VISION SCIENCE AND EYE HEALTH JOURNAL

CASE REPORT

Neurotrophic Keratopathy Post-Herpes Zoster Ophthalmicus Infection

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Dates:
Received: 23 April 2024
Revised: 16 July 2025
Accepted: 18 July 2025
Published: 26 July 2025

DOI:
https://doi.org/10.20473/vsehj.v4i3.2025.91-94

Abstract

Introduction: Neurotrophic keratopathy (NK) is a degenerative disease of the corneal epithelium caused by disruption of corneal trigeminal innervation, resulting in reduced corneal sensitivity, epithelial damage, and impaired corneal healing. It can be caused by various factors, such as viral infections (e.g. herpes simplex keratoconjunctivitis and herpes zoster), chemical or physical trauma, corneal surgery, and intracranial lesions. Management of NK is based on clinical severity to promote corneal healing and prevent progression to stromal melting or perforation. **Case Presentation:** A 64-year-old male presented with a three-month history of a whitish plaque on the right eye, accompanied by redness, foreign body sensation, and decreased vision. The patient had a history of herpes zoster ophthalmicus (HZO) on the left side of the forehead in June 2022. Ophthalmologic examination revealed a 4 x 5 mm corneal epithelial defect with stromal infiltrates and decreased corneal sensitivity in the left eye, consistent with stage 2 neurotrophic keratopathy. Ancillary tests revealed reduced tear production and instability of the tear film. The patient was treated with topical antibiotics, lubricants, cycloplegics, and systemic doxycycline, with weekly follow-up and no evidence of active bacterial or fungal infection. **Conclusion:** Neurotrophic keratopathy can occur as a complication of post-HZO infection. Early diagnosis, severity-based treatment, and close monitoring are crucial for achieving epithelial healing and preventing further corneal damage. Prognosis depends on the degree of sensory impairment and the response to treatment.

Keywords: neurotrophic keratopathy (NK); neurotrophic keratitis, herpes zoster ophthalmicus (HZO)

Introduction

Neurotrophic keratopathy (NK) is a degenerative disease of the corneal epithelium caused by disruption of the corneal trigeminal innervation, resulting in reduced corneal sensitivity, epithelial damage, and impaired corneal healing. NK can be caused by various factors, including viral infections (such as herpes simplex keratoconjunctivitis and herpes zoster), chemical trauma, physical trauma, corneal surgery, and intracranial lesions. Systemic disorders such as diabetes, multiple sclerosis, and leprosy can also contribute to the disease.[1],[2],[3],[4]

This virus causes both ocular and extraocular manifestations. Herpes zoster ophthalmicus (HZO) occurs when there is involvement of the ophthalmic branch of the trigeminal nerve in viral reactivation. HZO can result in decreased corneal sensitivity, which can lead to NK.[1],[3],[5],[6],[7]

Mackie in Guerra et al.[8] divides the degree of NK into three stages. The first stage is characterized by epithelial changes, including punctate keratitis, epithelial hyperplasia, ocular surface irregularities, stromal scarring, corneal neovascularization, a thicker tear film, and decreased tear break-up time.[8] The second stage is characterized by a persistent epithelial defect, which an anterior chamber reaction may follow may follow.[8] The third stage is characterized by ulceration, which can progress to stromal melting and ultimately lead to corneal perforation.[8]

In general, the management of NK is based on clinical severity to trigger corneal healing and prevent the progression of corneal damage to melting

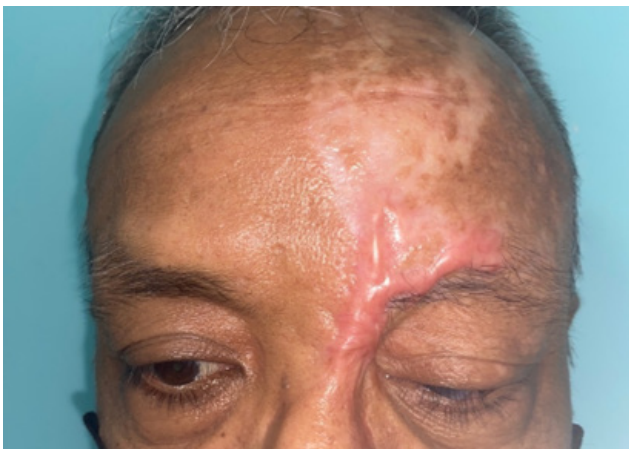

Figure 1. Clinical appearance shows a cicatricial scar caused by herpes on the left periocular area

stroma and even perforation. The prognosis for NK is variable. Factors that affect prognosis in patients include sensory damage to the cornea and the response to the therapy administered. The more severe the corneal sensory damage, the greater the likelihood of progression of corneal damage.[2],[9]

