

## Severe, unilateral, unresponsive keratoconjunctivitis sicca in 16 juvenile Yorkshire Terriers

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### Abstract

**Objective** To present ophthalmic findings, clinical data, and treatment outcomes of 16 juvenile Yorkshire Terriers with severe unilateral keratoconjunctivitis sicca.

**Results** Each of the 16 dogs exhibited extreme unilateral dryness associated with blepharospasm, mucoid discharge, and corneal vascularization. Ages of affected dogs at presentation ranged from 5 months to 4 years. Mean Schirmer tear test (STT) result for affected eyes was 1 mm/min. Topical application of 0.2% cyclosporine to the affected eye was not associated with improvement in STT values in any dog. Clinical signs subjectively improved with topical application of 20% chondroitin sulfate ophthalmic solution in some dogs, and transposition of the parotid duct was performed in three dogs. Histopathologic examination in one dog failed to show evidence of orbital lacrimal gland tissue. Clinical signs, age of presentation, disease severity, and lack of response to treatment are consistent with breed-related unilateral aplasia or hypoplasia of the lacrimal gland.

**Conclusion** Lacrimal gland aplasia or hypoplasia should be considered in young dogs with severe unilateral ocular dryness, especially female Yorkshire Terriers.

**Key Words:** congenital alacrima, developmental defect, KCS, keratoconjunctivitis sicca, Yorkshire Terrier

### INTRODUCTION

Canine keratoconjunctivitis sicca (KCS) is a common ocular disease characterized by a variable diminution of the aqueous layer of the precorneal tear film, and resulting in desiccation and inflammation of the conjunctiva and cornea.<sup>1-3</sup> While ocular pain, conjunctivitis, corneal melanosis, and corneal vascularization may be present depending on the stage of the disease, the main clinical sign is the presence of mucoid ocular discharge. For this reason, KCS may be misdiagnosed as bacterial conjunctivitis.<sup>1,2</sup>

In dogs, KCS is commonly characterized as an immune-mediated disorder, occasionally associated with systemic autoimmune conditions.<sup>1-3</sup> Other causes of KCS include infectious disease, such as distemper, toxicity due to sulfonamides or other drugs, surgical removal of the gland of the third eyelid, facial trauma, and congenital alacrima.<sup>1-8</sup>

Breed and sex predisposition to KCS have been proposed.<sup>1-3,5,9,10</sup> The English Bulldog, Lhasa Apso, Shih Tzu, West Highland White Terrier and Cocker Spaniel are recognized worldwide as predisposed breeds.<sup>1,3</sup> A female predisposition to KCS was reported in West Highland

White Terriers, and female dogs were also more affected than male dogs in other clinical trials.<sup>1,9-11</sup>

Little information exists regarding congenital alacrima. In particular, predisposed breeds, clinical signs associated with this syndrome and treatment and prognosis of affected dogs are poorly described. The purpose of this paper was to describe clinical findings and treatment outcomes for 16 juvenile Yorkshire Terriers with severe unilateral keratoconjunctivitis sicca suggestive of congenital alacrima.

### CASE HISTORIES

Sixteen Yorkshire Terriers were presented to the Ophthalmology Unit of the School of Veterinary Sciences (University of Buenos Aires) and the Surgery Unit of the School of Veterinary (University of Zaragoza) between August 1999 and February 2004. Each patient had a chronic history of severe, unilateral blepharospasm and variable amounts of mucoid discharge from and over the surface of the affected eye (Figs. 1–3). Twelve affected dogs were female and four were male. Chi-square analysis of this gender distribution suggested female dogs were significantly more frequently



**Figure 1.** Right eye of a 2-year-old, female Yorkshire Terrier with unilateral and severe keratoconjunctivitis sicca (STT 0 mm/min) and associated blepharospasm, blepharitis, copious mucoid discharge, and superficial corneal vascularization.



**Figure 2.** Left eye of a 2-year-old, female Yorkshire Terrier with unilateral keratoconjunctivitis sicca (STT 4 mm/min) of 3 months duration. Blepharospasm, blepharitis, mucoid discharge, and superficial corneal vascularization can be observed.



**Figure 3.** Left eye of an 11-month-old, male Yorkshire Terrier with unilateral and severe keratoconjunctivitis sicca (STT 0 mm/min) and associated blepharospasm and mild mucoid discharge.

affected than were male dogs ( $P = 0.05$ ). No dogs were neutered and a familial relationship between the dogs was known for only two dogs, which were mother and daughter. The dogs ranged in age from 5 months to 4 years (mean  $\pm$  standard deviation (SD):  $2.1 \pm 1.4$  years; median: 2 years). Duration of clinical signs before presentation ranged from 3 to 24 (mean  $\pm$  SD:  $9.1 \pm 6.9$ ; median: 6) months. All dogs had been treated with various topical ophthalmic antibiotics by the referring veterinarians, without resolution of clinical signs. None of the dogs had been treated with sulfonamides or had undergone surgery involving the third eyelid gland. A history of trauma or infectious disease could not be obtained in any dog.

