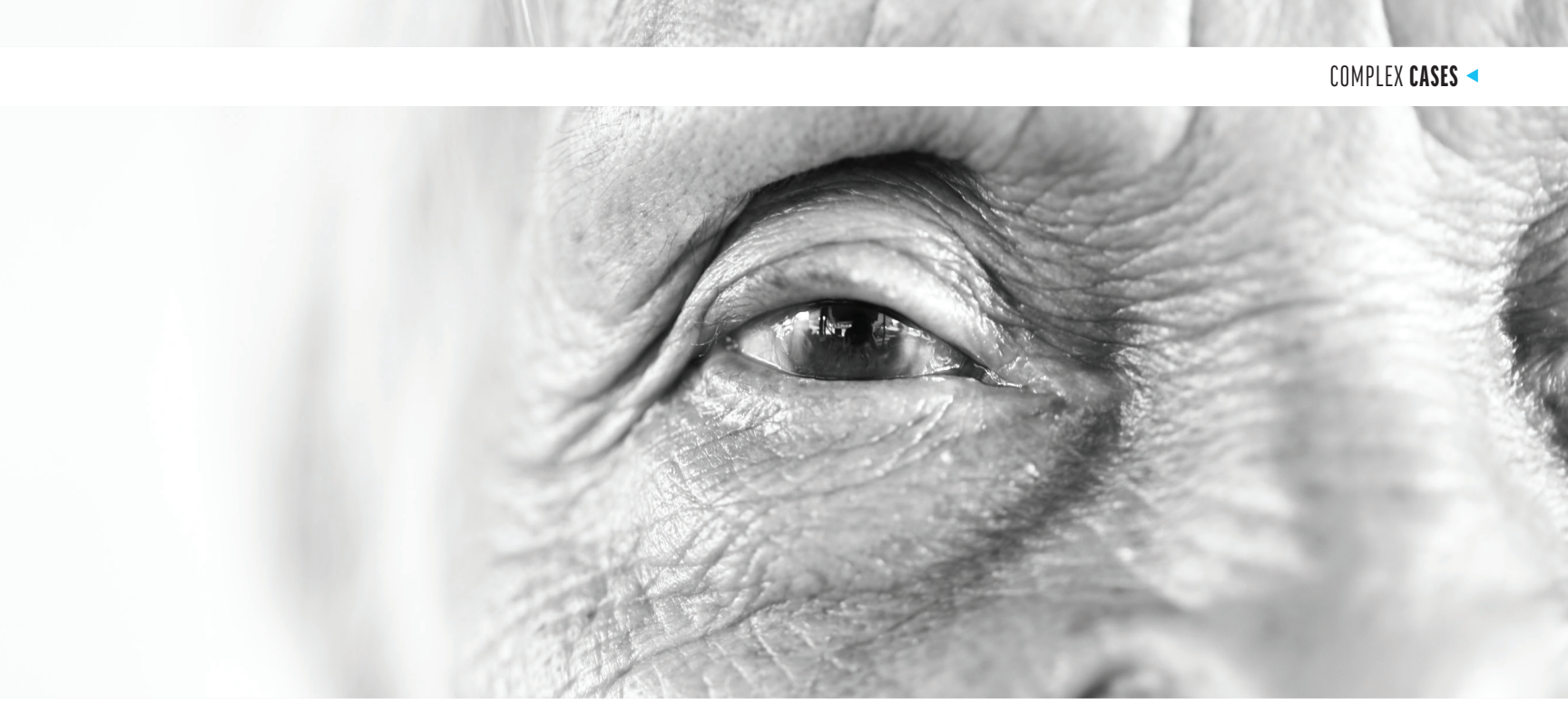

AT NERVE'S END: NEUROTROPHIC KERATITIS IN A MONOCULAR PATIENT

How to proceed in challenging cases such as this.

BY KATIE RACHON, OD, FAAO, DIPL ABO

How many times have you seen a cornea with noticeable superficial punctate keratopathy (SPK), only to look back at the chief complaint in disbelief, as it states, "Patient denies pain and irritation"? When the patient feels their dryness, it is easy to educate and treat them, but it's more of a challenge when they don't understand their own symptoms.

The literature suggests neurotrophic keratitis (NK) is rare, affecting only 20 per 100,000 people, but these numbers may not accurately reflect the reality of the disease.[1] In this case, I discuss a patient with multifactorial NK that goes from bad to worse.

