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Concomitant Malignant Pulmonary Peripheral Nerve Sheath Tumour and Benign Cutaneous Peripheral Nerve Sheath Tumour in a Dog

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Summary

Peripheral nerve sheath tumours (PNSTs) are neoplastic growths derived from Schwann cells, perineural cells or both. Malignant PNSTs (MPNSTs) are uncommon in domestic animals. This report describes the concomitant occurrence of PNSTs in a 10-year-old female cocker spaniel with a clinical history of respiratory impairment. Grossly, there was a large infiltrative mass in the caudal lobe of the right lung; smaller nodules were observed in the other lobes of the right lung. Furthermore, a small encapsulated cutaneous nodule was observed on the left hindlimb. Histopathology of the pulmonary tumours revealed the proliferation of pleomorphic spindle-shaped cells with moderate mitotic index arranged in interwoven bundles and concentric Antoni A and Antoni B patterns; invasion of the adjacent pulmonary tissue was observed. The cutaneous nodule consisted of neoplastic mesenchymal cells in interwoven bundles with concentric whorls, but without the marked anisokaryosis, binucleation and infiltrative growth seen in the pulmonary tumour. Immunohistochemistry revealed that both tumours were immunoreactive for vimentin, glial fibrillary acidic protein and S100 protein, but were negative for factor VIII. These findings are indicative of a MPNST in the lung with a concomitant benign PNST in the limb. This case represents the first report of a primary MPNST in the lung of a dog. This neoplastic growth should be included in the differential diagnosis of primary malignant pulmonary tumours of dogs.

Keywords: dog; immunohistochemistry; lung; malignant peripheral nerve sheath tumour

Peripheral nerve sheath tumours (PNSTs) are a heterogeneous group of neoplasms of the peripheral nerves that originate from Schwann cells, perineural cells or both (Gross *et al.*, 2005; Suzuki *et al.*, 2014). In veterinary medicine, this group of neoplasms is often referred to as PNSTs because there is no distinct histopathological subclassification and it is difficult to perform ancillary tests to determine the specific cell of origin; moreover, there are no prognostic differences between subtypes of PNSTs (Koestner and Higgins, 2002; Gross *et al.*, 2005). Although primary PNSTs are uncommon in domestic animals, there are reports in dogs, cats, pigs, sheep, horses, goats and cattle (Ramires *et al.*, 2007; Sugiyama *et al.*, 2008; Boonsriroj *et al.*, 2014; Grossi *et al.*, 2014; Kegler *et al.*, 2014; Resende *et al.*, 2015).

Older dogs are more predisposed to develop PNSTs and there is no apparent sex predisposition (Koestner and Higgins, 2002). PNSTs described in domestic animals are frequently located unilaterally and originate from spinal nerves or the brachial plexus. Less

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common sites of origin are the lumbosacral plexus, and subcutaneously at sites of distal peripheral nerves, on the trunk, distal legs or internal viscera (Brehm *et al.*, 1995; Koestner and Higgins, 2002; Gross *et al.*, 2005; Suzuki *et al.*, 2014). In dogs, primary PNSTs have been described in the central nervous system (Pumarola *et al.*, 1996), vagus nerve (Yap and Pratschke, 2016), myocardium (Wohlsein *et al.*, 2005; Thomason *et al.*, 2015), testis (Rothwell *et al.*, 1986), liver (Park *et al.*, 2011), ocular region (Duke *et al.*, 2015; Kang *et al.*, 2017), spleen (Bergmann *et al.*, 2009; Suzuki *et al.*, 2014), gingiva, nasal cavity (Suzuki *et al.*, 2014), tongue (Baratt *et al.*, 2015) and the diaphragm (Patterson *et al.*, 2008). To our knowledge, there are no reports of a primary pulmonary PNST in the dog.

PNSTs are usually nodular or lobulated masses that can range from soft to firm in consistency, white to grey in colour, and usually have a shiny and smooth surface (Koestner and Higgins, 2002; Gross *et al.*, 2005). Benign PNTs are well-circumscribed, encapsulated nodules or masses that are microscopically composed predominantly of small spindle-shaped cells embedded in a delicate collagenous stroma (Koestner and Higgins, 2002). The tumour cells are arranged as interwoven bundles, streams or concentric whorls (Antoni type A pattern) and can have areas of reduced cellular density, where the cells have small dark nuclei and are embedded in a loose fibrous stroma (Antoni type B pattern). The neoplastic cells may also show palisading or herringbone patterns (Gross *et al.*, 2005) and they have mild cellular pleomorphism and rare mitotic figures (Koestner and Higgins, 2002).

