Refractory neurotrophic keratitis in a young adult: A case report on the role of multimodal therapies

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SUMMARY

Neurotrophic keratitis (NK) is a rare, degenerative corneal disease that presents significant treatment challenges. We present a case of a 20-year-old female with a history of recurrent herpetic stromal keratitis (HSK) who developed bilateral NK complicated by persistent epithelial defects (PED), superimposed infective keratitis and band keratopathy (BK). A 20-year-old female with history of recurrent herpetic stromal keratitis with recurrent corneal epithelial defect initially presented with left eye pain, redness, and photophobia. Best-corrected visual acuity (BCVA) was 6/6 in the right eye and 6/12 in the left with a central epithelial defect of 5.4×5.8 mm. Despite treatment for corneal epithelial defect, symptoms worsened bilaterally as she developed recurrent HSK with PED. The diagnosis of NK was diagnosed and treated with lubricants, bandage contact lens, temporary tarsorrhaphy, punctal plug and initiation of autologous serum eye drops. However, she developed superimposed mixed bacterial and fungal infective keratitis while on autologous serum eye drop, necessitated temporary cessation of serum drops and initiation of antimicrobial therapy. Following treatment, the infective keratitis resolved but epithelial defect was persistent. Insulin eye drops were initiated, yielding only partial improvement. Subsequently, the patient developed BK. EDTA chelation with basement membrane polishing was performed, leading to complete resolution of PED and BCVA improvement to 6/12 in both eyes. This case illustrates the complexity of NK management and highlights the value of a multimodal approach in achieving successful clinical outcomes.

INTRODUCTION

Neurotrophic keratitis (NK) is a rare, degenerative disease of the cornea resulting from impaired trigeminal innervation, leading to reduced or absent corneal sensation and poor epithelial healing. It affects fewer than 5 individuals per 10,000 population.[1] Common causes include herpetic keratitis, intracranial lesions, and neurosurgical trauma to the ophthalmic branch of the trigeminal nerve. Ocular risk factors such as chemical burns, corneal dystrophies, long-term topical medications, and anterior segment surgery, as well as systemic conditions like diabetes, leprosy, and multiple sclerosis, have also been implicated.[2]

Managing NK remains a significant clinical challenge. Conventional therapies include preservative-free artificial tears, tarsorrhaphy and use of therapeutic contact lenses.[4] More recent approaches explore topical agents such as autologous serum eye drops, which offer essential growth factors that support epithelial repair.[3,4,6]

Insulin eye drops have also shown promising results in persistent epithelial defects (PED) refractory to standard treatments.[5-7] In addition, band keratopathy (BK) which is a complication seen in longstanding ocular surface disease, can be effectively managed with ethylenediaminetetraacetic acid (EDTA) chelation and polishing, which improve both vision and comfort.[8-10]

This case report presents a challenging case of bilateral NK complicated by PED, superimposed infection, and BK, successfully treated using a multimodal approach. The case highlights the utility of combining established and novel therapies to achieve epithelial healing and visual rehabilitation.

CASE PRESENTATION

A 20-year-old female with underlying allergic rhinitis first presented to our clinic at the age of 15 with a 3-day history of bilateral eye redness, tearing, itching and blurred vision. The best-corrected visual acuity (BCVA) was 6/7.5 in the right eye (RE) and 6/6 in the left eye (LE). Both eyes demonstrated macropapillae with conjunctival injection, clear cornea, deep and quiet anterior chambers and clear lenses. Other ocular examinations were unremarkable. She was diagnosed with bilateral allergic conjunctivitis and commenced on topical olopatadine 0.1% twice daily (BD) in both eyes (BE).

