Malignant peripheral nerve sheath tumour in a dog presenting as a pseudo aneurysm of the left jugular vein: a case report

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ABSTRACT: The authors report an autopsy case of a malignant peripheral nerve sheath tumour in a 9-year-old female Akito-ino dog, presenting as a pseudo aneurysm of the left jugular vein. Signs and symptoms included swelling of the neck and legs, dyspnea, malaise and weight loss. Post-mortem examination revealed a tumour mass (8 × 6, 5 × 6 cm), localized to the left paravertebrally, and on the level of C7 to T2 vertebral bodies; additional masses were observed in both lungs, heart and left kidney. On the basis of necropsy, histological findings and immunophenotype, the tumour was classsified as a malignant peripheral nerve sheath tumour. Immunohistochemistry especially positivity for S-100 protein can be helpful in distinguishing this type of neoplasm from other malignancies with similar morphologies.

Keywords: malignant peripheral nerve sheath tumour; dog; tumour

Malignant tumours arising from peripheral nerves or displaying differentiation along the lines of the various elements of the nerve sheath (Schwann cell, perineural cell, fibroblast) are collectively referred to as malignant peripheral nerve sheath tumours (MPNSTs). In human pathology this term replaces a number of previously used designations, including malignant Schwannoma, neurofibroma, sarcoma and neurogenic sarcoma (Enzinger and Weiss, 1995; Miettinen, 2003; Garcia et al., 2004; Fletcher, 2007; Ramirez et al., 2007).

The most common sites for MPNSTs are the proximal parts of lower and upper extremities, the paraspinal region of the trunk, and the head and neck region. Those arising from a major nerve commonly show fusiform swelling of the adjacent nerve and those originating from a pre-existing benign tumour may show a zoned appearance microscopically, although often this is not evident. Most commonly they occur in lungs, bones, pleura, and liver but a spread by the meningeal route is also possible. Histologically, most MPNSTs are high-grade tumours with a high mitotic rate and commonly induce necrosis. The most common histological patterns include a high-grade fibrosarcomatous mass composed of densely packed sheets of plump but relatively uniform spindle or oval cells; distinctive features that may suggest neural differentiation are the abrupt alternation between cellular and more myxoid areas and the apparent perivascular accentuation or whorling of tumour cells which sometimes extends directly into vessel walls and leads to thrombosis (Enzinger and Weiss, 1995; Miettinen, 2003; Fletcher, 2007).

MPNSTs, which are rare in domestic animals, have, nevertheless, been described in cattle, sheep, goats, horses, dogs and cats (Uchida et al., 1992; Ramirez et al., 2007). Canine MPNSTs may show variable histological patterns as seen with human MPNSTs, although their characteristics are not

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well established. Therefore, diagnosis of MPNSTs is often confused with other soft tissue tumours (Chijiwa et al., 2004).

This report describes the histomorphological and immunohistochemical characteristics of a MPNST in a 9-year-old female Akito-ino dog presenting as a pseudo aneurysm of the left jugular vein.

Case presentation

A 9-year-old female Akito-ino dog had been administered ambulatory medical care from September 1th, 2000 to October 1th, 2000 because of swelling of the left side of the head, neck and anterior extremities, and dyspnoea. On September 22nd 2000, an "aneurysm" of the left jugularis vein was surgically removed. After operation, oedemas disappeared but dyspnoea and poor mobility persisted. Subsequently, food intake also declined and the dog died on October 2nd, 2000.

The autopsy revealed an encapsulated tumour, localized on the left paravertebrally, by the C7 to T2 vertebrae, and adhering to the vertebral column. Grossly, the tumour was 8 × 6, 5 × 6 cm. An analysis of a cut section demonstrated that the tumour was firm, white to tan with areas of hemorrhage and necrosis. 150 ml of brown fluid was found in the thoracic cavity. The lung surfaces were covered by nodules, and in a cut section of the lungs dozens of nodules grey to white in colour, and of firm consistency, were observed. Fields of necrosis and bleeding were also discernible and white, small and firm nodules were found in the myocardial tissue.

