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A Case of Noninflammatory Corneal Edema Following Anterior-Posterior Radial Keratotomy (Sato's Operation) Successfully Treated by Topical Corticosteroid

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Background: Corticosteroids seem to affect the functions of corneal endothelial cells directly in addition to their anti-inflammatory effect.

Case: A 69-year-old man presented with blurred vision in his left eye and decreased visual acuity in both eyes. He had received anterior-posterior radial keratotomy for myopia in both eyes 40 years earlier.

Observations: Both eyes showed mild corneal stromal edema in the pupil area. We diagnosed the condition as corneal edema secondary to cell loss and dysfunction of corneal endothelium after surgery. One month later, the stromal edema was further advanced in the left eye. Corneal thickness had increased from the initial value of 619 μm to 631 μm, and corrected visual acuity had decreased from 0.5 to 0.06. There were no signs suggesting inflammatory reaction. The left eye was then treated with topical corticosteroid eyedrops and subconjunctival corticosteroid injection. Two months later, corneal thickness had decreased to 546 μm and visual acuity had improved to 0.5.

Conclusions: This case shows that topical corticosteroids may be effective in treating corneal edema by producing an anti-inflammatory effect and possibly activating the endothelium.
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Key Words: Anterior-posterior radial keratotomy, central corneal thickness, corneal edema, corneal endothelial cell, corticosteroid.

Introduction

Corneal transparency is maintained by the barrier function of the epithelium, the unique structure of the stroma, and endothelial cell functions. When the endothelial functions are impaired, the corneal stroma swells and corneal transparency deteriorates as a result of corneal edema.[1] The loss of the physiologic functions of the corneal endothelium is caused by a decrease in the number of endothelial cells and/or by the impairment of endothelial cells. Effective therapy against the loss of endothelial cells—such as that suffered as a result of bullous keratopathy—has not been established, except by surgically supplying endothelium by penetrating keratoplasty.

However, corticosteroids have been used to treat endothelial dysfunction resulting from inflammatory reactions in the anterior chamber, such as anterior uveitis. Corticosteroids are mainly used in ocular therapy as anti-inflammatory and immunosuppressive agents.[2] Although it is known that corticosteroids influence the function of cells like fibroblasts, the role of corticosteroids in noninflammatory corneal diseases such as bullous keratopathy is not yet understood. Several studies have reported that topical corticosteroids affect endothelial cell function in rabbits,[3,4] and suggest that corticosteroids might activate corneal endothelial cells and enhance the cell functions. Although there have been several studies of topical corticosteroids in normal human corneal endothelium, which can seldom proliferate, the results have not been in agreement.[5–7]

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We successfully treated a case of corneal edema following anterior-posterior radial keratotomy (Sato's operation)[8] with topical corticosteroids for the purpose of activating the corneal endothelium. In this case, we succeeded in eradicating stromal edema, reducing corneal thickness, and improving visual acuity.

Case Report

The patient, a 69-year-old Japanese man, complained of blurred vision in the left eye and decreased visual acuity in both eyes. He had undergone anterior-posterior radial keratotomy in 1958. He had noticed left blurred vision for 4 years before coming to see us, and had been treated with eyedrops of hyperosmotic sodium chloride and Ofloxacin (Tarivid®). Because his symptoms did not improve and his visual acuity gradually decreased, he was referred to the Department of Ophthalmology of the Yamaguchi University Hospital on May 20, 1997. At his first visit, his best corrected visual acuity was 0.9 OD and 0.5 OS. Intraocular pressure was 8 mm Hg OD and 6 mm Hg OS. Slit-lamp examinations showed bilateral radial incision scars (the optical zone was about 7 mm) in the anterior and posterior corneal stroma, and retrocorneal membrane at the peripheral cornea. In the pupil area, corneal stromal edema was slightly visible in both eyes, but it was hard to detect any difference between the right and left eyes by slit-lamp examination. Measured by specular microscope (SP-2000P; Topcon, Tokyo), the thickness of the central cornea was greater in the left eye than in the right eye (564 μm OD, 619 μm OS). Moderate nuclear cataracts were observed in both eyes. No signs suggesting inflammatory reactions, such as corneal infiltration, conjunctival injection, or inflammatory cells in aqueous humor, were observed in either eye. The cellular density of the corneal endothelium measured by specular microscope (Noncon Robo; Konan, Hyogo) decreased to 915/mm^2 in the right eye, and was uncountable in the left eye. No remarkable change was observed in the fundus of either eye.

As the patient had previously undergone anterior-posterior radial keratotomy without any observable inflammatory reaction, we diagnosed his problem as corneal edema induced by cell loss and dysfunction of corneal endothelium after surgery. At the initial examination, however, we considered the possibility that the decrease of visual acuity in the left eye was due mostly to cataracts, because the corneal stromal edema in the pupil area was slight. Therefore, we did not begin treatment for corneal edema. On June 24, 1997, there was advanced stromal edema in the pupil area of his left eye (Figure 1). Although both visual acuity and corneal thickness in the right eye did not change, in the left eye the best corrected visual acuity decreased to 0.06 and central corneal thickness increased to 631 μm. Intraocular pressure was 6 mm Hg OD and 6 mm Hg OS. As in his first visit, there were no signs of an inflammatory reaction. In order to activate corneal endothelial cell function, we administered a subconjuntival injection of 0.3 mL dexamethasone sodium phosphate (Decadrone®) and eyedrops of betamethsone sodium phosphate (Rinderon®) in his left eye and lomefloxacin HCl (Lomeflon®) to prevent opportunistic infection.

