

## CASE REPORT

# Leiomyoma of the third eyelid in a dog

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## Abstract

A 14-year-old neutered male Dachshund presented for the evaluation of oculus dexter (OD) third eyelid elevation ongoing for approximately 2 months. Complete ophthalmic examination revealed a large, nonpainful, well-demarcated, soft mass at the base of the right third eyelid causing elevation and mild hyperemia. The mass was freely moveable with the third eyelid, and no right globe deviation was noted. No other abnormalities were noted on physical examination, routine blood chemistry, complete blood count, serum T4, urinalysis, or urine cortisol/creatinine ratio. Ocular B-mode ultrasonography showed an anechoic, well-demarcated, homogenous, soft tissue mass at the base of the third eyelid with no orbital extension. A leiomyoma was diagnosed after multiple punch biopsies were obtained from the palpebral surface of the mass. The right third eyelid was excised surgically. Histopathology confirmed a completely excised, nodular, unencapsulated, expansile mass within the third eyelid. Positive smooth muscle actin and negative S-100 immunohistochemistry confirmed a leiomyoma. Bundles of normal smooth muscle were also present adjacent to the mass. The mass was compressing the adjacent lacrimal gland and associated with moderate dacryoadenitis. Twelve months postoperatively, the right globe position and motility remain normal with no evidence of mass regrowth. To the author's knowledge, this is the first reported case of a leiomyoma of the third eyelid in any species. In this case, the mass was completely excised and no regrowth has occurred twelve months after surgery. This case along with independently reviewed canine third eyelids clearly demonstrates the presence of smooth muscle within the canine third eyelid.

**Key Words:** canine, eyelid leiomyoma, leiomyoma, smooth muscle, third eyelid

## INTRODUCTION

Canine leiomyomas are benign tumors arising from smooth muscle and are most commonly found in the gastrointestinal tract.<sup>1–7</sup> These tumors may also occur in a variety of other locations including the heart,<sup>8</sup> urinary system,<sup>9–12</sup> uterus,<sup>13</sup> mesosalpinx,<sup>14</sup> vagina,<sup>15,16</sup> trachea,<sup>17</sup> and nasopharynx.<sup>18</sup> Angioleiomyomas, uncommonly reported in dogs, arise from vascular smooth muscle and may occur in a variety of locations. Although leiomyomas are benign, they may cause serious disease secondary to compression or displacement of adjacent abdominal or alimentary structures.<sup>1,2,5,6</sup> Leiomyomas may also produce insulin-like growth factors that cause hypoglycemia in affected canine patients.<sup>19–21</sup> In spite of their relative commonness in

other locations in dogs, there is only one report of a canine intraocular leiomyoma, arising from the iris in a dog.<sup>22</sup>

In the human literature, there are multiple reports of ocular or periocular leiomyomas arising from the orbit,<sup>23</sup> eyelid,<sup>24,25</sup> conjunctiva,<sup>26</sup> iris,<sup>27–29</sup> ciliary body,<sup>30–33</sup> and choroid.<sup>34,35</sup> Ocular leiomyomas are considered rare<sup>36,37</sup> as these case reports are very sporadic throughout the literature. Additionally, a 1994 study revealed that many earlier intraocular 'leiomyomas' were misdiagnosed; immunohistochemistry on previous cases confirmed many of these tumors to be melanocytic lesions.<sup>38</sup> Thus, ocular leiomyomas may be even rarer than the literature would suggest. Mesectodermal leiomyomas are benign intraocular tumors arising from the ciliary body epithelium, a cell

of neural crest origin.<sup>39</sup> Although routine histopathology may be highly suggestive of a leiomyoma, a definitive diagnosis of leiomyoma can only be made with immunohistochemistry, as the clinical and microscopic appearance of these tumors may be similar to other tumors such as melanocytic neoplasia, gastrointestinal stromal tumors (GISTs), and other spindle cell tumors.<sup>2,3,38</sup> This was also highlighted in a 2007 study of canine small intestinal and cecal tumors that demonstrated distinct immunohistochemical differences between gastrointestinal smooth muscle and stromal tumors, resulting in many tumors being reclassified.<sup>40</sup>

The herein present case report describes a primary canine third eyelid leiomyoma diagnosed with histopathology and immunohistochemistry. To the authors' knowledge, this is the first report of a primary third eyelid leiomyoma in any species. The mass was surgically excised with no regrowth reported twelve months postoperatively. This case report also definitively demonstrates the presence of native smooth muscle within the canine third eyelid, the presence of which has previously been indeterminate.