CASE PRESENTATION

A 72-year-old female was referred to our cornea specialist for a band keratopathy in her only functioning (left) eye. She had a history of multiple penetrating keratectomies OU, cataract extraction OU, and a penetrating injury OD that left her with no light perception. She had trace SPK managed with artificial tears, without complaints of dry eye symptoms. At her initial visit, she had no complaints except blurry vision OS, and her BCVA was 20/200 OS. She was taking difluprednate ophthalmic emulsion 0.05% (Durezol, Novartis) once daily OS to prevent corneal transplant rejection and brimonidine tartrate ophthalmic solution 0.2% (Alphagan, Allergan) twice daily OS for mild mixed-mechanism glaucoma, in addition to the artificial tears. The cornea specialist placed collagen punctal plugs in both lower lid puncta, and the patient was scheduled for a superficial lamellar keratectomy with ethylenediaminetetraacetic acid 3% (EDTA) and mitomycin C 0.02% to prevent corneal haze.

At the patient's 1-day postoperative appointment, her VA was 20/60—an immediate improvement. She had a bandage contact lens in place, and a small central epithelial defect was noted. She was using difluprednate three times daily OS, moxifloxacin (Vigamox, Novartis) three times daily

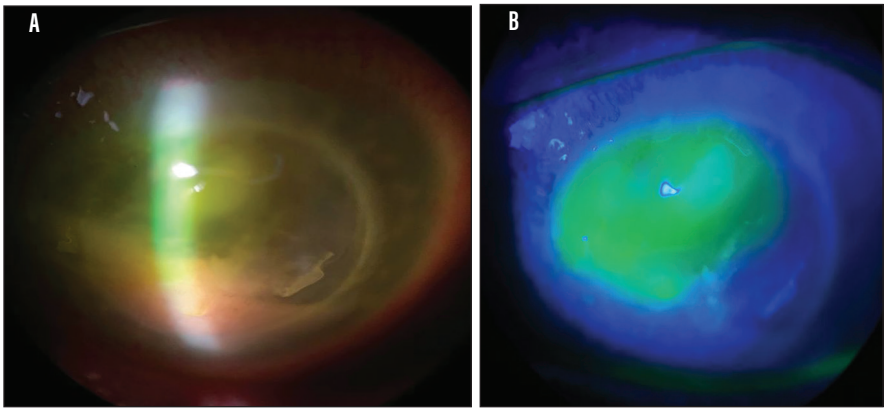

Figure 1. The patient's corneal ulcer progression with hypopyon. Imaging shows the dense infiltrate paracentrally in the graft tissue and inferior hypopyon (A) and the large epithelial defect highlighted with fluorescein (B).

OS, brimonidine twice daily OS, and artificial tears twice daily. The patient was asked to increase artificial tear use and to return in 5 days to remove the bandage contact lens and replace it with a Prokera Biologic Corneal Bandage (BioTissue).

At her follow-up visit, the patient's VA was 20/80, and when the bandage contact lens was removed, her epithelial defect was centrally located from limbus to limbus. I applied the amniotic tissue and taped her eyes to minimize blinking and decrease discomfort. When she returned 3 days later, the amniotic membrane had completely dissolved. The cornea had diffuse 3+ SPK, and there were two remaining epithelial defects: a central 1 mm by 1 mm defect and another of the same size at the 2:00 clock position in the midperiphery. Despite improvement, I placed another cryopreserved amniotic membrane to close the persistent defects.

At her follow-up visit 2 weeks after surgery, all epithelial defects had resolved, but her cornea still had 2+ diffuse SPK. She did not report any pain or discomfort. The amniotic membrane's polycarbonate ring was removed, and a bandage contact lens was placed to continue to promote healing from the superficial keratectomy.

CASE DISCUSSION

Superficial keratectomy can be performed to smooth the corneal surface in the case of corneal dystrophies, scarring, band keratopathy, and recurrent epithelial erosion. Standard postoperative care includes 1-day, 5- to 7-day, and 1-month visits, with drops including an antibiotic and a steroid. Bandage contact lenses stay in place for 1 week, or until the epithelial defect is healed, with the exception being recurrent epithelial erosion, where the contact lens should be maintained for 2 months. The normal expectation for epithelial healing is within days. Many surgeons recommend amniotic membrane placement if the epithelial defect is persistent at the 1-week postoperative visit.

EDTA can be used during superficial keratectomy to break down calcium deposits for band keratopathy. After epithelial debridement, EDTA is soaked on the cornea using sterile sponges, paper, or a well for 3 minutes at a time until the calcium is gone, which can take several rounds lasting from minutes to an hour. The chemical is toxic to the cornea, so care must be taken to avoid the limbal stem cells. Potential side effects of EDTA are pain, edema, scarring, and persistent epithelial defects.