Thorough ophthalmic examination including the Schirmer tear test (STT) (Schering Plough Animal Health Co., Kenilworth, NJ, USA), measurement of intraocular pressure (IOP) using applanation tonometry (Tonopen, Mentor, Norwell, MA, USA), application of fluorescein stain, slit-lamp biomicroscopy (Kowa SL-14, Kowa, Tokyo, Japan), and direct and indirect ophthalmoscopy was performed in all dogs. Results of the STT in the affected eye ranged from 0 to 7 mm/min (mean  $\pm$  SD,  $1 \pm 2$ ; median, 0). In 11 dogs,

the STT in the affected eye was 0 mm/min. Results of the STT in the unaffected eye ranged from 11 to 17 mm/min (mean  $\pm$  SD,  $14 \pm 2$ ; median, 15). IOP was normal in all dogs. Affected eyes had blepharitis, mild conjunctival hyperemia, and variable degrees of superficial corneal vascularization with a dry appearance to the ocular surface. Corneal melanosis was not observed in any dog. The rest of the anterior segment examination and the fundic examination revealed no abnormalities in any dog. Signs of cranial nerve dysfunction were not observed in any dog and no other relevant clinical signs were detected during the general physical examination.

Eleven dogs were initially treated with 0.2% cyclosporine ophthalmic ointment (Optimmune, Schering Plough, Buenos Aires, Argentina and Zaragoza, Spain) three times daily for 30 days. A mild reduction in the amount of mucoid discharge and blepharospasm was observed in these eyes; however, none of the treated eyes showed improvement in their STT values at revisit examinations during this time. In fact, STT results declined by a further 3 mm/min and 4 mm/min, respectively, in the two dogs receiving this treatment. The remaining five dogs that did not receive cyclosporine, along with those three in which cyclosporine

was unsuccessful, were treated twice daily with 20% chondroitin sulfate ophthalmic solution (Tears, Labyes, Buenos Aires, Argentina). All eyes receiving 20% chondroitin sulfate ophthalmic solution showed subjective improvement in ocular comfort as evidenced by reduced blepharospasm.

Open (lateral approach) parotid duct transposition (PDT) was performed in three dogs, and a good result was obtained in two. Excessive salivary secretion and facial dermatitis occurred in the third. A nylon ligature was performed around the duct to decrease salivary secretion in this dog.

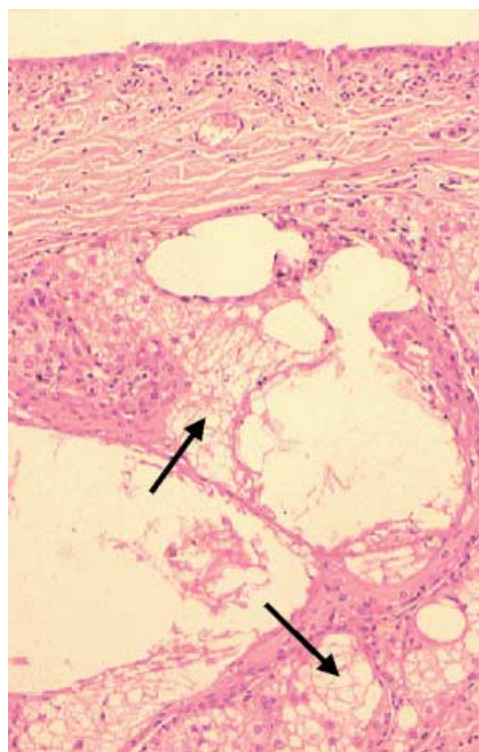
History, signalment, clinical signs, age of presentation, disease severity, and lack of response to medical treatment suggested that these dogs had breed-related unilateral aplasia or hypoplasia of the lacrimal gland. Based on this presumptive diagnosis, biopsy of the lacrimal glands of the affected eye was proposed in seven dogs but no owner consented to this. However, a 5-year-old, female dog, which had undergone PDT, experienced acute spinal cord compression due to intervertebral disk protrusion and underwent reduction surgery 2 years after the original ophthalmic diagnosis. This dog was subsequently euthanized owing to neurologic disease, and a tissue sample was collected from the site of the orbital lacrimal gland, fixed in paraformaldehyde and routinely processed for histologic examination. Light microscopic examination of a hematoxylin and eosin-stained section of this tissue revealed absence of acini and ducts consistent with aplasia. A few lobules of sebaceous glands were observed (Fig. 4). Biopsy of the third eyelid lacrimal gland was not performed in this dog.

During the 4.5-year study period, only one other dog with history, signalment, clinical signs, and response to therapy suggestive of congenital alacrima was presented to the authors. This was a 1-year-old, female Chihuahua. This dog was treated with 20% chondroitin sulfate ophthalmic solution and showed a similar response to the Yorkshire Terriers treated in this way.

