Case Report

Long-term clinical outcome of corneal endothelial degeneration managed with keratoleptynsis in a Chihuahua dog

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Abstract

A 9-year-old spayed female Chihuahua presented with a 2-month history of progressive corneal edema in the left eye. Slit lamp biomicroscopy showed moderate corneal edema, instability of the axial corneal epithelial surface, and an anterior cortical opacity of the lens. Based on these results, a diagnosis of canine endothelial degeneration was made with the incidental finding of an incipient cataract in the left eye. Keratoleptynsis successfully managed the corneal edema for 28 months after surgery without corneal ulceration. This case study underscores the need for an early surgical approach using keratoleptynsis for dogs with a progressive nature of canine endothelial dystrophy.

Keywords: conjunctiva, cornea, edema, keratoconus, corneal transplantation

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Introduction

Canine corneal endothelial degeneration (CED) is a corneal disease characterized by bilateral corneal edema, occasional asymmetric development, bullous keratopathy, and ulcerative keratitis caused due to the premature degeneration of endothelial cells, which could even result in visual impairment (Gwin *et al*., 1982). Certain breeds, including the Boston Terrier, Chihuahua, Dachshund, German Shorthaired and Wirehaired Pointers, may inherit this condition. However, it can also develop with age or as a secondary result of factors like trauma, glaucoma, uveitis, lens luxation, intraocular surgery, and toxins. (Shull *et al*., 2018).

Palliative medical therapy using topical 5% NaCl has been used to reduce corneal edema. It has also been recently reported that a topical rho-associated kinase inhibitor can regenerate corneal endothelial cells damaged due to cryoinjury in dogs (Miyagi *et al*., 2019; Samuelson, 2013). Several surgical options for the management of CED have been reported in the veterinary literature such as thermokeratoplasty, superficial keratectomy combined with conjunctival hood flap (a modified keratoleptynsis), and Descemet's stripping endothelial keratoplasty (Boo *et al*., 2019; Horikawa *et al*., 2016; Michau *et al*., 2003). Among them, thermokeratoplasty has been recommended as a surgical intervention for the condition. However, recent studies have shown that keratoleptynsis alleviates corneal edema and prevents subsequent complications such as corneal ulcers, which can compromise vision in dogs and horses (Giannikaki *et al*., 2020; Kim *et al*., 2021; Kim *et al*., 2023; Scherrer *et al*., 2017). Therefore, the purpose of this report was to describe the long-term outcomes of keratoleptynsis as a surgical treatment option for CED.

Case history

A 9-year-old spayed female Chihuahua was presented with a 2-month history of progressive corneal edema at the ventrotemporal area in the left eye, which had been medically managed with antibiotics (q12h) and a 5% NaCl ophthalmic solutions (Muro128®; Bausch & Lomb Incorporated, Tampa, FL, USA, q4h). A complete ophthalmic evaluation was performed including neuro-ophthalmic evaluations, Schirmer tear test (STT: Schirmer Tear Test; MSD, USA), fluorescein staining (Fluorescein sodium®, Opti-tech Eyecare, Allahabad, India), slit lamp biomicroscopy (HS-7000®; Huvitz Co., Ltd., Korea), rebound tonometry (Tonovet®; Icare, Vantaa, Finland) and indirect ophthalmoscopy (Heine Omega 500®, Heine, Germany).

Throughout the study duration, the right eye showed no significant abnormalities and was not further monitored after the last visit. The subsequent ocular examinations pertain to the left eye. Menace response, dazzle reflex, and direct/indirect pupillary light reflexes were present. The STT measurement was 15 mm/min, and the intraocular pressure was 9 mmHg. Uptake of fluorescein staining was not observed on the corneal surface. Anterior segment findings included: moderate corneal edema at the ventrotemporal area, mild conjunctival hyperemia, instability of the axial corneal epithelial surface identified by punctate fluorescein staining, and anterior cortical opacity of the lens (Figure 1). There were no remarkable abnormalities in the posterior segment. Clinical diagnosis of CED typically involves excluding other underlying factors such as glaucoma, uveitis, persistent pupillary membrane, endophthalmitis, lens luxation, keratitis, and damage from surgery or toxins. Based on the clinical evaluation, a diagnosis of CED and incipient cataract was made in the left eye.