By July 1, one week after treatment with topical corticosteroids, the subjective symptoms had subsided, and the best corrected visual acuity in his left eye had improved to 0.2. Central corneal thickness had also decreased slightly to 613 μm, but little change was observed in his right eye (570 μm). Intraocular pres-

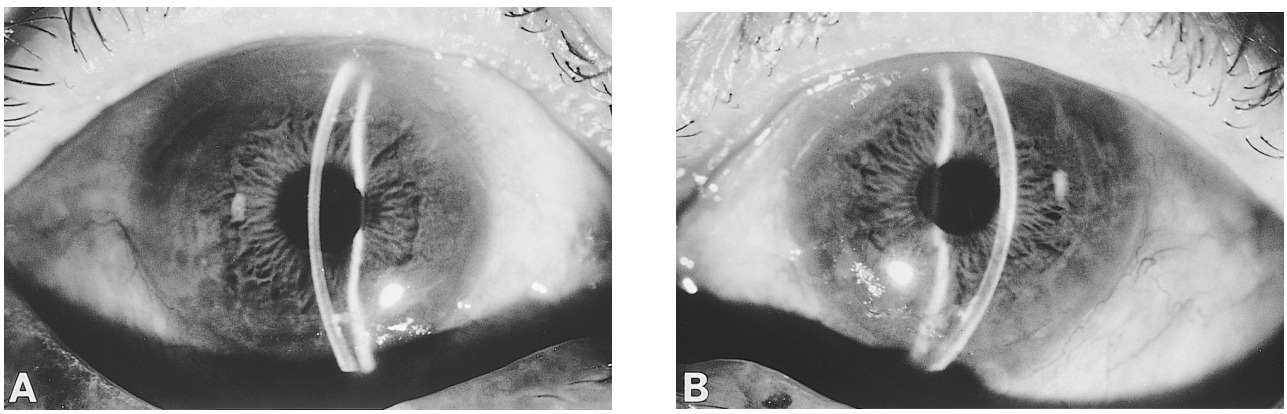

Figure 1. Slit-lamp photographs of right (**A**) and left (**B**) eyes on June 24, one month after initial visit. Radial incision scars in anterior and posterior corneal stroma and retrocorneal membrane at peripheral cornea were observed. In pupil area, advanced corneal stromal edema was observed in left eye (**B**) compared to right eye.

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sure was 9 mm Hg OD and 9 mm Hg OS. We administered subconjunctival dexamethasone to the left eye on July 1 and July 29. On August 26, two months after treatment, the stromal edema in the left eye had vanished from the pupil area, and the central corneal thickness had decreased to normal (546 μm) (Figure 2). Intraocular pressure was 9 mm Hg OD and 9 mm Hg OS. The best corrected visual acuity had also improved to 0.5 OS (Figure 2). We had not been able to observe the corneal endothelium of the left eye by specular microscope since the first visit, but now the corneal endothelial cell density was countable (714 cells/mm^2) because the corneal edema had vanished. For other parameters of the corneal endothelium, the coefficient of variation was 0.39, and the percentage of hexagonal cells was 53% (Figure 2). We continued to prescribe eyedrops of betamethasone sodium phosphate for his left eye. His visual acuity and central corneal thickness remained stable. At his last visit to us, August 25, 1998, the best corrected visual acuity was 0.4 and central corneal thickness was 550 μm in his left eye. In the right eye, which did not receive corticosteroid therapy, few changes were observed in either central corneal thickness or visual acuity during follow-up visits.

Discussion

We report a case of noninflammatory corneal edema following anterior posterior radial keratotomy (Sato's operation) treated by topical corticosteroids for the purpose of activating the corneal endothelium. In this case, the corneal edema disappeared, corneal thickness decreased, and visual acuity improved.

Corneal transparency deteriorates as a result of corneal edema or abnormal deposition on the stroma. Corneal thickness is a very useful marker clinically, because it reflects stromal water content. When either the endothelial barrier function or the active fluid pump function is lost, the corneal stroma swells, and its transparency is damaged, according to the pump-leak theory.[1] Although a specular microscope enables us to determine quantitative or morphological abnormalities of the endothelium in a clinical setting, we do not have any means of detecting abnormalities in each endothelial cell. Therefore, measuring corneal thickness is a useful and sensitive means of detecting endothelial dysfunction. In this case, we could observe the effect of corticosteroids on the corneal endothelium, with corneal thickness and visual acuity as markers.

