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## Proceedings

### Exotic Animals

#### CANINE KERATOCONJUNCTIVITIS SICCA

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Canine keratoconjunctivitis sicca (KCS) is a common disease characterized by chronic inflammation of the lacrimal gland, conjunctiva and cornea which leads to a qualitative and quantitative modification of the precorneal tear film (PTF). The condition is usually defined as a diminution of tear production. However, even though several late clinical signs of the disease arise from a decrease of tears, early changes on the ocular surface are due to qualitative deficiencies even in presence of normal quantity of tears.

KCS is often misdiagnosed by the clinician as bacterial conjunctivitis and commonly treated with different topical antibiotics. The patient improves while treated but the clinical signs reappear days or weeks after the discontinuation of the treatment. The condition progresses to severe corneal opacities and lately to blindness.

#### THE PRECORNEAL TEAR FILM

The PTF is composed by three layers. The outer is an oily layer secreted by the meibomian glands which retards tear evaporation and stabilizes its surface. It is mainly composed of cholesterol. The intermediate layer is the aqueous tear component produced by the orbital and nictitans lacrimal glands. It contains over 70 different compounds such as proteins, inorganic salts, glucose, urea, vitamins, growth factors, and provides oxygen, nutrients, and lubrication to the avascular cornea. The deepest layer is composed of mucin secreted by conjunctival goblet cells. It serves to anchor the aqueous tear to the hydrophobic corneal epithelium.

#### ETIOLOGY OF KCS

Different causes can produce a reduction in tear production. Canine Distemper virus, sulfonamide toxicity, long term using of atropine and facial nerve injury are some of them.

However, the etiology of canine KCS can often not be determined. In humans, severe KCS is associated with Sjögren's syndrome, a condition characterized by autoimmune reactions in the lacrimal and salivary glands. Serologic and histopathologic studies in dogs revealed similar findings to those characteristic of human autoimmune KCS.

Sjögren's syndrome in man is often associated with polyglandular autoimmune exocrinopathy including chronic hepatitis, intestinal disorders, seborrhea, etc. These patients can also exhibit polyarthritis, allergy, hypothyroidism. *Many dogs with KCS associate dry eye with seborrhea or atopy and rheumatoid factor was positive in some dogs with KCS. Based on these findings, the majority of canine KCS cases are considered as an autoimmune disease. **Because of that, canine KCS should be considered as a syndrome.***

## CLINICAL SIGNS

Most of the dogs with KCS are presented with a history of chronic, recurrent, non specific keratoconjunctivitis. **The hallmark of the disease is the presence of mucoid ocular discharge.** These eyes look like undergoing bacterial conjunctivitis and this is the reason for the misdiagnosis. Other clinical signs are diffuse conjunctival hyperemia, superficial corneal vascularization, corneal cellular infiltrates and pigmentary keratitis. Corneal damage leads to blindness.

It is very important to remark that non ocular clinical signs are usually present. Skin disorders are commonly associated with KCS; according to own data, over 90% of Cocker spaniels with dry eyes present seborrhea and over 70% of Shih tzu and Lhasa apso have atopy. These skin problems affect the eyelids producing changes in the composition of the PTF.

## DIAGNOSIS

The presence of mucoid ocular discharge in a patient with a history of non specific recurrent conjunctivitis should be considered as the key to make a diagnose of keratoconjunctivitis sicca. Clinical signs of superficial corneal disease such as vascularization or pigment, are usually present in these dogs.

The diagnosis is easily confirmed by using the Schirmer tear test (STT). The STT, a quick and easy test, should be performed as a routine part of the ophthalmic examination in any dog, but it must be used in every dog of a predisposed breed with conjunctivitis, even with no other clinical signs of dry eye.

It should be noted that the disease starts before the STT values become abnormal. Qualitative changes in tears can be associated to the first inflammatory changes in the lacrimal glands even with normal or slightly decreased values of STT. *This means that the disease should be considered not only as "dry eye" but as a wider syndrome with an early stage with "wet eye", usually most difficult to diagnose, and a typical stage of keratoconjunctivitis sicca easy to diagnose by clinical signs and STT. Whereas the term keratoconjunctivitis sicca, worldwide used, refers only to the advanced stage of the disease, we prefer to call these cases as **Canine Immune-mediated***

**Lacrimal Syndrome (CILS).**

Other diagnosis tests are the Break up Time (BUT) and the Phenol Red Thread Tear Test. The BUT evaluates the time in which the PTF shows punctate dry spots after instillation of a drop of fluorescein maintaining the eye in an open position. Normal values are about 15 to 20 seconds. The phenol red test consists of a thread of 75 mm in length impregnated with phenol red, which is a pH indicator. The thread is placed in the lower conjunctival fornix for 15 seconds and the alkaline tears change its color from yellow to orange. The mean of absorption is 35 mm per 15 seconds.

**TREATMENT**

Traditional medical therapy has consisted of replacing the lost tears but these solutions primarily, do not have any effect on the inflammatory process which continue progressing and secondarily, do not contribute with some of the most important compounds of tears such as nutrients, antimicrobial agents or growth factors. Moreover, because of their quick evaporation, they have to be administrated frequently. Some of these substitutes are polyvinyl pyrrolidone, polyvinyl alcohol, methylcellulose and lately hyaluronic acid.

Starting from the evidences of autoimmune etiology, a new treatment has been applied for KCS in the last years. Cyclosporine A (CsA), a noncytotoxic immunosuppressant, has been used because of its effects on tear production. *CsA proved to be effective on interrupting the immune-mediated reaction against lacrimal glands, cornea and conjunctiva, but the drug is also a lacrimomimetic agent even in normal eyes, and has an antinflammatory effect too.* Different formulations for topical use of CsA have been developed as eyedrops or ophthalmic ointment, and several clinical trials have demonstrated their therapeutic effects.

In one study (Herrera et al, 1994), 373 dogs with KCS were treated using 2% CsA oily solution (corn oil). Normal STT values were obtained after treatment in 319 patients (85,5%). When the patients were divided into two groups according to their STT values at the beginning of treatment: group 1: STT values between 6 to 10 mm/min and group 2: STT values < 6 mm/min, the response to treatment was better in group 1 (93,6%) than in group 2 (80,5%). Some particular responses were seen in these dogs: a) some patients with no changes on the STT values showed a marked improvement on their corneoconjunctival signs indicating that the clinical improvement does not depend only on the amount of tears; b) some other patients with dermatological problems i.e. seborrhea (specially Cocker), showed an improvement on their ocular signs but the skin around the eyelid area got worst.

In other clinical trial (Herrera et al, 1996), 73 dogs with KCS (mean of STT: 6,52 mm/min) were treated using a CsA 0,2% ophthalmic ointment. After 28 days of treatment the mean of STT values was 16,31 mm/min.

Some new immunosuppressants such as tacrolimus and pimecrolimus are being evaluated presently. Preliminary results obtained by the author using topical 0,05% tacrolimus, showed similar therapeutic effects than CsA.

Finally, **KCS is a common but misdiagnosed disease. Diagnosis can be made using**

**the Schirmer tear test but initial clinical changes can be present even with normal values of STT. Therapeutic response will be better as earlier the diagnosis can be done.**

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