

Peripheral Nerve Sheath Tumor in the Upper Eyelid in a Dog

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ABSTRACT

Background: Peripheral nerve sheath tumors are most commonly found on the head and neck regions of both dogs and people. Schwannomas are rarely observed in ophthalmic areas. When they occur, ocular Schwannomas are usually located in the orbit, uveal tract and conjunctiva. The occurrence of uveal schwannoma, a subset of PNST has been well documented in the veterinary literature. PNST has never been observed in the eyelids of dogs. Therefore, the present report aimed to describe the surgical treatment and outcome of a PNST located in the upper eyelid of a dog.

Case: A 9-year-old, spayed female mixed-breed dog was referred for evaluation of a large mass involving the right upper eyelid for a duration of approximately one month. The inspection revealed sero-sanguinolent discharge and an oval-shaped mass occupying more than 70% of the right upper eyelid. A presumptive diagnosis of eyelid neoplasia was considered most likely. Excision of the entire mass with a 2 cm margin was performed. The third eyelid and dorso-medial bulbar conjunctiva were also removed. Upper eyelid reconstruction was performed based on a similar technique previously described in cats (lip-to-lid flap). As a result, neoplastic spindle cells exhibited immunoreactivity for S100 and intense cytoplasmic staining for vimentin, supporting the diagnosis of schwannoma. Fifteen days later, the margins of the subdermal pattern flap were healed and skin sutures were removed. On the last follow-up, 9 months post-surgery, the dog was visual, and the flap was well incorporated and covered the ocular surface. Ten months later, another large mass arising from the right inferior palpebral conjunctiva was observed. Once ultrasound revealed orbital invasion exenteration combined with orbitectomy were performed, and the defect was covered with an auricular axial pattern flap. The second tumor had the same histological and immunohistochemical characteristics of the first mass. Both tumors expressed Ki67; however, the PI in the second mass was higher (7.9%) than the first (3.4%).

Discussion: Reported eyelid neoplasms in dogs include adenomas and adenocarcinomas of the meibomian glands, melanomas, fibroma, fibrosarcoma, histiocytoma, mastocytoma, lipomas, papillomas, and squamous cell carcinomas. To the author's knowledge, however, this is the first case description of a PNST affecting the eyelid in a dog. The histologic distinction between PNSTs and other spindle cell tumors, including myxosarcoma, fibrosarcoma, leiomyosarcoma, hemangiopericytoma, and melanoma can be challenging and requires immunohistochemical staining. S100 is an acidic protein that identifies various nervous tissue cells, including Schwann cells, and the majority of canine PNSTs diffusely express this molecule. As in the case presented here, neoplastic cells of different ocular and adnexal structures were also positive for S100 and vimentin in all PNSTs previously reported in the veterinary literature. This is the first report of PNST affecting the eyelid in a dog. The lip-to-lid flap is a feasible technique to reconstruct the upper eyelid following wide surgical removal of a tumor in dogs. However, the authors suggest radical surgery combining orbitectomy, exenteration and a miocutaneous flap if PNST is diagnosed in the eyelids of dogs. They also caution once recurrence is possible and can be more aggressive.

Keywords: lip-to-lid transposition, S100, vimentin, desmin, Ki67, dog.

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INTRODUCTION

Schwannomas are benign tumors derived from the Schwann cells of the peripheral nerve sheath. These tumors are generally presented as solitary masses that can be located in soft tissues throughout the body. It has a smooth surface and grows slowly [7,13]. The occurrence of uveal schwannoma, a subset of PNST has been well documented in the veterinary literature [10]. In dogs, however, there are only 4 reports of PNSTs arising from ocular structures other than the iris, one involving the third eyelid [14], three the retrobulbar space [1,2,6] and only one where both of the corneas of the same patient were affected [8]. To the author's knowledge, PNST has never been observed in the eyelids of dogs. Therefore, the present report aimed to describe the surgical treatment and outcome of a PNST located in the upper eyelid of a dog.

CASE

A 9-year-old, spayed female mixed-breed dog, weighing 19 kg was referred to Federal University of Mato Grosso (Brazil) Ophthalmology Service for evaluation of a large mass involving the right upper eyelid for a duration of approximately one month. The inspection revealed sero-sanguinolent discharge and an oval-shaped mass occupying more than 70% of the right upper eyelid. The mass was firm on palpation and had a pedunculated characteristic; it was ulcerated

at the cutaneous side of the eyelid, and measured 3.9 x 4.4 cm (Figure 1A). The palpebral conjunctiva and the top of the third eyelid of the affected side showed an irregular aspect and were mildly hyperemic (Figure 1B).

The dog was alert and the ophthalmic and general physical examination did not revealed abnormalities. Ocular ultrasonography did not show significant findings. Blood count and biochemical profile were unremarkable, and thoracic radiographs did not reveal any signs of lung metastasis.

