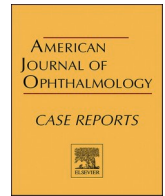


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## Unilateral pediatric neurotrophic keratitis due to congenital left trigeminal nerve aplasia with PROSE (prosthetic replacement of the ocular surface ecosystem) treatment

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### ABSTRACT

**Purpose:** To present a 3-year-old female patient with a non-familial, isolated, unilateral case of left corneal anesthesia with MRI-confirmed congenital left trigeminal nerve aplasia.

**Observations:** A corneal epithelial defect was noted in the left eye after an 8-week trial of recombinant human nerve growth factor. Subsequent evaluation and fitting of a PROSE (prosthetic replacement of the ocular surface ecosystem) lens led to healing of the corneal epithelium and visual acuity improvement from 20/300 to 20/70.

**Conclusions and Importance:** A scleral lens may be a possible treatment for those with neurotrophic keratitis in which a trial of topical lubrication and human nerve growth factor has not been effective.

### 1. Introduction

The diagnosis of neurotrophic keratitis in the pediatric population is a rare phenomenon. In adults, several acquired etiologies exist including herpetic infections, diabetes, neoplastic, vascular, and inflammatory. In children, while the same potential exists for various causes, congenital lesions also gain prominence. Congenital trigeminal anesthesia is a possible cause of neurotrophic keratitis in the pediatric population. It can present as part of a constellation of congenital anomalies and in isolation. It can be bilateral or unilateral. It can encompass the entire distribution of the trigeminal nerve or be isolated to the cornea. Here, we present a 3-year-old Caucasian female patient with a non-familial, isolated, unilateral case of left corneal anesthesia with MRI-confirmed congenital left trigeminal nerve aplasia.

### 2. Case report

A 3-year-old Caucasian female patient presented with decreased left corneal sensitivity noticed when she was poked in the eye at age 1 and did not react. She was noted to occasionally scratch or rub her left eye. Past medical and birth history were not significant with the exception of an umbilical hernia. Past family history was negative for familial corneal

hypoesthesia or any neurological or congenital disorders. The lack of corneal sensitivity was determined to be due to a trigeminal nerve lesion. Punctal occlusion and aggressive lubrication failed to treat the corneal anesthesia.

On referral to the cornea clinic at Baylor College of Medicine, patient was CSM (central, steady, maintained) OU. Tonometry yielded stp (standard pressure) OU. No APD (afferent pupillary defect) was detected OU. Full extraocular movements were present OU. V1 and V2 cutaneous sensitivity of the forehead and cheeks was noted to be normal bilaterally. The left cornea had absent sensitivity with the Q-tip test, while sensitivity was intact in the right cornea. The external exam, lids/lashes, conjunctiva, sclera, anterior chamber, iris, and lens were normal OU, as well as the cornea OD. The left cornea was noted to have central anterior stromal scarring with no epithelial defect, but the epithelium was irregular and had a healing line. Oxervate (cenegermin), a topical ophthalmic recombinant human nerve growth factor solution, was started six times per day for eight weeks.

On follow-up examination after completing the 8-week course of Oxervate, biomicroscopic findings were similar to those found at the first visit with the significant exception that an oval epithelial defect (4mm vertically by 5mm horizontally), in addition to the central anterior stromal opacity were noted in the left cornea. Because of the

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apparent lack of response to Oxervate, a recommendation to fit the left eye with a PROSE (prosthetic replacement of the ocular surface ecosystem) lens was made. Importantly, an MRI obtained two weeks later demonstrated congenital aplasia of the trigeminal nerve (Fig. 1). There was also enhancement of the left anterior chamber suggestive of inflammation (Fig. 2).

The patient was evaluated for a PROSE device. At that time, the treatment included application of preservative free artificial tears every 30 minutes during the day with mineral oil ointment at night.

At the consultation visit, uncorrected Snellen visual acuity was 20/300 in the left eye. On slit lamp examination, the left eye had grade 2 diffuse conjunctival injection with a central epithelial defect (approximately 4.5mm x 2mm) with surrounding stromal haze and diffuse grade 4 superficial punctate keratitis (Fig. 3). The slit lamp examination of the right eye was unremarkable. A trial PROSE device with a base curve of 8.00 mm and diameter of 16.0 mm was placed on the left eye. An adequate fit with complete vault over the cornea was achieved, and the patient tolerated the PROSE device well.

