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CASE REPORT
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Indolent Corneal Ulcer in a Calf

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ABSTRACT

***Background*:** Corneal ulcers or lesions are considered emergencies in veterinary practice and may have a prolonged course. Treatment is typically based on antibiotic therapy and the use of autologous or heterologous serum, which may be combined with other adjuvant drugs. Therapeutic decisions aim to provide an environment conducive to corneal tissue regeneration, ensuring the preservation of ocular structures and the patient's visual capacity. This report aims to describe a case of an indolent and refractory corneal ulcer in a Holstein calf, with the purpose of elucidating the therapeutic measures adopted and illustrating the patient's visual recovery process.

***Case*:** A 4-month-old Holstein calf was admitted to the Large Animal Veterinary Hospital with complaints of apathy, pale mucous membranes, nasal and ocular discharge, and diarrhea. Additionally, physical examination revealed a whitish spot in the left eye, which, upon ophthalmic examination with fluorescein staining, was diagnosed as a corneal ulcer. Initial treatment included equine heterologous serum, 0.3% ciprofloxacin eye drops, and 1 mg diclofenac eye drops, with approximately 0.1 mL administered. After 9 days, the clinical condition worsened, with increased ulcer diameter, more pronounced conjunctival edema, photophobia, and blepharospasm. As a result, keratotomy was chosen as a therapeutic alternative to promote proper corneal remodeling. The procedure was performed under general anesthesia and occurred without complications. Following the surgery, treatment with moxifloxacin eye drops was initiated. Within 2 days, tissue neovascularization and a slight reduction of the ulcer were observed, leading to complete healing 20 days after the procedure. However, a corneal scar was noted, which was treated with prednisolone eye drops for 2 days. The corticosteroid was selected due to several favorable properties, including high intraocular concentration, ease of passage between epithelial cells, and slow absorption rate. After this therapeutic approach, only a slight residual scar remained. The animal was discharged without significant visual impairment.

***Discussion*:** The corneal tissue plays a crucial role in the visual mechanism; therefore, when affected, it requires attention, as the greater the number of compromised layers, the lower the cornea's regenerative capacity. Infectious bovine keratoconjunctivitis is an ocular condition of infectious nature, mainly caused by *Moraxella bovis*, which leads to severe ocular inflammation and may progress to corneal ulceration if not treated early. In the case in question, it was a deep ulcer, which contributed to a longer recovery time until complete healing. Treatment is based on the use of antibiotics and other topical drugs, as well as more invasive techniques aimed at controlling inflammation, ensuring ocular integrity, preserving visual capacity, halting lesion progression, and minimizing potential scarring. Corneal ulcers are considered emergencies in veterinary practice, demanding the clinician's full attention and immediate treatment to avoid irreversible damage to the animal's vision and ocular tissues. Logical reasoning should be applied to evaluate the type and severity of the ulcer, with a therapeutic approach focused on promoting an ideal environment for corneal epithelium regeneration. Thus, decisions must be made quickly, efficiently, and carefully, and the treatment should be reassessed and adjusted whenever necessary, aiming to restore corneal health.

Keywords: ulcerative keratitis, cattle, melting ulcer, ophthalmology.

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INTRODUCTION

The cornea is 1 of the layers that make up the structure of the eyeball and is divided into 5 layers: epithelium, basement membrane, stroma, Descemet's membrane, and endothelium [9]. The cornea is characterized as a non-pigmented tissue, with several functions, such as maintaining the shape of the eyeball along with the sclera and protecting the inner structures. However, to properly perform these functions, its natural properties must be in ideal condition, with good surface uniformity, low cellular density in the stroma, and relative dehydration [4].

When any of these mechanisms fails, the disorders appear. Corneal ulcers are characterized by a defect or rupture of the epithelium and may have various causes [9]. Keratopathies range from superficial erosions to perforations of the cornea itself [4] and are classified according to etiology, involvement, and depth [9]. In cattle, infectious bovine keratoconjunctivitis is the most significant ocular disease in livestock, which can progress to corneal ulceration. Clinical signs of ulceration include photophobia, tearing, blepharospasm, conjunctival hyperemia, miosis, and corneal edema [11].

