Use of grid keratotomy for the treatment of indolent corneal ulcer in a llama

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Abstract — A case of indolent corneal ulcer in a llama (Llama glama) is described. Diagnostic testing included a complete ophthalmic examination with corneal cytologic and histopathologic examination. Successful management involved grid keratotomy and topical application of neomycin-polymixin-bacitracin and atropine 1% ointments. Weekly follow-up examinations are described until healing was considered complete.

Case description

A 13-year-old, 120 kg, castrated male llama (Llama glama) was examined at the Boren Veterinary Medical Teaching Hospital, Oklahoma State University, for a unilateral corneal ulcer of the right eye.

The ulcer had been diagnosed 12 d previously by the referring veterinarian and treatment had involved topical application of neomycin-polymixin-bacitracin ointment (3.5 mg neomycin sulfate, 10 000 units polymixin B sulfate, 400 units bacitracin zinc, The Butler Co. Dublin, Ohio, USA), q12h, and topical application of atropine 1% ointment (Bausch and Lomb Pharmaceutical, Tampa, Florida, USA), q12h.

The llama had also received oxytetracycline (Liquamycin LA200; Pfizer Animal Health, Exton, Pennsylvania, USA), 2.4 g, IM, 3 d after the ulcer was diagnosed by the referring veterinarian. The cause of the initial ulcer was unknown. It was speculated that the cornea may have suffered traumatic insult, perhaps from feeding hay in an elevated rack feeder.

The purpose of this report is to describe the diagnosis and management by grid keratotomy of an indolent corneal ulcer in a llama.
ointment was increased to q8h to help to ensure adequate prophylactic antimicrobial concentrations. Neomycin-polymixin-bacitracin ointment was selected for its broad spectrum of activity against gram-positive and gram-negative organisms to prevent the serious complication of secondary corneal stromal bacterial infection (2). Atropine 1% ointment was decreased to q24h, because the pupil was fully dilated (Atropine was utilized to alleviate the potential pain caused by the axon reflex from corneal nerve endings, creating a secondary anterior uveitis including ciliary muscle spasm [3]). Additionally, the llama was fed hay on the ground.

The corneal samples provided adequate cellularity for evaluation and showed a cell population consisting entirely of squamous epithelial cells. No inflammatory cells, fungal elements, or neoplastic cells were seen. Histopathologic study revealed squamous metaplasia with no evidence of infectious agents. A diagnosis of indolent corneal ulcer was made, based on the historical findings of a refractory epithelial corneal ulcer with positive fluorescein staining, nonadhered epithelium at the margins of the ulcer, and exclusion of ongoing corneal damage by infectious causes, abnormalities of the eyelids, or precorneal tear film (4,5).

Seven days after initial presentation (day 7), with fluorescein staining, the nasal half of the ulcer appeared reepithelialized (Figure 1). However, when the epithelium was touched with a cellulose sponge (Ultracell Medical Technologies, North Stonington, Connecticut, USA), it lifted off the ulcer surface, leaving the size of the ulcer unchanged from the initial presentation. Proparacaine 0.5% (Alcon Laboratories, Fort Worth, Texas, USA) was instilled in the eye and epithelial debridement and grid keratotomy over the corneal defect, using a 64 Beaver blade, were performed with the patient standing and under minimal head restraint. Colibri forceps were used to remove all nonadhered epithelium. Gridlines were made 1 mm apart, extending into the superficial stroma in horizontal, vertical, and diagonal directions (Figure 2). Medical therapy was amended to applying atropine 1% ointment q3d to maintain mydriasis; application of the neomycin-polymixin-bacitracin ointment was maintained at q8h.

On day 14, the inferior corneal blood vessels had receded and the superior vessels had progressed slightly. The ulcer had reepithelialized, with the exception of a 3-mm circular area in its superotemporal aspect, where epithelium was present but nonadherent. The results of neuroophthalmic examinations, including menace and pupillary light responses, remained normal throughout the treatment period.

Proparacaine 0.5% was instilled in the eye, the nonadhered epithelium was removed with Colibri forceps, and a grid keratotomy was performed with a 64 Beaver blade in the horizontal and vertical planes over the remaining focal defect. Due to the small size of the remaining ulcer and the lack of cellular infiltrate, application of the neomycin-polymixin-bacitracin ointment was decreased to q12h daily and that of the atropine 1% ointment to q7d to maintain mydriasis. On day 21, the focal ulcer was smaller with adherence of epithelium, but thickened epithelium was present at the temporal aspect (Figure 3). Proparacaine 0.5% was instilled in the eye and a small grid keratotomy was performed over the temporal edge of the thickened epithelium, using a 64 Beaver blade. Application of the atropine 1% ointment was discontinued, as the pupil had remained well dilated on the tapering dosage with no evidence of secondary anterior uveitis, but that of the neomycin-polymixin-bacitracin ointment was continued q12h. On day 28, the focal area of thickened epithelium was smoother, with a small crevice of fluorescein uptake remaining at the temporal edge. The remaining cornea was clear, with the exception of faint grid lines visible at the original ulcer site and focal vascularization toward the spot of thickened epithelium. On day 38, the 3-mm lesion was fluorescein negative and appeared smooth, with some thickened epithelium and fibrosis. The area was surrounded by very focal vascularization. Grid lines remained visible in the otherwise clear cornea. Application of the neomycin-polymixin-bacitracin ointment was decreased to q24h for 5 d, then discontinued. On day 45, the cornea was clear with the exception of faint
grid lines and receding corneal vessels (Figure 4). During the ensuing 8 mo, there was no recurrence of the ulcer and vision remained normal.

