COMPANION OR PET ANIMALS

Inflammatory pseudotumour arising in the epidural space of a dog

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SUMMARY
A one-year five-month-old labrador retriever was presented with acute-onset pelvic limb ataxia, gradually progressing to paraplegia. CT and MRI demonstrated an extradural mass lesion at T11 and T12. The dog underwent haemilaminectomy, dorsal laminectomy and resection of the mass. Results of histopathology and immunohistochemistry suggested that the mass was an inflammatory pseudotumour (IPT). The dog’s condition improved after surgery, with no recurrence of clinical signs eight months after surgery. To the author’s knowledge, this is the first report of IPT arising in the epidural space in dogs. Although rare, IPT should be included as a possible differential diagnosis for extradural mass in dogs. Excision may result in a good outcome in dogs with IPT in the epidural space.

BACKGROUND
Inflammatory pseudotumour (IPT) is a tumour-like lesion characterised by myofibroblastic spindle cells accompanied by mixed inflammatory cell infiltrates of lymphocytes, plasma cells, eosinophils and histiocytes (Coffin and Fletcher 2002, Gartner and others 2002, Böhme and others 2008, Gleason and Hornick 2008, Loderstedt and others 2010). IPTs are well recognised in the human literature as focal and benign mass lesions that may occur at any location in the body. In the veterinary literature, on the other hand, there are only few reports (Gartner and others 2002, Böhme and others 2008, Knight and others 2009, Tursi and others 2009, Loderstedt and others 2010, Swinbourne and others 2014). Here, we report an extremely rare canine case of IPT arising in the epidural space.

CASE PRESENTATION
A one-year five-month-old castrated male labrador retriever presented with a two-month history of progressive ataxia and paraplegia in the pelvic limbs. The dog was bright and alert but unable to walk. On physical examination, the dog displayed non-ambulatory paraplegia, and abdominal palpation revealed an enlarged urinary bladder. Neurological examination revealed hyperreflexia and absence of superficial pain perception in both pelvic limbs. Neuroanatomical localisation was to the T3–L3 spinal cord segments. Complete blood cell count and blood chemical analysis results were within reference ranges, and thoracolumbar radiography showed no remarkable changes.

INVESTIGATIONS
CT revealed a mass as a region of slightly increased density in the spinal canal at levels T11 and T12. There was no vertebral erosion. MRI demonstrated a 1.6×0.8 cm relatively well-circumscribed extradural mass, which showed isointensity on T1-weighted (T1W) and T2-weighted (T2W) images (Fig 1). Contrast-enhanced T1W images after intravenous injection of gadolinium revealed mild homogenous contrast enhancement of the mass. The spinal cord was compressed by the mass from the dorsal aspect. CT and MR findings were consistent with a mass lesion in the epidural space.

OUTCOME AND FOLLOW-UP
Histological examination revealed that the mass was mainly composed of spindle cells with abundant lymphoplasmacytic infiltration. The spindle cells had mildly anisokaryotic nuclei, little mitotic activity and no abnormal mitoses (Fig 2a). Immunohistochemical evaluation showed that almost all the spindle cells were positive for vimentin (Fig 2b) and smooth muscle actin (SMA) (Fig 2c), whereas a few subsets of the spindle cells were positive for desmin. The spindle cells were negative for cytokeratins and S-100 protein. Immunohistochemical results were consistent with a myofibroblastic derivation of the spindle cell population. From these findings, the diagnosis of IPT was made.

The dog improved steadily after surgery with no neurological deficit. Follow-up MR imaging was performed 10 days after surgery. No lesion was observed and recurrence was not detected. At present, eight months postoperatively, the dog has no recurrence of clinical signs.

DISCUSSION
The pathogenesis of IPT remains unknown; however, various causes have been suggested, such as an immunological host response to infectious agents, fibrogenic cytokine production and neighbouring necrotic tissue or chronic inflammation (Coffin and Fletcher 2002, Gartner and others 2002, Böhme and others 2008, Loderstedt and others 2010). For this reason, the lesions diagnosed as IPT have a broad spectrum of biological behaviour ranging from benign tumour-like lesions to malignant tumours, and there is an ongoing debate as to whether the nature of IPT is an inflammatory, reactive or a self-limiting neoplastic process (Böhme and others 2008, Gleason and Hornick 2008, Loderstedt and others 2010). Inflammatory myofibroblastic tumour (IMT) is a lesion belonging...
to the IPT group and is known to display malignant rather than benign behaviour (Böhme and others 2008).