The aim of this manuscript is to report a case of indolent and refractory corneal ulcer in a Holstein calf, in order to elucidate therapeutic measures and illustrate the process of visual recovery in the patient.

CASE

A 4-month-old Holstein female calf was admitted to the Large Animal Veterinary Hospital of the Federal University of Lavras (UFLA). The complaint included apathy, pale mucous membranes, nasal and ocular discharge, and diarrhea. Among the various alterations identified during the physical examination, a whitish spot on the left eye stood out. Upon ophthalmic examination, a corneal ulcer was diagnosed using a positive fluorescein test (Figures 1 & 2).

The treatment administered consisted of the instillation of equine heterologous serum, 0.3% ciprofloxacin eye drops[1] [Ciloxan® - 0.1mL, topical application, 5 times a day, during 9 days], and diclofenac eye drops[2] [Still® - 0.1mL, topical application, 5 times a day, during 9 days]. The medications were applied directly to the cornea using a 1 mL syringe. The administered volume was approximately 0.1 mL, enough to cover the entire corneal surface.

After 9 days of treatment, the clinical condition worsened, with an increase in the ulcer diameter, more pronounced conjunctival edema, photophobia, and blepharospasm (Figure 3). The ulcer was classified as indolent and refractory to treatment, as a deficiency in the adhesion between the corneal epithelium and stroma was identified. This diagnosis was made through fluorescein staining, which adheres to the exposed stroma and extends underneath the detached epithelial edge.

To stimulate proper corneal remodeling, a linear keratotomy was performed which is a surgical procedure indicated for refractory indolent ulcers. It involves the excision of the corneal epithelium and a portion of the underlying stroma, with up to one-third of the affected corneal stroma potentially removed. Healing occurs by 1st intention [15]. The procedure was performed under general anesthesia, and the prior administration of flunixin meglumine, a non-steroidal anti-inflammatory drug, was recommended to reduce inflammation, uveitis, edema, and postoperative pain. The technique was performed without complications (Figure 4). Following the surgical intervention, the animal resumed the previous medical treatment, but this time with the heterologous serum instilled every 12 h, ciprofloxacin eye drops every 6 h, and diclofenac eye drops every 8 h.

After 5 days of treatment, the cornea still did not show the expected response. Therefore, it was decided to replace the ciprofloxacin-based eye drops with moxifloxacin-based drops[3] [Cloridrato de moxifloxacino® - 0.1 mL, 4 times a day]. Two days after this change, signs of tissue neovascularization and a slight reduction in the ulcer were already evident. Complete healing was observed 20 days after the surgical procedure (Figure 5).

After treatment was concluded, the cornea remained with a small scar, which was treated with prednisolone-based eye drops[3] [Acetato de prednisolona® - 0.1mL, twice daily, for 7 days]. The choice of corticosteroid use was based on favorable criteria for its effective absorption and action on the cornea, such as higher intraocular concentration, ease of passage between epithelial cells, and slow absorption. The animal was discharged with a slight residual scar on the cornea, consisting of a small whitish spot.

