

A Corneal Sequestrum Case Study

Brittany Nichole Szafran

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Advisor:

Caroline Betbeze, DVM, MS, DACVO

Introduction

A corneal sequestrum is an uncommon condition in cats affecting the corneal epithelium and stroma. Corneal sequestra are characterized by an amber-to-black rounded lesion on the cornea that can range from a depth of 1/3 of the corneal stroma to Descemet's membrane.^{1,12} They are generally painful, causing noticeable ocular discomfort in affected cats. The cause is unknown, but there are a variety of factors and diseases that have been known to predispose cats to this condition including corneal trauma, keratoconjunctivitis sicca, brachycephalic conformation, corneal ulcers, entropion, Feline Herpesvirus-1, Chlamydia psittaci, and grid keratotomies.^{1,7,12} Persians, Himalayans, and domestic shorthair breeds are over-represented.¹² Although it generally only affects cats, it has been reported in a horse and two dogs. A case study from 2000 at the Royal Veterinary College in London diagnosed a corneal sequestrum in a Shetland pony with concurrent keratoconjunctivitis sicca (KCS) and a corneal ulcer.⁹ A case study from 2008 was the first to diagnose a dog, a Shih tzu with a history of a corneal ulcer, with a corneal sequestrum, and a second case study in 2013 diagnosed one in a Cairn terrier with chronic KCS.^{3,4}

History and Presentation

A 3-year-old male, intact, long-haired Scottish fold presented to the Veterinary Specialty Center in Starkville, Mississippi on May 9th, 2016 for a second opinion of a corneal ulcer of the left eye that had not completely healed over the course of 4-5 months, despite treatment by another veterinarian. The client first noted the patient exhibiting blepharospasm of the left eye in July of 2015. At this time, the patient was prescribed Neo-Poly-Dex ophthalmic suspension, but the problem would recur each time treatment was discontinued. In December of 2015, a corneal ulcer was diagnosed by a fluorescein stain, and the patient was prescribed atropine ophthalmic

solution, ofloxacin ophthalmic solution, and Remend® corneal repair gel. The client reported that at this time, the ulcer began to heal, but recurred when treatment was discontinued. A grid keratotomy and entropion surgery were performed on the left eye in January 2016 after the ulcer had not completely healed, and the patient was prescribed amoxicillin orally, topical autologous serum, and Meloxicam orally. Despite treatment, the ulcer did not improve, and the patient was prescribed bacitracin neomycin polymyxin B ophthalmic ointment. Several months passed without resolution of the ulcer and the patient continued to display clinical signs of discomfort, blepharospasm and excessive tearing, so the client decided to seek a second opinion.

Upon presentation, the patient was bright, alert, and responsive. His vital parameters were within normal limits (temperature: 102.2 ° F, pulse: 184 beats per minute, respiration: 44 breaths per minute), and he had a normal body condition score of 4/9. His heart and lungs auscultated normally. An initial evaluation of the eyes revealed OS blepharospasm and a 5-6 mm diameter black, raised, circular area within the left cornea. The black area was surrounded by thickened corneal epithelium and there was superficial corneal vascularization extending from the limbus to the lesion. The conjunctiva was hyperemic and there was evidence of dark-colored mucoid discharge at the medial canthus. The right eye was normal. There were no abnormalities noted on physical examination aside from the abnormalities involving the left eye.

