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SUTURELESS AMNIOTIC MEMBRANES (PROKERA) FOR FILAMENTARY KERATITIS: A CASE SERIES

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ABSTRACT

Purpose
To report a case series of refractory filamentary keratitis successfully managed with sutureless amniotic membranes resistant to other management strategies.

Methods
Three cases are discussed with anterior segment photography who were diagnosed with filamentary keratitis and successfully managed with sutureless amniotic membranes, after experiencing limited relief with standard treatments.

Conclusions
This case series demonstrates the complex management of patients with filamentary keratitis who had failed with traditional therapies and were successfully managed with sutureless amniotic membranes. All three patients demonstrated improvement in both ocular signs and symptoms following amniotic membrane application to the ocular surface.

Keywords: *filamentary keratitis, sutureless amniotic membranes*

Filamentary keratitis is an ocular surface disorder characterized by adherence of mucin and epithelial cells to the cornea.[1] Patients with filamentary keratitis may present with variable symptoms, including increased levels of pain, due to the irregularity of the corneal surface and the presence of epithelial defects, necessitating rapidity of treatment. The condition has been linked to various ocular and systemic diseases. Traditional treatment may entail debridement of the filaments, lubrication, punctal occlusion, acetylcysteine, autologous serum, topical anti-inflammatories, topical cyclosporine, bandage contact lenses, and scleral lenses.[2] Amniotic membranes have utility in the treatment of ocular surface disorders due to their anti-inflammatory and epithelial healing properties. The availability of sutureless amniotic membranes allows this treatment option to be more easily and readily performed in office. Presented here are the cases of three patients who were diagnosed with filamentary keratitis and successfully managed with sutureless amniotic membranes, after experiencing limited relief with standard treatments.

CASES

Patient 1

A 74-year-old African American female presented with complaints of foreign body sensation and photophobia in both eyes; however, her left eye was more

severe than her right. She also reported episodes of intermittent pain and irritation that were quickly relieved with the use of artificial tears. Ocular history was remarkable for neurotrophic keratopathy OU, diagnosed 3 years prior. She had been previously diagnosed with filamentary keratitis and was using cyclosporine 0.05% ophthalmic emulsion (Restasis®, Allergan, Inc., Irvine, CA) BID OU, and preservative-free artificial tears every one-hour OS. She had been fit previously with bandage soft contact lenses following removal of her corneal filaments.

Corrected visual acuities were 20/30 OD and 20/50 OS, pinhole no improvement. All other entrance testing was unremarkable. Slit lamp examination revealed 3+ meibomian gland (MG) dysfunction, lid wiper epitheliopathy (LWE), an incomplete blink, and trace conjunctival injection OU. The right cornea had 1+ diffuse punctate epithelial erosions that stained with both fluorescein and lissamine green, and the left eye had 3+ coalesced punctate epithelial erosions and three inferior filaments. Intraocular pressures by Goldman applanation tonometry were 14 mmHg OD and 15 mmHg OS. Dilated fundus examination was unremarkable.

An assessment of filamentary keratitis secondary to neurotrophic keratopathy (confirmed by corneal sensitivity testing), MG dysfunction, and incomplete lid closure was made. Over the course of two months, the filaments continually recurred even after multiple debridements and application of soft bandage contact lenses. During this period, she also had lid wiper debridement and MG expression performed in office. She was taking oral Omega-3s, and was instructed to use OCuSOFT® Plus lid wipes (OCuSOFT, Rosenberg, TX), at home heat therapy and preservative-free ointment (Refresh P.M.®, Allergan, Irvine, CA) at night. It was advised that the patient begin oral antibiotics for her MG dysfunction, but the patient declined.

