was observed, and the subjective symptoms disappeared. Thus, corneal perforation improved the symptoms, and we believe that the above-mentioned mechanism alleviated inflammation.

Similarly, in Case 2, the previous physician administered aggressive anti-amoeba treatment, although no improvements were observed. Subsequently, during treatment at our hospital, corneal perforation occurred; therefore, the dose was reduced, and careful follow-up was performed. Thereafter, the subjective symptoms and conjunctival hyperemia improved markedly. We believe that

the same mechanism alleviated the inflammation in this patient. In addition to the anti-inflammatory mechanism described above, multiple mechanisms were involved in this patient. Inflammation caused by the crystalline lens cortex melting was also involved in Case 1, and it is possible that inflammation was triggered by the outflow associated with perforation. Our findings suggest that the symptoms and clinical findings of AK may be alleviated following corneal perforation. These two cases suggest that assertive perforation of the cornea can be one of the treatments for refractory AK. However, there are a few reports on the effects of aqueous humor substances on the cornea. Studies examining large cohorts of patients with AK are required to clarify the pathogenesis and prognosis of severe AK.

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