CONJUNCTIVITIS IN DOGS AND CATS

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CONJUNCTIVITIS IN DOGS

In dogs conjunctivitis is rarely caused by primary conjunctival pathogens. The differential diagnosis includes systemic causes (canine distemper, rickettsial disease), parasites (thelazia), allergies (often seasonal and frequently associated with allergic dermatitis), trauma, and keratoconjunctivitis sicca.

Most canine conjunctivitis is initiated by some form of trauma, such as keratoconjunctivitis sicca (KCS), exposure to irritating substances such as shampoos and dips, or secondary to primary adnexal disorders (entropion, ectopic cilia, trichiasis, lagophthalmos). Bacteria are found in the conjunctival sac of normal dogs (Gram-positive) and rarely induce inflammation on their own. Bacterial conjunctivitis occurs when the predisposing insult alters normal homeostasis and allows bacteria to proliferate. Conjunctivitis in dogs is also secondary to chronic skin disease; this form of conjunctivitis is especially common in dogs with pyoderma or seborrhea, and rarely resolves unless the underlying skin condition can be corrected. In some geographic locations allergies constitute a major cause of conjunctival inflammation. Allergic conjunctivitis is often associated with other general signs of allergic skin disease such as face rubbing and paw licking, however, conjunctivitis may be the only clinical sign.

The diagnostic approach to the canine conjunctivitis patient should always include a careful adnexal exam and a Schirmer's tear test. The most important consideration in treatment is to correct the primary underlying abnormality. If tear production is low the primary treatment should be the twice daily application of either cyclosporine (0.2 percent ointment or 1 percent solution) or 0.03 percent tacrolimus1. Tacrolimus is an immusuppressive drug that exerts its effects via inhibition of calcineurin. Treatment with broad spectrum antibiotics is also indicated, (triple antibiotic). Corticosteroids are used in combination with antibiotics to reduce the associated inflammatory response and for allergic conjunctivitis (neomycin, polymyxin, 0.1 percent dexamethasone).

FELINE CONJUNCTIVITIS

Chlamydial Conjunctivitis

In contrast to dogs, nearly all cases of conjunctivitis in cats are due to a primary pathogen. Chlamydiophila felis (formerly Chlamydia psittaci) is a primary conjunctival pathogen of cats, and concurrent, clinically relevant respiratory disease is uncommon. Initially unilateral, it progresses to become bilateral in 7 days. Spread to other household cats is common. Chemosis and serous discharge are characteristic clinical signs. Cytoplasmic inclusions are seen in conjunctival epithelial cells only early in disease (first 7-10 days). Chlamydia vaccines are available, but they are similar to vaccines for feline herpesvirus in that they decrease the severity of infection but do not prevent infection. Following recovery from infection organisms are shed for long periods of time from the gastrointestinal and urogenital tracts. The exact site of latency, however, is not clearly understood. It is appropriate to treat acute Chlamydial conjunctivitis empirically with topical antibiotics. Chlamydia are sensitive to tetracycline, erythromycin and chloramphenicol. Chlamydia are not sensitive to aminoglycosides. The carrier state can be eradicated with either a 3 week course of doxycycline or therapy with azithromycin (Zithromax; 5 mg/lb QD for 21 days). Conjunctival scrapings are sometimes helpful in identifying chlamydial conjunctivitis as intracytoplasmic inclusion bodies are found transiently during acute stages of the disease. IFA procedures on conjunctival scrapings may be helpful for confirmation, but false negative results are common.

Feline Herpesivus Type 1 (FHV-1)

Feline herpesvirus-1 replicates in the epithelium of nasal mucosa, conjunctiva, tonsil, and nasal turbinates, and tissue damage is due to viral cytolysis during active infection. Typically, this process is most severe in immunologically naive cats undergoing their first or primary infection. The ability of FHV-1 to induce rapid and severe lysis of susceptible cells is presumably responsible for symblepharon formation in young cats. FHV-1 replicates to a limited extent in corneal epithelium to produce micro-dendritic lesions. Corneal lesions occur in a biphasic pattern on days 3 and 12 of primary infection, the latter peak reflecting virus released following lysis of the conjunctival epithelium. Stromal viral replication apparently occurs little or not at all. Following primary infection, FHV-1 resembles other alpha herpesviruses by establishing latent infections in the trigeminal ganglia, and possibly other tissues, which persist for the life of the host.

FHV-1 is thought to be the most common cause of conjunctivitis in cats. The virus is ubiquitous with world wide distribution, and has features characteristic for alpha herpesviruses; latency is established in the trigeminal ganglia, recurrence is common, especially with stress or systemic disease, and a chronic carrier state develops with intermittent virus shedding and/or recrudescent disease. In cats < 6 months, concurrent upper respiratory tract infection is common. In adults, conjunctivitis may occur with or without concurrent respiratory involvement; signs are recurrent conjunctivitis or keratitis, and may last weeks to months. Clinical findings vary depending upon the severity and duration of disease. Conjunctivitis in acute disease is characterized by severe hyperemia, and serous to mucopurulent discharge. After severe conjunctivitis in young cats, symblepharon formation (adhesion of conjunctiva to itself or cornea) can occur. Keratoconjunctivitis sicca is a common complication of chronic conjunctivitis in adult cats. Although mild epithelial keratitis is common during primary infection, keratitis is most significant as a sequelae to recrudescence infections. The clinical signs are usually unilateral in adult cats, and frequently unassociated with signs of upper respiratory infection.