Soft bandage contact lenses (lotrafilcon A, Alcon, Fort Worth, TX) were prescribed for continuous wear and were replaced every 30 days. The patient was prescribed topical antibiotics to use over the bandage contact lenses four times daily. The patient was instructed to aggressively lubricate the ocular surface with preservative free artificial tears (Refresh Optive Sensitive PF [Allergan, Irvine, CA]) and ointments and had collagen punctal occlusion of the inferior puncta performed OU. She also continued twice daily dosing of cyclosporine in both eyes. The patient was not able to tolerate scleral lenses and was ultimately managed with sutureless amniotic membranes OU. The amniotic membrane was placed on the left eye first and 2 weeks later was placed on the right eye. After the amniotic membrane had dissolved and the outer ring was removed, her ocular signs and symptoms improved OU. Visual acuity improved to 20/25 OD, 20/30 OS. Corneal staining decreased to trace diffuse punctate staining OD and 1+ diffuse punctate staining OS. Her ocular signs and symptoms remained stable for 6 months and she had no recurrence of filaments in either eye with her continued treatment regimen of warm compresses, Omega-3s, topical cyclosporine bid OU, and non-preserved artificial tears QID OU. A summary of treatments is outlined below in Table 1 and Figures 1–3.

Patient 2

A 72-year-old Hispanic female presented with complaints of foreign body sensation, tearing, and itching that had been fluctuating for the past year in both eyes; however, the left eye was more pronounced. The patient's ocular history was remarkable for herpes simplex keratitis and neurotrophic keratopathy. Her medical history was remarkable for breast cancer. She was using preservative-free artificial tears (TheraTears® preservative-free, Akorn, Lake Forest, IL) every 30 minutes to one-hour OU and preservative-free ointment every evening in both eyes, which provided intermittent relief.

Corrected visual acuities were 20/30 OD and 20/60 OS, no improvement with pinhole. Confrontation visual fields, extraocular motilities, and pupils were within normal limits OU. Slit lamp examination revealed inferior punctal plugs OU, 1+ MG dysfunction OU, trace LWE OU, 1+ conjunctival staining and injection OU, trace inferior punctate epithelial erosions OD, and 1+ diffuse punctate epithelial erosions OS. The left cornea also had several two nasal and three superior corneal filaments. Intraocular pressures by Goldman applanation tonometry were 17 mmHg OD, OS. Dilated fundus examination was unremarkable.

TABLE 1 Patient 1, Summary of Treatments

Current Therapy	Restasis® 0.05% BID OU Preservative-free artificial tears every one-hour OS History of soft bandage contact lenses OS
IEI Initial Visit	Debridement of filaments Warm compresses Omega-3s OCuSOFT Plus lid wipes Refresh PM Restasis 0.05% BID OU Preservative-free artificial tears QID OU
2-week follow-up	Meibomian gland expression
1-month follow-up	Debridement of filaments Bandage contact lenses OU Collagen punctal plug occlusion of inferior puncta OU
2-month follow-up	Sutureless amniotic membrane OS 2 weeks later Sutureless amniotic membrane OD

An assessment of filamentary keratitis secondary to neurotrophic keratopathy and MG dysfunction was made. Two filaments OS continued to recur despite debridement of the filaments and LWE, bandage contact lens application, and hourly lubrication with preservative-free artificial tears, gels, and ointments for three months as the patient was hesitant to try other therapies. During this period, the patient was also managed with warm compresses (Bruder mask, Bruder Healthcare, Alpharetta, GA) and Omega-3s. The patient was fit with a sutureless amniotic membrane OS and remained stable for three months (her last follow-up) following its application with improvements in ocular signs and symptoms. Best corrected visual acuity improved to 20/25 OS (Figure 4–6).

Patient 3

A 68-year-old Asian female presented with long-standing complaints of a "tight" feeling at the nasal canthus of both eyes with associated stinging. She

FIG. 1 Patient 1, corneal staining OS, status-post debridement of corneal filaments, 1-month follow-up.