## CLINICAL REPORT

### *Ophthalmic examination*

A fourteen-year-old neutered male short-haired Dachshund presented to a private referral hospital's Ophthalmology Service for the evaluation of recurrent corneal ulceration oculus uterque (OU), blepharospasm OU, and white corneal opacities OU. Full ophthalmic examination with slit-lamp biomicroscopy (Kowa SL-15; Kowa Optimed, Torrance, CA, USA) and indirect ophthalmoscopy (Keeler Vantage Plus; Dan Scott and Associates, Westerville, OH, USA) performed by a board-certified veterinary ophthalmologist (RM) revealed mild enophthalmos OU, mild intermittent blepharospasm OU, mild-to-moderate hyperemia OU, paraxial ventrotemporal dense mid to anterior corneal stromal lipid opacifications OU and multifocal wispy arborizing anterior stromal limbal-based corneal vascularization temporally and ventrotemporally extending variable distances into the corneal stroma OU. A large, nonpainful, well-demarcated, soft mass at the base of the right third eyelid causing third eyelid elevation was also identified (Fig. 1). Save for the previously mentioned mild OU enophthalmos, there was no OD globe deviation or strabismus. There was normal ocular motility and an otherwise normal neuro-ophthalmic examination. The mass was freely movable within the right third eyelid. Schirmer tear test values were 18 mm/min OD and 15 mm/min OS (Schirmer Tear Test; Merck and Company, Inc., Whitehouse Station, NJ, USA), and intraocular pressures were 8 mmHg OD and 8 mmHg OS measured by applanation tonometry (Tonopen XL; Reichert Technologies, Depew, NY, USA). The tear film breakup time (TBUT), measured as previously described,<sup>41</sup> was decreased in both eyes (3 s OD, 5 s OS), consistent with a

qualitative tear deficiency. There was no corneal or conjunctival fluorescein stain retention OU. The patient was visual with a normal intraocular examination OU.

Based on the ophthalmic examination, diagnoses of OU qualitative tear deficiency, OU corneal lipidosis, OU mild keratitis, and OD third eyelid mass were made. Recommendations were made for systemic workup to identify any underlying systemic factors contributing to the corneal lipidosis along with an ocular ultrasound and biopsies of the third eyelid mass. Topical therapy was instituted with 0.2% cyclosporine (small strip OU BID; Optimmune, Merck, White House Station, NJ, USA) and an artificial lacrimomimetic (1 drop OU BID; Refresh Celluvisc, Allergan, Irvine, CA, USA) for the qualitative tear deficiency.

### *Diagnostics*

Systemic diagnostics including routine blood chemistry, complete blood count, serum triglycerides, serum T4, and urinalysis were within normal limits. A urine cortisol/creatinine ratio was 6, which is consistent with normal adrenal function. Based on these diagnostics, no further investigation of adrenal or thyroid function was performed.

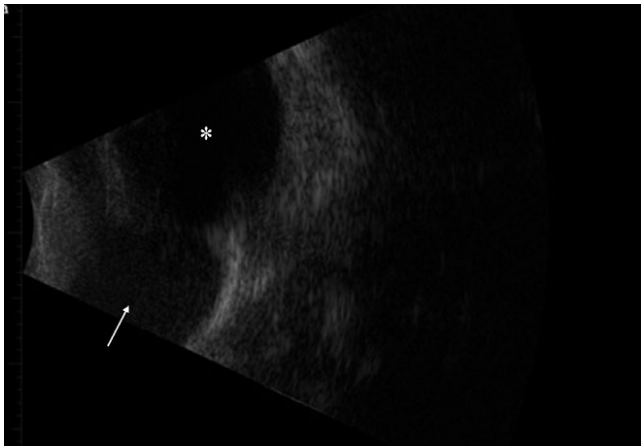
The patient presented again for ocular ultrasound and biopsies of the third eyelid mass. Ophthalmic examination revealed marked improvement in the patient's overall



**Figure 1.** Front (a) and side (b) photographs of the patient at initial presentation are depicted. There is elevation of the third eyelid OD and a ventral periocular mass effect. The position and motility of the right globe were normal.

comfort. The hyperemia and enophthalmos had resolved OU. The limbal-based corneal vascularization had resolved, and the tear film breakup time (TBUT) was normal in both eyes (>15 s OU). No other changes in the ophthalmic examination were noted. The right third eyelid mass appeared unchanged.