A fine-needle aspirate of the palpebral tumor was not elucidative, even so, a presumptive diagnosis of eyelid neoplasia was considered most likely. Excision of the entire mass with a 2 cm margin was performed. The third eyelid and dorso-medial bulbar conjunctiva were also removed (Figure 1C). Upper eyelid reconstruction was performed based on a similar technique previously described in cats [12]. The excised tissues were fixed in 10% formalin and subjected to histopathological evaluation. Amoxicillin¹ (20 mg/kg q12 h) and oral meloxicam² (0.1 mg/kg q24 h) were prescribed for 5 and 3 days, respectively, during the post-operative period.

Based on the histological findings, a spindle cell tumor was suggested (Figure 2A) and an immunohistochemical panel for S100³, vimentin, and desmin³ were used for differential diagnosis. As a result, neoplastic spindle cells exhibited immunoreactivity for

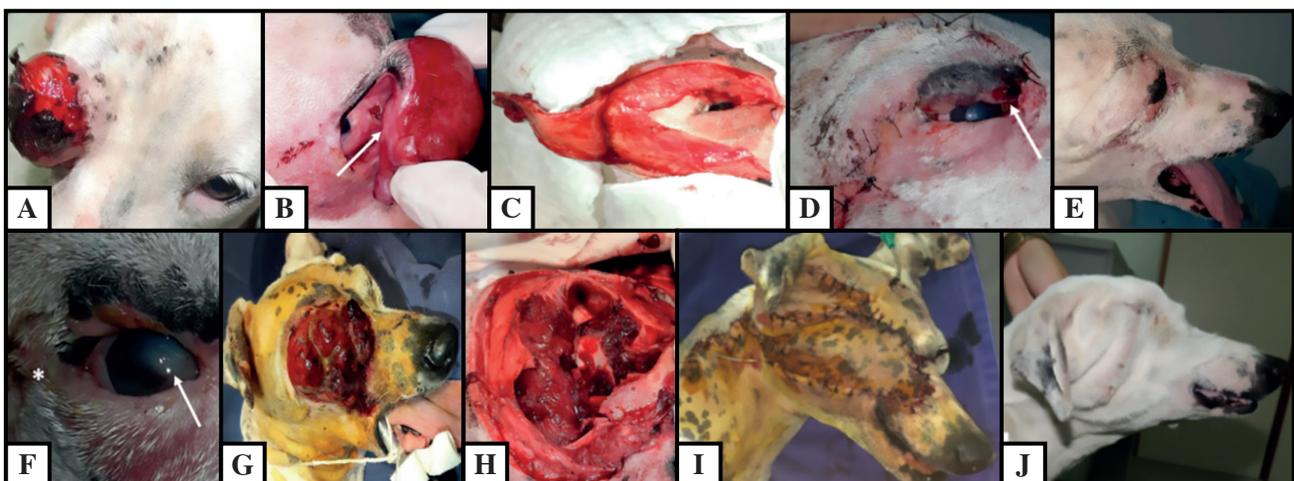


Figure 1. Clinical photograph of a 9-year-old female, spayed mixed-breed bitch at the time of initial presentation depicting a large oval-shaped mass occupying more than 70% of the right upper eyelid (A). The palpebral conjunctiva and the top of the third eyelid of the affected side showing mild hyperemia and an irregular aspect (arrow) (B). Intraoperative photograph after radical resection of 90% of the right upper eyelid, the entire third eyelid, and the dorsal aspect of the bulbar conjunctiva; the subdermal plexus (lip-to-lid) flap is ready to be transposed (C). Fifteen days after surgery, the graft and donor-site defect healed but a small visible point of necrosis was observed at the tip of the transposed lip near the medial canthus (arrow) (D). Nine months after surgery showing good cosmetic result (E); a corneal scar (arrow) and mild signs of keratoconjunctivitis sicca (asterisk) are depicted OD (F). Ten months after the first surgery depicting the recurrence of a large mass arising from the right inferior palpebral conjunctiva (G). Intraoperative photograph after radical resection combining exenteration, orbitectomy, and an auricular axial pattern flap (H-I). No local recurrence was observed 60 days after the second surgery (J).

S100 and intense cytoplasmic staining for vimentin, supporting the diagnosis of schwannoma (Figure 2B & 2C). No desmin immunoreactivity was detected (Figure 2D). Neoplastic cells were not found in the bulbar conjunctiva and the third eyelid.