In dogs, spleen (Gartner and others 2002) and meningeal (Loderstedt and others 2010) IPTs and nasal (Swinbourne and others 2014), mitral valve (Tursi and others 2009), orbital, cutaneous (Knight and others 2009) and bladder IMTs (Böhme and others 2008) have been described. In these reports, IPT and IMT displayed similar findings. On microscopic examination, masses were composed of a mixture of spindle cells and marked infiltration with inflammatory cells (Gartner and others 2002, Böhme and others 2008, Knight and others 2009, Tursi and others 2009, Loderstedt and others 2010, Swinbourne and others 2014). The spindle cell population demonstrated slight-to-moderate atypia and little mitotic activity (Gartner and others 2002, Böhme and others 2008, Knight and others 2009, Tursi and others 2009, Loderstedt and others 2010, Swinbourne and others 2014). The spindle cell population demonstrated slight-to-moderate atypia and little mitotic activity (Gartner and others 2002, Böhme and others 2008, Knight and others 2009, Tursi and others 2009, Loderstedt and others 2010, Swinbourne and others 2014). Immunohistochemical characteristics of the spindle cells were strong diffuse expression of vimentin, variable expression of SMA and desmin and no expression of cytokeratin and S-100 protein (Gartner and others 2002, Böhme and others 2008, Knight and others 2009, Tursi and others 2009, Swinbourne and others 2014).

In human beings, the degree of myofibroblastic differentiation expressed by muscle markers varies among cases and locations within a mass (Böhme and others 2008, Gleason and Hornick 2008, Swinbourne and others 2014). Because of this variable expression, it is difficult to distinguish IMT from IPT on the basis of immunohistochemical findings alone. Therefore, evaluation of microscopic features remains the main tool to diagnose IMT (Böhme and others 2008, Gleason and Hornick 2008, Swinbourne and others 2014). In human IMT, characteristic histological patterns include fasciitis-like, compact spindle cell and hypocellular fibrous patterns, which are often seen in combination within the same mass lesion (Coffin and others 1995, Coffin and Fletcher 2002, Coffin and others 2007, Gleason and Hornick 2008). Typically, the spindle cells have plump ovoid to tapering nuclei, palely eosinophilic cytoplasm and one or two small nucleoli. Approximately one half of cases contain ganglion-like cells: larger polygonal cells with abundant

FIG 1: MRI reveals a mass lesion (arrow head), which compressed the spinal cord (arrow) from the dorsal direction in the epidural space at the T11–T12 levels. The mass lesion is isointense to the spinal cord parenchyma on T2-weighted sagittal (a), transverse images (b) and T1-weighted image (c). The postcontrast T1-weighted transverse (d) and dorsal (e) images reveal a mild homogenous enhancing. There is no abnormality in the adjacent bone.

FIG 2: Section of tissue removed from epidural space demonstrates proliferation of spindle cells with an infiltrate of lymphocytes and plasma cells. The spindle cells had mildly anisokaryotic nuclei, little mitotic activity and no abnormal mitoses (a) H&E, ×400. Immunohistochemical staining of the spindle cells shows diffuse strong reactivity for vimentin (b) and smooth muscle actin (c) ×400.
amphophilic to eosinophilic cytoplasm, large vesicular nuclei and eosinophilic nucleoli. Mitotic activity is generally low and atypical mitoses are rare. These changes have also been observed in dogs (Böhme and others 2008, Tursi and others 2009). In our case, there was no evidence for diagnosing IMT definitely. Consequently, the authors judged that IPT was more fitted for a diagnosis rather than IMT.

In the future, histopathological and immunohistochemical findings, together with biological behaviour, of mass lesions of myofibroblastic origin need to be accumulated. To diagnose IMT, pathologists need to consider various aspects and to make a consensus. Recently, expression of anaplastic lymphoma kinase (ALK) and mutations of ALK-related gene have been proposed as useful in diagnosing IMT in human beings (Coffin and Fletcher 2002, Coffin and others 2007, Gleason and Hornick 2008). If the presence of these molecules were confirmed by clonality studies, clonal characteristics including ALK might be added as one of the criteria for diagnosing IMT in dogs.

The differential diagnosis considered in extradural mass without bone destruction includes lymphoma, myelolipoma, steatitis and empyema (Lavely and others 2006, Ueno and others 2007, De Stefani and others 2008, Aikawa and others 2008, De Stefani and others 2010), which differ from the signal intensity in our case. However, the signal intensity on the T2W images is thought to be variable within the IPT (Seol and others 2005). Therefore, hypointensity on T2W images is not diagnostic for IPT. Without a histopathological evaluation, differentiating the diagnoses is difficult.

In the present case, immunohistochemical characteristics of the spindle cells, only slight adhesion of the tumour to the dura mater and lack of bone involvement indicated that the lesion did not derive from the dura mater, periosteum or nerve root. However, the fact that it occurs in a variety of anatomic sites suggests that IPT may arise in any tissue in which myofibroblasts are inherent. It was presumed that the origin of the mass might have been myofibroblasts residing in the ligamentum flavum.

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Contributors TK wrote the first draft of the manuscript and rewrote new drafts based on input from coauthors. TK and NW took MRI and CT, and performed surgery. YS provided a pathological diagnosis. MS carried out physical and neurological examinations, X-ray and blood test, and planned diagnostic imaging. All authors read and approved the final manuscript.

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