The patient was sedated with dexmedetomidine (375 mcg/m<sup>2</sup> IV; Dexdomitor, Zoetis, Florham Park, NJ, USA) and butorphanol (0.4 mg/kg IV; Torbugesic, Fort Dodge, Fort Dodge, IA, USA). After sedation, ocular ultrasound imaging (10 MHz UBM probe; Aviso, Quantell Medical, Bozeman, MT, USA) was obtained and showed an anechoic to mildly hypo-echoic, well-demarcated, homogenous, soft tissue mass at the base of the third eyelid with no orbital extension (Fig. 2). Based on the ultrasound and readily accessible location for tissue sampling, biopsies of the mass were pursued. After routine surgical preparation, local anesthetic was injected subconjunctivally on the palpebral surface of the third eyelid overlying the mass with 2% injectable lidocaine (0.15 mL subconjunctival; MWI, Boise, ID, USA). Several 4-mm punch biopsies (disposable biopsy punch; Miltex, York, PA, USA) were obtained from the palpebral surface of the third eyelid in the body of the firm, intrapalpebral mass and submitted for histopathologic examination. The conjunctival defect was closed with simple interrupted 6-0 vicryl (Ethicon; Johnson and Johnson, New Brunswick, NJ, USA) sutures. The patient's dexmedetomidine sedation was then reversed using atipamezole (375 mcg/m<sup>2</sup> IM; Antisedan, Zoetis, Florham Park, NJ, USA). The patient recovered routinely and was discharged with topical diclofenac (1 drop Q12 h OD; Nexus Pharmaceuticals, Vernon Hills, IL, USA) and topical Optimune as previously prescribed.



**Figure 2.** A representative ultrasonographic image of the patient's third eyelid is shown. The globe is positioned toward the top of the photograph (asterisk), and the mass is depicted by the arrow. The soft tissue density mass is well-demarcated, homogenous, and anechoic to mildly hypo-echoic. The mass was freely moveable with the third eyelid and showed no further orbital extension or involvement.

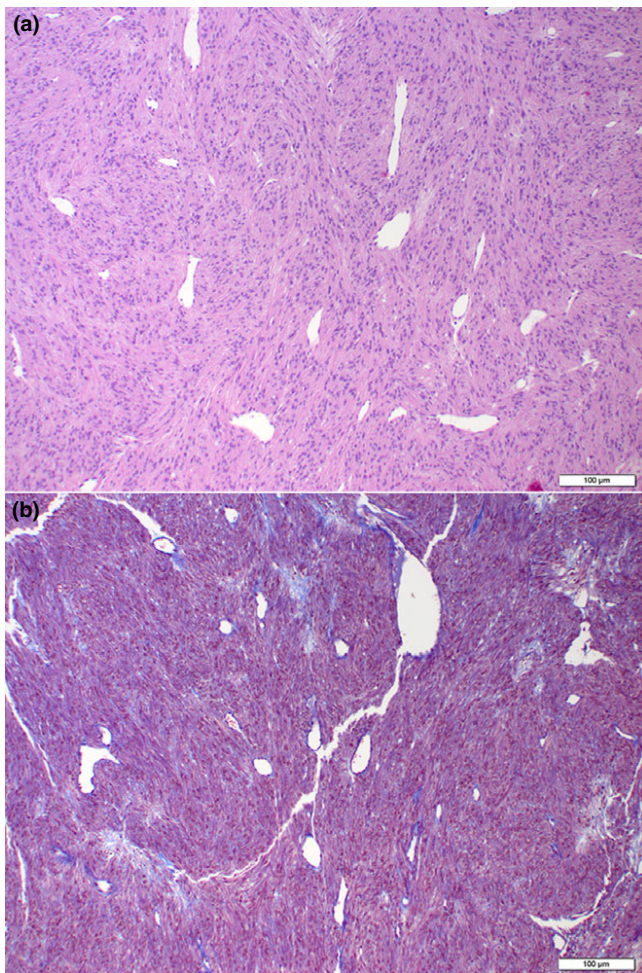
### *Third eyelid biopsy histopathology*