After pre-medication with meloxicam (0.1 mg/kg IV; Metacam®, Boehringer Ingelheim, Spain), midazolam (0.2 mg/kg IV; Midazolam®, Bukwang Pharm., Korea) and butorphanol (0.2 mg/kg IV; Butorphan®, Myungmoon Pharm., Korea) were injected intravenously as pre-anesthestic medications. General anesthesia was induced with propofol (5 mg/kg IV; Provive®, Myungmoon Pharm., Korea) and maintained with isoflurane (Ifran®, Hana Pharmaceutical Co., Ltd, Korea) and oxygen. The periocular region was clipped and prepared with three washes of 0.5% diluted povidone-iodine solution alternating with saline. The patient was positioned in a dorsal recumbency and draped. After outlining the outermost border line of the edematous corneal area with a Swann-Morton 64 microsurgical blade (SM 64®, Swann-Morton Ltd, UK), the tip of the edematous cornea excised was slightly undermined with the blade to insert a 2.6 mm crescent microsurgical knife (Kai Medical, Tokyo, Japan) for superficial keratectomy. The dissected edematous cornea and limbus were excised with corneal scissors. To separate a thin conjunctival tissue from the Tenon`s capsule, a small amount of 0.9% physiologic salt solution was injected immediately below the conjunctival surface and then the needle was advanced to the fornix as much length and width as the corneal flap with confirming the view of the needle through the conjunctiva. This conjunctival tissue was dissected with Stevens curved tenotomy scissors and sutured into the margin of the exposed stromal layer in the shape of a conjunctival hood graft with 8-0 polyglactin 910 (coated Vicryl®, Ethicon, Somerville, NJ, USA). Postoperative topical medications included 0.3% ofloxacin (Ofloc®; Bynexs Pharmaceutical Co., Ltd., Busan, Korea. q6h), 0.3% hyaluronic acid (Hyalon®, Samcheondang Pharmaceutical Co., Ltd., Hwaseong-si, Gyeonggi-do, Korea. q6h), and 5% NaCl ophthalmic solution (q4h). Additionally, the systemic oral medication consisted of doxycycline 5.0 mg/kg twice a day (Doxycycline Hyclate, Kukje Pharm., Korea) and meloxicam 0.1 mg/kg once a day (Meloxifen®, Kukje Pharm., Korea) for a week.

Results and Discussion

The patient was examined every 2 to 3 months until 28 months after surgery. For the management of post-operative corneal pigmentation, 0.2% cyclosporine (Optimmune ophthalmic ointment®, MSD animal health, Merck & Co., Inc., Rahway, NJ, USA) and 0.3% hyaluronic acid were continued twice a day. During the follow-up examination, 3 months postoperatively, partial pigmentation and neovascularization had

occurred at the edge of the conjunctival graft, but there was no abnormality in the passage of light through the thin graft, which was confirmed by retroillumination using slit lamp biomicroscopy (Figure 2. A and A1). During the follow-up assessment performed 19 months after surgery, extremely mild corneal edema developed around the edge of the ventral graft (Figure 2. B and B1). Both pigmentation and neovascularization slowly progressed to the region of unstable axial corneal epithelial surface identified by punctate fluorescein (Figure 2. C and C1). The left eye remained comfortably free from corneal ulceration; however, mild visual impairment was noted on the temporal side as evidenced by vision tests such as the menace response and cotton ball test during the study period.

