



Review

Ocular manifestations of feline viral diseases

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ABSTRACT

Feline viral diseases are common and cats can be presented with a variety of clinical manifestations. Ocular disease associated with viral pathogens is not unusual, particularly with viruses causing upper respiratory tract disease in cats, such as feline herpesvirus type 1 and feline calicivirus. These agents mainly cause ocular surface disease. Other viruses, such as feline immunodeficiency virus and feline coronavirus, can cause uveitis, while feline leukemia virus can induce ocular lymphosarcoma. This review covers the most common viral pathogens of cats that cause ocular manifestations, the specific features of the ocular diseases caused by these viruses and therapeutic recommendations.

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Introduction

Viral diseases in cats are a common occurrence, sometimes presenting both diagnostic and therapeutic challenges to veterinarians. Ocular manifestations of viral disease are many and varied, depending on the inciting pathogen. Familiarity with the clinical and ocular manifestations of the common viral pathogens of cats might help to direct diagnostic testing and therapy. This review describes the most common feline viral infections that could have an ocular manifestation, how to recognize which viral pathogen might be responsible, therapeutic options for treating ocular disease and prognosis.

Feline herpesvirus

Feline herpesvirus type 1 (FHV-1) is the most common viral pathogen of cats that causes ocular disease. It is a DNA virus that belongs to the subfamily *Alphaherpesviridae* and develops neuronal latency following primary infection. The trigeminal ganglion is a known site of latency for FHV-1, but the virus can persist in a quiescent form in ocular tissues, particularly the cornea (Townsend et al., 2004; Stiles and Pogranichniy, 2008).

Clinical signs

FHV-1 causes upper respiratory tract disease (URTD) and conjunctivitis or keratitis via its cytopathic effect on epithelial cells.

Cats affected by both primary infection and viral recrudescence are likely to have ocular disease. Conjunctivitis is the most common ocular condition (Fig. 1), followed by corneal epithelial ulceration and keratitis, with or without ulceration (Fig. 2). Conjunctivitis is manifested by conjunctival hyperemia, with or without chemosis, tearing and discomfort. The nictitating membrane can sometimes be elevated due to pain or swelling. The early inflammatory response is neutrophilic and a purulent ocular discharge is common. Dendritic epithelial corneal ulceration is the classic herpetic lesion and, if evident, is helpful in making the diagnosis. However, many cats with FHV-1-related ocular disease are presented with geographic epithelial ulcers. Both of these types of epithelial ulcers can be seen after staining with fluorescein. Rose Bengal will highlight dendritic ulcers, but is irritating and a topical anesthetic should be used before this stain is applied. Keratitis without corneal ulceration can also occur in cats, manifesting as corneal vascularization, with or without inflammatory cell infiltrates (Fig. 2). Corneal disease from FHV-1 is almost always accompanied by conjunctivitis.

Other corneal conditions, such as sequestra and eosinophilic keratitis, have been associated with FHV-1 (Nasissse et al., 1998; Dean and Meunier, 2013). These conditions are more likely to occur with chronic FHV-1-associated ocular disease. Typically, primary infection with FHV-1 is self-limiting, lasting a few weeks, followed by clinical recovery. However, some cats develop chronic conjunctivitis that does not resolve spontaneously. Chronic conjunctivitis, or recurrent conjunctivitis, can occur bilaterally, but it is not uncommon for only one eye to be affected. This might lead the clinician to erroneously assume that FHV-1 could not be the underlying pathogen.

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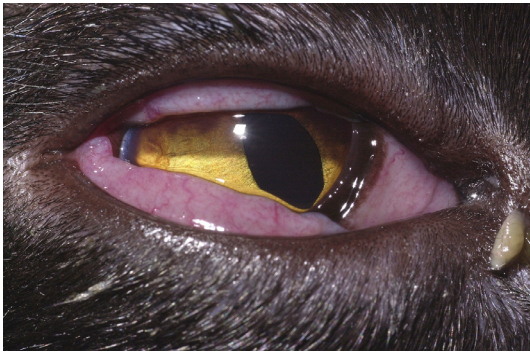


Fig. 1. Conjunctivitis caused by feline herpesvirus type 1 in an adult cat. Note conjunctival hyperemia, chemosis and purulent ocular discharge. The diagnosis was made based on virus isolation from a conjunctival swab.



Fig. 2. Keratitis without corneal ulceration caused by feline herpesvirus type 1 in a kitten. Note corneal vascularization and edema. Conjunctivitis is also present. The diagnosis was made based on virus isolation and positive PCR results from a conjunctival swab.

Diagnosis

The diagnosis of FHV-1 can sometimes be problematic, particularly in the adult cat. A history of recurrent episodes of conjunctivitis or corneal ulceration, especially if accompanied by sneezing, might allow for a presumptive diagnosis. Conjunctival cytology, if performed in the early phase of the disease, will show a neutrophilic inflammation. As the disease becomes more chronic, a mixed pattern of neutrophils, lymphocytes and plasma cells will be seen. Eosinophils and occasional mast cells might also be present. Intracuclear viral inclusions are generally not visible.

