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Primary leiomyosarcoma of the jugular vein in a dog

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Abstract

A four-year-old, male, Labrador retriever was referred for removal of a spindle cell sarcoma involving the right jugular vein. A post-contrast CT scan showed a seven-centimeter subcutaneous mass originated from the right external jugular vein, which was partially obstructed and showing contrast stasis, suggested a primary intravascular tumor of the jugular vein. The mass was resected, and histological evaluation was consistent with grade II intravenous spindle cell sarcoma of the jugular vein. Immunohistochemical positivity for vimentin, desmin, and α SMA antibody and negativity for S-100 protein confirmed venous leiomyosarcoma. The dog received five doses of intravenous doxorubicin, and there was no recurrence of the tumor 30 months post treatment. In dogs, primary intravascular sarcomas are rare and primary venous leiomyosarcoma has not been described. A venous tumor may be considered as a differential diagnosis in dogs with ventral neck swelling.

Keywords: Dog, Doxorubicin, Intravascular sarcoma, Jugular vein, Leiomyosarcoma.

Introduction

Primary intravascular sarcoma is rare in dogs and only intra-arterial tumors have been reported (Anderson *et al.*, 1988; Callanan *et al.*, 2000; Mellanby *et al.*, 2003; Ranck *et al.*, 2008; Cohen *et al.*, 2010; Lee *et al.*, 2011; Stieger-Vanegas *et al.*, 2016). In people, primary intravascular sarcomas also are rare and almost all intravenous sarcomas were classified as leiomyosarcomas (Burke and Virmani, 1993). In humans, a high metastatic rate has been reported for intravenous leiomyosarcoma (Tilkorn *et al.*, 2010).

Leiomyosarcoma is rare in companion animals. In the dog, it is most common in the alimentary tract, spleen, and liver and is considered to have a moderate to high metastatic tendency (Kapatkin *et al.*, 1992).

To authors' knowledge, primary venous leiomyosarcoma has not been described in dogs. This report describes clinical, tomographic and pathological features, treatment and outcome of a primary leiomyosarcoma of the jugular vein in a dog.

Case history

A four-year-old, 39.3 kg, male Labrador retriever was referred for removal of a spindle cell tumor involving the right jugular vein. The dog had been examined initially at a primary care clinic because of a neck swelling that had increased in size over 2 weeks. Cytological evaluation of aspirate collected by fine needle biopsy revealed spindle cell sarcoma. Excisional biopsy was attempted at the primary care clinic but abandoned because of severe hemorrhage. Computed tomography (CT) showed a 7.2 cm x 5.7 cm x 5.2 cm mass at the thoracic inlet in the right caudoventral neck

area (Fig. 1). The mass originated from the right external jugular vein, which was dilated cranially and joined the tumor in an S-configuration. Post-contrast CT showed partial obstruction of the right external jugular vein and contrast stasis. The right internal jugular vein, carotid artery, retropharyngeal and cervical lymph nodes, and thyroid gland were normal as were the thoracic and abdominal findings. The CT results were consistent with a primary intravascular venous tumor or extravascular tumor with secondary involvement of the right external jugular vein and venous thrombosis.



Fig. 1. 3D volume-rendered CT image of the ventral cervical region highlighting the vascular structures of the neck. The mass involving the right external jugular vein is clearly visible as well as the associated distention of the jugular vein and its S-configuration, proximal to the mass.

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Physical examination of the dog at the referral clinic showed a longitudinal, 10-cm, surgical wound in the caudal third of the ventral neck region. A 7-cm, firm, painless, subcutaneous mass that extended cranially from the thoracic inlet could be palpated in the region of the wound. There was no apparent vascular obstruction or venous stasis. The cervical lymph nodes were unremarkable, and results of a complete blood cell count and serum biochemical analysis were within the reference intervals.

The dog was premedicated with dexmedetomidine (5 µg/kg IM Dexdomitor, Pfizer Italia srl, Milan, Italy) and butorphanol (0.1 mg/kg IM Dolorex, Intervet Italia srl, Latina, Italy) and a catheter was placed in the lateral saphenous vein. The dog was pre-oxygenated via a face mask, and anesthesia was induced with propofol (2 mg/kg IV Rapinivet, Intervet Italia srl, Latina, Italy) and maintained with oxygen and isoflurane after endotracheal intubation. The dog was placed in dorsal recumbency with the head extended and the ventral aspect of the neck was prepared for aseptic surgery. The surgical wound was resected, and a clean margin was maintained around the entire periphery of the tumor during its removal. The right external jugular vein was isolated, exposed with blunt dissection, and ligated (2.0 polyglyconate) cranial and caudal to the mass, which was then resected and submitted for histologic examination (Fig. 2).

