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FELINE EOSINOPHILIC KERATITIS—A REVIEW

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ABSTRACT

Eosinophilic keratitis is a disease occurring in cats, horses and rabbits. Its clinical signs include blepharospasm, discharge, chemosis, conjunctival hyperaemia and the presence of corneal ulceration. The typical signs of the disease are white to pink plaques on the cornea accompanied with keratitis. The diagnosis of the disease has to be confirmed with cytology examination and the presence of eosinophils and mast cells in the specimen. Local application of corticosteroids and cyclosporine has good therapeutic effect and has been recommended in all affected species. In samples collected from cats, the presence of feline herpes virus DNA has been reported. Eosinophilic keratitis might be caused by an aberrant immune response or reaction to unknown allergic stimuli. The primary cause of the disease is currently unknown.

Key words: corneal plaque; cyclosporine; feline eosinophilic keratitis

INTRODUCTION

Feline eosinophilic keratitis (FEK), also known as proliferative keratitis or eosinophilic keratoconjunctivitis, or firstly described as corneal eosinophilic granuloma, is a chronic corneal disease [2, 10]. D e a n, M e u n i e r [4] suggested an alternative name for the disease as eosinophilic ocular surface disease as it affects not only the cornea but also the conjunctiva and sometimes the third eyelid. The clinical signs of the disease appear as an immune mediated response to unknown antigenic stimuli [22]. The disease usually occurs in cats [3, 6, 9, 12, 13, 14], horses [18] and rabbits [8]. The clinical signs can appear bilaterally but in most cases (66 % of cases) [14] and (80 % of cases) [22] unilateral appearance is observed. In some cases at the beginning, unilateral appearance can be observed while with progressing the eyes can be affected [22]. FEK is most often observed in middle aged, young, castrated male cats [12, 14] The most common affected breed is Domestic Short-haired cat (DSH). The analysis of 35 affected cats revealed that 30 of them were DSH, three were Domestic Long-haired, and one Siamese and one Maine Coon [22].

The clinical signs of FEK are usually typical changes of the cornea—inflammation with the white plaques, granulation and sometimes ulceration. The disease has a progressive character, in the initial stages the lateral or nasal corneal quadrants are affected. With the development of the disease, the entire cornea can be affected leading to vision impairment [11, 22]. The diagnosis is confirmed with cytological examination of the cornea. The basic recommended therapy in the case of FEK, is the topical application of dexamethasone, prednisolone and cyclosporine [3, 22].

There are few reports regarding the eosinophilic keratoconjunctivitis in rabbits. The clinical signs in this species included bilateral purulent discharge, dacryocystitis, conjunctivitis, and ulcerative keratitis, conjunctiva with hyperaemia, chemosis and typical white plaques on the bulbar and palpebral conjunctiva, as well as the eyelid margins. Cytology confirms the presence of macrophages, lymphocytes, plasma cells and polymorphonuclear cells containing intracytoplasmic eosinophilic granules. As reported in the literature; the treatment included ofloxacin eye drops and topical neomycin-polymyxin B-dexamethasone eye solution four times daily and artificial viscous tears. The improvement of the status was observed within one week. Dexamethasone eye drops twice daily were applied as continuation of the therapy while relapse has been observed in one case after 20 days of application with 0.2 % cyclosporine ointment. Despite these observations, cyclosporine is recommended in rabbits affected with eosinophilic keratoconjunctivitis. Similarly in cats, infectious diseases and environmental factors have been considered as a possible aetiology of eosinophilic keratoconjunctivitis in rabbits [8, 24, 25].

Similarly to cats and rabbits, in horses eosinophilic keratoconjunctivitis manifests as a raised band of 1 to 2 mm subepithelial plaques on the cornea. The additional clinical signs include blepharospasm, epiphora, yellow-to-white mucoid discharge, chemosis, conjunctival hyperemia, and corneal ulceration. The presence of eosinophils and segmented neutrophils, mast cells, plasma cells, and lymphocytes during cytology examination can be revealed. Histological examination of samples collected from the equine cornea showed the presence of degenerated collagen fibres infiltrated by eosinophils, neutrophils, lymphocytes, plasma cells, and macrophages. The therapy in horses is similar to that recommended for cats and rabbits. It has been reported that a 3 week treatment with corticosteroids caused complete resolution of the corneal changes [18, 26].