Diagnosis of herpesvirus infections. Clinical signs - Dendritic ulceration is the only sign that is pathognomonic. Cytology is of little

diagnostic value because FHV-1 inclusions do not stain with routinely used cytologic stains and in chronic infections inclusions are few. Immunofluorescence (IFA) of conjunctival smears is good in acute cases, but usually negative when chronic, presumably because viral antigen is limited, and when present coated with secretory antibody. Serology aids in documenting exposure, and strongly suggestive of active infection if the titer exceeds 1:200. Virus isolation is a definitive test, but it is reliable only in the early course of infection, and is largely impractical. The advent of polymerase chain reaction (PCR) technology has allowed us to significantly improve our ability to detect ocular pathogens. The principle of the assay is that small amounts (theoretically a single molecule) of DNA can be exponentially amplified under the appropriate conditions without the need for initial purification and cloning procedures. For FHV-1, the segment of DNA amplified for described assays is from the thymidine kinase gene. The PCR assay may be used to look for FHV-1 DNA in any biological sample. In conjunctivitis, inferior cul de sac swabs are collected after instillation of topical anesthetic and placed in 1 cc of phosphate buffered saline (PBS). Alternatively, or for epithelial keratitis, scrapings may be collected. Keratectomy or other tissue specimens are similarly placed in PBS. In any event, the more cellular material that is collected, the better the chances of obtaining a positive result. Once collected, samples should be frozen (-20□C) and not allowed to warm appreciably prior to analysis to avoid loss of target DNA. Although PCR testing is the most sensitive method for detecting FHV-1 DNA, the clinical usefulness of the test is limited by the inability of the test to distinguish between persistent viral DNA and that associated with active infections.

Treatment of acute herpesvirus infections. Treatment of acute viral conjunctivitis consists of topical, prophylactic antibiotics (erythromycin or tetracycline ophthalmic ointment) to prevent secondary or opportunistic infections. Antiviral therapy is not indicated unless the condition becomes chronic.

Treatment of chronic conjunctivitis. Topical antiviral therapy is unpredictably effective. Idoxuridine, adenine arabinoside, and trifluridine (Viroptic) are used topically2,3. Trifluridine is the only antiviral commercially formulated. Although trifluridine is the most effective antiviral in vitro, the drug's cost and the high rate of conjunctival irritation limit its clinical effectiveness. My preference is to start with 0.1 percent idoxuridine solution. Antiviral solutions are administered up to 5 times daily initially, then TID-QID as needed for symptomatic control. Systemic acyclovir (Zovirax; 200 mg/BID) may be beneficial but may cause bone marrow depression. The role of vaccination in the prevention and treatment of FHV-1 infection remains controversial. Numerous vaccines have been developed and tested in virus challenge studies. Unfortunately, a vaccine has not been developed that prevents the disease, although most have at least some effect on diminishing its severity. Most available vaccines are parenteral, modified live vaccines that are shown to stimulate humoral immunity. The fundamental reason for the poor efficacy of these vaccines is that persistent infections with FHV-1 (and HSV-1) are not affected by neutralizing serum antibodies. In order to prevent disease due to these α-herpes viruses, production of effective mucosal immunity in the conjunctiva and respiratory tract is required. A modified live vaccine designed for topical inoculation has been available for many years, but is infrequently used. Vaccination has been shown to have no effect on latency. Vaccination should probably be avoided in cats with stromal keratitis. Interferons are a group of cytokines that play diverse immunologic and antiviral functions. Viral infection stimulates cells to secrete IFN into the extracellular space. Interferon then binds to specific receptors on neighboring cells, and through mechanisms not fully understood, prevents the spread of infection. Topical interferon therapy has been shown to be effective in preventing herpes simplex virus infections of humans. Most studies done with IFN treatment alone have shown little efficacy on established infections. IFNα (2 X 106 units/g) ointment used to treat genital herpes reduced virus shedding and healing from 15 to 6.2 days. Veterinary ophthalmologists commonly prescribe topical interferon (10,000 units/ml) for FHV-1 infected cats, however, response to therapy is unpredictable. The effects of systemic IFNα in experimental FHV-1 infection have been previously studied; 108 units/kg were administered subcutaneously BID on two consecutive days, and animals were inoculated after the first 2 doses were given. Although disease was not prevented, cumulative clinical scores were lower for cats treated with IFNα. However, it remains to be proven whether interferons given after exposure will have the same beneficial effect. The use of antiinflammatory drugs in the management of FHV-1 infections remains controversial. Due to the well documented potential for reactivating latent infections, systemic corticosteroid therapy is contraindicated in FHV-1 infected cats. Due to the ability of locally administered corticosteroids to allow what would have been a self limiting conjunctival infection to become a chronic corneal infection, topical corticosteroids are contraindicated in all cases of primary ocular FHV-1 infection. Because corneal opacification in chronic stromal keratitis occurs secondary to an exuberant immune responses to viral proteins, corticosteroids are indicated in such cases. It is prudent, however, to always treat concurrently with a topical antiviral. Arginine is an essential amino acid for replication of many herpes viruses. It has previously been demonstrated that combinations of low concentrations of arginine, and high concentrations of L-lysine in tissue culture media can suppress replication of HSV-14,5. We have recently shown that this is true for FHV-1 also. Lysine is thought to exert its inhibitory effects by competing with arginine for incorporation into the virus, thereby producing a non-infective virus particle. The currently recommended dose of L-lysine is 500 mg mixed with the food daily.

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