Diagnostic Approach

The diagnostic approach to this patient was a full ophthalmologic exam. To evaluate the patient's vision, the menace, tracking, and dazzle responses were evaluated. All responses were normal bilaterally. Next, the globes were evaluated for their size, position, and motility, which were also within normal limits bilaterally for a brachycephalic cat. An evaluation of the eyelids and conjunctiva revealed normal nictitating membranes bilaterally, but mild hyperemia of the

conjunctiva OU was noted. The pupils were found to be of normal size bilaterally, and both the direct and consensual pupillary light reflexes were normal. Evaluation of the iris, lens, and vitreous was normal bilaterally with no evidence of aqueous flare. Upon examination of the corneas, the right cornea was found to be normal. The left cornea contained a raised, circular, necrotic plaque located centrally and somewhat ventral on the cornea. This was consistent with a corneal sequestrum. Superficial vascularization was present on the ventral and dorsal aspects of the corneal and extended directly to the abnormality. The corneal also contained some edema in this area. Proparacaine drops were administered bilaterally as a local anesthetic in order to perform a fluorescein stain and applanation tonometry. The intra-ocular pressures were unremarkable at 20 mmHg OD and 18 mmHg OS. The fluorescein stain was negative OD, but some of the fluorescein stain was adherent to stroma near the OS corneal abnormality. Tropicamide ophthalmic solution was utilized to dilate the pupils for a fundic exam, which was normal bilaterally. The results of this ophthalmologic exam were consistent with an OS corneal sequestrum and surrounding corneal ulceration.

Pathophysiology

Four layers comprise the cornea: the epithelium, stroma, Descemet's membrane, and the endothelium. A typical corneal sequestrum affects the epithelium and portions of the superficial stroma, but it may extend to Descemet's membrane in severe cases. The exact cause is unknown, but a corneal sequestrum occurs when there is coagulation necrosis of the corneal stroma.¹⁵ The cause of the dark pigmentation is also unknown; however, melanin particles and porphyrins have been suggested as potential causes. Studies have shown that porphyrins, hemoproteins responsible for causing red or brown tears in rats and mice, are not present in feline lacrimal glands or corneas, but melanin particles have been identified.^{11,15} On

histopathology, the lesion consists of necrotic stromal lamellae, and there may or may not be inflammatory cell infiltrate.^{12,15} Differential diagnoses for a corneal sequestrum can include a corneal foreign body or a ruptured corneal ulcer with prolapse of the iris. However, because a corneal sequestrum has a unique appearance, an amber-to-black plaque present on a feline cornea upon examination is diagnostic.¹⁵

In the current case, the patient is identified as a long-haired Scottish fold. This is not one of the over-represented breeds; however, the patient's coat consisted of a color-point pattern. A study from 1981 suggested a possible genetic link between color-point patterns and corneal sequestra.⁵ Similar to that of Persian or Himalayan cats breeds, the patient had a brachycephalic conformation. Brachycephalic cat breeds are at risk for developing lagophthalmos and entropion due to their facial conformation, and it has been suggested that they have decreased corneal sensitivity when compared with domestic shorthaired cats.¹⁶ Collectively, this may increase their likelihood to have chronic exposure keratitis, predisposing them to corneal ulcer formation.⁹ The patient's initial diagnosis was a corneal ulcer. When the ulcer did not heal with medical management, a grid keratotomy and surgical correction of entropion was performed. One retrospective study on lower eyelid entropion in cats found that 37% of cats in one of their study groups presented with concurrent entropion and corneal sequestrum.¹⁶ Another retrospective study found that 4 out of 13 feline eyes treated with a grid keratotomy for a non-healing corneal ulcer developed a corneal sequestrum, suggesting the procedure may predispose cats to developing this condition.^{5,6} From the prior medical records provided by the client, it was unclear if the sequestrum developed prior to or following the grid keratotomy and entropion correction surgery. It is likely in this case that a variety of factors contributed to the development of this patient's corneal sequestrum.