Corticosteroids have a powerful anti-inflammatory effect on inflammatory corneal edema, but the effect of corticosteroids in noninflammatory corneal diseases is uncertain.[2] Several researchers have reported the effect of topical corticosteroids on endothelial cell function. Previous studies have demonstrated a decrease in corneal thickness in response to eyedrops[3] and subconjunctival or intravenous injection of

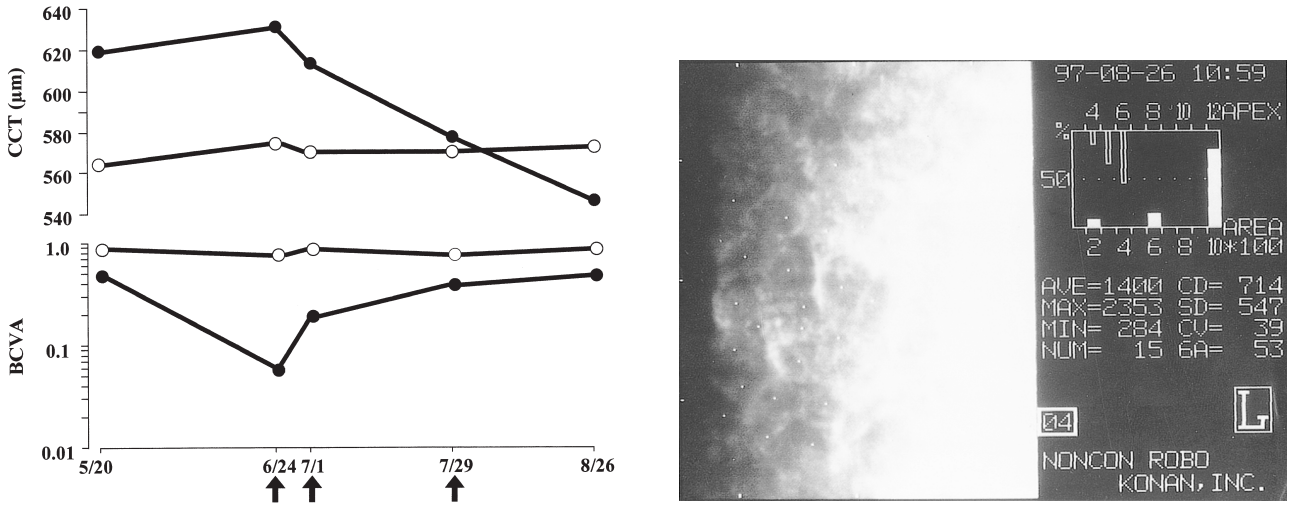

Figure 2. (Left) Central corneal thickness (CCT) measured by specular microscope and best corrected visual acuity (BCVA). ○: OD, ●: OS. CCT of left eye had decreased after administration of topical corticosteroids. BCVA in left eye had decreased by June 24, but administration of topical corticosteroids improved acuity to level of first visit. Little change was observed in right eye not receiving corticosteroid treatment, during follow-up visits. Arrows indicate subconjunctival administration of dexamethasone sodium phosphate to left eye. (Right) Specular photograph of corneal endothelium of left eye. We were first able to observe the corneal endothelium with specular microscope on August 26 when corneal edema had disappeared. Cell density was 714 cells/mm^2.

corticosteroids[4] using rabbit models. These results suggest that corticosteroids might activate corneal endothelial cells. However, the effect of corticosteroids on the human corneal endothelium has been controversial. Some groups[5] reported that topical corticosteroids did not affect corneal thickness or the barrier and pump functions of corneal endothelium in normal humans. Others[6] reported a small increase in normal corneal thickness in response to topical corticosteroids. However, the responses to corticosteroids by a normal cornea might differ from those of an injured or damaged cornea. Sunga et al[9] reported that topical corticosteroids decreased corneal thickness when corneal edema was present, as in the case of endothelial cell damage. Wilson et al[7] investigated the effect of topical corticosteroids on corneal endothelial function in Fuchs' dystrophy, and observed no statistically significant differences in corneal thickness, endothelial permeability, or pump function. However, this study had no explanation for a significant decrease in both the endothelial permeability and the pump rate of the placebo groups. Although the effect of corticosteroids on the human cornea remains ambiguous, in our study it is possible that corticosteroids might have directly influenced the functions of corneal endothelial cells.

Two months after treatment with corticosteroids, we observed that corneal thickness had decreased to normal and that corneal edema was no longer present in the pupil area. In addition, visual acuity also improved with decreasing corneal thickness. Furthermore, we were able to observe the corneal endothelium with a specular microscope and objectively estimate the transparency of the cornea and the absence of edema. In the near future, our patient will require penetrating keratoplasty and cataract surgery to restore visual acuity. However, in light of the critical shortage of donor corneas, especially in Japan, the present study suggests that topical corticosteroids might be useful for the nosotropic treatment of noninflammatory corneal edema until an operation can be performed. These results further suggest that corticosteroids might activate endothelial cell functions. The direct effect of corticosteriods on corneal endothelial functions has not been studied sufficiently, however, and further studies are needed.

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