

**SHORT PAPER**

Primary Splenic Peripheral Nerve Sheath Tumour in a Dog

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Summary

An 8-year-old crossbred dog was presented with a one-month history of progressive weakness, respiratory impairment and abdominal distension. Surgical exploration revealed the presence of a splenic mass that infiltrated the mesentery and was adherent to the stomach and pancreas. The mass was composed of highly cellular areas of spindle-shaped cells arranged in interlacing bundles, streams, whorls and storiform patterns (Antoni A pattern) and less cellular areas with more loosely arranged spindle to oval cells (Antoni B pattern). The majority of neoplastic cells expressed vimentin, S-100 and glial fibrillary acidic protein (GFAP), but did not express desmin, α -smooth muscle actin or factor VIII. These morphological and immunohistochemical findings characterized the lesion as a malignant peripheral nerve sheath tumour (PNST). Primary splenic PNST has not been documented previously in the dog.

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Keywords: dog; peripheral nerve sheath tumour; spleen

Peripheral nerve sheath tumours (PNSTs) represent a heterogeneous group of lesions classified into benign schwannoma, benign neurofibroma, malignant schwannoma and neurofibrosarcoma (Hendrick *et al.*, 1998; Koestner *et al.*, 1999). Schwannomas originate from Schwann cells only, whereas neurofibromas and neurofibrosarcomas are mixed tumours composed of Schwann cells and perineural cells (Hendrick *et al.*, 1998; Goldschmidt and Hendrick, 2002). Some authors, however, prefer to distinguish only between benign and malignant PNSTs (Hendrick *et al.*, 1998; Goldschmidt and Hendrick, 2002) since differential diagnosis based upon morphology alone is difficult.

PNSTs are uncommon in animals and occur mostly in dogs, cattle and cats (Summers *et al.*, 1995; Hendrick *et al.*, 1998; Goldschmidt and Hendrick, 2002). Benign PNSTs (BPNSTs) of the nervous system are rare in dogs and cats and are found incidentally in cattle (Summers *et al.*, 1995; Koestner *et al.*, 1999). Malignant PNSTs (MPNSTs) of the nervous system

are most commonly seen in dogs (Koestner *et al.*, 1999).

Benign PNSTs of the skin are uncommon in cats and rare in dogs (Hendrick *et al.*, 1998). In cattle, multiple benign cutaneous PNSTs may arise within the subcutis and the nerve plexuses (Hendrick *et al.*, 1998; Goldschmidt and Hendrick, 2002). Malignant cutaneous PNSTs are uncommon in cats and extremely rare in large animals (Goldschmidt and Hendrick, 2002). The true incidence of canine dermal malignant PNST is difficult to estimate since confirmation of the diagnosis requires immunohistochemical examination that was not performed routinely in the past.

Although rare, PNSTs arising within the thoracic cavity and abdomen have been described in man (Bui *et al.*, 2004; Khan *et al.*, 2006; Rahman *et al.*, 2006; Vyas *et al.*, 2006; Tashiro *et al.*, 2007), horses (Pascoe, 1982; Andreasen *et al.*, 1993; Kirchhof *et al.*, 1996; Stoica *et al.*, 2001; Quinn *et al.*, 2005), dogs (Stoica *et al.*, 2001; Essman *et al.*, 2002; Aupperle *et al.*, 2007; Patterson *et al.*, 2008; Sugiyama *et al.*, 2008), cats (Stoica *et al.*, 2001) and cattle (Stoica *et al.*, 2001). Herein we report the clinical,

microscopical and immunohistochemical findings related to the occurrence of a PNST within the spleen of a dog. To the best of our knowledge, primary splenic PNSTs have not been described previously in man or animals.

An 8-year-old, neutered female, crossbred dog was presented with a one month history of progressive weakness, respiratory impairment and abdominal distension. Clinical examination revealed loss of general body condition, mild hypothermia (body temperature 37.6°C), low heart rate (64 beats/min) and a generalized mild increase in lung sounds on inspiration. The abdomen was distended, with palpable enlargement of the spleen. Haematological and serum biochemical examinations revealed the presence of a stress leucogram, thrombocytosis and mild hypoglycaemia. The urinary sediment was unremarkable. Ultrasonography confirmed the presence of a large splenic mass, with suspected rupture but minimal peritoneal effusion. There were no lesions suggestive of metastasis on thoracic radiography. On laparotomy, the mass was seen to infiltrate the mesentery and was attached to the fundic area of the gastric wall and to the distal left limb of the pancreas (Fig. 1). Aberrant vessels had formed between the splenic mass and the caudal pole of the left kidney. The tumour was dissected from the surrounding tissue and the aberrant vascular trunk ligated. After partial gastrectomy and pancreatectomy, the tumour was completely excised and had a weight of 600 g. Follow-