Treatment and Management

The treatment of choice for a corneal sequestrum is a keratectomy with or without a conjunctival graft, or corneoconjunctival transposition (CCT).¹² During a keratectomy, the necrotic corneal tissue is dissected out until only clear cornea remains. If the corneal dissection is able to be superficial (less than 50% corneal depth), the keratectomy alone can be curative. In these cases, a contact lens or partial temporary tarsorrhaphy may be placed to protect the surgical site while it heals.¹⁵ If the corneal dissection exceeds 0.3 mm, or half the corneal thickness, additional support may be warranted.^{1,7} In these cases, a corneoconjunctival transposition (CCT), xenograft (BIOSIS, ACELL, or amniotic membrane), or a conjunctival graft be performed. These procedures provides additional support to the area which assists with healing. During a corneoconjunctival transposition, a pedicle of healthy cornea with conjunctival attachment adjacent to the site of the sequestrum is transposed over the keratectomy site. This provides both tectonic support and a vascular supply to the affected area. Because the defect is filled with corneal tissue, the cornea heals clear and minimal scarring is left behind.¹ In opposition, a conjunctival graft will leave behind a partial scar. To minimize scarring from a conjunctival graft, the conjunctival pedicle may be trimmed, but this will require a follow-up visit with a local anesthetic and possibly sedation.⁷ Alternatives to a corneoconjunctival transposition or conjunctival graft include equine amniotic membrane trans-plantation, a heterologous penetrating keratoplasty using canine corneal tissue, and a small intestinal submucosal graft typically from porcine origin which can aid in healing and decrease scarring.^{2,7,14} Corneal sequestra have been reported to recur in up to 25% of cases, but one study reported that use of a CCT or conjunctival graft can help to prevent recurrence.^{1,12}

Corneal sequestra may be managed medically if financial constraints are an issue, the lesion appears to be superficial on the cornea, and it is not causing any discomfort to the patient.⁵ This is a rare case as most corneal sequestra are painful. Medical management consists of topical antibiotics to prevent secondary infections, analgesics, anti-viral medications if concurrent FHV-1 infection, topical atropine to cause cycloplegia and relieve pain, ocular lubricants, bandage contact lenses, and an E-collar to prevent self-trauma.^{5,12,15} With medical management, the corneal sequestrum may eventually slough off; however, there is a risk that the sequestrum could worsen, get deeper, and require a more invasive surgery to remove it than when it was first detected. Surgical correction will relieve any discomfort and prevent the sequestrum from extending further into the cornea.¹² These medical treatments are also commonly used as adjunctive therapy when the sequestrum is removed surgically.

Case Outcome

The client elected to return to the Mississippi State University College of Veterinary Medicine (MSU-CVM) on May 11th, 2016 for the patient to undergo a superficial keratectomy with the potential of a grafting procedure depending on the depth of the keratectomy. Pre-operative bloodwork was within normal limits, and the patient was determined to be a good candidate for anesthesia. During the procedure, the corneal abnormality was dissected until a clear area of cornea remained, and the abnormal tissue was submitted for histopathology. The area removed was approximately 50% corneal thickness and was found to be 6 mm by 10 mm. A graft did not have to be performed, but a contact lens was placed and a partial temporary tarsorrhaphy was performed to protect the surgical site during the healing process. Recovery of the patient was uneventful. Post-operatively, the patient was monitored in the MSU-CVM intensive care unit, and the only complication was an increased temperature of 103.6 ° F that

subsided after a dose of robenacoxib. Retrospective case studies in cats have shown that opioids, such as hydromorphone, can cause post-operative hyperthermia in cats.¹¹ Pre-operatively, the patient in this case report received methadone, so this could have been the cause of the patient's hyperthermia post-operatively. While reports on hyperthermia in cats receiving methadone are scarce, one experimental study found an increase thermal threshold with this drug.¹²

The patient was discharged on ofloxacin ophthalmic solution, oral robenacoxib, and transmucosal buprenorphine. Histopathology of the lesion was consistent with a corneal sequestrum and chronic bacterial keratitis. A recheck examination was performed on May 16th, 2016. At this time, the keratectomy site facet appeared to be healing well, and the area did not take up any stain when a fluorescein stain was performed. After this recheck, the patient was lost to follow-up, but a brief call with the client 6 months post-surgery revealed that the sequestrum had not recurred and only a faint scar was still visible.

