

CASE REPORT

Spinal epidural and synovial lipomatosis in a 3-year-old Eurasian dog receiving sustained steroid therapy

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Abstract

This report describes a spinal cord epidural and synovial lipomatosis in a 3-year-old neutered male Eurasian dog. This dog presented for ambulatory paraparesis and was previously treated with immunosuppressive dosages of prednisolone for 2 years. Computed tomography (CT) myelography and magnetic resonance imaging (MRI) images identified dorsal compression of the thoraco-lumbar spinal cord by hypertrophic epidural fat. Histological examination identified extensive well-differentiated mature adipose tissue in the subepithelial area of the tarsal synovium. Prednisolone is a reported predisposing factor in humans with lipomatosis.

KEYWORDS

dog, epidural lipomatosis, fatty infiltration, synovial lipomatosis

1 | INTRODUCTION

Lipomatous tissue is defined as an overgrowth of non-encapsulated adipose tissue (Bancroft et al., 2006). The pathological manifestations are mostly mature adipocyte tissue without biological characteristics of malignant neoplasia. The pathogenesis remains elusive, but an association with chronic inflammation (Fujita et al., 2016; Rao et al., 2011) or abnormal lipid metabolism (Zhang et al., 2021) has been suspected in the human literature (Fujita et al., 2016; Rao et al., 2011). Prolonged exogenous steroid use, exposure to high level of endogenous steroid, obesity and post-surgical changes have been thought to be involved in the pathogenesis of spinal epidural lipomatosis in people (Kim et al., 2019; Zhang et al., 2021). Trauma, chronic inflammation and short bowel syndrome were described as comorbidities of synovial lipomatosis in human cases (Malkoc & Korkmaz, 2018). In dogs, this condition has been anecdotally reported to affect the parotid salivary glands (Madarama et al., 2015; Pellegrino et al., 2019), pancreas (Muresan et al., 2019), subcutaneous tissues (Sechi et al., 2016), synovium (Orekhova & Schwarz, 2021) and epidural lumbosacral space (Meij et al., 1996). This report describes the first case of synovial and thoraco-lumbar epidural lipomatosis in a young adult Eurasian dog.

2 | CASE HISTORY

A 3-year-old male neutered Eurasian dog was presented for evaluation of a several-week history of ambulatory hindlimb paresis, urinary incontinence and loss of appetite. The dog had previously been diagnosed with lymphoplasmacytic enteritis and follicular colitis by endoscopic biopsies 2 years before consultation. An immunosuppressive treatment of prednisolone at 2 mg/kg per day initially then tapered to a current dose of 0.7 mg/kg per day, associated with omeprazole (1 mg/kg twice daily), had then been initiated for 2 years. A hydrolysed diet had also been prescribed. Then, 3 months prior to presentation, the dog had been diagnosed with a non-erosive immune-mediated polyarthritis based on mild synovial neutrophilic pleocytosis, normal joint radiography and negative serology for anaplasmosis, ehrlichiosis, borreliosis and leishmaniasis. Cyclosporin (Atopica, Elanco), and 1 month later, leflunomide (Arava, Sanofi) was added to the prednisolone.

Upon presentation, mild paraparesis was noted. Diffuse spinal pain upon palpation of the thoraco-lumbar segment was elicited. Postural reactions and spinal reflexes were normal. We suspected T3-L3 myelopathy or osseous spinal affection: discospondylitis, spinal