Case presentation

A 64-year-old patient, came to the infection and immunology polyclinic at Dr. Soetomo Regional General Hospital, Surabaya, East Java, Indonesia, with complaints of a whitish plaque appearing on the black part of the right eye for the past three months. Red eyes, a gritty feeling, and a decrease in vision accompany complaints. The patient previously visited dr. Soegiri Regional General Hospital, Lamongan, East Java, Indonesia, and was given various types of drops, however, unfortunately, the patient forgot the name of the medicine. The whites in the patient's right eye expanded, and vision became increasingly blurry; therefore, the patient was referred to Dr. Soetomo Regional General Hospital, Surabaya, East Java, Indonesia.

The patient had a history of herpes infection in June 2022 with complaints of minor, fluid-filled bruises appearing in the left facial area, especially on the forehead. The patient visited a general practitioner and received two types of medication, namely antiviral drugs and fever reducers. After two weeks of treatment, the patient was declared cured. The patient had no history of hypertension, diabetes mellitus, allergies, trauma, or previous eye surgery.

The results of dermatological examination on the right forehead found multiple hyperpigmented macular lesions of the trigeminal branch of the ophthalmic branch of the trigeminal nerve (Figure 1). On ophthalmological examination, the best corrected visual acuity of the right eye was 6/12 and 1/60 in the left eye, and no improvement with pinhole. Move both eyeballs normally in all directions. Intraocular pressure (IOP) in the right eye is within normal limits, and per palpation in the left eye is within normal limits, the anterior segment of the right eye is within normal limits (Figure 2). On the left eye, minimal blepharospasm, conjunctival hyperemia, and ciliary injection were found. On the cornea, a positive result of the fluorescein test was found, measuring 4 x 5 mm in diameter, with stromal infiltrates, edema, and decreased sensitivity in all parts of the cornea. The Van Herick (VH) grade III was found to have no flares and cells with a round pupil, a slightly cloudy lens (Figure 3). The Schirmer test revealed 10 mm on the right eye and 7 mm on the left eye, with tear break-up time resulting in eleven seconds on the right eye and five seconds on the left eye.

The patient was prescribed Cenfresh eye drops, one drop once daily in both eyes; Moxifloxacin eye drops, one drop every four hours in the left eye; Doxycycline tablets, 100 mg twice daily by mouth; Chloramphenicol eye ointment, once daily in the left eye at night; and Atropine 1% eye drops, one drop every 12 hours in the left eye. The patient's condition was evaluated weekly. Corneal ulcer scraping revealed no bacterial or fungal infection in the left eye. The laboratory results were within normal limits.

Discussion and conclusions

NK is a degenerative disease of the corneal epithelium caused by disruption of the corneal trigeminal innervation, resulting in reduced corneal sensitivity, epithelial damage, and impaired corneal healing. Corneal sensory nerves play a crucial role in maintaining the anatomical integrity, transparency, and function of the cornea, particularly the epithelial layer. The causes of NK are varied (Table 1). NK is a rare, degenerative corneal disease affecting approximately five people per 10,000. The most common cause is herpetic keratitis. The prevalence of NK is estimated to be less than five

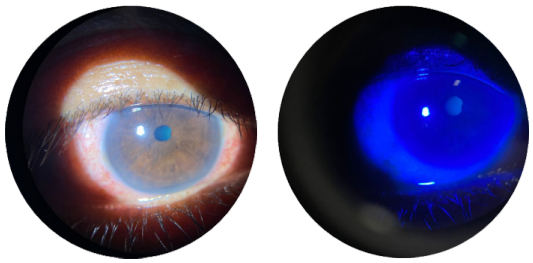

Figure 2. Anterior segment examination of the right eye is within normal limits.

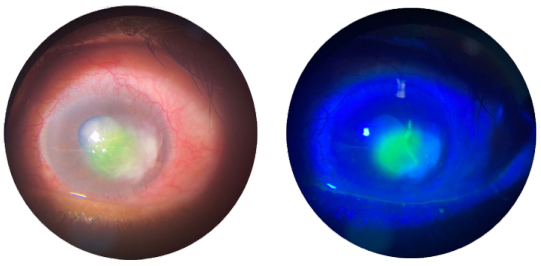

Figure 3. Anterior segment examination of the left eye shows a corneal defect.

Table 1. Etiology of NK.