## DISCUSSION

Keratoconjunctivitis sicca is a common condition in dogs. One of the most common causes of this syndrome is immune-mediated destruction of the lacrimal glands, which tends to occur in adult dogs, is typically bilateral, and has an insidious onset until aqueous deficiency is severe enough to produce signs of ocular surface dryness. The Yorkshire Terrier is not a breed usually affected by the immune-mediated form of KCS.<sup>1</sup> The dogs in this study were all affected with severe clinical signs at an early age. Besides immune-mediated dacryoadenitis, KCS may be caused by toxicity associated with sulfonamides,<sup>5,6</sup> infectious disease, such as canine distemper virus,<sup>4</sup> facial and trigeminal nerve disorders,<sup>8</sup> and surgical excision of the third eyelid gland.<sup>7</sup> Evidence of these causes was not found in any patient presented in the current study.

Congenital alacrima, caused by aplasia or hypoplasia of the lacrimal gland, has been frequently mentioned but not



**Figure 4.** Photomicrograph of a tissue sample obtained from the dorsolateral orbit of a 5-year-old, female Yorkshire Terrier with keratoconjunctivitis sicca and suspected congenital alacrima. Note the absence of acini, ducts, inflammatory cells, or fibrosis consistent with aplasia of the lacrimal gland. Vacuolated cells (arrows) represent sebaceous glands (H&E,  $\times 40$ ).

well described.<sup>1,3,5</sup> Aguirre *et al.* reported three cases of congenital KCS in a series of 71 dogs affected with dry eye.<sup>5</sup> Although these authors described congenital KCS as more common in miniature or small-breed dogs, there was no full description of the clinical characteristics of these three dogs. In the current report, all but one of the affected dogs in a 4.5-year period were Yorkshire Terriers, suggesting that Yorkshire Terriers are predisposed to this syndrome. A sex predisposition for KCS has been suggested by some authors,<sup>1,3</sup> and in other studies female were more commonly affected than male dogs.<sup>10,11</sup> In the study presented here, female ( $n = 12$ ) were presented three times more commonly than male dogs ( $n = 4$ ) and this difference bordered on significant.

Congenital aplasia or hypoplasia of the lacrimal gland should be considered when a young dog of a small breed is presented with signs attributable to severe, unilateral reduction in the aqueous layer of the precorneal tear film. This diagnosis is supported by a lack of history suggestive of trauma, infectious disease, toxicity, or previous surgery of the third eyelid. All of the dogs presented here met these criteria. Although confirmation of the diagnosis by biopsy of the lacrimal glands was not possible in most dogs in the present series because of lack of owner consent, histopathologic

examination performed in one dog was consistent with lacrimal gland aplasia. Unfortunately, examination of the gland of the third eyelid was not performed in this dog. However, the extremely low STT values obtained in most affected eyes in the dogs presented here suggests that both lacrimal glands were involved.

Treatment of these dogs was problematic, which is understandable if most had glandular aplasia or hypoplasia. Cyclosporine is an immunosuppressive drug that produces immune modulation of the ocular surface and lacrimal glands with associated increased tear production.<sup>1,3,11-13</sup> However, this therapeutic effect depends on the presence of viable lacrimal gland tissue, and failure to effect an increase in STT result in dogs with lacrimal gland aplasia or hypoplasia should be expected. Eleven of the dogs presented here were initially treated using 0.2% cyclosporine ophthalmic ointment but all failed to show improvement in STT values. Although some had mild reduction in mucoid discharge and blepharospasm, this may have been due to the anti-inflammatory or lubricating properties of the drug. Cyclosporine was not used at higher concentrations in these dogs because previous clinical trials performed by one of the authors (HDH) showed no clinical differences in the STT values of dogs with KCS treated with cyclosporine at variable concentrations (data not published).

Chondroitin sulfate ophthalmic solution was used in three of the 11 dogs that failed to improve with cyclosporine, and as an initial treatment in five additional dogs. This drug subjectively appeared to be more effective than cyclosporine in reducing discomfort and mucoid discharge. This probably occurred as a result of its lacrimomimetic properties.<sup>3,14</sup> The use of chondroitin sulfate as medical treatment of recurrent corneal erosions has recently been described;<sup>15</sup> however, there is a paucity of references concerning the clinical use of tear substitutes like chondroitin sulfate and hyaluronic acid. In addition, 20% chondroitin sulfate ophthalmic solution is highly viscous and would aid lubrication and protection of the ocular surface, reduce desiccation, and provide some nutrition of the cornea.

Open PDT was performed in three dogs and was associated with excessive salivary secretion and facial dermatitis in one of these. Other reported complications of this technique, such as superficial band keratopathy caused by calcium precipitates or a failure to salivate,<sup>1,3,5,16,17</sup> were not observed in the dogs undergoing PDT in this study. The PDT technique should be considered when no improvement in clinical signs is achieved with other therapies.

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