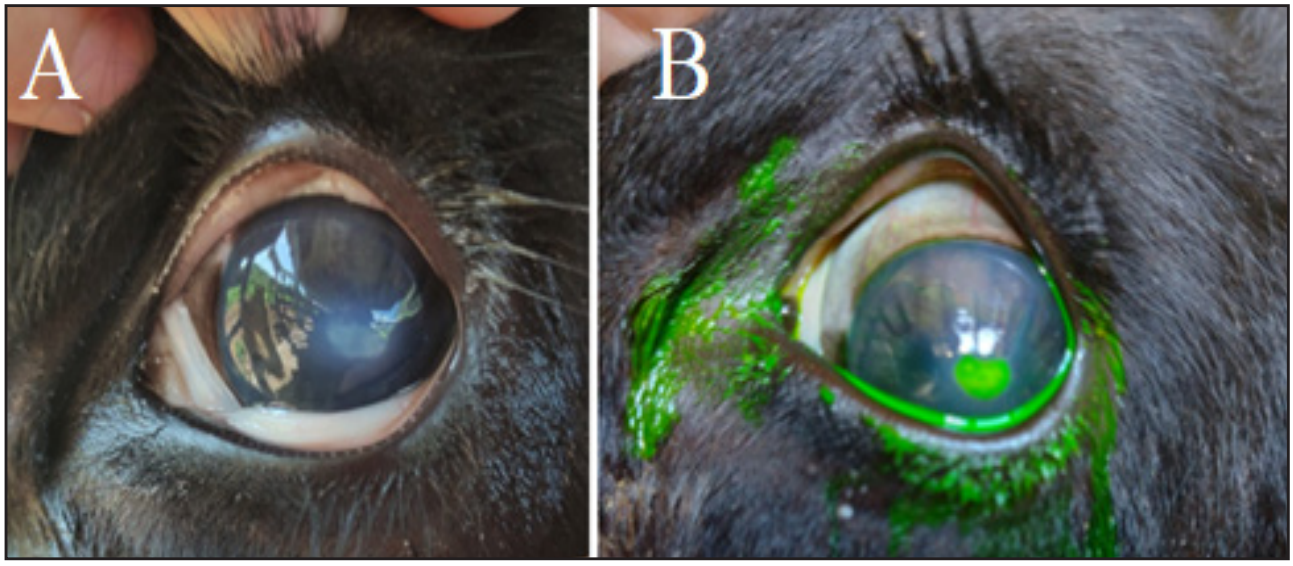

Figure 1. Ophthalmic examination of the left eye of a 4-month-old Hosltein calf with an indolent corneal ulcer. A- Corneal alteration presented on initial clinical examination. B- Corneal ulcer confirmed by fluorescein test.

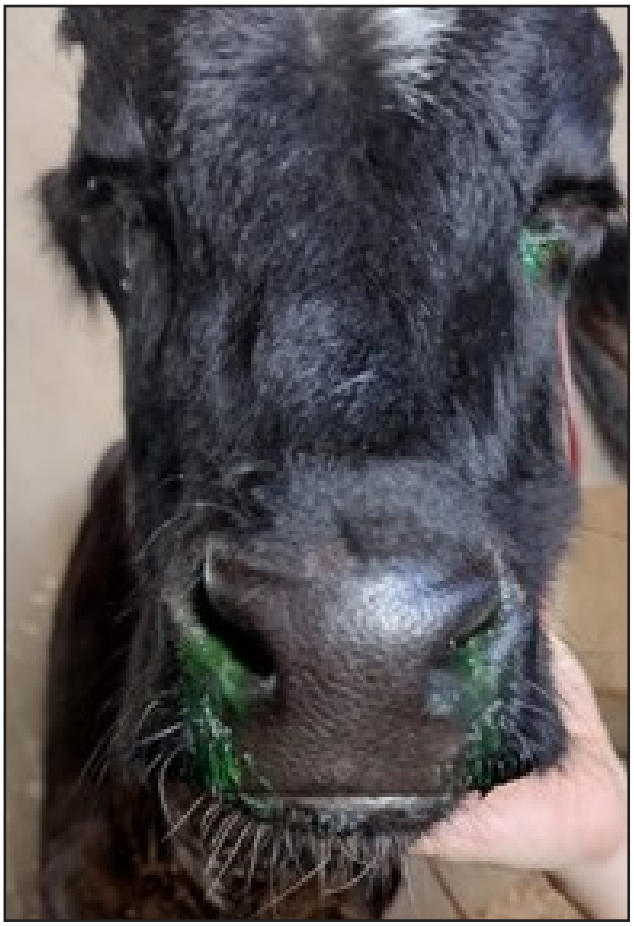

Figure 2. Ophthalmic examination of a 4-month-old Holstein female bovine with an indolent corneal ulcer, showing flurescein refluxing through the nostrils, demonstrating the integrity of the lacrimal duct confirmed by the fluorescein test.