Examined sections contained sections of a mass that were composed of interlacing bundles and fascicles of spindle-shaped to polygonal cells with indistinct borders and scant, clear to eosinophilic cytoplasm that extended away from the nucleus in delicate streams (Fig. 3). Nuclei were round to oval with finely stippled chromatin and 1-2 distinct nucleoli. Anisocytosis and anisokaryosis were mild. The mass also had numerous, mildly dilated, occasionally branching vessels lined by flattened to slightly plump endothelial cells. A Masson's trichrome stain was performed, and staining was consistent with muscle (Fig. 3). A diagnosis of leiomyoma was made; however, an angioleiomyoma could not be excluded.

### *Right third eyelid excision*

Based on the histopathology results and location of the mass, recommendations were made for surgical excision of the right third eyelid with histopathologic evaluation. The patient was premedicated with acepromazine (0.02 mg/kg IM; Fort Dodge, Fort Dodge, IA, USA) and hydromorphone (0.1 mg/kg IM; West Ward, Eatontown, NJ, USA) prior to general anesthesia. Anesthetic induction was achieved with propofol (4 mg/kg IV; Propofol, Abbott Animal Health, North Chicago, IL, USA) to effect. General anesthesia was maintained after endotracheal intubation with inhalant isoflurane 1-2% in oxygen (Isoflo; Abbott Animal Health, North Chicago, IL, USA). After endotracheal intubation and anesthesia maintenance, cefazolin (22 mg/kg IV; WG Critical Care LLC, Paramus, NJ, USA) and carprofen (2.2 mg/kg SQ; Rimadyl, Zoetis, Florham Park, NJ, USA) were then administered. The patient was positioned in sternal recumbency, and the right eye was prepped routinely for surgery (Fig. 4). Prior to excision, an encircling conjunctival incision was made at the base of the third eyelid with a #15 blade. Metzenbaum scissors were used to undermine the bulbar and palpebral conjunctiva on either side of the third eyelid within the fornices to provide a section of conjunctiva available for surgical closure after third eyelid excision. The right third eyelid was excised at the base as previously described<sup>42</sup> and submitted for histopathology. The conjunctiva was closed with simple continuous 6-0 vicryl (Ethicon; Johnson and Johnson, New Brunswick, NJ, USA) sutures using with care to place the knots deep within the dorsonasal and ventrotemporal fornices on either end of the incision to avoid contact with the cornea.

The patient recovered from general anesthesia routinely. Postoperatively, the patient received hydromorphone (0.05 mg/kg IV Q6 h). The patient was discharged with topical OD diclofenac (1 drop OD Q8 h), Optimune (small strip OU Q12 h) neomycin-polymyxin-gramicidin (1 drop OD Q8 h; Neopolygram, Bausch and Lomb, Inc., Tampa, FL, USA), and artificial tear ointment (small strip OD Q6 h; Puralube, Fera Pharmaceuticals,



**Figure 3.** Photomicrographs from an incisional biopsy of the third eyelid mass are depicted. The mass is composed of interlacing bundles of spindle-shaped cells with mild pleomorphism that frequently surround mildly dilated vessels H&E stain 10× magnification. (a) Neoplastic tissue stains red with a Masson's trichrome stain (b, 10× magnification), consistent with muscle. Small amounts of blue staining collagen are visible, usually surrounding vessels.

Locust Valley, NY, USA) along with oral tramadol (2 mg/kg PO for 5 days; Amneal Pharmaceuticals, Glasgow, KY, USA) and carprofen (2.2 mg/kg PO Q12 h; Rimadyl, Zoetis, Florham Park, NJ, USA).