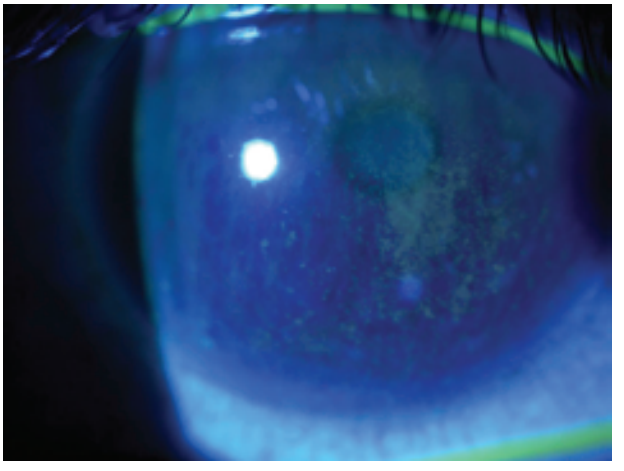


FIG. 2 Patient 1, Sutureless amniotic membrane, ProKera® OS.

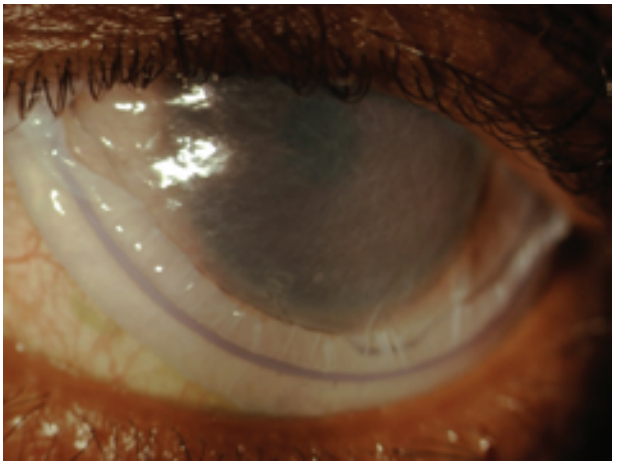


FIG. 3 Patient 1, 6-months post-ProKera® OS, decreased corneal staining and no filaments present.

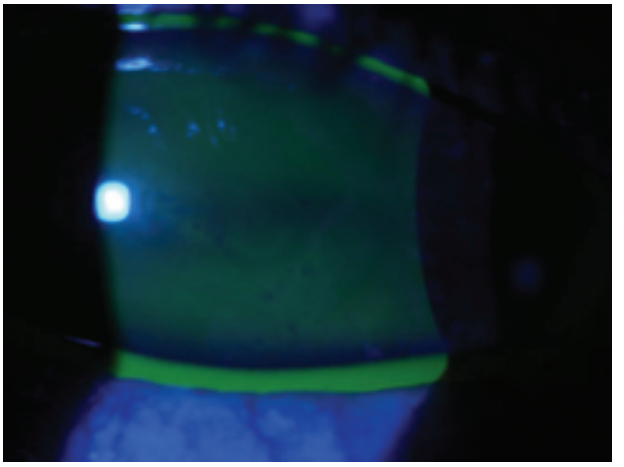


FIG. 4 Patient 2, corneal filaments OS, 1+ diffuse punctate staining.

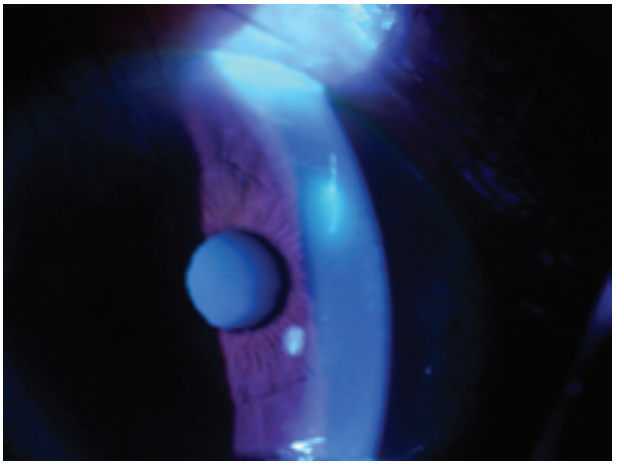


FIG. 5 Patient 2, sutureless amniotic membrane, ProKera® OS, dissolving.