PROSE treatment was initiated in the left eye for the purpose of protecting the ocular surface from exposure and promoting healing of the epithelial defect. A smaller diameter (15.0mm) initial device was ordered to ease application and removal for the parents. The diameter was eventually increased to 16.5 mm to provide more conjunctival coverage. Visual acuity eventually improved to 20/70 with the PROSE device.

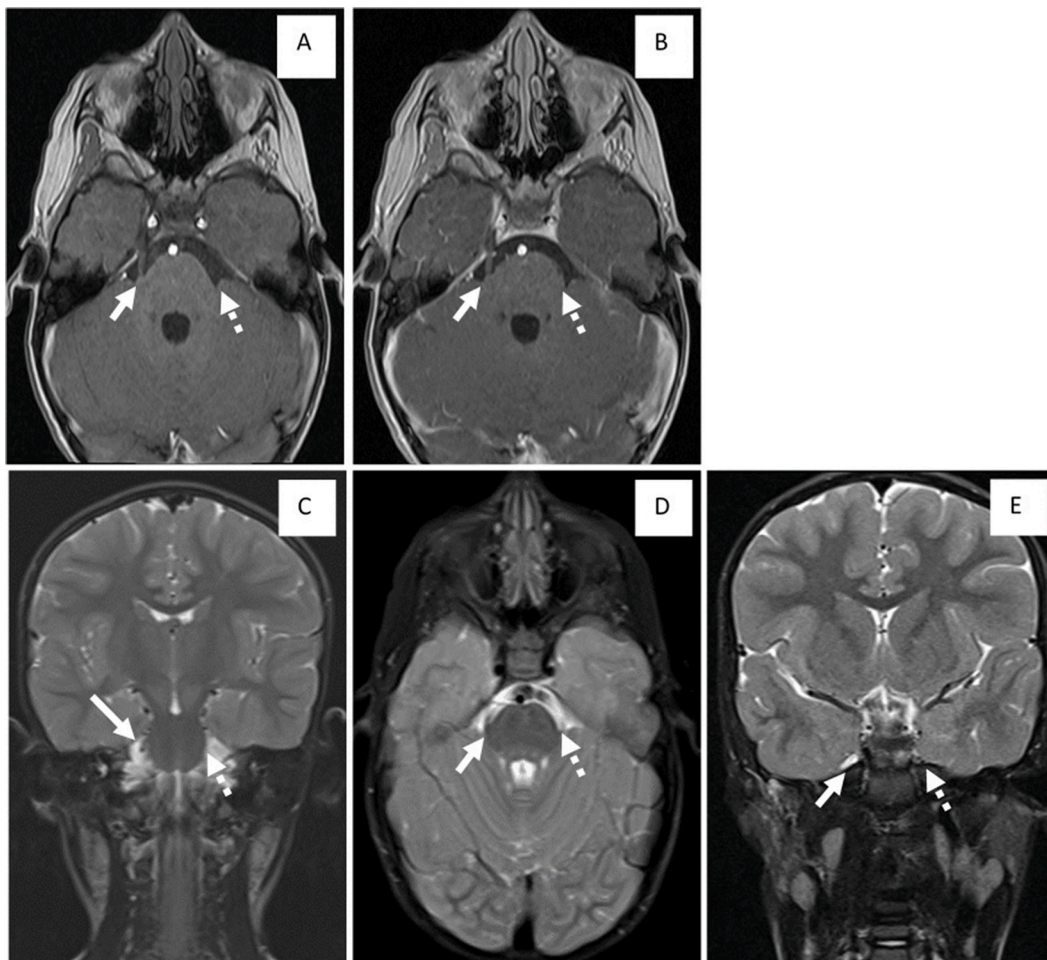
The epithelial defect healed after 9 days of daily PROSE wear—worn during the day and removed while sleeping (Figs. 4 and 5).

Daily wear of the PROSE device was continued with installation of ointment at night when the device was removed. The patient returned to her home in Texas and is being examined locally.