#### *Right third eyelid and mass histopathology*

Examined sections of third eyelid contained a well-demarcated, unencapsulated, nodular, expansile mass at the base of the third eyelid that compressed the adjacent third eyelid lacrimal gland (Fig. 5). The mass was composed of dense bundles of polygonal to spindle-shaped cells with indistinct borders, scant to moderate, eosinophilic to pale eosinophilic, homogeneous to finely vacuolated cytoplasm, and round, oval, or cigar shaped, lightly hyperchromatic nuclei with 1–2 distinct nucleoli. Anisocytosis and anisokaryosis were mild to moderate, and there were two



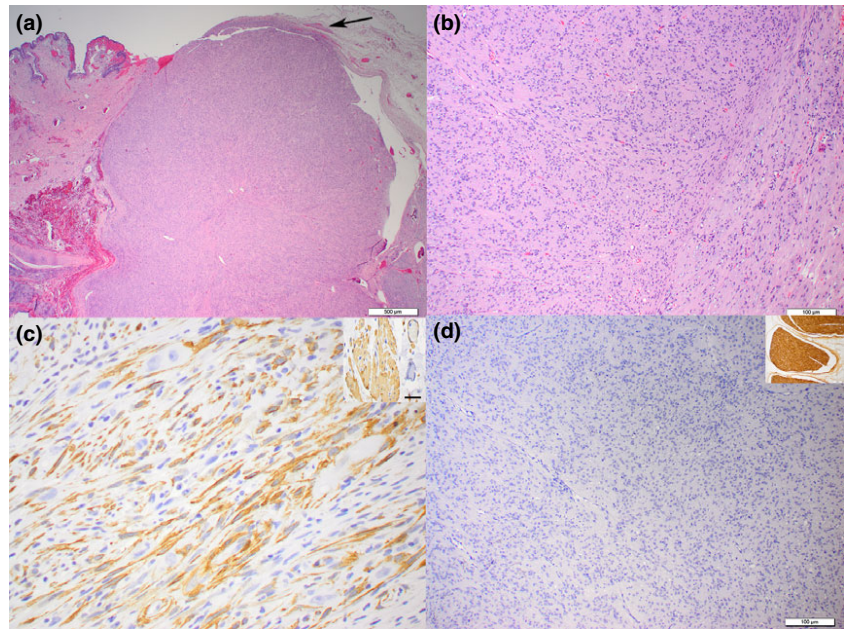
**Figure 4.** A photograph of the patient at the time of third eyelid surgical excision preoperatively to treat an OD third eyelid mass is depicted with a view from the front (a) and side (b). The mass has grown significantly since the time of initial presentation (see Fig 1). There is dramatic elevation of the OD third eyelid and a prominent ventral and rostral periocular mass effect. At this time, the right globe is also enophthalmic secondary to the mass.

mitotic figures in 10 high-powered fields of view. In some areas, neoplastic cells were separated by numerous round to oval vacuoles containing mucinous material, and there were few, small, scattered foci of mineralization. In the adjacent third eyelid lacrimal gland, ducts and acini were often ectatic with intraluminal neutrophils, macrophages, and debris, and the interstitium was mildly expanded by lymphocytes and plasma cells. Immunohistochemical staining was performed using  $\alpha$ -smooth muscle actin and  $\alpha$ -S100 antibodies. Neoplastic cells were diffusely and strongly positive for smooth muscle actin (Fig. 5) but were diffusely negative for S-100 (Fig. 5).

#### *Clinical outcome and results*

The patient presented for evaluation 12 days postoperatively. The conjunctival incision was healed. The suture knots were visible in the fornices and causing mild conjunctival hyperemia. These were thus removed along with the conjunctival suture using topical proparacaine (Alcaine; Alcon Laboratories, Fort Worth, TX, USA). The

**Figure 5.** Photomicrographs from the excised third eyelid mass are depicted. The mass is well demarcated and is composed of densely packed, interlacing bundles of spindle-shaped cells. A small bundle of normal smooth muscle is evident at the base of the tumor (arrow) H&E stain (a, 2× magnification). Neoplastic cells are spindle shaped and are arranged in relatively well-organized bundles and fascicles. Anisocytosis and anisokaryosis are mild, and mitoses are rare. Nuclei are round, oval, or cigar shaped and lightly hyperchromatic. Occasional cells have clear or lightly basophilic vacuoles H&E stain (b, 10× magnification). Immunohistochemistry using anti-smooth muscle actin antibody (c, 40× magnification). Neoplastic cells exhibit strong positive staining Inset: positive control Immunohistochemistry using anti-S100 antibody (d, 10× magnification). Neoplastic cells are diffusely negative for S100 Inset: Positive control.