AETIOLOGY

The aetiology of the disease is uncertain [22]. It is presumed to be an immune-mediated disease or the reaction to unknown allergic stimuli. Analysis of this aberrant immune response suggest type I or IV hypersensitivity reaction in the case of FEK [16, 17]. It has been detected that Feline herpes virus type 1 (FHV-1) is present in corneal scraping in 76 % of the cats affected with FEK [13, 22]. The diagnostic tests performed in a study conducted on 33 affected cats included cytological examination of the cornea and conjunctiva and real-time quantitative polymerase chain reaction (PCR) for the detection of feline herpesvirus type 1 (FHV-1). It has been revealed that viral DNA was present in 54.4 % of the cats [4]. To compare, only 5.9 % positive for FHV-1 DNA samples has been detected in the samples collected from healthy feline corneas. Additionally, roles for mycoplasma and chlamydia in cases of feline conjunctivitis and keratitis have been described but none of the reports have pointed to it in eosinophilic/ proliferative keratitis [5].

DIAGNOSTICS

The typical clinical signs of FEK are single or multiple focal plaques on the corneal surface. The changes resemble granulation tissue and can be white, yellow or pink [11]. The inflammatory process of the disease involves blepharospasm with a mucoid sometimes purulent discharge, superficial vascularisation and oedema of the cornea. Additionally, conjunctivitis with severe chemosis with rarely cobblestone appearance can be observed [12, 14]. In some cases, the third eyelid can also be affected and eyelid margins depigmented [11]. Corneal ulceration is observed on an eye affected with the disease in 25 % of the affected cats. According to the reports, corneal defects are usually superficial and heal within 5 days of antibiotic therapy [15].

The diagnosis of the disease is based on clinical signs. It should always be confirmed with a cytological examination. In cytology, the samples collected from the cornea, the presence of eosinophils, mast cells and neutrophils are confirmed. Additionally, hyperplastic or/and dysplastic epithelial cells can be observed [11]. In a study conducted on 35 cats affected with FEK, 97.1 % had eosinophils present and 71.4 % mast cells in the corneal cytologic specimens;

Fig. 1. A—White corneal plaques in a cat with eosinophilic keratitis; B—The same eye as in A after 7 days of therapy with topical dexamethasone 3 times daily; C—The same eye as in A, B, after 21 days of therapy with topical dexamethasone 3 times daily

the cells typically absent in unaffected feline cornea. Therefore, the characteristic clinical signs—changes on the cornea and cytology results are pathognomonic in the case of feline eosinophilic (proliferative) keratitis. Lymphocytes, and plasma cells are less often present in specimens but they can also occur in the case of FEK [22]. FEK is reported to affect both corneal epithelium and stroma [16, 17].

Samples from superficial layers of the cornea contain squamous epithelial cells, cellular debris, including eosinophilic granules, and mast cells with lower numbers of intact eosinophils. According to Prase, Winston eosinophils and lymphoid cells are predominantly visible in deeper scrapings [17], (more eosinophils than mast cells). It has been also reported that mast cells are most frequent in scrapings that avoid the white surface exudate [19].

The differential diagnosis of FEK include: FHV-1, keratitis, keratomycosis, corneal neoplasia, acid fast granuloma and foreign body granuloma [12, 14].