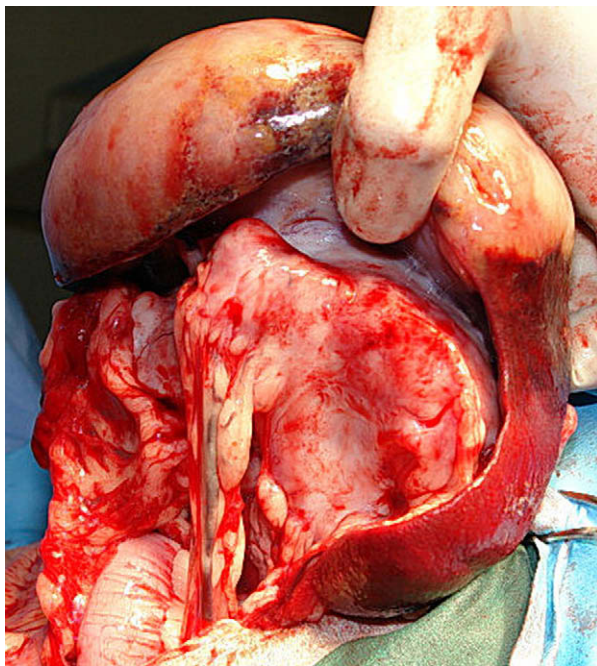


Fig. 1. Splenic tumour during surgery. The mass infiltrates the mesentery and is attached to the stomach and the pancreas.

ing discharge, the dog remained well for three months, but thereafter started to vomit. An ultrasound examination at this time revealed the presence of masses within the liver and mesentery. The dog was humanely destroyed without permission for necropsy examination.

The excised spleen contained a non-encapsulated, multilobulated, infiltrative, marbled mass (5 × 7.5 × 11 cm) of soft consistency. Representative samples taken from the lesion were fixed in 10% neutral buffered formalin, processed routinely and sections were stained with haematoxylin and eosin (HE). Serial sections were subject to immunohistochemical examination with the following primary antibodies (all from Dako, Glostrup, Denmark unless otherwise stated): rabbit polyclonal anti-factor VIII (1 in 400), rabbit polyclonal anti-S-100 (1 in 400; Zymed, San Francisco, USA), mouse monoclonal anti-Desmin (1 in 200; Novocastra Ltd, Newcastle UK), mouse anti- α -smooth muscle actin (1 in 2000), mouse anti-vimentin (1 in 20,000; Sigma, St Louis, USA), mouse anti-glial fibrillary acidic protein (GFAP; 1 in 3000) and rabbit polyclonal anti-human c-kit (1 in 200). Secondary detection was performed with an avidin–biotin–peroxidase kit according to the manufacturer's instructions (Vector laboratories, Burlingame, CA, USA).

Microscopically, the mass was non-encapsulated, poorly demarcated and replaced the majority of the splenic parenchyma. Neoplastic tissue infiltrated the surrounding adipose tissue and mesentery. The mass had a biphasic growth pattern. Some regions were highly cellular and composed of interlacing bundles and streams of spindle-shaped cells growing in a storiform pattern or as whorls around blood vessels and nerves. These cells had poorly defined eosinophilic fibrillar cytoplasm and spindle-shaped basophilic nuclei and were associated with variable amounts of collagenous stroma (Antoni A pattern; Fig. 2). Other areas were less cellular and composed of loosely arranged spindle to oval cells with inconspicuous cytoplasm and a small hyperchromatic round nucleus surrounded by a copious myxoid, often microcystic, matrix (Antoni B pattern). In these areas numerous lymphatic vessels were markedly dilated (Fig. 3). The mitotic rate in both areas was less than one per ×400 high-power field. Immunohistochemical labelling revealed that almost 100% of the neoplastic cells expressed cytoplasmic vimentin, S-100 and GFAP (Fig. 4), but there was no expression of desmin, α -smooth muscle actin, factor VIII or c-kit. These findings supported a diagnosis of a primary splenic malignant PNST.

