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. 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 the presence of a normal quantity of tears. Often misdiagnosed by the clinician as bacterial conjunctivitis, KCS is commonly treated with different topical antibiotics. The patient improves while under treatment, but the clinical signs reappear days or weeks after the treatment is discontinued. The condition progresses to severe corneal opacities and, in an end-stage, to blindness.

The PTF

The PTF is composed of three layers. The outer layer is made oily through the secretions of 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, and growth factors, and provides oxygen, nutrients, and lubrication to the avascular cornea. The deepest layer, composed of mucin secreted by conjunctival goblet cells, 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 use of atropine, and a facial nerve injury are some of them. The etiology of canine KCS can not often be determined. In human patients, 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, and seborrhea. Patients can also exhibit polyarthritis, allergies, and hypothyroidism. Many dogs with KCS experience dry eye with seborrhea or atopy. 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. Canine KCS should be considered a syndrome.

Clinical Signs

A history of chronic, recurrent, non-specific keratoconjunctivitis is seen in most cases of dogs with KCS. The hallmark of the disease is the presence of mucoid ocular discharge. The eyes appear to be undergoing bacterial conjunctivitis and this can often lead to 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 note that non-ocular clinical signs are also usually present. Skin disorders are commonly associated with KCS; according to the author’s data, over 90% of cocker spaniels with dry eyes present seborrhea and over 70% of shih tzu and lhasa apso breeds 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 crucial to make a diagnosis of KCS. Clinical signs of superficial corneal disease, such as vascularization or pigment, are also usually present. Diagnosis can be confirmed by using the Schemer tear test (STT). The STT, which is quick and easy, should be performed as a routine part of the ophthalmic examination in any dog. It is mandatory in every dog of a predisposed breed with conjunctivitis, even when there are no other clinical signs of dry eye.
The disease starts before the STT values become abnormal. Qualitative changes in tears can be associated with the first inflammatory changes in the lacrimal glands, even with normal or slightly decreased values of STT. The disease should be considered not only as ‘dry eye’, but as a wider syndrome with an early stage of ‘wet eye’, usually the most difficult stage at which to diagnose, and a typical stage of KCS easier to diagnose. The term keratoconjunctivitis sicca, used worldwide, refers only to the advanced stage of the disease. The author prefers to refer to the earlier stages as canine immune-mediated lacrimal syndrome (CILS).

Other diagnostic tests include the ‘break-up-time’ (BUT) and the ‘phenol-red-thread tear test’. BUT evaluates the time in which the PTF shows punctuated dry spots after the instillation of a drop of fluorescein whilst maintaining the eye in an open position. Normal values range from 15 to 20 seconds. In the phenol-red test, a 75mm-long thread, impregnated with phenol-red (a pH indicator), is placed in the lower conjunctival fornix for 15 seconds and the alkaline tears change color from yellow to orange. The mean of absorption is 35mm/15secs.

Treatment

Traditional medical therapy has largely consisted of replacing the lost tears with substitutes; these include polyvinyl pyrrolidine, polyvinyl alcohol, methylcellulose, and hyaluronic acid. This solution does not have a primary effect on the inflammatory process, which continues progressing, nor does it contribute to some of the most important compounds of tears, such as nutrients, antimicrobial agents, or growth factors. Also, because of their quick evaporation, the substitutes have to be frequently administered.

Based on autoimmune etiology evidence, a new treatment has been recently used for KCS. Cyclosporine A (CsA), a non-cytotoxic immunosuppressant, has been used because of its effects on tear production. It has proved to be effective on interrupting the immune-mediated reaction against lacrimal glands, cornea, and conjunctiva. The drug is a lacrimomimetic agent, even in normal eyes, and also has an anti-inflammatory effect. Different formulations for the topical use of CsA have been developed, such as eye-drops and ophthalmic ointment. Several clinical trials have demonstrated their therapeutic effects.

In one study, 373 dogs with KCS were treated using a 2% CsA oily solution (corn oil). Normal STT values were obtained after treatment in 319 patients (85.5%). At the beginning of treatment, the patients were divided into two groups, according to their STT values; group one’s STT values were between six and 10mm/min, and group two’s STT values were less than 6mm/min. The response to treatment was better in group one (93.6%) compared with the group two response (80.5%). Particular responses were also seen in these dogs. Some patients with no changes on the STT values showed a marked improvement in their corneoconjunctival signs, indicating that the clinical improvement does not depend purely on the amount of tears; other patients with dermatological problems, for example, seborrhea (especially in cocker spaniels), showed an improvement in their ocular signs, although the skin around the eyelid area got worse.

In another clinical trial, 73 dogs with KCS (mean of STT: 6.52mm/min) were treated using a CsA 0.2% ophthalmic ointment. After 28 days of treatment, the mean of STT values was 16.31mm/min.

Some new immunosuppressants, such as tacrolimus and pimecrolimus, are currently being evaluated. The results obtained by the author, using a topical 0.5% tacrolimus solution, showed similar therapeutic effects to CsA.

In conclusion, KCS is a common but often misdiagnosed disease. Diagnosis can be made using the STT, taking into account the fact that initial clinical changes can be present even with normal values of STT. An early diagnosis will substantially enhance the therapeutic response.