Fifteen days later, the margins of the subdermal pattern flap were healed and skin sutures were removed. Only one small visible point of necrosis was observed at the tip of the transposed lip near the medial canthus (Figure 1D). The necrotic margin was removed and left to heal by second intention. Ten days later, the patient presented with mild mucous discharge from the operated eye. The STT was 11 mm/min and a small axial corneal ulcer was diagnosed in the right eye. Topical 0.03% tacrolimus⁴, carboxymethylcellulose lubricating gel⁵, and tobramycin⁶ were prescribed. Three days after the follow-up, the corneal ulcer was healed. On the last follow-up, 9 months post-surgery, the dog was visual, and the flap was well incorporated and covered the ocular surface (Figure 1E). The right eye showed mild signs of keratoconjunctivitis sicca (KCS), once the owner reported that he was not able to follow the prescription in a continuous manner (Figure 1F).

Ten months later, another large mass arising from the right inferior palpebral conjunctiva was observed (Figure 1G). Once ultrasound revealed orbital invasion exenteration combined with orbitectomy were performed, and the defect was covered with an auricular axial pattern flap (Figure 1H). Although the second tumor had the same histological and immunohistochemical characteristics of the first mass (Figure 2E – 2H), additional staining for Ki67³ was used to investigate the biological behavior of both masses. The Ki67 proliferation index (PI) was defined as the percentage of positive nuclei determined by counting up to 1,000 nuclei in the selected fields (×400). Both tumors expressed Ki67; however, the PI in the second mass was higher (7.9%) than the first (3.4%) (Figure 2I and 2J). Despite no local recurrence was observed 60 days after the second surgery (Figure 1I), the general health status of the dog worsened substantially, the patient developed disseminated lymphadenomegaly and an enlarged right hind limb with a tumor-like appearance. The owner elected euthanasia and the histopathology of the limb revealed histiocytic sarcoma unrelated to the ocular tumors.

DISCUSSION

Reported eyelid neoplasms in dogs include adenomas and adenocarcinomas of the meibomian glands, melanomas, fibroma, fibrosarcoma, histiocytoma, mastocytoma, lipomas, papillomas, and squamous cell carcinomas. For all the above-mentioned diseases, benign neoplasms outnumber malignant tumors by a ratio of 3 to 1 [15]. Other masses with benign histological behavior that can affect the eyelids of dogs less

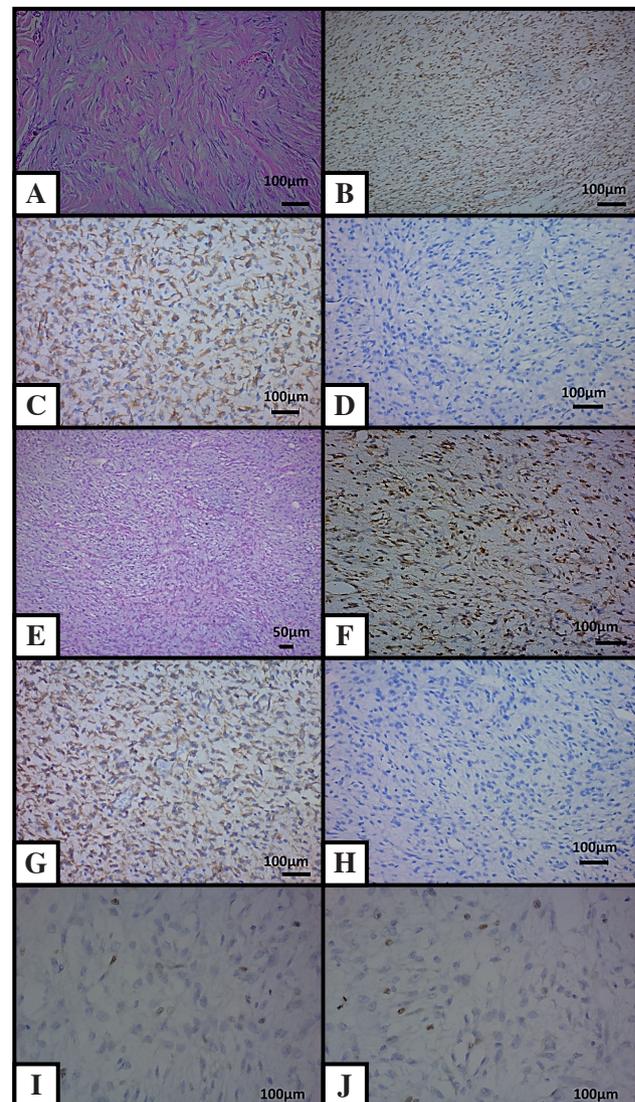


Figure 2. Photomicrographs of the first (A) and second tumor (E) [H&E]. Observe that neoplastic cells are composed of juxtaposed spindle cells intersecting in various directions, with pleated and spiral-shaped areas, arranged in a moderate myxoid stroma (A). Note that the second tumor shows similar histological characteristics of the first mass (E). Immunohistochemical characterization of neoplastic cells in the first (B-D) and second tumor (F-H). Spindle cells demonstrate moderate cytoplasmic labeling for S100 (B,F) and intense cytoplasmic staining vimentin (C,G). Neoplastic spindle cells did not exhibit immunoreactivity to desmin (D,H). Photomicrograph displaying the immunohistochemical nuclear expression of Ki67 in the first (I) and second tumor (J). The proliferative index observed in the second tumor was higher (7.9%) than the first (3.4%).

frequently are the hamartomas and the granular cell tumors [5,9]. To the author's knowledge, however, this is the first case description of a PNST affecting the eyelid in a dog.