On the basis of morphological appearance it is difficult to differentiate PNST from other mesenchymal tumours, particularly those of perivascular origin

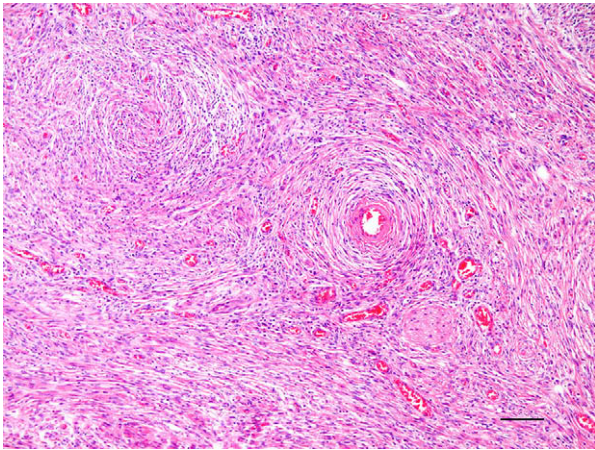


Fig. 2. Highly cellular area composed of interlacing bundles, streams and whorls of spindle-shaped cells (Antoni A pattern). HE. Bar, 50 μ m.

(Stoica *et al.*, 2001; Goldschmidt and Hendrick, 2002). Definitive diagnosis requires immunohistochemistry (IHC), electron microscopy or genetic analysis (Stoica *et al.*, 2001). No specific immunohistochemical markers are able to define a PNST, so a panel of reagents is generally employed. PNSTs are, like all spindle cell tumours, positive for vimentin, indicating a mesenchymal origin (Pérez *et al.*, 1996; Chijiwa *et al.*, 2004). S-100 identifies Schwann cells and consequently most PNSTs express this molecule (Koestner *et al.*, 1999; Chijiwa *et al.*, 2004). There may be variable expression of GFAP, nerve growth factor receptor (NGFR) and neuron specific enolase (NSE) (Koestner and Higgins, 2002; Chijiwa *et al.*, 2004). However, other tumours may also express the combination of S-100, GFAP, NGFR and NSE (Chijiwa *et al.*, 2004). The inclusion of antibodies specific

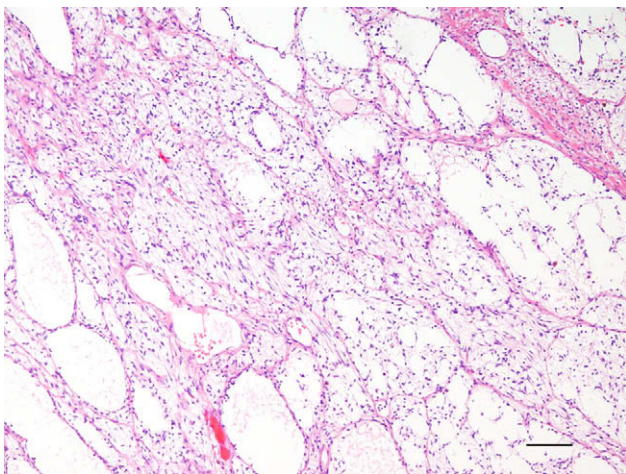


Fig. 3. Area of less cellular, more loosely arranged spindle cells, surrounded by a copious myxoid matrix (Antoni B pattern). HE. Bar, 50 μ m.

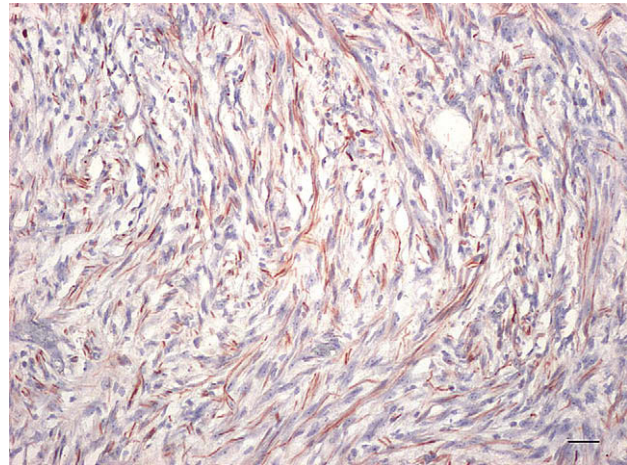


Fig. 4. Neoplastic spindle cells with cytoplasmic expression of GFAP. IHC. Bar, 50 μ m.

for factor VIII, desmin and α -smooth muscle actin in the diagnostic panel can assist in distinguishing tumours of vascular or myofibroblastic origin. Use of immunolabelling for c-kit can exclude the possibility of gastrointestinal stromal tumour (GIST). In the present case, confirmation of the identity of this tumour was only made possible following evaluation of the lesion immunohistochemically with such a panel of antisera.

Acknowledgment

The authors thank Dr. Chiara Brachelente for performing the c-kit immunohistochemistry.

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[Received, October 29th, 2008]
 [Accepted, March 30th, 2009]