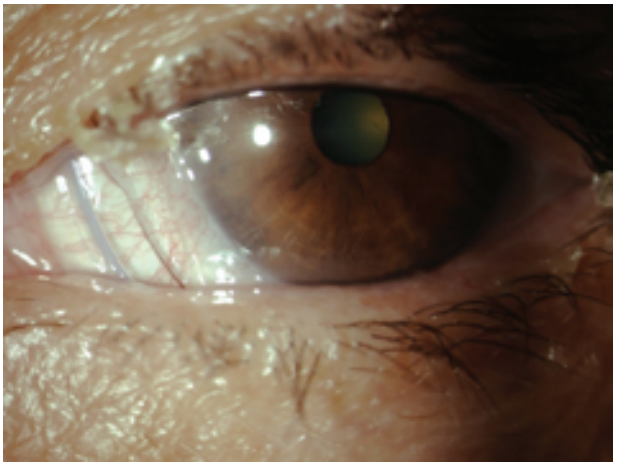
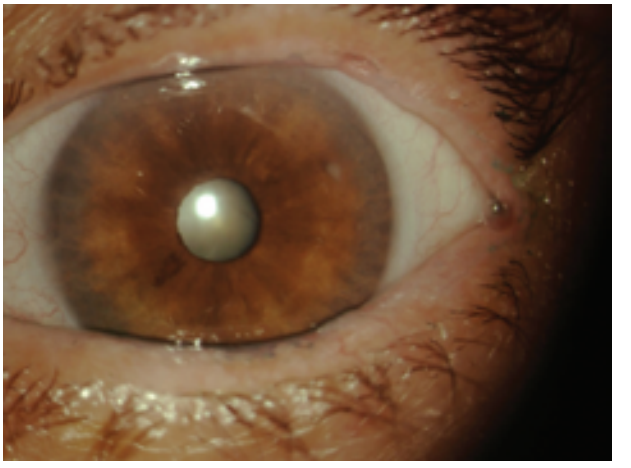


FIG. 6 Patient 2, 3 months post-ProKera® OS, no filaments present.



also reported episodes of intermittent blurry vision. The patient's past ocular history was remarkable for pterygiectomy OS and her medical history was remarkable for hypertension. The patient was using non-preserved artificial tears (Refresh Celluvisc, Allergan Inc., Irvine, CA) every one-hour OU which provided minimal relief.

Best-corrected visual acuities were 20/25 OD and 20/30 OS, no improvement with pinhole. Confrontation visual fields, extraocular motilities, and pupils were within normal limits OU. Slit lamp examination revealed a 2-mm nasal pterygium OD, 1-mm temporal pterygium OD and 0.5-mm nasal pterygium OS, as well as grade 1+ diffuse conjunctival injection OU, severe conjunctivochalasis OU, trace diffuse punctate epithelial erosions OU, and a small anterior stromal scar inferior nasal OS. Both corneas also had superior arcuate staining with lissamine green, and several superior corneal filaments OU with two additional paracentral filaments OS. The patient also had bilateral reflex blepharospasm and a reduced tear break-up time of 1 second in each eye. Intraocular pressure by Goldmann applanation was 14 mmHg OD and 15 mmHg OS. Dilated fundus evaluation

was unremarkable excepting age-related combined cataract in each eye, which was likely contributing to the reduction in best-corrected visual acuity.