Tissue samples from encapsulated tumour mass, liver, kidneys, lungs and heart were fixed in 10% buffered formalin, embedded in paraffin wax, sectioned at 5 μm thick sections and stained

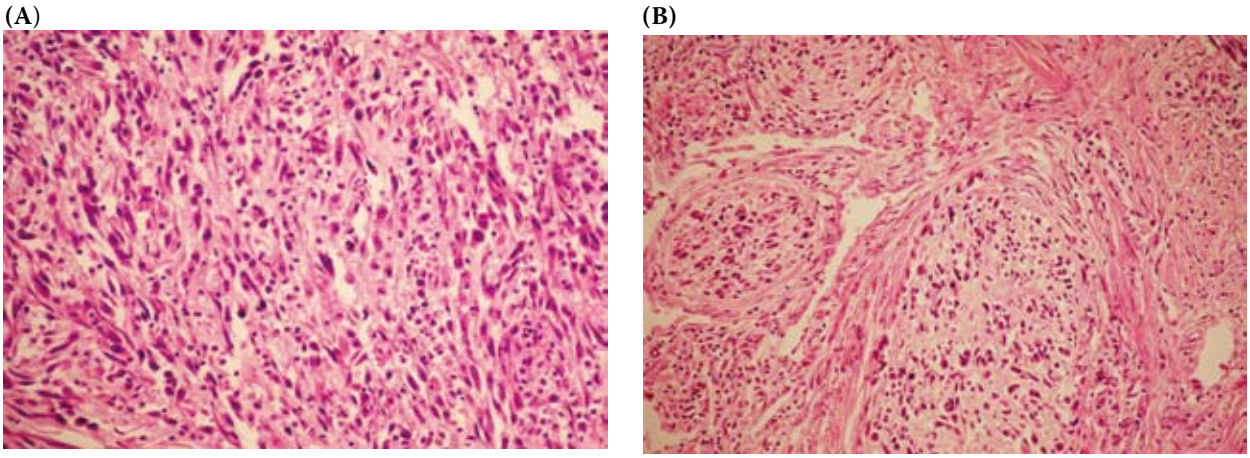

Figure 1. Malignant peripheral nerve sheath tumour. Spindle-shaped cells arranged in fascicles and sheats (A) and whorled structures within a tumour (B). (A and B, H&E, 200×)

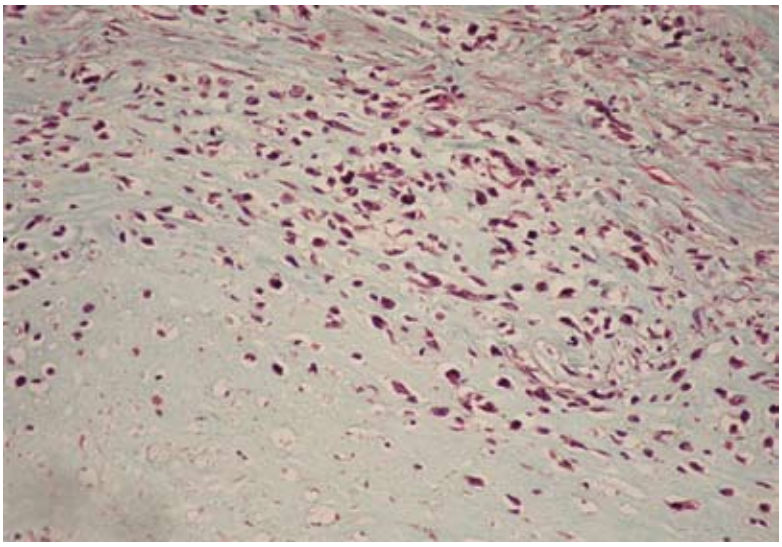

Figure 2. Cartilaginous metaplasia was present in a portion of the tumour mass (Masson's trichrome, 200×)