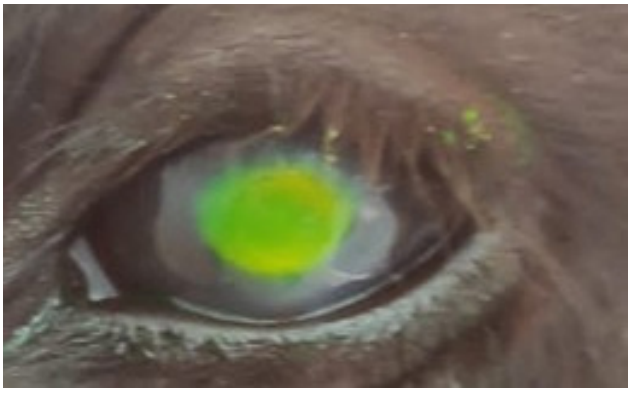

Figure 3. Ophthalmic examination of the left eye of a Holstein calf with a noticeable worsening of the ulcer (larger diameter) when compared to Figure 2B.

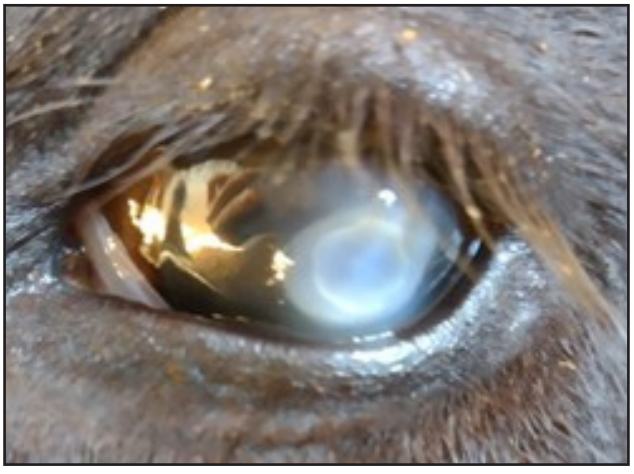

Figure 4. Ophthalmic evaluation of the left eye of a Holstein calf in the immediate postoperative period after keratotomy.

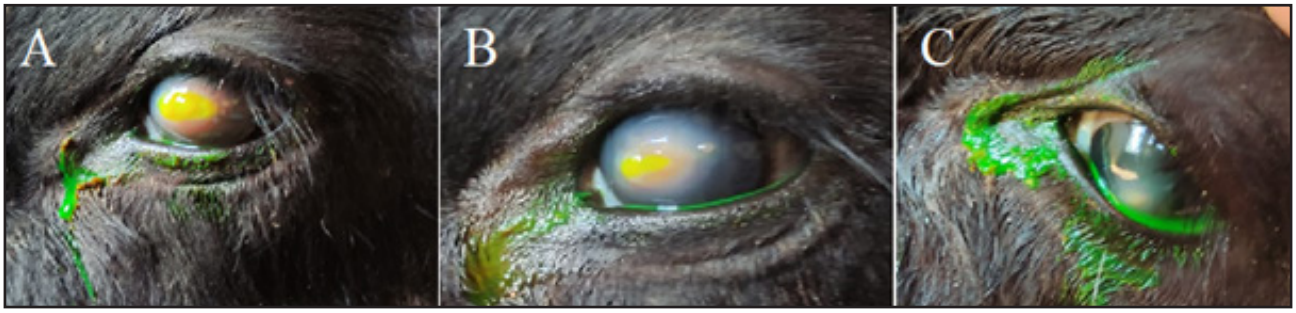

Figure 5. Ophthalmic examination of the left eye of a 4-month-old Holstein calf with an indolent corneal ulcer. A- Two days after changing the antibiotic eye drops, there is a slight reduction in ulceration. B- Seven days after changing the antibiotic eye drops, a significant reduction in ulceration. C- Complete closure of the ulcer, before starting treatment with prednisone eye drops.

DISCUSSION

Infectious bovine keratoconjunctivitis (IBK) is an ocular condition of infectious nature, with the main etiological agent being the bacterium *Moraxella bovis* [2]. During the disease, the excessive increase in bacterial load in the ocular microbiota poses a major challenge to the recovery of the affected eyeball [8]. When not diagnosed early, this scenario may worsen the lesion and the intensity of symptoms, which can be clinically evaluated through signs such as ocular pain, photophobia, blepharospasm, epiphora, synechia, among others [11]. This condition can progress to corneal ulceration, significantly compromising the prognosis and the well-being of the patient.