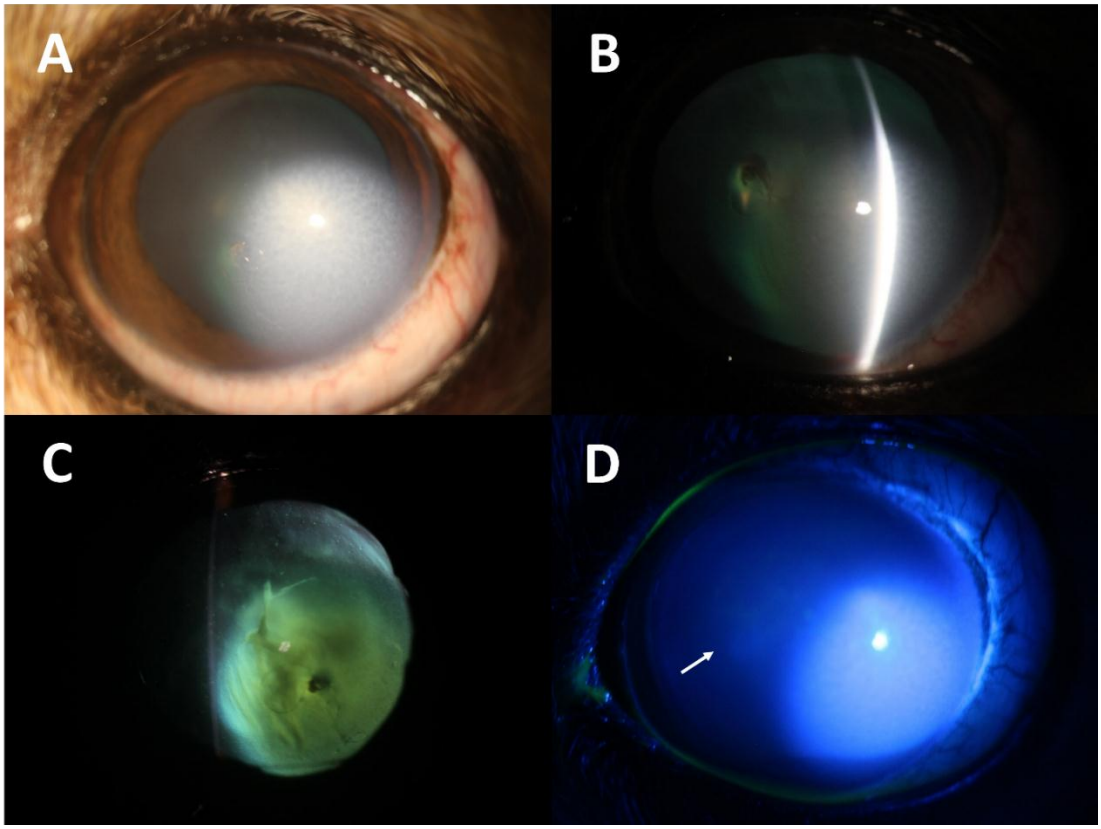

Figure 1 Slit lamp biomicroscopic photographs of the left eye at initial presentation. (A) Image with direct diffuse illumination. Note the moderate corneal edema and conjunctival hyperemia in the ventrotemporal area. (B) Image with direct focal illumination shows a relatively higher corneal thickness at the area of corneal edema. (C) Image with retroillumination clearly exhibits a borderline area of corneal edema. (D) Punctate fluorescein staining image demonstrates the instability of the axial corneal epithelial surface (arrow).

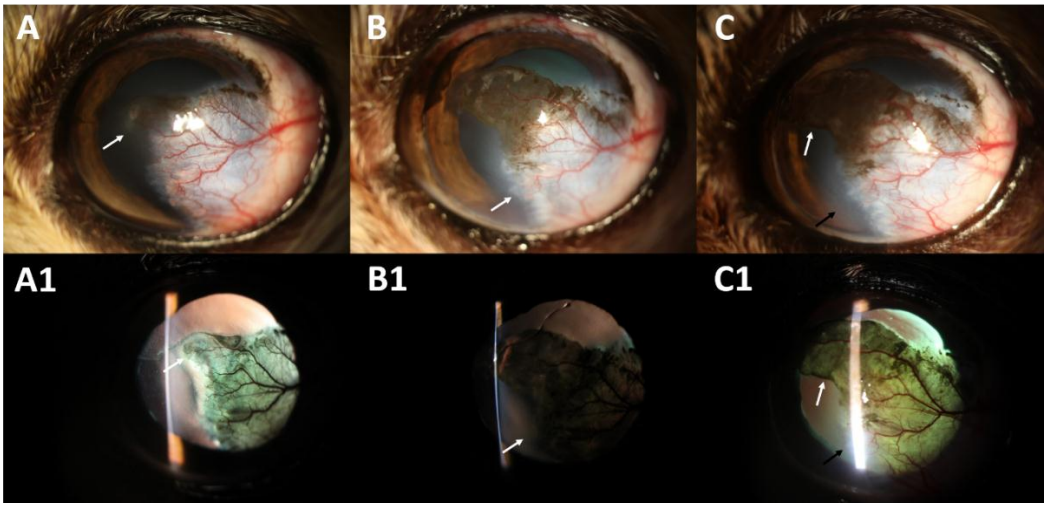

Figure 2 Slit lamp biomicroscopic photographs at 3 (A and A1), 19 (B and B1) and 28 months (C and C1) after keratoleptynsis. Images A to C with direct diffuse illumination and A1 to C1 with retroillumination. (A and A1) Note the partial pigmentation and neovascularization at the edge of the conjunctival graft (arrow). (B and B1) Note the extremely mild corneal edema developed around the edge of the ventral graft (arrow). (C and C1) Note both pigmentation and neovascularization have slowly progressed to the unstable zones of the axial cornea epithelial surface, which was identified by punctate fluorescein staining (white arrow), and corneal edema to the ventral area (black arrow).