ophthalmic examination was otherwise unremarkable, excepting the previously described small lipid corneal opacities. The Schirmer tear test values were 24 mm/min OD and 17 mm/min OS (Schirmer Tear Test; Merck and Company, Inc., Whitehouse Station, NJ, USA), and intraocular pressures were 14 mmHg OD and 13 mmHg OS measured by applanation tonometry (Tonopen XL; Reichert Technologies, Depew, NY, USA). Recommendations were made for long-term topical Optimune (small strip OU Q24 h). Artificial tear ointment OD was recommended for 2 weeks with instructions to discontinue after that. All other medications were discontinued.

The patient presented for evaluation 3 months after surgery (Fig. 6). The right conjunctival surfaces were normal with the absence of the right third eyelid. Except for the previously described corneal lipidosis, the ophthalmic examination was normal. Schirmer tear test values were 17 mm/min OD and 22 mm/min OS (Schirmer Tear Test; Merck and Company, Inc., Whitehouse Station, NJ, USA). No corneal ulceration or episodes of discomfort had occurred since surgery.

Telephone conversation with the owners 12 months after surgery revealed that there had been no change in the patient's general or ocular condition or appearance. No clinical signs of keratoconjunctivitis sicca had been noted as the owners described bright, clear, comfortable eyes in the patient. The owners had continued the Optimune therapy OU Q24 h and were still administering the medication.

#### *Histology of selected canine third eyelids*

Several sections of separate canine third eyelids were examined histologically to evaluate for the presence of native smooth muscle. Strips of normal smooth muscle were consistently noted within the canine third eyelid.

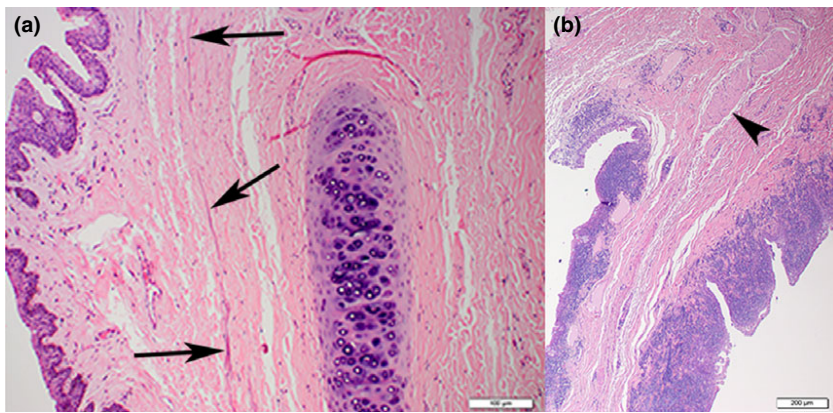


**Figure 6.** A photograph of the patient 3 months after third eyelid excision OD is depicted. The right globe position and motility are normal with normal facial symmetry. Both eyes are comfortable with a normal pre-ocular tear film.

There were variations among patients and sections as to the amount of smooth muscle present (Fig. 7), but it was consistently noted on canine third eyelid histology.

#### DISCUSSION

The described case herein is the first reported leiomyoma of the third eyelid in any species, to the authors' knowledge. This tumor was diagnosed based on histopathology and immunohistochemistry. As has been previously documented,<sup>3,38,40</sup> it is very important to perform immunohistochemistry on suspected leiomyomas as these tumors may histologically appear similar to other tumors. In our case, the tumor displayed clear histologic characteristics of mesenchymal origin. The tumor exhibited polygonal to



**Figure 7.** Photomicrographs of two canine third eyelids are depicted (10× magnification a, 2× magnification b) highlighting the variability in amount of smooth muscle present in canine third eyelid sections. Smooth muscle is present as larger bundles near the base of the third eyelid (arrowhead, a) and as thin, barely perceptible strips extending along most of the length of the third eyelid (arrows, b) in two representative samples H&E stain.