An assessment of filamentary keratitis secondary to superior limbic keratoconjunctivitis was made. The filaments and associated symptoms continued to recur after repeated episodes of debridement, bandage contact lens application, and hourly lubrication with preservative-free gels, tears, and ointments over the course of three months. The patient was fit in a sutureless amniotic membrane OS and was stable for two months following its removal. She showed improvement in signs and symptoms. Eventually, she was fit into 18.2-mm scleral lenses with toric peripheral curves and started on topical cyclosporine 0.05% ophthalmic emulsion (Restasis®, Allergan Inc., Irvine, CA) for long-term management of the ocular surface disease (Figure 7 and Figure 8).

DISCUSSION

Filamentary keratitis is a chronic, recurrent corneal condition characterized by multiple filaments attached to areas of compromised corneal epithelium.[3–6] It is most often seen in patients with dry eye disease and is often a result of the mechanical friction between the ocular surface and palpebral epithelium.[2–6] Documentation of the presence and amount of LWE is important and debridement may be considered in order to prevent recurrence.[7] Patients at an increased risk for the development of filamentary keratitis include those with a history of ocular surgery, ocular surface inflammation, ocular surface disease (superior limbic keratoconjunctivitis, viral keratoconjunctivitis, MG dysfunction), recurrent corneal erosions, neurotrophic keratopathy, bullous keratopathy, or poor lid apposition (ptosis, lagophththalmos).[2,5,6,8–12] These patients may also have underlying systemic connective tissue disorders.[9] Blinking of the lids may pull on the loose ends of the filaments, which could create multiple epithelial defects and cause symptoms of pain and irritation. Patients often present with complaints of foreign body sensation, discomfort, photophobia, pain, blurred vision, and reflex blepharospasm. Examination often reveals a reduced tear break-up time, punctate epithelial erosions and mucus filaments attached the corneal surface that stain with vital dyes. As demonstrated by this case series, treatment usually includes multiple approaches, as long-term management of filamentary keratitis can prove challenging and the root cause of the patient's ocular surface disease needs to be addressed to ensure success.

Traditional treatment for filamentary keratitis usually begins with mechanical removal of the filaments and lubrication of the ocular surface to decrease inflammation.[5] Aggressive lubrication is recommended hourly with preservative-free artificial tears, gels, and ointments as well as management of underlying MG dysfunction such as lid hygiene, warm compresses, gland expression, oral medications.[4,13] Previous literature

FIG. 7 Patient 3. Corneal filaments OS.

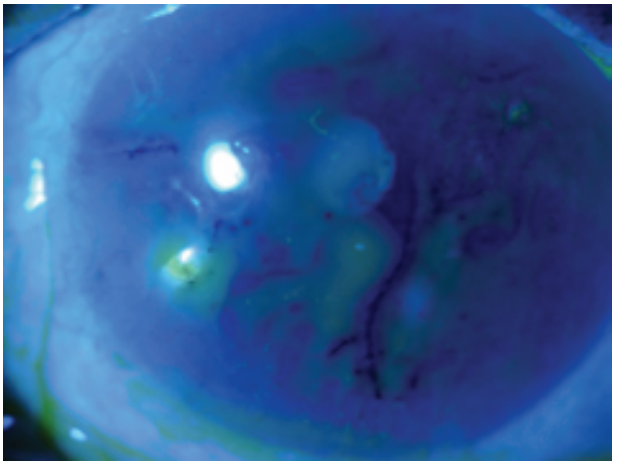
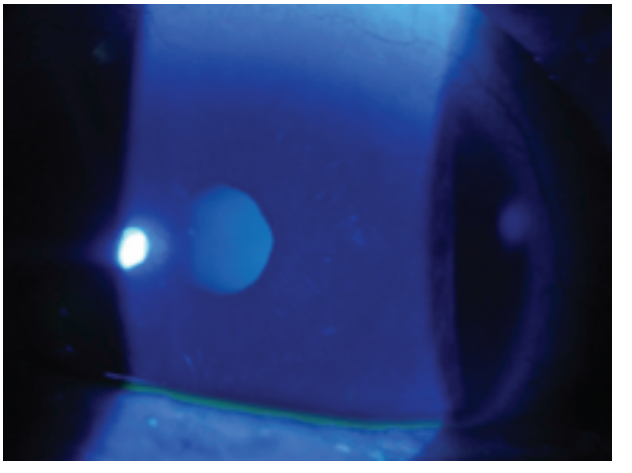