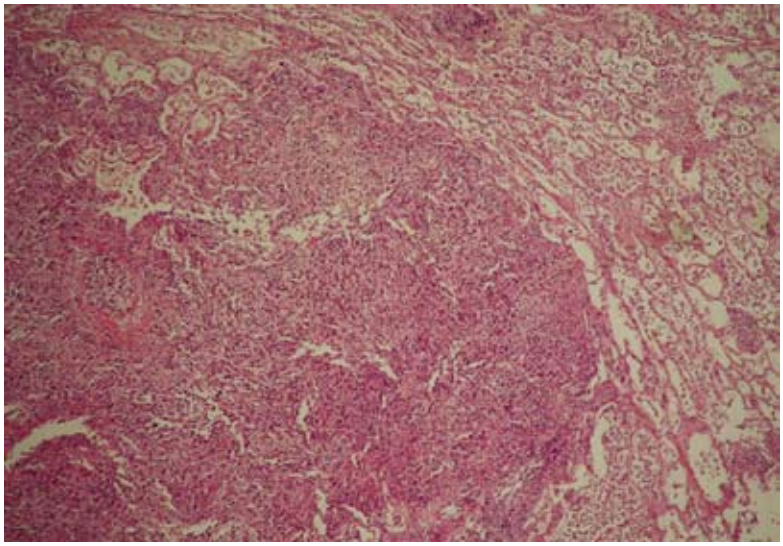

Figure 3. Metastatic deposit of malignant peripheral nerve sheath tumour in the lung (H&E, 100×)

with haematoxylin and eosin (H&E), Alcian Blue – periodic acid-Schiff (AB-PAS) and Masson's trichrome. Representative material was stained with a panel of antibodies using the labeled streptavidin-biotin-peroxidase complex method according to the manufacturer's instructions (LSAB Kit, Dako, Glostrup, Denmark). The primary antibodies used were mouse monoclonal antibodies for vimentin (VIM; clone V9), cytokeratin (CK; clone AE1/AE3), α-smooth muscle actin (SMA; clone 1A4), melanocytes (clone PNL2), and rabbit polyclonal antibody for S-100 protein. The chromagen was 3, 3'-diaminobenzidine (DAB), and the slides were lightly counterstained with Meyer's haematoxylin. All reagents were acquired from the Dako Company (Glostrup, Denmark).

Histologically, the tumourous mass was composed of a dense population of spindle-shaped cells arranged in fascicles, whorls or sheets (Figure 1a,b). Neoplastic cells had hyperchromatic, oval to ellipsoid nuclei, and fine eosinophilic cytoplasms. The tumour contained areas of heterotopic elements and mature islands of cartilage (Figure 2). Confluents necrotic areas and haemorrhagic foci could also be seen. Numerous mitotic figures were observed (> 10/high-power field). The periodic acid-Schiff reaction demonstrated small amounts of mucopolysaccaride between neoplastic cells. Unencapsulated metastatic growth was observed in lungs (Figure 3), left kidney and heart.

The nuclei and cytoplasm of the neoplastic cells were immunoreactive for S-100 protein (Figure 4) while the vimentin antibody was strongly and multifocally reactive in the cellular cytoplasm (Figure 5). Cytokeratin, SMA and PNL2 were completely negative.

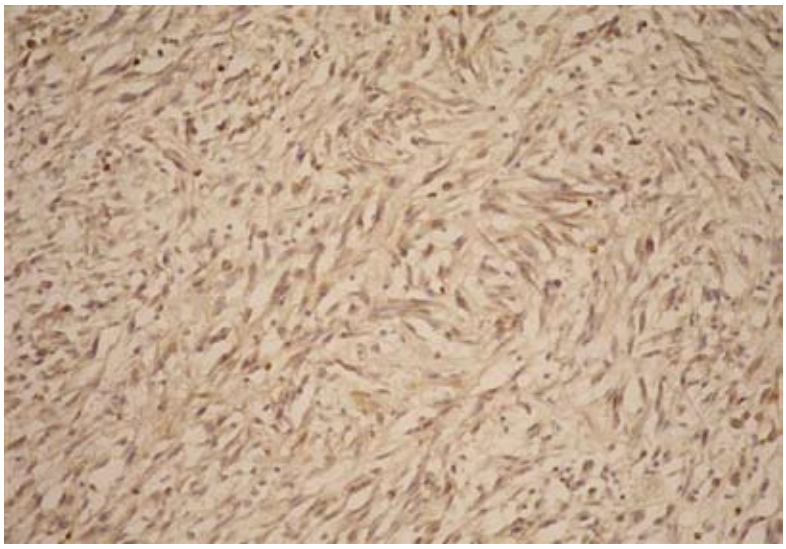

Figure 4. Diffuse immunoreactivity of the spindle-shaped tumour cells to S-100 protein (Streptavidin-biotin-peroxidase complex method, Meyer's haematoxylin counterstain, 200×)