On her most recent follow-up after wearing the PROSE lens for 16 weeks, she was tolerating the lens well. The corneal epithelium remains healed with punctate epithelial erosions that stained with fluorescein in the central cornea. Visual acuity with PROSE and over refraction was 20/70 + 1.50. This level of acuity was felt to be due to stromal opacity, refractive error and amblyopia. Patching for 2 hours per day was recommended for the right eye.

### 3. Discussion

Neurotrophic keratitis (NK) is a degenerative corneal condition caused by damage to – or, in this unique case, maldevelopment of the trigeminal (V) cranial nerve root, leading to a decrease or lack of corneal sensation.<sup>1,2</sup> The trigeminal sensory nerve fibers play a key role in providing signals for tear production.<sup>1,2</sup> With loss of normal neural function, the ocular surface desiccates due to a decrease in reflex tear secretion and blinking and the cornea is thus vulnerable to insult. Spontaneous epithelial breakdown may occur due to the lack of trophic factors supplied by the trigeminal nerve that preserve corneal integrity.<sup>1-3</sup> Reduced corneal sensitivity and impaired corneal healing are characteristic of NK, which can make the patient's recognition and healing of corneal damage more challenging.<sup>1,2</sup> These features of the condition can lead to corneal scarring, thinning, stromal ulceration, and perforation, all of which can be visually debilitating.<sup>1,2</sup>



**Fig. 1.** Absent left trigeminal nerve A—axial T1 precontrast, B—axial T1 postcontrast, C—coronal T2 FS (fat-suppressed), D—axial T2 FS; absent left Meckel's cave E—coronal T2 FS \*normal is indicated by solid arrow, absent is indicated by dotted arrow.

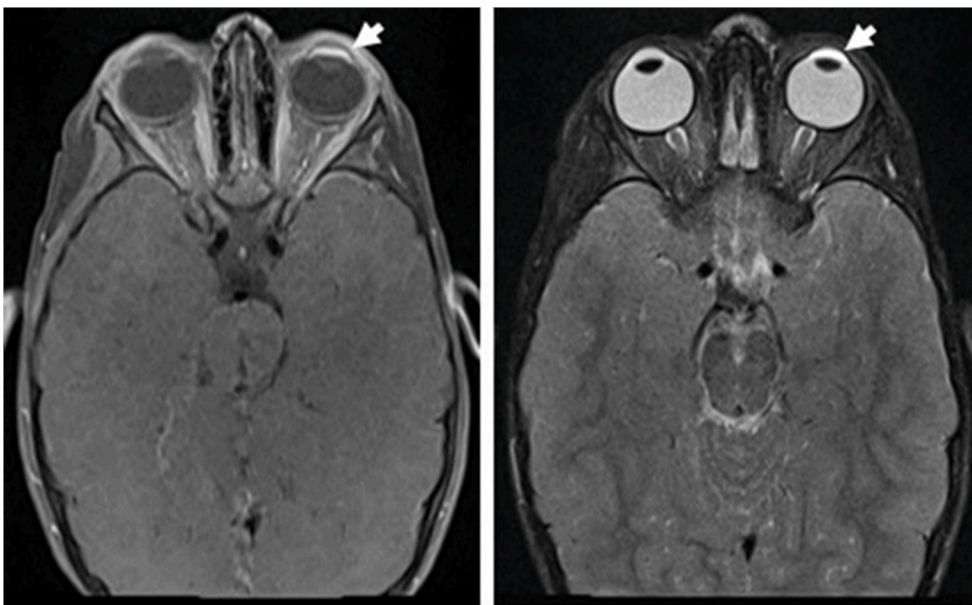


Fig. 2. Enhancement in left anterior chamber (arrow) left—axial T1 postcontrast, right—axial T2 FS.