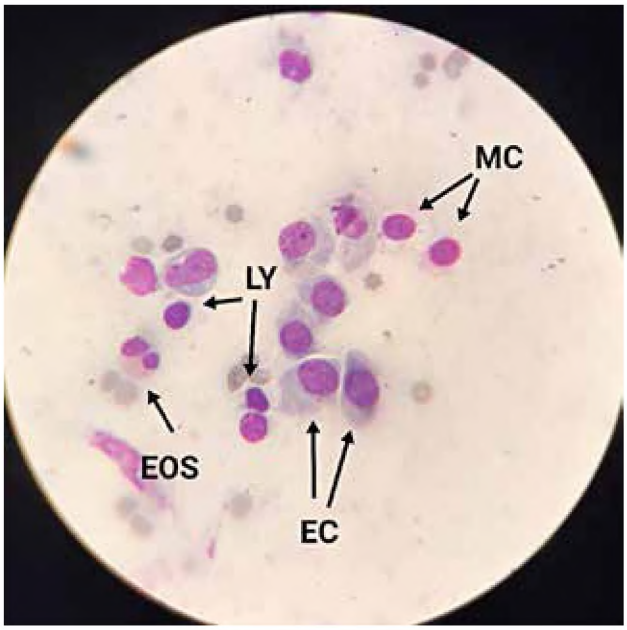

Fig. 2. Cytology sample from corneal lesion of affected cat

We can see different populations of cells, with the highest number of epithelial cells (EC), some with dark brown pigment granules. Mast cells (MC) with purple staining cytoplasmatic granules, eosinophil (EOS) with segmented nucleus and eosinophilic cytoplasmatic granules and small lymphocytes (LY) are also present

TREATMENT

Corticoids are the drugs of choice in the case of FEK. Traditionally, they are applied topically or systemically. Due to knowledge regarding the presence of FHV-1 DNA in cases of FEK, treatment using corticosteroids requires caution. Immunomodulatory drugs may develop reactivation of a virus from latency and a worsening of the status [11]. Good results were also observed in cases treated with ophthalmic antiviral agents or famciclovir, although in many cases additional immunomodulatory therapy was required. Additionally, in cases with higher risk of ulceration, it is recommended to use famciclovir with systemic treatment of corticosteroids while corticosteroids may lead to recrudescence FHV-1 that lead to dendritic ulceration [11, 14]. Oral administration of megestrol acetate was also recommended, although its side effects including adrenocortical suppression, *diabetes mellitus,* mammary hyperplasia, neoplasia and also behavioural changes, and hair loss makes it rarely a drug of choice in the case of FEK and patients should be always controlled during therapy [11].

Cyclosporine is an alternative treatment. It is recommended in cases with ulceration while cyclosporine does not affect re-epithelialization of the cornea and does not have cytotoxic effects [21]. However, the development of marginal blepharitis during the treatment of FEK with cyclosporine was reported in 1.5 % of cats [22]. Additionally, intolerance including irritation, chemosis and conjunctival hyperaemia were also reported in some of the cats treated with cyclosporine [1, 22]. Cyclosporine applied in commercially available ocular ointment in 0.2 % concentration had good therapeutic effects only in 2 from 5 cats, as the 3 developed ocular irritation [1]. The other study revealed improvement after treatment of the same ointment in one cat as well in 4 cats treated with 1 % cyclosporine in corn oil [20]. The analysis of 35 cats treated with 1.5 % cyclosporine in corn oil twice and three times daily for 5 months revealed good results in the vast majority of cases affected with FEK [22]. Other studies suggest also good tolerance in felines for 1—4 % cyclosporine in olive oil [7].

Analysis of safety and therapeutic effects of allogeneic feline adipose-derived mesenchymal stromal cells revealed also good therapeutic effects. The cells were implanted subconjunctivally around the ocular surface affected with lesions. The study was performed in five cats and in all cases the reduction of clinical signs were observed. During the therapy none of the animals had systemic or local complications. In this study improvement of the status was observed in the first 4 weeks, while corneal cytology was negative for eosinophils and mast cells after 2 months of treatment. Complete remission of the disease was observed in cats after 6 months [23].

In severe cases of FEK superficial keratectomy was recommended, although in most cases a topical treatment (prednisone, dexamethasone) will be satisfactory [15, 16]. Most cases have a good response to a treatment, although disease has to be controlled while recurrence has been observed in 64 % of the cats [12]. Feline eosinophilic keratitis is a disease that cannot be cured, but only controlled. It is recommended for long-term and in some cases, life-long treatment with a required low effective dose.

CONCLUSIONS

The feline eosinophilic keratoconjunctivitis is a common disease in ophthalmic practices. The typical signs of the disease need to be confirmed with cytology. The exact pathogenesis of this proliferative keratoconjunctivitis is still unknown but it is presumed to be the result of hypersensitivity reaction to an unknown stimuli. This hypothesis is supported by the response to immunomodulation therapy, however the disease requires further research.

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