The excised tissue was fixed in 10% buffered formalin, processed routinely, and embedded in paraffin wax for histologic and immunohistochemical examination. Sections were stained with hematoxylin and eosin. A streptavidin/peroxidase complex method (Vectastain Kit, Vector Laboratories Inc., Burlingame, CA, USA) was used for immunohistochemical staining. The primary antibodies used included rabbit polyclonal desmin antibody (polyclonal, Santa Cruz), mouse monoclonal vimentin antibody (clone 3B4, Dako), α -smooth muscle actin antibody (α SMA, clone 1A4, Scytek), and S-100 protein antibody (clone 4C4.9, Scytek). The expression of Ki67, a cellular marker for proliferation and prognostic indicator, was evaluated by incubating tissue sections with primary Ki67 antibody (MIB-1 mAb, DAKO, Carpinteria, CA). The tumor was encapsulated and pedunculated, and histologic evaluation showed a neoplasm composed of spindle cells arranged in interlacing bundles with a herringbone pattern and no interstitial collagen matrix (Fig. 3).

There were occasional, thin-walled, blood vessels. Neoplastic cells had indistinct borders, an intermediate nuclear-to-cytoplasmic ratio, and a moderate amount of lightly eosinophilic cytoplasm. Nuclei were round to oval, often cigar-shaped, or blunt-ended, with finely granular chromatin and one central magenta nucleolus. Mitotic figures ranged from 0-4 per high-power field (11 mitotic figures per 10 HPF), and there was

moderate anisocytosis and anisokaryosis with karyomegaly and occasional bizarre cells. Moderate multifocal foci of necrosis were evident (<50%). Histologic findings were consistent with intravenous spindle cell sarcoma of the jugular vein, most likely of smooth muscle origin (leiomyosarcoma). Based on the grading system for soft tissue sarcoma using histotype, mitotic index, and necrosis, the neoplasm was classified as grade II sarcoma (Dennis *et al.*, 2011).

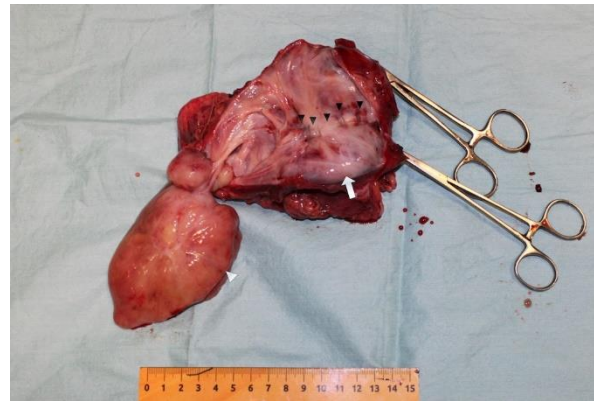


Fig. 2. The resected right external jugular vein has been opened longitudinally revealing the tunica intima (white arrow) and the leiomyosarcoma. The tumour has been turned over to show its pedunculated shape (white arrowhead) and the suture on the internal side of the jugular vein (black arrowheads) from the initial surgery.

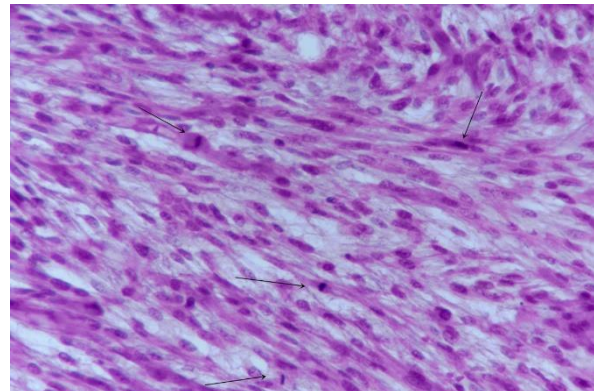


Fig. 3. The neoplasm was composed of spindle cells arranged in interlacing bundles and in a herringbone pattern. The cells have indistinct cell borders, a moderate amount of lightly eosinophilic cytoplasm, and oval or cigar-shaped nuclei. Several mitoses are evident (arrows) (H&E stain; bar = 100 µm).

Immunohistochemical staining with vimentin, desmin, and α SMA antibodies was positive in all sections (Fig. 4). Neoplastic cells were uniformly negative for S-100 protein, typically expressed in peripheral nerve sheath tumour, confirming the diagnosis of leiomyosarcoma. Ki67 positive cells were uniformly distributed in the neoplasm, and the Ki67 index was 30-40%, which was considered high.

