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Immune mediated keratitis in horses
Brian C. Gilger
Department of Ophthalmology, North Carolina State University, Raleigh, North Carolina, USA.

INTRODUCTION
Corneal diseases are the most common ocular abnormalities in horses. Nonulcerative keratopathies are characterised as chronic corneal lesions with cellular infiltrate, vascularisation and variable degrees of ocular discomfort. Causes of nonulcerative keratitis include onchocerciasis, bacterial infections, fungal infections, infiltrative neoplasia, corneal degeneration and immune-mediated inflammation. Chronic corneal opacities with mild to moderate cellular infiltrate and vascularisation, without secondary uveitis or severe ocular discomfort, and not associated with infectious agents, have been described as immune-mediated keratitis (IMMK).

DIAGNOSIS
Diagnosis of IMMK is made if there is a progressive or chronic (>3 months duration) nonulcerative recurrent corneal opacity with or without mild signs of keratitis with cellular infiltrate, corneal vascularisation, and ocular discomfort (i.e. mild epiphora, slight blepharospasm). Other characteristic features include lack of secondary uveitis or severe discomfort, lack of microorganisms, and clinical improvement with anti-inflammatory medications. In cases of epithelial, superficial or midstromal IMMK (see description below), ocular cytology and culture collection should be attempted to rule out infectious causes of the lesions. If the diagnosis is still in doubt, a superficial keratectomy/biopsy should be considered.

CLINICAL CHARACTERISTICS
Clinical features of IMMK are based on the depth of the corneal lesion, and 4 distinct levels have described. These include epithelial, superficial stromal (45% of cases), mid-stromal (27%) and endothelial (23%). With endothelial IMMK, there is commonly focal or diffuse corneal oedema and pigment deposition on at the endothelial surface. Unilateral presentation of IMMK is most common (85%). There is no breed or gender predilection and the average age of diagnosis of all clinical manifestations is approximately 12 years.

TREATMENT
Treatment for IMMK is dependent on the clinical characteristics/type of IMMK that is present. Epithelial, superficial stromal and mid-stromal IMMK are initially treated with topical neomycin, polymyxin and dexamethasone (q. 6 h; Alcon Laboratories) or topical neomycin, bacitracin and polymyxin (Bausch & Lomb) (e.g. following creation of a epithelial defect during diagnostic corneal scraping) with 0.2% cyclosporine topically (q. 12 h; Schering-Plough). Topical neomycin, polymyxin and dexamethasone HCl (q. 6 h) added following re-epithelialisation of the corneal wound. Once the lesion has resolved, then the neomycin, polymyxin, and dexamethasone is tapered and discontinued, while the topical cyclosporine is maintained at q. 24 h. If the lesions persist, then a superficial keratectomy, with or without a conjunctival graft, is recommended. Several horses had been tapered off all medications after corneal healing with a keratectomy and conjunctival graft. The deeper the lesion, the more slowly and incompletely one would expect resolution of the lesions with therapy.

Horses with endothelial IMMK have a poor prognosis and lesions probably will persist or progress despite therapy. Horses with endothelial IMMK may also develop bullous keratopathy and corneal ulcers resulting in discomfort. If not ulcerated, treatment is initiated with topical neomycin, bacitracin and dexamethasone (q. 6 h), and cyclosporine (q. 12 h). If ulcerated, then topical neomycin, bacitracin and polymyxin is recommended with use of topical nonsteroidal anti-inflammatory drugs (NSAIDs, e.g. flurbiprofen, bromfenac). In fact, some excellent responses have been observed with endothelial IMMK with primary brofenac (Xibrom, Alcon) therapy, although the high cost of this medication has limited its chronic use.

DISCUSSION
Four types of IMMK in horses have been described and the location of the inflammation dictates the clinical signs observed and response to therapy. Superficial stromal keratitis appears as a diffuse, mild to moderate yellow to white, cellular infiltrate with diffuse superficial vascularisation. Most of these horses respond to constant topical medical therapy and even surgical removal of the lesion. Mid or deep stromal cellular infiltrate is less common and appears as diffuse, yellow to white, cellular infiltrate with mild surrounding corneal oedema and vascularisation. This type of IMMK responds best to chronic
steroid and cyclosporine A therapy. Endothelitis appears as cellular infiltrate at the endothelium with associated diffuse corneal oedema. This type of inflammation is the least amenable to therapy, but use of the NSAID brofenac has shown some promise.

Prior to treatment with anti-inflammatory or immuno-suppressive medication, careful consideration of the inciting cause must be made. The most common cause of cellular infiltrate in the equine cornea is infectious agents (i.e. stromal abscess), and because topical anti-inflammatory medications may allow infectious agents to proliferate, these medications are strictly contraindicated. It is recommended in all horses with corneal cellular infiltrate that diagnostic samples be collected to rule out infectious organisms. These would include corneal cytology, culture and sensitivity (bacterial and fungal), and corneal biopsy (histopathology, bacterial and fungal culture).

The possible pathogenesis of IMMK in horses is that the immune system has recognised a self-antigen in the cornea (i.e. molecular mimicry) or a foreign protein or organism antigen within the cornea. An underlying infectious agent may be either the inciting or perpetuating cause (or both) in many horses with IMMK. The microorganism may be directly inciting active inflammation or may have induced immunological cross-reaction with self-antigen in the cornea. Immunological cross-reaction with self-antigens has been well documented with leptospiral organisms or their DNA in the equine cornea. Further study is warranted to define the pathogenesis of IMMK and determine why the horse is particularly susceptible to immune-mediated ocular disease.

FURTHER READING

NOTES