spindle cell shape, low mitotic index, scant intercellular connective tissue matrix, and an intermittent ‘whorling’ cell pattern, which may be histologic features of other types of tumors. Because this tumor was not located within the gastrointestinal tract, a gastrointestinal stromal tumor, which may appear similar to a leiomyoma, was not considered. Peripheral nerve sheath tumors and melanocytic neoplasia have been reported within the globe and in the facial region in dogs;<sup>43–46</sup> therefore, these tumors were considered important differential diagnoses. In this case, smooth muscle actin (SMA) staining was positive and S-100 staining was negative, clearly differentiating the tumor as a leiomyoma. The initial biopsy samples showed frequent, prominent, often dilated blood vessels within the tumor; thus, an angioleiomyoma was initially considered. However, once the tumor was available in its entirety for review, an angioleiomyoma was ruled out based on a histologic lack of similarly prominent vasculature, and a leiomyoma was diagnosed.

Leiomyomas are benign tumors and, as such, do not metastasize, but may be locally expansive and can become very large. In dogs, these tumors are most commonly found in the GI tract and are one of the most common GI tumors.<sup>2–4,40,47</sup> In the GI tract, these tumors cause morbidity related to adjacent structure involvement; effects are usually due to compression or obstruction. In our case, the leiomyoma caused third eyelid elevation, but was found primarily as an incidental finding. This patient presented to the ophthalmologist for clinical signs of his qualitative tear deficiency. By the time the mass was removed, it had grown to a large enough size that the facial appearance of the patient was altered and the third eyelid was significantly elevated (Fig. 4). Likely, had the mass continued to grow and this been the only clinical ocular abnormality, the patient would have been presented to the ophthalmologist for these changes. Because the mass was limited to the third eyelid, removal of the third eyelid in its entirety was warranted. In retrospect, excision of the mass without removal of the third eyelid could have been attempted. However, this mass was quite extensive and it is unlikely that both complete excision of the mass and preservation of the third eyelid anatomy would have

been achieved. A primary mass of the third eyelid is one of the rare indications for complete removal of this structure as removal of the associated lacrimal gland is considered detrimental.<sup>48</sup> In our case, close monitoring of the quantitative tear production was considered important during follow-up. In addition, the possibility of clinical keratoconjunctivitis sicca was discussed with the client prior to surgical removal of the third eyelid. The patient’s quantitative and qualitative tear production remains normal 12 months after surgery on once-per-day lacrimostimulant therapy. Whether the quantitative tear production would have been affected had this medication not been administered is unknown. In this patient’s case, this medication was administered to treat a qualitative tear deficiency, for which the patient was already clinical prior to removal of the lacrimal gland.

This case is interesting in that it is the first reported case of leiomyoma in the periorcular region of a dog, but also because it clearly demonstrates the presence of native smooth muscle within the canine third eyelid. Not only does this tumor originate from smooth muscle and by default shows the presence of smooth muscle in this location, and there were also bundles of normal smooth muscle at the base of the mass within our patient’s third eyelid (Fig. 5). This prompted the authors to critically examine other canine third eyelids. A random selection of normal canine third eyelids or third eyelids submitted for other conditions clearly demonstrated the presence of smooth muscle (Fig. 7). There were variations among patients and sections as to the amount of smooth muscle present (Fig. 7), but it was consistently noted on canine third eyelid histology and was exclusively at or near the base of the third eyelid along the margins of, and usually parallel to, the gland. Previously, the presence of native smooth muscle within the canine eyelid was undecided, being more commonly reported as a consistent feature of the feline third eyelid. Further research is needed to elucidate the full role of this muscle in the dog.

Leiomyoma may occur within the canine third eyelid. In our case, surgical excision carried an excellent prognosis with no tumor recurrence to date 12 months after surgery. This report also definitively illustrates the presence

of native smooth muscle within the canine third eyelid. Further work is needed to determine the function of the smooth muscle in this location. Serial evaluation of the quantitative tear production in any patient after third eyelid excision is warranted.

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