

WEIRD CORNEAS: EVERYTHING THAT IS FLUORESCEIN NEGATIVE

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Keratitis is defined as inflammation of the cornea as characterized by the presence of blood vessels on a normally exquisitely avascular structure. You can further break these down into ulcerative keratitis and non-ulcerative keratitis. If your patient is fluorescein negative and there is no history of a previous ulceration, there are a few diseases you should consider. In the most basic sense, anything that causes chronic irritation to the surface of the eye will cause vascularization and pigmentation even in the absence of overt ulceration. The most common cause of this keratitis is dry eye or keratoconjunctivitis sicca. As part of your evaluation of any red eye, a Schirmer tear test, fluorescein stain and intraocular pressure reading are indicated in order to rule this disease out.

If tear production is normal (≥ 15 mm/min) then consider the other causes of non-ulcerative keratitis. The first consideration should be chronic mechanical irritation. This would include entropion, trichiasis or foreign bodies. In these situations, the vascularized cornea should match with the source of the irritation. Keep in mind that most brachycephalic dogs have some degree of medial canthal entropion and keratitis. The pug in particular has a high percentage of normal dogs with triangles of pigment in the medial cornea. If you do not see an underlying cause for the corneal vascularization, you should consider immune-mediated forms of keratitis in which the body sends inflammatory cells and blood vessels to the cornea for unknown reasons.

Chronic superficial keratitis is the most common immune-mediated keratitis in the dog. It historically went by the name pannus and has a classic appearance. Typically, pannus presents with bilateral (but often asymmetric) vascularization and pigmentation of the lateral cornea. These patients are typically comfortable when first presenting to the veterinarian although in advanced stages, there can be discomfort and discharge. Shepherds are over-represented in the disease, but CSK can be diagnosed in almost any dog. Although we do not understand the underlying pathophysiology, we do know that the disease is substantially exacerbated by exposure to UV light. As such, this disease is far more aggressive and difficult to treat at high elevations or in desert environments. Dogs in these regions of the country may consider UV protective goggles (Doggles or RexSpecs) to reduce the UV exposure to the cornea. Treatment is predicated on the principles of treatment for all immune-mediated disease, immune suppression. Initially a steroid is the best option to reduce the vascularization on the cornea. The key to control and maintenance of this disease is to hit hard and taper slowly. The two appropriate topical steroids available on the market are 0.1% dexamethasone which is usually combined with neomycin and polymyxin and 1% Prednisolone acetate. Either medication is likely to work. It is recommended that treatment be initiated at four times daily with a weekly taper (depending on the severity) until the cornea is free of blood vessels. This is considered clinical control and some level of anti-inflammatory chronically may be necessary to maintain this control. Given the potential negative consequences of long-term steroid use, many practitioners start their patients with this disease on an immunomodulator such as cyclosporine or tacrolimus concurrently with the steroid. The goal of this approach is to wean slowly off of the steroid and use the other drug for long term maintenance. Keep in mind that the pigment on the cornea is unlikely to go away so use the presence or absence of vessels to assess control.

Pigmentary keratitis in the absence of overt vessels is a common finding in brachycephalic breeds. It is potentially associated with medial canthal entropion and general exposure. For this reason, many ophthalmologists advocate closing down the medial canthus to prevent prolonged irritation. This author is less inclined to perform this surgery as pigmentary keratitis is usually self-limiting in brachycephalic breeds and those that are going to progress to complete pigmentation do so despite surgical closure of the canthus. Tacrolimus and cyclosporine have supportive roles in the treatment of this disease as they can control underlying irritation and potentially break up corneal pigmentation. These patients should be checked for dry eye disease as that will hasten and worsen pigment.

Lipid keratopathy could be considered a non-ulcerative keratitis and is split into two forms. One is the inherited form which involves bilateral, central deposits of lipid and is inherited. This is common in cavalier King Charles spaniels, Shetland sheepdogs, huskies and a multitude of other breeds. As there is no inflammatory component, treatment is not indicated. This is differentiated from lipid deposits associated with inflammation of the cornea (typically post-ulceration). In these cases, steroids are known to make lipid deposits significantly worse and, in fact, chronic topical steroids can cause lipid deposits. Although rare, systemic lipid metabolism

abnormalities can cause or worsen lipid keratopathy. In a patient with progressive lipid deposits, it is recommended that thyroid, serum chemistry and fasting triglycerides be tested. A low fat diet is also recommended to prevent high circulating lipids in the blood stream.

Endothelial dystrophy/degeneration is caused by impaired function of the corneal endothelium resulting in chronic edema of the cornea. Endothelial dystrophy occurs bilaterally although the severity of the disease and onset may be asymmetric. Typically the edema is first noticed in middle aged dogs if due to dystrophy, and older dogs if due to degeneration. Endothelial degeneration can result from severe uveitis, glaucoma, or trauma. No treatment is required in the early stages of the edema; however, in later stages the edema may become severe enough for fluid pockets to develop in the corneal epithelium (bullous keratopathy). These pockets may rupture, creating corneal ulcers. Therapy is palliative using hyperosmotic 5% sodium chloride to reduce edema enough to allow epithelial adhesion and topical antibiotics to prevent secondary infection. Topical sodium chloride will not result in a clinically significant decrease in the cloudy appearance of the cornea however. Referral for surgical therapy to scar the cornea may be required in severe cases.

Cats: The feline corollary to chronic superficial keratitis is eosinophilic keratitis. This disease is notable for the presence of white to yellow plaque lesions. These lesions are associated with blood vessels and can be flat or raised (sometimes dramatically). Diagnosis is achieved via cytology. The presence of even one eosinophil on a corneal cytology is enough to confirm a diagnosis of this disease. What is more complicated is the intertwined relationship between eosinophilic keratitis and feline herpesvirus. It is unclear if these are comorbidities or if herpesvirus actively contributes to eosinophilic keratitis but the diseases often co-exist. As such, one runs the risk of reactivating latent herpesvirus when starting topical immunosuppression designed to control the eosinophilic keratitis. For this reason, some advocate starting oral famciclovir 90mg/kg BID for 3 weeks while simultaneously starting 1% prednisolone acetate TID-QID. Due to the extremely rare but potential anaphylactic reaction to neomycin or polymyxin, neo/poly/dex is not recommended for cats when alternatives are available. As with CSK in the dog, the key to control of this disease is to start at a high frequency and do a very slow taper (one step down every 2 weeks). Control is defined as a lack of plaques and a reduction of blood vessels on the cornea.

As with CSK, starting a topical t cell modulator like tacrolimus or cyclosporine with the prednisolone acetate can allow the patient to be tapered off of the pred acetate. Eosinophilic keratitis sometimes requires life-long management but frequently cats experience isolated episodes and can come off of medication. If the cornea ulcerates, it is necessary to discontinue the topical steroid while allowing the ulceration to heal. If an anti-viral was not started already, a topical or oral antiviral should be started if a cat with eosinophilic keratitis ulcerates. Cidofovir can be applied topically twice daily while vidarabine, idoxuridine and other topical anti-virals typically need to start at 4-6 times daily for a few days before decreasing to four times daily. In rare cases of resistant eosinophilic keratitis, control can be achieved with megestrol acetate, however, given the potential catastrophic systemic risks of using this medication, it should be reserved for use by specialists who have exhausted all other options.