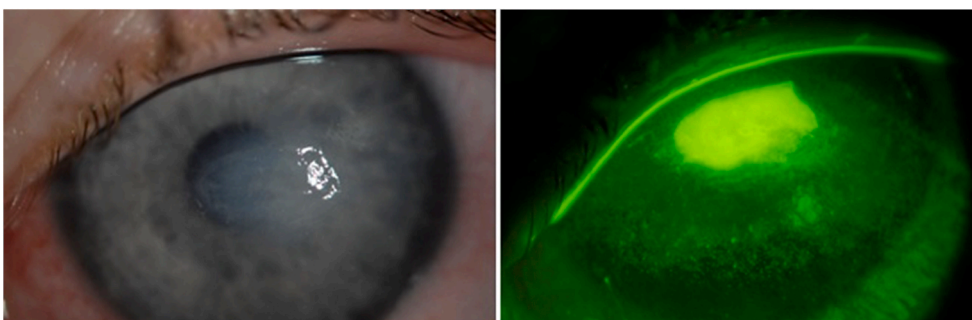


Fig. 3. Large central epithelial defect in the left eye on presentation, seen in white light and in cobalt blue light with sodium fluorescein dye. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

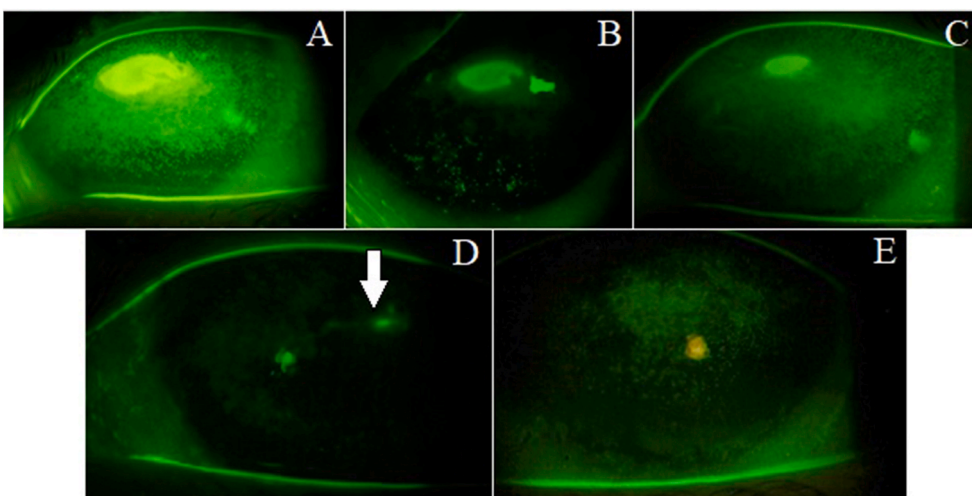


Fig. 4. The course of healing of the left eye noted with PROSE wear over a period of 9 days, left to right (day 2, 3, 4, 5, and 9). The arrow depicts the defect in image D to differentiate it from the reflection seen to the left.



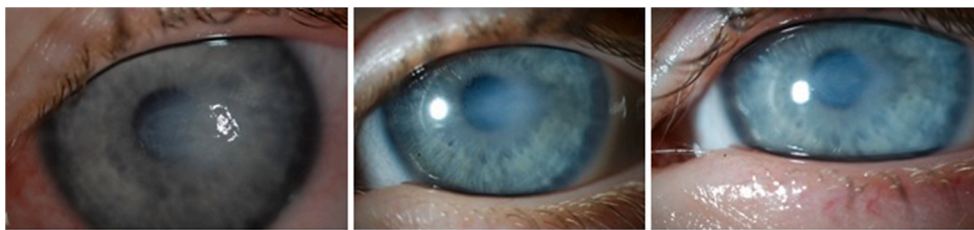


Fig. 5. From left to right, appearance of the left cornea on presentation, after 9 days, and after ~3.5 months of PROSE treatment. Note the increase in visibility of iris details and pupillary margin especially temporally in the rightmost image.

An important cause of neurotrophic keratitis in the pediatric population is congenital trigeminal anesthesia. It typically presents bilaterally, and a unilateral presentation is uncommon, unless due to a specific trigeminal nerve lesion as in our case.<sup>4</sup> It is also typically limited to the sensory component of the trigeminal nerve because of the trigeminal nerve's embryology. The sensory root of the trigeminal nerve arises from the neural crest cells whereas the motor root arises from the ventral part of the developing neural tube.<sup>5</sup> A unique peculiarity of our case is the presence of a subclinical left anterior uveitis detected on MRI. This is likely due to loss of trigeminal innervation causing increased vascular permeability and a subsequent inflammatory cascade.