References

1. Andrew S, Tou S, Brooks D. Corneconjunctival transposition for the treatment of feline corneal sequestra: a retrospective study of 17 cases (1990–1998). *Veterinary Ophthalmology* [serial online]. June 2001;4(2):107-111.
2. Barachetti L, Giudice C, Mortellaro C. Amniotic membrane transplantation for the treatment of feline corneal sequestrum: pilot study. *Veterinary Ophthalmology* [serial online]. September 2010;13(5):326-330.
3. Bouhanna, L., Liscoët, L. B., & Raymond-Letron, I. (2008). Corneal stromal sequestration in a dog. *Veterinary Ophthalmology*, 11(4), 211-214. doi:10.1111/j.1463-5224.2008.00627.x

4. Dubin A, Pizzirani S, Beamer G. Corneal sequestrum in a dog with chronic unilateral keratoconjunctivitis sicca. *Journal Of The American Veterinary Medical Association* [serial online]. December 15, 2013;243(12):1751-1755.
5. Featherstone H, Sansom J. Feline corneal sequestra: a review of 64 cases (80 eyes) from 1993 to 2000. *Veterinary Ophthalmology* [serial online]. July 2004;7(4):213-227.
6. La Croix NC, van der Woerd A, Olivero DK. Nonhealing corneal ulcers in cats: 29 cases (1991–1999). *Journal of the Veterinary Medical Association* 2000; 218: 733–735.
7. Laguna F, Leiva M, Costa D, Lacerda R, Peña Gimenez T. Corneal grafting for the treatment of feline corneal sequestrum: a retrospective study of 18 eyes (13 cats). *Veterinary Ophthalmology* [serial online]. July 2015;18(4):291-296.
8. Maggs, D., Miller, P., Ofri, R., & Slatter, D. (2008). *Slatter's Fundamentals of Veterinary Ophthalmology*. St. Louis: Saunders.
9. McLellan, G. J., & Archer, F. J. (2000). Corneal stromal sequestration and keratoconjunctivitis sicca in a horse. *Veterinary Ophthalmology*, 3(2/3), 207-212. doi:10.1046/j.1463-5224.2000.3230207.x
10. Newkirk K, Hendrix D, Keller R. Porphyrins are not present in feline ocular tissues or corneal sequestra. *Veterinary Ophthalmology* [serial online]. September 2, 2011;14:2-4.
11. Niedfeldt, R. L., & Robertson, S. A. (2006). Postanesthetic hyperthermia in cats: a retrospective comparison between hydromorphone and buprenorphine. *Veterinary Anaesthesia & Analgesia*, 33(6), 381-389. doi:10.1111/j.1467-2995.2005.00275.x
12. Sandmeyer LS, Breaux CB, Grahn BH. Diagnostic Ophthalmology. *The Canadian Veterinary Journal*. 2010;51(11):1295-1296.

13. STEAGALL, P. M., CARNICELLI, P., TAYLOR, P. M., LUNA, S. L., DIXON, M., & FERREIRA, T. H. (2006). Effects of subcutaneous methadone, morphine, buprenorphine or saline on thermal and pressure thresholds in cats. *Journal Of Veterinary Pharmacology & Therapeutics*, 29(6), 531-537. doi:10.1111/j.1365-2885.2006.00800.x
14. Townsend W, Rankin A, Stiles J, Krohne S. Heterologous penetrating keratoplasty for treatment of a corneal sequestrum in a cat. *Veterinary Ophthalmology* [serial online]. July 2008;11(4):273-278.
15. Webb, T. (2013, January 17). Corneal Sequestrum. Retrieved November 03, 2016, from <http://www.vin.com/Members/Associate/Associate.plx?from=GetDzInfo&DiseaseId=545>
16. White J, Grundon R, Hardman C, O'Reilly A, Stanley R. Surgical management and outcome of lower eyelid entropion in 124 cats. *Veterinary Ophthalmology* [serial online]. July 2012;15(4):231-235.