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An overview of ulcerative keratitis in Dogs and Cats

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Abstract

Ulcerative keratitis, also known as the corneal ulcerative disease is a prevalent ophthalmic affection, particularly among the brachycephalic breeds of dogs and cats. This ailment often presents itself as a secondary complication arising from various underlying eye disorders. The avascular nature of the cornea impedes the reparative and regenerative mechanisms. By focusing on identifying and rectifying the root issues, we can significantly contribute to the prevention and management of this condition.

Keywords: Cornea, ulcer, Fluorescein dye test, keratomalacia, Feline herpes virus

Introduction

Ulcerative keratitis is characterized by the loss of corneal layers, often resulting from trauma (physical or chemical), infection, or any inflammatory conditions associated with anatomical abnormalities. The incidence of corneal ulcers among ophthalmic disease conditions is about 0.38%. Brachycephalic breeds like Boxers and Pugs are highly susceptible to corneal ulcerative diseases. The cornea comprises five anatomical layers: the anterior epithelium, basement membrane, stromal layer, descemet's membrane, and endothelium. The thickness of the corneal layer varies between 0.5-0.8 mm in dogs and cats. Histologically, corneal epithelium is stratified, squamous, and non-keratinized. The stromal layer, constituting around 90% of the cornea's thickness, consists of keratocytes, collagen, and a ground substance that provides essential structural support. Corneal layers are shielded by the preocular tear film, conjunctiva; and both eyelids (Hartley, 2010). The imbalance between corneal protection and corneal abrasion rate results in the development of corneal ulcers.

Etiology

The insufficient production of tear film and eyelid dysfunction makes the cornea vulnerable to damage. Keratoconjunctivitis sicca (KCS) is a common ophthalmic condition that is characterized by diminished tear film production. Lagophthalmos, paralysis of the trigeminal nerve and facial nerve (neurotrophic factors) contribute to defective eyelid functions. The trigeminal nerve contributes major sensory innervation to the cornea and lacrimal gland. The compromised nervous function leads to insensitive cornea and KCS in animals. The excessive loss of corneal epithelium is often associated with conditions such as ectropion, ectopic cilia, distichiasis, and trichiasis. Moreover, immune-mediated complex deposition due to vascular diseases and prolonged use of inhalant anaesthetics and anticholinergics tends to develop corneal ulcers in animals (Kirschner, 1990).

The imbalance between the proteolytic enzymes (proteases and collagenases) produced in normal corneal wound healing significantly leads to stromal degradation. Moreover, the normal bacterial inhabitant of the eye *Pseudomonas aeruginosa* releases exogenous proteases and also stimulates endogenous proteolytic enzymes. These enzymes aggravate the corneal stromal layer destruction, contributing to keratomalacia in dogs and cats (Balland *et al*., 2016). Brachycephalic cat breeds, short-haired domestic cats, Persian and Himalayans are predisposed to corneal ulcerative diseases. The queen Persian is prone to superficial ulcers. Feline herpes virus (FHV) infection has a great impact on the occurrence of corneal ulcers among the cat population. The virus replicates within the epithelial cells and leads to cytopathic effects such as corneal erosion and inflammation (Hartley, 2010).

Ulcers can be classified as simple or complicated based on the depth of corneal layers involved and duration of healing. Simple ulcers are affects superficially without any stromal involvement and heal within 7 days, whereas complicated ulcers exhibit a contrasting pattern, extending deeper into the tissues beyond the surface layers. As a result, their healing process tends to be more prolonged and intricate. Indolent ulcers are non-healing superficial abrasions of the cornea with non-adherent lips. It is more common in dogs than in cats. FHV-1 infection is suspected to be a leading cause of indolent ulcers in cats. *Staphylococcus aureus* is the primary bacterial infection found in dogs with corneal ulcers, contributing to the gelatinous appearance of affected eyes (Farghali *et al*., 2021).

Normal reparative mechanism

Reparative mechanisms vary for each layer of the cornea, and the timing of healing similarly diverges across these layers. The corneal reepithelization occurs within 7 days after damage, whereas the stromal layer takes even weeks and months for regeneration. Complicated stromal wounds utilize vascular healing, with fibrovascular ingrowth from the nearby limbus, depositing granulation tissue at the injured site. Uncomplicated wounds, on the other hand, undergo avascular healing through keratocytes transforming into active fibroblasts, generating fresh collagen and glycosaminoglycan covering the damaged area. The corneal epithelization in cats requires about 2 weeks of time period. The endothelium has a limited capacity for regeneration in cats. The excessive loss is compensated by the spreading and thinning of existing cells.