CASE FOLLOW-UP

Forty days after the surgery, the patient returned to have the bandage contact lens removed and the epithelium assessed. Her BCVA was 20/80, and her cornea still showed

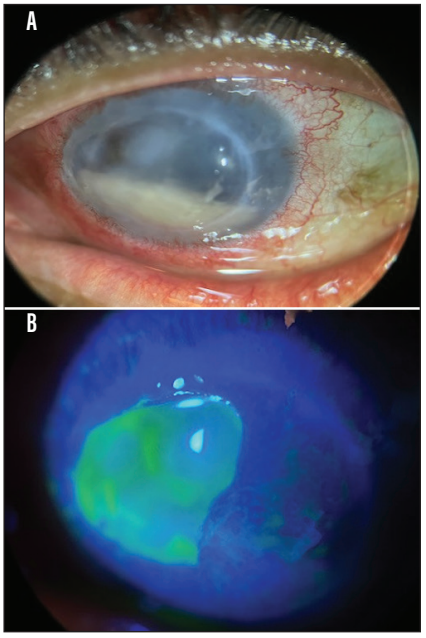

Figure 2. Imaging shows improvement in the density of the infiltrate and cornea (A)—the coagulated inferior hypopyon is clearer—and in the epithelial defect with fluorescein staining (B).

diffuse 2-3+ SPK. She maintained that she did not have any pain, and before topical anesthetic was applied, corneal sensitivity was determined to be 0% in the inferior, nasal, and temporal quadrants.

With the persistent SPK and almost near absence of corneal sensitivity, the patient was diagnosed with stage one NK and prescribed recombinant human nerve growth factor cenegermin-bkbj ophthalmic solution 0.002% (Oxervate, Dompé) six times daily to promote corneal nerve regeneration.

Three weeks after her diagnosis, the patient presented for an emergency visit due to decreased vision and new soreness OS. She had not yet begun the cenegermin drops. Her VA was counting fingers at the face. She had a new central epithelial defect, stromal edema, and anterior chamber cells and flare. She was instructed to increase difluprednate to every 2 hours and start cyclopentolate every night at bedtime OS for pain.

When the patient returned the next week, her vision had decreased to hand motion, and she now had

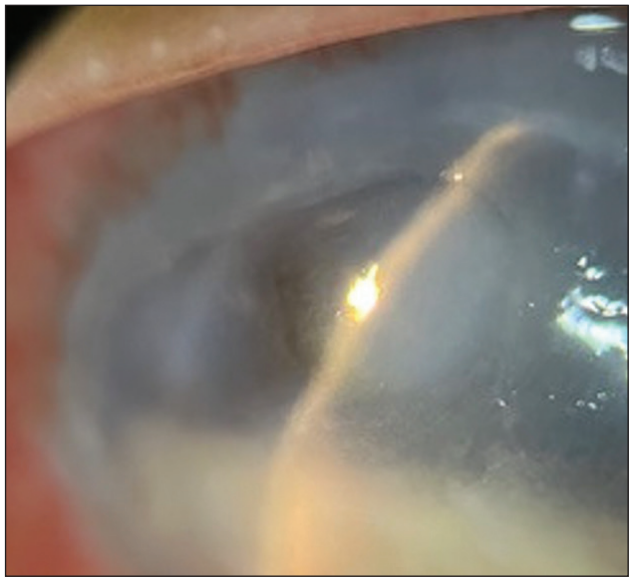

Figure 3. Superior nasal thinning can be seen along the graft-host junction in this patient.

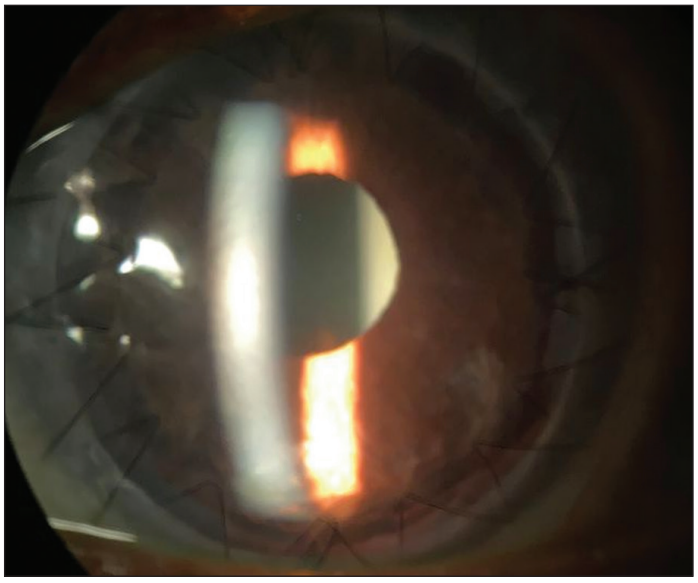

Figure 4. Signs of a healing penetrating keratoplasty, without edema or haze, are evident in this slit-lamp image.