In October 2022, three years later, she developed bilateral eye redness with discomfort. The BCVA was 6/12 in RE and 6/15 in LE. Examination revealed macropapillae, conjunctival injection, and central corneal epithelial defects without stromal infiltrates in both eyes. Corneal sensation was reduced bilaterally. A diagnosis of bilateral herpetic epithelial keratitis was made, and she was commenced on oral acyclovir 400 mg five times daily for 10 days, followed by a prophylactic dose of 400 mg twice daily for four months, along with topical moxifloxacin 0.5% 4-hourly, olopatadine

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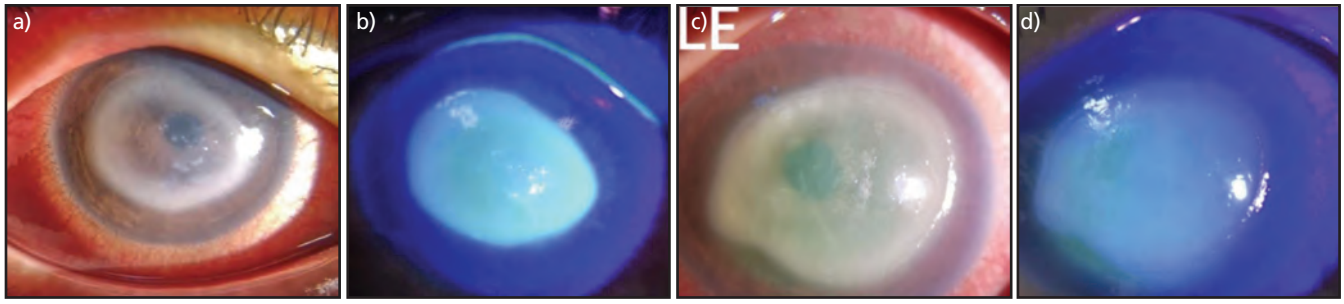

Fig. 1: Anterior segment photos at diagnosis: (A, B) right eye, (C, D) left eye, with diffuse illumination and fluorescein staining showing a ring of stromal infiltrate with oedematous cornea and large, central epithelial defect

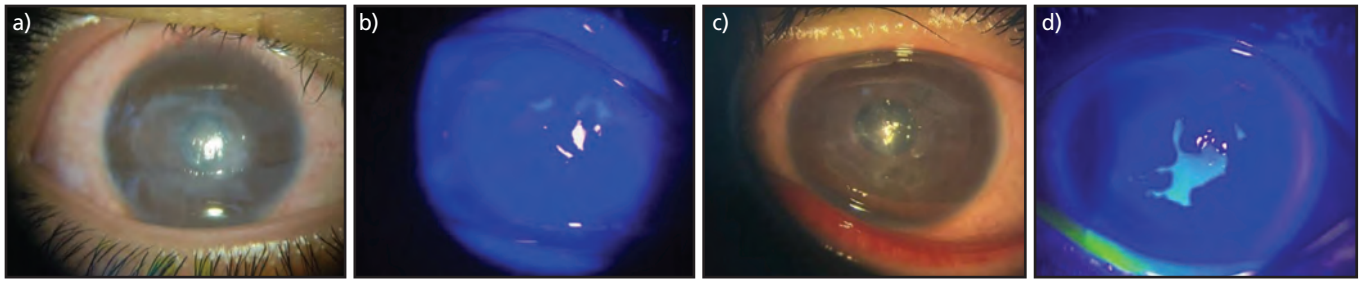

Fig. 2: Photos post-autologous serum therapy: (A, B) right eye, (C, D) left eye showing improvement of ring stromal infiltrate with persistent epithelial defect

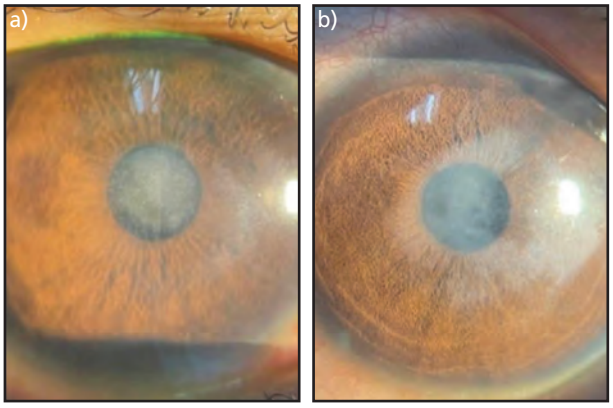

Fig. 3: Photos six-months post-EDTA chelation and polishing: (A) right eye, (B) left eye showing residual stromal fibrosis.

0.2% every morning and preservative-free artificial tears (ATPF) hourly in both eyes. The epithelial defects resolved, with improvement of BCVA in both eyes to 6/7.5, and she remained asymptomatic for one year.