Definitive tests for the presence of FHV-1 include virus isolation, fluorescent antibody staining and PCR. PCR has become the most commonly utilized test. Samples from both the eye and oropharynx should be submitted. PCR is highly sensitive and specific, although variability amongst laboratories exists. However, a negative test does not rule out FHV-1 as the inciting agent, nor does a positive test prove that the virus is the cause of clinical signs. Several studies have demonstrated that cats with clinically normal eyes can have positive PCR results for FHV-1 from conjunctival samples (Stiles et al., 1997; Burgesser et al., 1999). However, a positive PCR result in the face of clinical disease consistent with FHV-1 should allow the clinician to proceed with reasonable certainty of a correct diagnosis. If diagnostic testing is not performed, or if results are negative in the face of clinical disease consistent with that caused by FHV-1, anti-viral therapy can be instituted and the response to treatment determined.

Treatment

Treatment of conjunctivitis, corneal ulceration or keratitis caused by FHV-1 should include specific anti-viral therapy. Corneal ulcers caused by FHV-1 alone should only involve the epithelium. If a stromal ulcer exists, a secondary bacterial pathogen is likely and would need more aggressive antibiotic therapy than would be instituted for a viral ulcer. Any loose epithelium should be removed by debridement with a cotton swab. Grid keratotomies should not be performed in cats, as this might worsen herpetic disease and lead to formation of a corneal sequestrum (La Croix et al., 2001). A broad-spectrum topical antibiotic, such as tobramycin, should be used if epithelial ulceration is present. Cleansing the eyes and removing discharge regularly is important.

Available anti-herpetic drugs are summarized in Table 1. Many of the topical anti-viral compounds are not available commercially or are available only in certain countries. Cidofovir is an intravenous drug used in human medicine for treatment of cytomegalovirus retinitis (Ahmed, 2011) and is the author's preferred topical drug in cats. Compounded into a 0.5% ophthalmic solution, it is efficacious against FHV-1 and is stable when stored frozen or refrigerated for at least 6 months (Fontanelle et al., 2008; Stiles et al., 2010). Additional benefits include lack of ocular irritation and a long tissue half-life, so that twice daily administration is adequate (Sandmeyer et al., 2005; van der Meulen et al., 2006). Acyclovir has a low efficacy against FHV-1 compared to its efficacy against human herpes simplex virus (HSV), and is not recommended for treatment of cats (Nasissse et al., 1989; van der Meulen et al., 2006). Idoxuridine, trifluridine and ganciclovir are all effective (Nasissse et al., 1989; Maggs and Clarke, 2004), but need to be used 4–6 times daily and can cause ocular irritation. The use of oral famciclovir (prodrug of the active agent penciclovir), frequently used for treating HSV, has become more commonly used in cats. It has been shown to be both safe and effective for short periods of 2–3 weeks (Thomasy et al., 2011); however, the optimal dose remains uncertain. The most recent information indicates that 40 mg/kg three times daily is likely to be effective (Thomasy et al., 2012), although, anecdotally, lower doses and frequencies are reported to be effective by some veterinary clinicians. A recent study of high dose topical recombinant human $\alpha 2b$ and feline ω interferon in a group of cats with naturally occurring viral keratoconjunctivitis found no beneficial effect of either interferon compared to placebo (Slack et al., 2013); thus, this treatment cannot be recommended.

The use of the amino acid L-lysine orally to treat FHV-1 in cats has met with mixed results. L-lysine is a competitive inhibitor of arginine, an amino acid necessary for synthesis of herpesviral proteins. In theory, excess ingestion of L-lysine will lead to decreased replication of FHV-1 through reduction in viral protein synthesis. In a placebo controlled experimental study, cats receiving 500 mg L-lysine every 12 h had less severe conjunctivitis than control cats (Stiles et al., 2002). In a study in which shelter cats were given 250 mg (kittens) or 500 mg (adults) L-lysine once daily in food, there was no difference in URTD in treated cats compared to untreated cats (Rees and Lubinski, 2008). In another study, shelter cats fed a diet high in L-lysine (5.7%) had no difference in the frequency of URTD signs compared to cats eating a diet with basal levels of L-lysine (1.7%) (Drazenovich et al., 2009). Anecdotally, it appears that some cats might benefit more than others from the administration of L-lysine. If this therapy is elected, a dose of 500 mg (adults) or 250 mg (kittens) twice daily with food should be used.

In some cats, particularly those with chronic FHV-1-related ocular disease, a topical anti-inflammatory drug might be indicated. Topical or systemic corticosteroids should be avoided, since the risk of exacerbating herpetic disease is high. The use of a topical

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