**Discussion**

A variety of ocular diseases have been reported in lamoids (6–8). The cornea represents the most common location of lesions, occurring in 41% of llamas with ocular disease (6). Reported conditions of the cornea of lamoids include ulcers from trauma, infection, or idiopathic etiologies; corneal edema; lacerations, keratitis; and degeneration (6,7). Despite the high frequency of corneal ulceration in lamoids (6), indolent corneal ulcer and its treatment by grid keratotomy have not been reported previously.

Indolent corneal ulcers are defined as chronic superficial corneal ulcers that do not respond to appropriate therapy in 5 to 7 d (4). Indolent ulcers have many etiologies, including ongoing mechanical irritation, infection, primary basement membrane defects, basal cell layer defects, and enzymatic or growth factor imbalances (9–11). Indolent ulcers are believed to occur as a result of a disorder of epithelial adhesion to the basement membrane, due to abnormal basement membrane formation, epithelial dystrophy, corneal sequestration, and enzymatic proteolysis (12). The lesion has been reported previously in dogs, cats, and horses (5,9,13–15). Animals of advanced age, such as this patient, may be predisposed to the development of indolent ulcers (11,14).

Treatments used for indolent ulcers include surgical epithelial debridement, including mechanical or chemical corneal debridement, grid or punctate keratotomy, keratectomy, and medical management, which may include antiprotease and antibiotic agents (5). Grid keratotomy involves incision of the cornea at 1–2 mm intervals over the ulcerated area, including 1–2 mm beyond the periphery of the lesion (4). These incisions extend into the healthy corneal stroma, exposing type-1 collagen of the stroma to the newly forming corneal epithelial cells to encourage adherence between the epithelium and the stroma (10,15). Grid keratotomy combined with epithelial debridement decreases healing times for indolent ulcers (5). Grid keratotomy has been reported previously in dogs, cats, and horses, but not in llamas (5,9,13–15). Prognosis for recovery is generally favorable in the absence of infection or severe corneal endothelial degeneration (14). Cytologic and histopathologic examination of the cornea in this case did not demonstrate infectious agents as complicating factors; however, the histologic appearance of the nonadhered epithelium did have characteristics of squamous metaplasia. An increase in mitotic figures and metaplasia may be seen in healing corneal epithelium (16), and can be mistaken for squamous cell carcinoma *in situ*.

Grid keratotomy was selected because of its superior efficacy over punctate keratotomy (4) and because the procedure can be carried out without the animal being under general anesthesia. Keratectomy is associated with rapid healing of indolent ulcers, but it requires the patient to be under general anesthesia. General anesthesia should be avoided, where possible, in ruminants and modified ruminants, such as llamas, to reduce the risk of complications, such as regurgitation of rumen contents, aspiration pneumonia, and nerve damage (17), and the associated economic costs. Keratectomy was not used in this case because of the rapid healing with the keratotomy. Within 7 d of the initial keratotomy, over 90% of the ulcer had healed. Why the remaining 3-mm defect did not heal as quickly as the remainder of the ulcer is not known. Adherent, thickened epithelium has been noted to impede indolent ulcer healing in dogs, which is overcome by either vascularization or keratectomy (Unpublished observations, Gilmour). In this case, keratectomy was deemed unnecessary, given the comfort of the patient (no blepharospasm and all epiphora resolved by day 14) and the minor area involved. The vascular response to the area was slow, minimal, and characterized by thin minimally branching blood vessels, which did eventually heal and remodel the defect.

**Figure 3.** Corneal ulcer, llama, day 21. The remaining temporal ulcer is reduced in size.

**Figure 4.** Day 45. The focal corneal neovascularization is receding. Faint gridlines from the original grid keratotomy are visible.
In addition to the medical therapies used in this case, systemic anti-inflammatory drugs may be used to help to alleviate the pain from secondary anterior uveitis (2). The patient in this report did not have evidence of anterior uveitis, based on a fully dilated pupil and clear aqueous humor. Although epiphora was present, no blepharospasm was ever noted on ophthalmic examinations; therefore, the use of systemic anti-inflammatory agents was not deemed necessary. Experimental topical therapies (18–21) have been evaluated in the treatment of indolent corneal ulcers in dogs, but they have not become a mainstay of treatment, as have corneal debridement and keratotomy.

Llamas are frequently used as guard, pack, and companion animals, making procedures that spare the globe and maintain vision essential for functional and esthetic reasons. Based on the success in this case, grid keratotomy may be a medically and economically sound treatment option for llamas with indolent corneal ulcers.

References