On 30 November 2023, one year later, she presented with left eye redness, tearing, and reduced vision in the LE. BCVA was 6/6 in RE and 6/12 in LE. LE examination revealed a central epithelial defect (5.4 × 5.8 mm) without stromal infiltrate. Four days later, she developed tearing, pain, and reduced vision in RE. BCVA had decreased to 6/60 in RE and counting fingers in LE. Both eyes demonstrated conjunctival injection and central epithelial defects (RE: 8.2 × 6.8 mm; LE: 5.4 × 5.8 mm). The cornea showed central stromal ring infiltrates with associated corneal oedema and Descemet's folds. Fine keratic precipitates were present bilaterally with 1+ anterior chamber cells in both eyes. Corneal sensation was significantly reduced bilaterally (Figure 1).

She was diagnosed with bilateral herpetic keratouveitis and commenced on oral acyclovir 800 mg five times daily, topical prednisolone acetate 0.1% twice daily, topical moxifloxacin 0.5% five times daily, ATPF every two hours and oral vitamin C 1 g daily. Despite treatment, the epithelial defects remained large with poor healing. A diagnosis of bilateral neurotrophic keratitis (NK) secondary to herpetic keratitis with persistent epithelial defects (PED) was made.

Topical autologous serum eye drops were initiated every two hours in both eyes, and oral acyclovir was continued at a prophylactic dose of 400 mg twice daily. Topical corticosteroids were discontinued in view of impaired

epithelial healing. A temporary central tarsorrhaphy was performed in the left eye. After three days of autologous serum therapy, the ring infiltrates became less dense, corneal oedema reduced and there was slight improvement in the epithelial defects bilaterally. BCVA improved to 6/12 in RE; LE vision was not quantifiable due to the tarsorrhaphy.

At one-week review, she reported worsening vision in RE. Examination revealed a new central stromal infiltrate within the pre-existing ring infiltrate, accompanied by an endothelial plug and a streak hypopyon. BCVA decreased to counting fingers. Corneal scraping was performed for Gram stain, full examination and microscopic evaluation (FEME), and culture and sensitivity (C&S). Based on clinical judgment, a diagnosis of mixed bacterial and fungal keratitis was made. While awaiting laboratory results, intensive broad-spectrum antibacterial and antifungal therapy was initiated, including topical gentamicin 0.9%, ceftazidime 5%, and amphotericin B 0.15% hourly. Autologous serum was withheld in RE during active infection but continued in LE. Corneal scrapings revealed no organisms, and cultures were negative. As the endothelial plug worsened despite treatment, therapy was switched to topical vancomycin 2% and voriconazole 1% hourly, leading to resolution of stromal infiltrates, endothelial plug, and hypopyon. Autologous serum was resumed in RE after four weeks.

At six-week follow-up, tarsorrhaphy in LE was discontinued due to minimal improvement in the epithelial defect. Over several months, the epithelial defects gradually reduced in size, with symptomatic improvement. At six months, she was asymptomatic with improvement of BCVA to 6/7.5 in RE and 6/12 in LE; however, PED persisted in both eyes, more marked in LE (Figure 2).

Given the persistent PED, she was started on topical insulin eye drops 0.5 IU four times daily (QID) and punctal plugs were inserted bilaterally. Progress remained slow despite multimodal therapy. At one-year follow-up, she developed bilateral band keratopathy (BK). In view of PED and BK, EDTA chelation with basement membrane polishing using a diamond burr was performed under general anaesthesia, followed by application of bandage contact lenses (BCL).

Four days post-procedure, complete resolution of PED was achieved. At one month, she had minimal residual stromal scarring and BCVA of 6/12 in both eyes. At six months post-procedure, residual stromal fibrosis persisted, more pronounced in LE (Figure 3). She was prescribed scleral contact lenses, which improved BCVA to 6/7.5 in both eyes. She expressed great satisfaction as she could resume her studies and driving.