Diagnostic approaches

The major diagnostic approaches include the Schirmer tear test (STT), Fluorescein dye test (FDT), Tear film break-up time (TFBUT), Rose Bengal staining, blink reflexes, cytology, and bacterial culture etc. The STT measures the basal and reflex tear production levels in animals. The normal value ranges from 15-25 mm/min in dogs and cats. The FDT is a vital stain used to demarcate the ulcerative lesion from a healthy, intact corneal epithelium. Fluorescein dye does not adhere to the Descemet's membrane in instances of deep stromal ulcers. However, in condition such as descematocoele, the ulcer bed lacks staining while the margin retains the presence of dye. The FDT shows typical staining in indolent ulcers with a distinct halo of stain around the ulcer border rather than sharp, distinct borders. The normal TFBUT in cats is 16.7 ± 4.5 s. The palpebral and corneal blink reflexes account for the trigeminal nerve and associated eyelid dysfunction. The motor nerve abnormalities cause inadequate contraction of the orbicularis oculi and result in lagophthalmos condition. The bacterial culture and sensitivity test are employed to confirm the etiology leading to the ulcerative corneal disease (Hartley, 2010).

Therapeutic strategies

The primary goal of treatment modalities for corneal ulcers is to effectively address the underlying cause. Supportive therapies, such as the administration of antibiotics and analgesics, play a crucial role in enhancing the efficacy of the primary treatment approach. These adjunctive measures help to potentiate the treatment and contribute to the overall improvement of corneal ulcers. Topical antibiotics mainly include gentamicin (0.3% solution), tobramycin (0.3% solution), vancomycin (5%) and triple antibiotic (neomycin, polymyxin B and bacitracin). Topical antibiotic administration is indicated for all forms of corneal ulcers as a preventive measure to counteract the secondary bacterial infection. The oral administration of doxycycline in cases of keratomalacia demonstrates a diverse range of effects, including the reduction of inflammation, inhibition of collagenase activity, and enhancement of corneal healing. The topical administration of corticosteroids and non-steroid anti-inflammatory drugs (NSAID) are contraindicated in corneal ulcers as they can predispose to infection, aggravate enzymatic destruction and retard healing of the cornea. Oral administration of NSAIDs like carprofen is found to be beneficial for management of corneal ulcers in animals. The collagenases and proteases produced by the host tissue could be controlled by administration of systemic anti-inflammatory drugs. It is recommended to employ mydriatic therapy with a 1% atropine solution (administered three times daily) to provide relief from pain and reflex uveitis that arise due to corneal nerve stimulation. Systemic administration of antibiotics and analgesics are indicated only in case of highly vascularized corneas or when conjunctival graft placement is involved. However, their ability to attain therapeutic concentration levels within the cornea is limited due to its avascular nature (Stanley, 2007).

Surgical management using conjunctival grafts is indicated for deep stromal ulcers in dogs and cats. The advantages of conjunctival grafts in corneal ulcer includes mechanical support, route of antibiotic and analgesic, supply of serum containing growth factors and presence of anti-collagenases. The five primary classifications of conjunctival grafts are island or free grafts, complete or 360-degree grafts, simple advancement or hood grafts, bridge grafts, and rotational pedicle grafts. Before grafting, the corneal edges undergo debridement. Polyglactin suture materials of sizes 7-0 to 9-0 are used for grafting techniques. The conjunctiva is dissected from underlying tenon's capsule and positioned according to the position of ulcers. Free grafts are used for small corneal ulcers, whereas central corneal ulcers with large diameters are corrected by complete or 360-degree grafts. Graft trimming occurs after full corneal healing, typically 6 to 8 weeks post-surgery. For corneal protection, lateral temporary tarsorrhaphy and third eyelid flap techniques are also recommended.

Cyanoacrylate tissue adhesive can be used to form a thin layer over the ulcer bed to promote the healing of corneal ulcers (Bromberg, 2002). Protease inhibitors like acetylcysteine (5%) and autologous serum are also alternatives to the surgical management of deep stromal ulcers. Many biomaterials like amniotic membrane, equine renal capsule, bovine

pericardium, porcine urinary bladder acellular matrix, and porcine small intestinal submucosa are used for corneal reconstruction (keratoplasty) in companion animals (Dulaurent *et al.*, 2014). Autologous platelet-rich plasma (PRP) administration via subconjunctival route is gaining momentum as a novel therapeutic strategy for the corneal ulcer healing (Farghali *et al.*, 2021; Sharun *et al.*, 2023). PRP serves as a cost-effective treatment and forms a robust repository of cytokines and growth factors, fostering the corneal regeneration. Allogenic mesenchymal stem cell administered via subconjunctival instillation for the healing of deep corneal wounds is a promising alternative for surgical techniques (Falcao *et al*., 2020).

Grid keratotomy combined with partial tarsorrhaphy, is the treatment of choice for indolent ulcers in dogs. In this technique, a cross hatches in the cornea is made using 25-gauge needle or tuberculin syringe. It is contraindicated in felines as they are predisposed to corneal sequestrum formation. Superficial keratectomy and punctate keratotomy are preferred in persistent corneal ulcer conditions.

An elizabethan collar is employed in all patients to prevent self-trauma and thereby exacerbation of corneal ulcer condition.

Conclusion

Systematic diagnosis and treatment of corneal ulcers are essential to avert potential ophthalmic emergencies, such as descemetocele. Addressing the underlying cause is crucial for effective therapy and subsequent ulcer healing. A proper supportive therapy with antibiotics and analgesics is essential to prevent future recurrences. Novel treatment modalities like cell therapy, PRP, and biomaterial implantation can serve as an alternative to surgical interventions and result in supreme healing of the cornea.

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