The histologic distinction between PNSTs and other spindle cell tumors, including myxosarcoma, fibrosarcoma, leiomyosarcoma, hemangiopericytoma, and melanoma can be challenging and requires immunohistochemical staining [13]. S100 is an acidic protein that identifies various nervous tissue cells, including Schwann cells, and the majority of canine PNSTs diffusely express this molecule. As in the case presented here, neoplastic cells of different ocular and adnexal structures were also positive for S100 and vimentin in all PNSTs previously reported in the veterinary literature [1,2,6,8,14]. Desmin is a protein of intermediate filaments and its expression is highly specific to muscle cells [13]. In our report, desmin was negatively expressed in the first and second tumors ruling out a tumor of muscle origin. The reasons to determine if the mass presented here expressed desmin was based upon the results of one study, which found that 77.5% of the samples of cutaneous PNST in dogs could be immunopositive for this marker [13]. Considering the invasiveness of the second tumor, we decided to use Ki67 to investigate the biological behavior of both masses. The expression of Ki67 allows the distinction between proliferating and quiescent cells and thus, predicts the further behavior of a specific pathology. The Ki67 is a useful marker for discriminating the biological behavior of canine cutaneous PNST, once 96% of the malignant masses display a Ki67 index higher than 6% [13]. In the present case, the first tumor that was removed showed a Ki67 proliferation index of 3.4% and could be already considered a malignant schwannoma. However, the recurrence of the same tumor 10 months later revealed a proliferation index of 7.9%, suggesting a much more aggressive growth.

Although described that the lip subdermal flap can be indicated to reconstruct the upper eyelid of dogs in a one-step fashion, to date, no reports using this technique have been found. The adaptation of this technique to reconstruct the upper eyelid of our dog proved successful in protecting the eye on the affected side [12]. Corneal abnormalities reported in the eye of the affected side may be associated with iatrogenic KCS due to the removal of the entire third eyelid. Impairment of tear production as well as microinjury to

the keratoconjunctival epithelium has been described when the lacrimal gland of the third eyelid is removed [3]. Despite the KCS developed by the present patient, good cosmesis and owner satisfaction were achieved with the lip-to-lid flap.

Previous reports have described that all PNSTs arising from the retrobulbar space or the third eyelid of dogs reoccurred after 5 to 7 months, and the patients died or were euthanized due to poor quality of life [1,2,6,8,14]. Similarly, in the patient of the present report recurrence of the tumor was observed 10 months after the removal of 90% of the upper eyelid, the entire third eyelid, and the dorso-medial aspect of the bulbar conjunctiva. Kafarnik *et al.* (2005) described the occurrence of PNST in 6 cats, where the upper eyelid was affected in four cats, the upper conjunctiva in two cats, and the lower eyelid in one cat [4]. All of the cats that underwent conservative surgical excision had an average of three recurrences of the tumor. Four of 6 cats that underwent wide excision with enucleation, exenteration or rhomboid flap had no recurrence of the tumor [4]. Coincidentally, in the dog of the present report, the right upper eyelid was affected, and the clinical aspect of the mass resembled the characteristics presented by the cats [4]. In our dog, tumor regrowth arose from the lower palpebral conjunctiva OD with invasion of the retrobulbar space, sparing the upper transposed lip and the eye; in addition, the Ki67 expression showed a much more aggressive behavior. Therefore, whenever possible, a preoperative biopsy and a histopathology study are recommended before electing reconstructive surgery in a dog presenting an eyelid mass with a similar appearance described here. It is unclear if the histiocytic sarcoma developed in the hind limb is linked to the PNSTs presented previously, once these tumors are of separate pathogenesis. It was described in a dog the occurrence of an orbital rhabdomyosarcoma and traumatic neuroma following enucleation for a uveal schwannoma, but authors of that report could not establish a link between those tumors [11].

This is the first report of PNST affecting the eyelid in a dog. The lip-to-lid flap is a feasible technique to reconstruct the upper eyelid following wide surgical removal of a tumor in dogs. However, the authors suggest radical surgery combining orbitectomy, exenteration and a miocutaneous flap if PNST is diagnosed in the eyelids of dogs. They also caution once recurrence is possible and can be more aggressive.

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