Malignant PNSTs (MPNSTs) are rare in man (Farid *et al.*, 2014) and domestic animals (Gross *et al.*, 2005; Suzuki *et al.*, 2014). Grossly, MPNSTs differ from benign PNSTs by being unencapsulated. Microscopically, MPNSTs consist of pleomorphic cellular populations with increased mitotic activity, intratumoural necrosis, haemosiderin deposition, infiltrative growth into surrounding tissue and metastasis to distant organs (Stoica *et al.*, 2001; Gross *et al.*, 2005). Moreover, MPNSTs may show areas of glandular, cartilaginous or osteoid differentiation (Chijiwa *et al.*, 2004; Gross *et al.*, 2005). This growth pattern explains the higher recurrence after surgical excision compared with benign PNSTs (Gross *et al.*, 2005).

A definitive diagnosis of PNST is obtained by histopathological evaluation, while immunohistochemistry (IHC) is required to distinguish these tumours from other sarcomas. PNSTs express S100 protein, glial fibrillary acidic protein (GFAP), vimentin, collagen IV and laminin (Koestner and Higgins, 2002; Suzuki *et al.*, 2014). This report describes the gross, histopathological and immunohistochemical findings in a primary pulmonary MPNST with a simultaneous benign cutaneous PNST in a dog.

A 10-year-old female cocker spaniel dog was presented to the Veterinary Teaching Hospital, Universidade do Oeste Paulista, São Paulo, Brazil, with a history of difficulty breathing. Clinical examination revealed tachypnoea and tachycardia. Thoracic radiography demonstrated a mass in the right lung with compression of the left lung and the heart. There was no history of previous tumours. The clinical status of the animal worsened, cardiorespiratory arrest was diagnosed and the dog died on the same day despite supportive therapy.

A routine necropsy examination performed soon after death revealed a large, 13 cm diameter, multilobulated soft white mass with firm areas, in the right caudal pulmonary lobe (Fig. 1); similar but smaller (1–8 cm diameter) nodules were observed in other lobes of the same lung. The left lung was congested, without the presence of masses. In addition, a 0.5 cm diameter cutaneous nodule was observed on the left hindlimb. Other significant gross findings included mild left ventricular concentric myocardial hypertrophy. Lymph node enlargement was not observed. Samples of the lungs and the pulmonary mass, as well as the cutaneous nodule, were collected, fixed in 10% neutral buffered formalin and processed routinely for embedding in paraffin wax. Sections were stained by haematoxylin and eosin and subjected to IHC using primary antisera specific for vimentin (V9 antibody at 1 in 100 dilution; Invitrogen, São Paulo, Brazil), GFAP (polyclonal antibody at 1 in 100 dilution; Zymed, San Francisco, California, USA), S100 protein (polyclonal antibody at 1 in 100 dilution; Zymed) and factor VIII

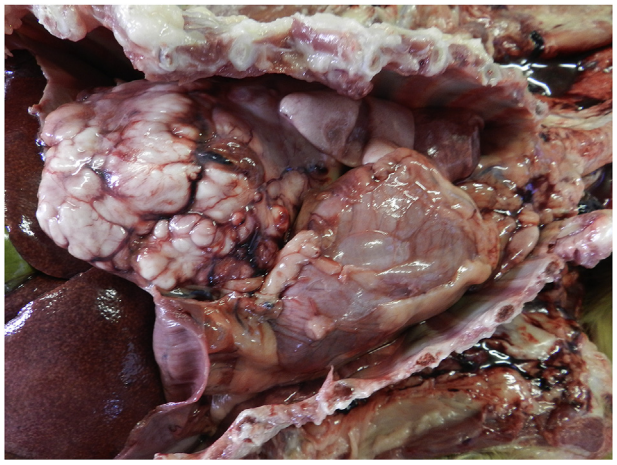

Fig. 1. White multilobular mass in the caudal right lung.