an ulcer (Figure 1). She was directed to increase moxifloxacin to every 2 hours while awake and begin topical gentamicin drops every 2 hours and alternate with moxifloxacin. She was instructed to decrease difluprednate to twice daily. The patient was seen the next day and started on oral doxycycline 100 mg twice daily and vitamin C 1,000 mg.

At day 3, the patient's vision was stable at hand motion, and the epithelial defect was improving (Figure 2). Her cornea showed 75% thinning from the 9:00 clock position to the 10:00 clock position along the donor cornea (Figure 3). The bacterial culture of the ulcer returned as *Staphylococcus aureus*, which is sensitive to moxifloxacin and gentamicin, so antibiotic management was not changed. Because she was showing improvement, the patient was kept on the same medications, and a collagen plug was placed in the upper left puncta to increase lubrication. She was also taught how to tape her eyelids shut to promote corneal healing.

Over the next 10 days, the patient showed significant improvement with resolution of the infiltrate and improvement of the epithelial defect. Bandage contact lenses were replaced at each visit, and antibiotics were decreased to four times daily OS. When the nasal epithelial defect reached 2 mm, a dehydrated amniotic membrane was placed. (A cryopreserved amniotic membrane was not used for fear that the polycarbonate ring would rub against the thinned cornea and cause perforation.) After resolution of the epithelial defect, the patient's VA was still counting fingers due to the irregularity of the corneal thinning, recurrent central calcium deposits, and coagulated hypopyon. She finally began the cenegermin drops and returned to the cornea specialist, who performed a penetrating keratoplasty, surgical peripheral iridotomy, and anterior and posterior synechiolysis OS.

At 1 month postoperative, the patient's transplant was healing as expected, and her VA was 20/50. After successfully completing treatment with cenegermin, her average SPK has only been trace, she has not had an epithelial defect, and she has regained corneal sensation. As she heals from the penetrating keratoplasty, we are maintaining the ocular surface with frequent lubrication and bandage contact lenses (Figure 4).

CASE CONCLUSION AND GENERAL MUSINGS

Although this patient had an ideal visual outcome of 20/50 from hand motion, many patients with poor epithelial cell growth go untreated. Often a thorough review of systemic or surgical history can help make the diagnosis of NK. Many conditions can cause diminished trigeminal nerve sensation, and if the patient doesn't have typical symptoms of dryness, a corneal sensitivity test is warranted. The earlier treatment is initiated, the better the visual outcome will be for the patient.

Topical options include a preservative-free artificial tear to reduce inflammatory proteins in the tear film, ointments and gels applied at nighttime, autologous serum tears, cenegermin drops, and antibiotics for bandage contact lenses or epithelial defects. Oral medications, such as tetracyclines, can also be prescribed.

In-office treatments include the use of amniotic membranes, punctal plugs, and bandage contact lenses. If the patient has lagophthalmos or is a chronic eye rubber, recommend lid taping and wearing a shield at night to help prevent loss of the lens. Surgical options include temporary

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or permanent tarsorrhaphies and amniotic membrane transplants that are sutured to the conjunctiva. In eyes with poor visual outcome, surgeons may consider a Gunderson flap.

Cenergermin drops specifically have been a game-changer in the treatment of NK since their FDA approval in 2018. The vast majority of patients are able to receive this medication free or at low cost. Benefits include its limited 8-week course; however, in some cases a second round is necessary. Patients need to ensure that either they or a caregiver can instill the drops six times daily, and they should be made aware that ocular discomfort can occur throughout the innervation process.

With a history of repeated corneal transplants, it's not surprising that our patient had a challenging and delayed healing process following her superficial lamellar keratectomy. As they say, "hindsight is 20/20." Although there was only trace corneal staining prior to surgery, it would've been a good idea to check for corneal sensitivity to see if additional treatment was needed. Moving forward, be on the lookout for the classic "stain without pain" and become familiar with the medications and procedures that can help with these challenging cases. ■

1. Saad S, Abdelmassih Y, Saad R, et al. Neurotrophic keratitis: frequency, etiologies, clinical management and outcomes. *Ocul Surf.* 2020;18(2):231-236.

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