Category	Details
Herpes infection	Simplex, leprosy, zoster
Pathological cornea trauma	Chemistry, operating contact lens wearers, laser-assisted in situ keratomileusis (LASIK), corneal incision, lamellar and penetrating dystrophic keratoplasty, lattice granular
Medication topical anesthetics	Timolol, Betaxolol, Trifluridine, Sulfacetamide
Cranial nerve V palsy	Neoplasm, trigeminal neuralgia, congenital facial trauma, aneurysm, riley-day syndrome, Möbius corneal hypoesthesia
Systemic disease	Diabetes, Vitamin A deficiency, multiple sclerosis, Adie syndrome

Table 2. Management of neurotrophic keratitis based on clinical level.

Stage	Findings	Clinical Management
I	Corneal irregularities and hyperplasia, small surface distribution of dry epithelium (Gaule's spots), superficial punctate keratopathy of the inferior conjunctiva, increased tear viscosity, decreased tear break-up time, superficial neovascularization, stromal scarring, corneal dellen	Complete termination topical treatment, use preservative-free artificial tear, treatment based on ocular surface disease
II	Persistent epithelial defects, descemet's membrane folds and stromal edema, anterior camera oculi inflammatory reaction with hypopyon (rare)	Corneal or scleral therapeutic contact lenses, tarsorafi, palpebral spring, Botulinum toxin type A
III	Corneal ulcer, perforation of the cornea, corneal stromal melting	Cyanoacrylate adhesive with protective contact lenses, conjunctival or tarsorrhaphy flaps, lamellar or penetrating keratoplasty

per 10,000 individuals, with causes including herpetic keratitis at 1.22/10,000 and postoperative procedures at 0.02/10,000. NK occurs in approximately 6% of cases of herpetic keratitis and 12.8% of cases of herpes zoster keratitis.[1],[2],[4],[8],[10]

This patient had a history of herpes in June 2022. The patient had complaints of minor, fluid-filled bruises appearing in the left facial area, especially the nose and forehead. The patient went to a general practitioner and was declared cured. The patient presented with eye complaints in February 2023. On dermatological examination, a cicatrix was found on the forehead and around the right eye, caused by a history of vesicular herpetic rash. A vesicular rash over the nasociliary nerve dermatome may indicate an ophthalmic complication of a herpes zoster infection. Involvement of the tip of the nose (Hutchinson sign) is considered a predictor of ocular manifestations. In several case series, it was found that 100% of patients with nasociliary involvement developed ocular pathology.

Corneal complications occur in 65% of cases of HZO. Corneal involvement can manifest as punctate epithelial keratitis, dendritic keratitis, stromal keratitis, or NK, which may occur over months to years. NK exhibits clinical characteristics of corneal epithelial changes, ranging from superficial punctate keratopathy to persistent epithelial defects and ulcers that can progress to stromal melting and corneal perforation. Damage to the trigeminal sensory fiber also affects the stimulation of the tear glands, so that tears are reduced. Patients with NK rarely complain of this symptom because of the lack of sensation in the cornea they experience. Mackie's classification of NK is divided into three stages (Table 2).

The second stage is characterized by a persistent epithelial defect, and an anterior chamber reaction may follow. The third stage is characterized by ulceration that can progress to stromal melting and ultimately lead to corneal perforation. Management of neurotrophic keratitis depends on the degree of severity seen from the clinical findings, as shown in Table 2.[1],[2],[5],[8]

In patients, corneal ulcers were found to be due to the reactivation of HZO infection. After administering topical medications for three weeks, there was a noticeable improvement. The last control was on May 2023. The patient was given additional therapy, including Occulenta gel three times a day and Vitamin C once a day. Miserocchi et al.[11] wrote that administering acyclovir orally twice daily at 400 mg for at least one year can reduce the recurrence rate of HZO infection.

The administration of autologous serum was stated by Lavaju et al.[9] to be beneficial in repairing damage in NK and preventing further complications. This is because autologous serum contains growth factors that stimulate the proliferation, migration, and maturation of corneal epithelial cells. High concentrations of insulin-like growth factor, substance P, and nerve growth factor in serum, which are not typically present in normal tear samples, contain neurotrophic factors that aid in healing the ocular surface.[4],[9],[12],[13]

The prognosis for NK is variable. Factors that affect prognosis in patients include sensory damage to the cornea and the response to the therapy administered. The more severe the corneal sensory damage, the more likely it is for the corneal damage to progress. In this patient, the prognosis is dubious due to decreased corneal sensibility in all regions. It may take some time to see the progress of the patient's corneal damage.[2],[4],[10],[13],[14]

NK is a complication that can occur after HZO infection. Early diagnosis, treatment based on severity, and good monitoring are important in promoting epithelial healing and preventing the progression of corneal damage. The prognosis for NK depends on the extent of sensory damage to the cornea and the response to therapy.

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