To our knowledge, this is the first unilateral isolated corneal anesthesia case with sparing of the V1 and V2 trigeminal cutaneous distribution in the English language ophthalmic literature. While unilateral isolated cases of congenital trigeminal anesthesia are infrequent, four have been reported in the literature dating back to 1972 (Table 1). The most recent case report in 2015 is the most similar to ours with unilateral ulceration of the cornea secondary to MRI-confirmed congenital trigeminal nerve agenesis with the notable exception of anesthesia in the distribution of all divisions of the trigeminal nerve.<sup>9</sup> The lack of facial anesthesia is a unique feature of our case. This is possibly due to a greater number of trigeminal nerve fibers present in the cornea; however, with left trigeminal aplasia noted on MRI, this explanation requires further exploration.

The treatment of congenital trigeminal anesthesia remains an area of active research. In the case of this patient, the epithelial defect did not heal or recur with topical lubrication and recombinant human nerve growth factor (NGF). A previous case report had demonstrated promising use of NGF to restore corneal epithelial integrity.<sup>10</sup> However, an 8-week trial of Oxervate was not effective in our patient and a therapeutic scleral lens was recommended. The benefit of scleral devices, like PROSE, is that the fluid-filled chamber of the lens allows for a constant bathing of the cornea with solution and prevents mechanical trauma. By doing this, the scleral lens (SL) provides the necessary environment for the cornea to recover and in turn promotes corneal healing. The SL additionally reduces the burden of frequent application of lubricant tears, which is particularly notable in a pediatric case. In addition to providing an environment for the healing of the epithelial defect, continued treatment with the SL is used to maintain the integrity of the cornea and prevent future epithelial defects.

In cases of ocular surface disease, the SL serves a protective and therapeutic role. The scleral lens is filled with preservative-free saline and then applied to the eye. The fit of the SL is optimized to rest gently on the conjunctival tissue overlying the sclera while completely vaulting the cornea and limbus without touch. Due to the fluid-filled chamber as well as the rigid nature of the device, scleral lens treatment allows for constant lubrication and protection of the ocular surface. The lens can be worn on a daily or continuous under close observation basis. Continuous short-term wear can be used to promote corneal healing. Daily long-term wear can protect the corneal epithelium from recurrent break down.

The secondary benefit that can occur with scleral lens treatment is an improvement in visual acuity. Irregular epithelium and scar tissue in the neurotrophic cornea may create irregular astigmatism that cannot be

**Table 1**  
Unilateral cases of congenital trigeminal anesthesia.

Author, Sex/Age, Year Published	Ocular Sensation	Facial Sensation
Stewart et al., F/11mo, 1972 <sup>6</sup>	Absent LE	L V1 absent
Hennis et al., F/1yr, 1989 <sup>7</sup>	Absent LE	L V1 absent
Hashmi et al., M/14yrs, 2004 <sup>8</sup>	Absent LE	L V1, V2, V3 absent
Ohana et al., M/7mo, 2015 <sup>9</sup>	Absent LE	L V1, V2, V3 absent

LE = left eye, RE = right eye, V1 = ophthalmic/V2 = maxillary/V3 = mandibular branches of the trigeminal nerve.

corrected by conventional means. The SL can correct for irregular astigmatism due to the rigid nature of the lens and the masking of surface irregularity by the fluid filled chamber.

In the case of this patient, the PROSE device was able to heal the persistent epithelial defect, and continued wear aims to prevent future defects from occurring.<sup>11</sup> An additional benefit was the improvement in vision from 20/300 to 20/70. This is particularly important due to the age of the patient to attempt to reduce amblyogenic risk. PROSE treatment will continue long-term for this patient and the PROSE device will be monitored and modified annually as needed.

#### 4. Conclusions

A scleral lens may be a possible treatment for those with neurotrophic keratitis in which a trial of topical lubrication and human nerve growth factor has not been effective.

#### Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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#### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

#### Declaration of competing interest

All authors have no financial disclosures.

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