DISCUSSION

Neurotrophic keratitis (NK) is a rare, degenerative corneal disease with a reported prevalence of ≤5 per 10,000 individuals.[1] It results from impairment of trigeminal innervation to the cornea, leading to loss of corneal sensation, decreased tear production, and disruption of epithelial metabolism and wound healing.[2] The corneal nerves are essential for maintaining ocular surface integrity; their loss initiates a cascade of epithelial breakdown, stromal melting, and potential perforation.[2] The most common aetiologies of NK include herpetic keratitis, diabetes mellitus, chemical or surgical trauma, and neurosurgical procedures.[2] In our patient, the contributing factors were recurrent herpetic keratitis, which may impair epithelial regeneration.[4]

Clinical presentation depends on the disease stage, as classified by Mackie2: Stage 1 - punctate epithelial keratopathy, tear film instability, conjunctival staining, and early stromal changes. Stage 2 - persistent epithelial defects (PED) with stromal oedema and loose epithelial margins. Stage 3 - corneal ulceration, stromal melting, and perforation. Our patient initially presented with Stage 2 NK, progressing to Stage 3, complicated by mixed bacterial–fungal keratitis and later band keratopathy (BK).

Management of NK is challenging, aiming to promote epithelial healing, suppress inflammation, and prevent stromal loss.[4] Conventional therapies include preservative-free lubricants, therapeutic contact lenses, and tarsorrhaphy.[4] Biologic therapies such as autologous serum eye drops provide epithelial growth factors, neurotrophic factors and vitamins that support corneal healing by promoting proliferation, migration and maturation of corneal epithelial cells and reduction in stromal fibrosis,[3,4,6] but their use carries a risk of microbial contamination.[3,6] Our patient developed secondary infection while on autologous serum, which improved after cessation and targeted antimicrobial therapy. The preparation of the eye drops was done at the transfusion medicine laboratory at HPUSM according to the Standard Operation Procedure (SOP). The process included collection of blood from the patient, centrifugation and packaging of the separated 100% serum in sterile eye drop vials. The patient was instructed regarding transport, proper storage of the eye drops in freezer and its proper use to minimize risk of contamination similar to previous literature.[3,6]

Topical insulin eye drops, as used in our case, are a novel option for refractory PED. Insulin shares structural similarities with insulin-like growth factor-1 (IGF-1) and promotes keratinocyte migration and proliferation.[5,6] Recent studies have reported successful epithelial closure in PED of various aetiologies, including herpetic keratitis, with minimal adverse effects.[6,7] The advantages of insulin include readily availability, cost effectiveness, excellent tolerance and absence of unfavourable side effects with no effect of serum glucose levels.[5-7]

Our patient's late course was complicated by BK, a frequent sequela of chronic ocular surface inflammation.10 EDTA chelation is an established treatment for complete removal symptomatic BK, effectively removing calcium plaques and improving the ocular surface.[9,10] In this case, there was PED with loose epithelium and poor adherence to underlying basement membrane hence EDTA chelation was combined with basement membrane polishing using a diamond burr (DBP). DBP has shown a lower rate of recurrences compared to epithelial debridement alone. The smooth surface left after polishing allows new epithelial growth and stimulate reactive fibrosis and extracellular matrix proteins that may contribute to stronger epithelial adhesion.[8] We observed

complete removal of BK with complete epithelial closure within four days following the procedure with significant visual recovery in our case.

This case demonstrates that even in severe, chronic NK complicated by infection and BK, good anatomical and functional outcomes can be achieved with a multimodal, stepwise approach. Early diagnosis, careful monitoring, and timely integration of both conventional and novel therapies—such as autologous serum, topical insulin, tarsorrhaphy, punctal occlusion, and EDTA chelation—are critical for preserving vision and quality of life in affected patients.

CONCLUSION

Refractory neurotrophic keratitis poses significant therapeutic challenges. This case highlights that even in advanced, refractory neurotrophic keratitis complicated by persistent epithelial defects, secondary infection, and band keratopathy, vision can be preserved with a structured, multimodal approach. Combining conventional measures such as tarsorrhaphy and punctal occlusion with novel therapies like autologous serum and topical insulin eye drops, followed by EDTA chelation and basement membrane polishing, resulted in complete epithelial closure and significant visual recovery. Early recognition, close monitoring, and timely escalation of therapy in neurotrophic keratitis is crucial. Further studies are needed to validate the role of topical insulin and combined surgical–medical strategies in similar complex cases.

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