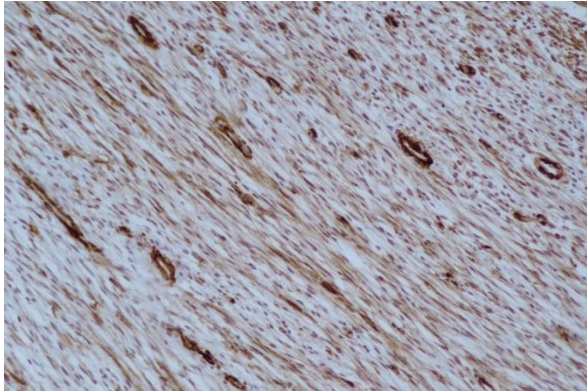


Fig. 4. Neoplastic cells showed moderate to strong α SMA immunelabeling. Small blood vessels within the tumour were strongly positive. Immunohistochemistry (IHC), diaminobenzidine, hematoxylin counterstain.

The dog was discharged the next day and healed without complications. At a follow-up examination 2 weeks postoperatively, the results of echocardiography were normal and the dog was treated with doxorubicin (30 mg/m² IV Doxorubicina, Teva Italia srl, Milan, Italy), administered over 20 minutes, once every 3 weeks for a total of five treatments. No chemotherapy side effects occurred.

The results of echocardiography 1 month after the last treatment were normal. The dog was examined clinically every three months, and there was no recurrence of the tumor at 30 months after the initial diagnosis.

Discussion

Primary intravascular sarcoma is rare in dogs and to our knowledge, only intra-arterial tumors have been reported and diagnosed histologically as aortic chondrosarcoma in 3 cases, pulmonary artery chondrosarcoma in 1 case, aortic angiosarcoma in 1 case, pulmonary artery poorly differentiated hemangiosarcoma in 1 case and pulmonary artery leiomyosarcoma in 1 case (Anderson *et al.*, 1988; Callanan *et al.*, 2000; Mellanby *et al.*, 2003; Ranck *et al.*, 2008; Cohen *et al.*, 2010; Lee *et al.*, 2011; Stieger-Vanegas *et al.*, 2016).

In people, primary intravascular sarcomas also are rare and may occur in great vessels of both the arterial and venous systems (Burke and Virmani, 1993). They are classified histologically as undifferentiated intimal sarcomas and differentiated sarcomas. Most of the latter are leiomyosarcomas and angiosarcomas (Burke and Virmani, 1993; Afzal *et al.*, 2015) and almost all intravenous sarcomas were classified as leiomyosarcomas (Burke and Virmani, 1993).

Leiomyosarcoma is rare in companion animals. In the dog, it is most common in the alimentary tract, spleen, and liver and is considered to have a moderate to high metastatic tendency (Kapatkin *et al.*, 1992). Pulmonary metastases were found in an adult dog euthanized

because of endoluminal arterial leiomyosarcoma (Callanan *et al.*, 2000). Of 12 people with venous leiomyosarcoma, 5 had high-grade leiomyosarcoma, 2 had distant metastases at the time of diagnosis, and 6 had distant metastases at the end of the study. All had pulmonary metastases, and the 3-year survival rate was 57% (Tilkorn *et al.*, 2010).

Based on a soft tissue grading system, the intravascular leiomyosarcoma described in this report was classified as grade II. It had an intermediate mitotic index and high Ki67 expression (Dennis *et al.*, 2011) suggesting malignant behavior (Ettinger *et al.*, 2006).

Because of the high risk of metastasis, adjuvant chemotherapy using a doxorubicin-based protocol was started; this is considered the best adjuvant treatment of dogs with high-grade soft tissue sarcoma (Ogilvie *et al.*, 1989) even though the efficacy of chemotherapy is not clear.

Edema in the head and neck region due to venous thrombosis or stasis did not occur in this dog, but was observed in 6 of 12 people with venous leiomyosarcoma (Tilkorn *et al.*, 2010). Despite the large size of the mass, the venous drainage of the head and neck could be afforded by the left external jugular vein and the internal jugular veins. Similarly, no local edema occurred after external jugular vein autografts were used to treat intrahepatic portosystemic shunts in dogs (Kyles *et al.*, 2001).

The diagnosis of leiomyosarcoma was based on histologic features (herringbone pattern, cigar-shaped nuclei), immunohistochemical expression of vimentin, desmin, and α SMA, and lack of expression of S100 (Frost *et al.*, 2003). An immunohistochemical panel that was recently introduced to better classify perivascular wall tumors was not used because frozen sections are required (Avallone *et al.*, 2007). Moreover, histological pattern was not characteristic of this group of tumours. Venous tumor may be considered as a differential diagnosis in dogs with ventral neck swelling.

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