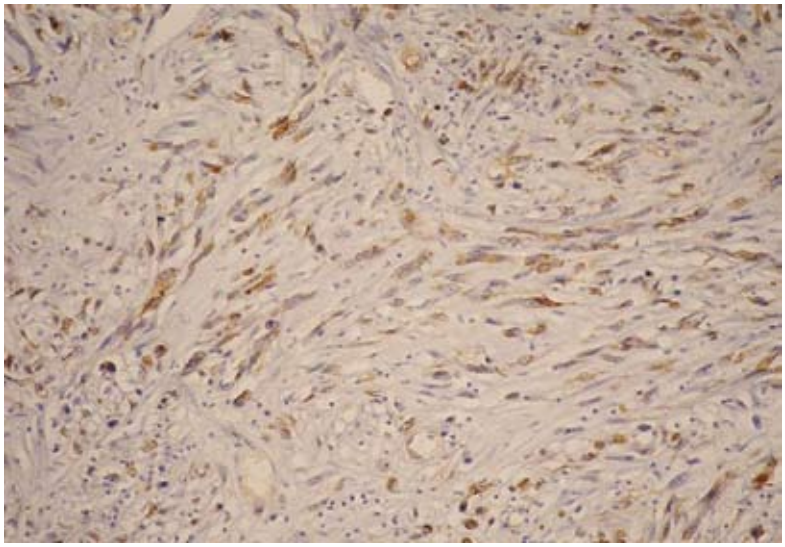

Figure 5. Focale intracytoplasmic immunoreactivity of the spindle-shaped tumour cells to vimentin (Streptavidin-biotin-peroxidase complex method, Meyer's haematoxylin counterstain, 200×)

Based on the morphological and immunohistochemical features, the tumour was classified as a MPNST with massive metastases in both lungs and heart, and micrometastases in the left kidney.

DISCUSSION

Malignant peripheral nerve sheath tumours arise from or differentiate toward cells within the endoneurium and perineurium. In a dog, these tumours arise sporadically and develop most commonly in cranial nerves, the spinal root and brachial plexus. For diagnosis of MPNST, one of following criteria must be met: (1) the tumour arises from a peripheral nerve; (2) the tumour arises from a preexisting benign or other malignant peripheral nerve sheath tumours; (3) the tumour displays histological features of Schwann or perineural cell differentiation as revelaed by immunohistochemistry or electron microscopy. Divergent differentiation in MPNSTs occurs in approximately 15% of cases (Huang et al., 2003).

In this case, histologically, there were areas of spindle-shaped to oval cells arranged in a fasciculated or whorled pattern, indicating the Antoni A pattern of schwannoma, distinct features that suggested neural differentiation.

It is relatively common to find metaplastic changes in nerve-sheath tumours, both benign and malignant. The most common secondary elements are cartilage and bone (Patnaik et al., 2002). In our case mature islands of cartilage were present. These findings are similar to those from human medicine (Enzinger and Weiss, 1995; Miettinen, 2003; Chijiwa et al., 2004; Fletcher, 2007).

The presence of heterologous elements containing mesenchymal and/or epithelial components is a rare feature in human nerve-sheath tumours, but very common in animal pathology (Patnaik et al., 2002; Huang et al., 2003; Garcia et al., 2004).

Brehm classified peripheral nerve sheath tumours into three anatomical groups: (1) a peripheral group including tumours involving nerves distal to the brachial or lumboscral plexus; (2) a plexus group comprised of tumours involving nerves of the brachial and lumbosacral plexus and those of spinal nerves distal to an intervertebral foramina; (3) a root group including tumours involving dorsal and ventral nerve roots and any tumours entering intervertebral foramina. The metastasis of MPNSTs into lungs has been reported in dogs, while in goats, this tumour developed systemic metastases (Okada et al., 2007).

Although systemic metastasis of this tumour is rarely seen in dogs, our case revealed massive metastases in lungs, heart and micrometastases in a cortex of the left kidney.

As differential diagnoses, fibrosarcoma, leiomyosarcoma and monophasic synovial sarcoma were considered. Also, because of the S-100 imunnopositivity of tumour cells, we considered a primary malignant melanoma as a differential diagnosis using clinical and melanoma markers. Establishing a diagnosis of MPNST can be difficult, and not always possible by classic histological examination.

In summary, this rare case report describes an advanced aggressive canine MPNST with metas-

tases in several internal organs. The use of immnunohistochemistry may be helpful in distinguishing this type of neoplasm from other malignancies with similar morphologies.

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