Based on the long-term clinical outcomes of CED, this case report demonstrated the usefulness of keratoleptynsis as an effective surgical option for progressive corneal edema, which had failed to respond to intensive medical treatments. This case study emphasizes the need for an early surgical approach for dogs with a progressive form of CED (Kim *et al*., 2021; Kim *et al*., 2023).

A topical 5% NaCl ophthalmic ointment has been found to reduce corneal thickness in normal dogs (Samuel *et al*., 2019**)**. Therefore, it was believed that the administration of the ophthalmic ointment may relieve the corneal edema caused by CED and delay its progression in patients. However, an earlier study reported that it appeared to be ineffective in humans with superficial bullae at the early stage of corneal edema (Knezović *et al*., 2006**)**. Likewise, based on previous studies, the efficacy of the topical agent has been found to be highly controversial in severely advanced corneal edema in dogs (Kim *et al*., 2021). Horses with profound corneal edema also did not respond positively to the topical agent (Scherrer *et al*., 2017). In the current case, despite the administration of the topical ophthalmic solution early in the development of the corneal edema, it continued to progress and eventually required surgery. The present findings indicate that topical 5% NaCl ophthalmic solution is likely ineffective in controlling early corneal edema in dogs. Accordingly, it is reasonable to conclude that surgical options for the corneal edema attributed to CED should be considered as early as possible.

Keratoleptynsis has been used as a surgical option for the treatment of CED in a clinical setting (Horikawa *et al*., 2016; Kim *et al*., 2021; Kim *et al*., 2023). It serves a dual purpose: it not only mobilizes conjunctival vessels to alleviate edema but also accomplishes corneal thinning through superficial keratectomy, thereby alleviating the workload on the remaining corneal endothelial cells (Horikawa *et al*., 2016). Several previous clinical studies in which modified keratoleptynsis technique were performed, have shown that it is useful for maintaining vision by managing severe corneal edema in extensive keratoconus associated with CED (Giannikaki *et al*., 2020; Kim *et al*., 2021; Scherrer *et al*., 2017). At the end of the long-term follow-up of 28 months in this case, the conjunctival graft was well integrated with the corneal stroma. The patient was comfortable without corneal ulceration after the surgery. Mild visual impairment was observed throughout the study period, attributed to the preserved transparency of the corneal region not shielded by the conjunctival flap.

The major complications of keratoleptynsis that have been previously reported included superficial corneal pigmentation and fibrosis, and the minor complications included were corneal edema and neovascularization (Kim *et al*., 2023). Another previous study described that conjunctival graft pigmentation occurred in 6 of the 18 eyes that underwent conjunctival hood flap combined with superficial keratectomy, a modified technique of keratoleptynsis (Horikawa *et al*., 2016). In current case report, similar complications, progressive pigmentation and neovascularization, were observed during the study period. These findings might be attributed to limbal epithelial stem cell deficiency prior to surgery and limbal-related surgery (Giannikaki *et al*., 2020). The application of topical corticosteroids, along with tacrolimus or compounded cyclosporine at concentrations exceeding 0.2%, following the initial healing stage can be considered to minimize post-operative complications. This approach aims to reduce neovascularization towards the surgical site (Horikawa *et al*., 2016). In addition, subtle corneal edema developed around the ventral graft margin, but progressed slowly. This is most likely due to progressive corneal decompensation of the peripheral corneal edema before surgery (Samuelson, 2013). Both this fact and the lack of response to medical treatment support the contribution of CED to the development of corneal edema in this case.

In the case report, keratoleptynsis was carried out to manage the progressive corneal edema arising from CED that was not responsive to a 5% NaCl ophthalmic solution. During the 28-month follow-up, mild corneal pigmentation in conjunction with neovascularization and slight corneal edema only around the conjunctival graft were recorded in a dog, who showed no signs of pain and corneal ulceration. The results highlight the early need for the surgical technique used in this case report to prevent progression of corneal edema and maintain long-term vision.

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