When the corneal tissue is injured, its regeneration depends on several factors, such as the severity and duration of the lesion, the extent of the defect, and how many layers are affected, as well as animal-related factors such as age, health status, and nutritional condition. The epithelium has great regenerative capacity, whereas the endothelium has very limited regeneration [4]. Superficial lesions may heal spontaneously, but during the healing process, proteases and collagenases released by the ocular metabolism are required for cleansing and removal of dead cells. However, when *M. bovis* invades the stroma, there is disorganization of collagen fibers followed by cellular necrosis, compromising tissue integrity and favoring the development of corneal ulcers [1].

The treatment of this condition is mainly based on the use of antibiotics and topical medications, the latter being the most commonly used route due to its ease of application and rapid absorption, allowing effective concentrations to be reached in the ocular tissue [14]. Moreover, in more severe cases, more invasive interventions such as corneal epithelial debridement may be necessary. Topically administered drugs are distributed through the cornea and non-corneal routes, such as the conjunctiva and sclera, and may also be drained by the nasolacrimal system or systemically absorbed through conjunctival vessels [4]. Other possible routes of administration include intravenous, subconjunctival, intraocular, and orbital.

To establish effective treatment, it is essential that the clinician identifies the primary cause of the lesion and assesses possible associated ocular abnormalities, such as entropion, dermoid, and neoplasms [9]. The therapeutic objective is to control inflammation, preserve ocular integrity, maintain visual capacity, stop the progression of the lesion, and minimize the risk of scarring [4].

In a study conducted by Silva [13] using 60 enucleated human eyes immersed in eye drops for 10 min, it was reported that the concentration of moxifloxacin in the cornea was about 5 times higher than that of ciprofloxacin. In the aqueous humor, this concentration was up to 3.5 times higher. However, drug penetration was not intense enough to raise toxicological concerns. Moxifloxacin may be used up to 4 times daily, and the clinician is responsible for deciding the frequency according to the severity of the lesion.

In addition to antibiotic therapy, the use of autologous or heterologous serum is well described in human ophthalmology and has been introduced in veterinary medicine. The serum is considered autologous when collected from the same animal, following prior evaluation of hydration, nutrition, and weight to ensure the animal is fit to be a donor. Heterologous serum is obtained from a different donor animal for later use [12]. In humans, serum is used as an adjuvant treat-

ment, especially in cases of ulcerative keratitis. In this case report, heterologous serum was chosen due to the animal's clinical condition, as apathy and dehydration made it unsuitable for autologous serum collection.

Topical application of serum is associated with improved healing rates, as well as providing comfort to patients with persistent epithelial defects. The benefits are believed to result from the high concentration of vitamin A, fibronectin, and growth factors, which promote epithelial health through cell proliferation, increased regenerative capacity, and involvement in homeostasis, healing, and neovascularization. Additionally, the anti-enzymatic activity of serum reduces degradation of the corneal stroma and is widely used in the treatment of indolent ulcers [3].

To manage pain and inflammation, nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used in human and veterinary medicine, including diclofenac. This acts by inhibiting cyclooxygenases and lipoxygenases in the arachidonic acid cascade, preventing the proliferation of inflammatory mediators [7]. However, the use of NSAIDs must be cautious, as they may delay corneal healing by reducing ligands for leukotriene receptors [6].

In addition to cautious NSAID use, corticosteroids must also be prescribed and administered with care. Topical application can have adverse effects such as increased intraocular pressure, decreased resistance to infections, cataracts, and delayed healing [5]. However, corticosteroids can be beneficial when collagen fibrils are deposited irregularly, leading to corneal scarring. Corticosteroids are associated with reduced scar formation [10]. In the studied animal, prednisolone eye drops were used after the treatment period due to the presence of a small corneal scar. This decision was justified by the corticosteroids' action in inhibiting collagen-forming activity, which causes the scar, and due to their short-term use.

Corneal ulcers are categorized as emergencies in veterinary medicine, requiring the clinician's full attention and rapid treatment to avoid further damage to the animal's vision and ocular tissues. A logical approach should be established regarding the type and severity of the ulcer, and treatment should aim to promote an ideal environment for corneal epithelium regeneration. Therefore, decisions must be made quickly, efficiently, and carefully, so that the recommended treatment can be promptly reassessed and modified if not effective, with the goal of restoring corneal health.

MANUFACTURERS

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