FIG. 8 Patient 3. 2-months post-ProKera® OS showing decreased corneal staining and no filaments present.



examining electron microscopy has demonstrated the role inflammation plays in filamentary keratitis; inflammatory cells and fibroblasts infiltrate a disrupted epithelial basement membrane below the filaments.[9] As filaments form, they exacerbate more inflammation due to the friction between the cornea and the lid.[9,11]

Many reports have discussed therapy options for controlling this inflammation and have found improvement, and in some cases resolution, of the filaments with topical steroids,[14] cyclosporine,[15] diclofenac,[16] acetylcysteine,[4,17] and autologous serum.[2] Some patients with inadequate tear production may benefit from punctal occlusion, as this prevents tears from exiting the eye via nasolacrimal drainage; however, close follow-up care should be maintained to ensure this does not cause an accumulation of inflammatory markers on-eye, perpetuating the cycle of inflammation.[5] Bandage contact lenses and scleral contact lenses have been utilized in the management of filamentary keratitis to assist with healing epithelial defects following debridement of the filaments and to minimize friction of the lids and cornea.[18]

A recent case report demonstrated immediate improvement in symptoms for a patient with filamentary keratitis when treated with autologous serum tears after other methods had failed.[2] Serum tears work by lubricating the ocular surface, minimizing friction, and improving health of the corneal nerves, in addition to having anti-inflammatory properties.[2,19,20] Other case reports have demonstrated the successful management of filamentary keratitis with blepharoptosis surgery and injection with onabotulinum-toxinA (BOTOX; Allergan Pharmaceuticals).[5,10] The toxin is injected into the pretarsal orbicularis near the eyelid margin of both the upper and lower eyelids causing blockage of acetylcholine release into the neuromuscular junction and resultant paralysis of the injected muscle.[5,21] This decreases the friction of the blink between the lid and the ocular surface, preventing the development of filaments; however, it also impedes the patient's visual axis.[5,10]

Cryopreserved amniotic membranes, such as the ProKera®(Biotissue, Inc. Miami, FL), contain anti-inflammatory mediators and a complex array of growth factors and cytokines, which help regenerate a healthy corneal epithelium and may reduce recurrence of filamentary keratitis.[22] Amniotic membranes have many useful properties to assist in the healing of the ocular surface: anti-inflammatory, anti-fibrotic, anti-vascularization, and anti-scarring effects, as well as the ability to promote epithelial regeneration.[23] Secondary to these properties, amniotic membranes are very useful in managing patients with filamentary keratitis and neurotrophic keratopathy as they reduce inflammation and fibrosis, prevent structural damage, and have antimicrobial properties.[23,24] Cryopreserved amniotic membranes have also been shown to restore corneal nerves in a small cohort of patients with ocular surface disease; increasing corneal nerve density which increases corneal sensitivity and reduces symptoms of dry eye.[25–27] The Dry Eye Amniotic Membrane (DREAM) study found that a single placement of a cryopreserved amniotic membrane resulted in improvement of both dry eye symptoms and signs based on an overall reduction of the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) scoring and improvement in corneal staining.[28]

After minimal improvement with traditional therapies, the anti-inflammatory properties of sutureless amniotic membranes, specifically the ProKera®, were successfully employed in three cases of filamentary keratitis. In all three cases, improvement in the ocular surface was noted and remained stable over several months. The ProKera® may be used for a wide range of ocular surface conditions and can be successfully used for patients with filamentary keratitis as an adjunct to other therapies.

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