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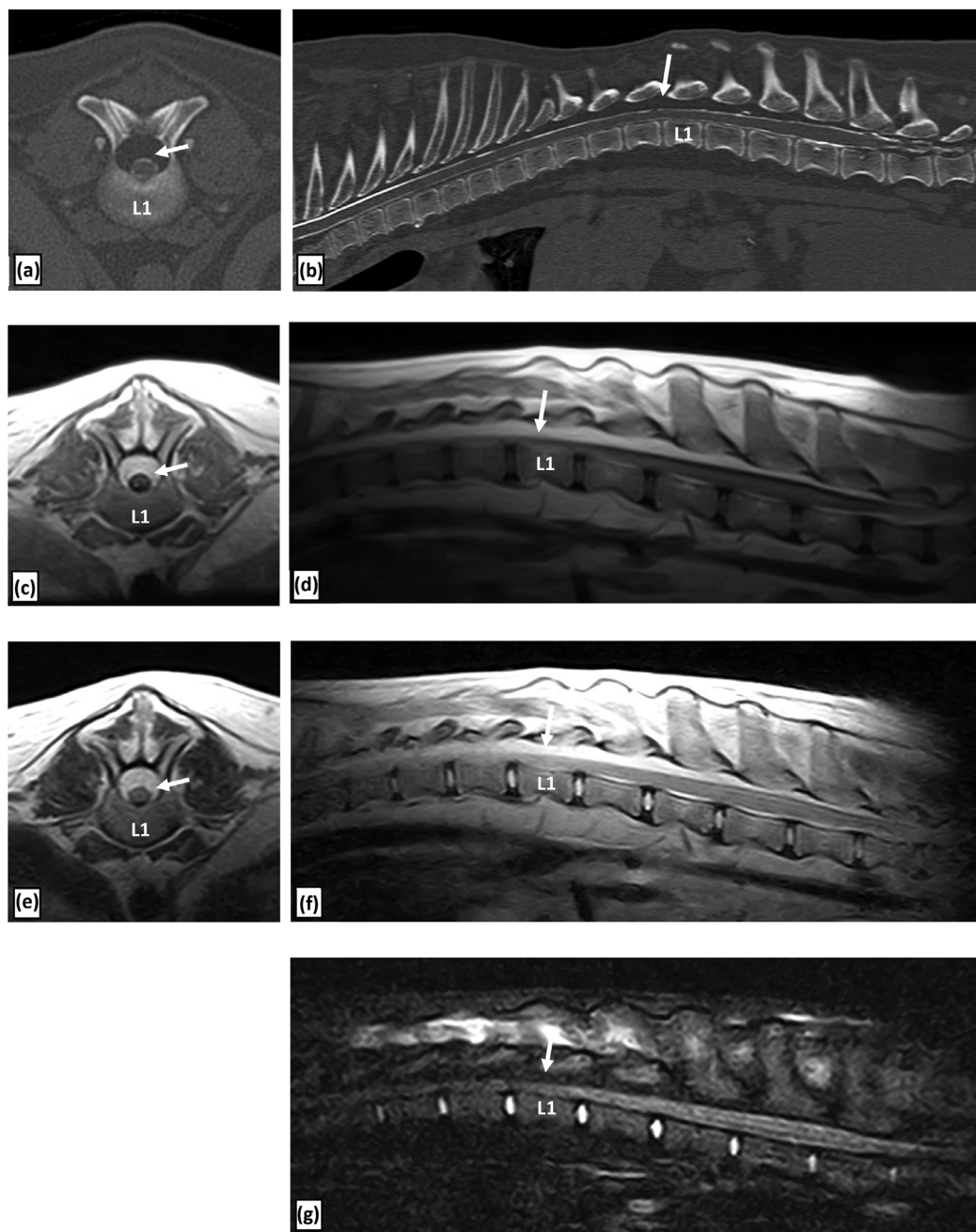


FIGURE 1 CT and MRI images showing epidural fat tissue (white arrow) extending dorsally to the spinal cord and associated with spinal cord atrophy. (a-b) Transverse and sagittal views of CT myelography showing thick dorsal epidural fat tissue at the first lumbar vertebrae (L1) and at the T8-L3 level, respectively. (c-d) Transverse (at the level of L1) and sagittal thoracolumbar T1 weighted MRI images showing extensive hyperintense material dorsally to the spinal cord. (e-f) Transverse and sagittal thoracolumbar T2-weighted MRI images showing hyperintensity of the material, which appeared hypointense on the fat-suppression sequence (G).

neoplasia, meningitis, spine malformations and less likely disc herniation or relapse of the polyarthritides were discussed.

Haematology revealed mild leucocytosis ($22.8 \times 10^9/L$) with mature neutrophilia ($20.3 \times 10^9/L$) and lymphopenia ($0.68 \times 10^9/L$). Biochemistry analysis revealed marked increases in alkaline phosphatase (5710 U/L), alanine aminotransferase (1389 UI/L) and gamma-glutamyltransferase (1433 U/L). These results were considered consistent with chronic steroid administration. This suspicion was confirmed

by liver aspirations showing clusters of hepatocytes with granular cytoplasm with uncolored storage material compatible with glycogen or lipids. The C-reactive protein level ($<7 \text{ mg/L}$, reference value $<7 \text{ mg/L}$) was within normal limits.

CT myelography (CT scanner, General Electric Brivo CT 385) revealed an extradural mass extending from the T8 to L3 vertebral canal segment causing spinal cord atrophy, mild dorsal compression and ventral displacement of the spinal cord (Figure 1). The mass had a

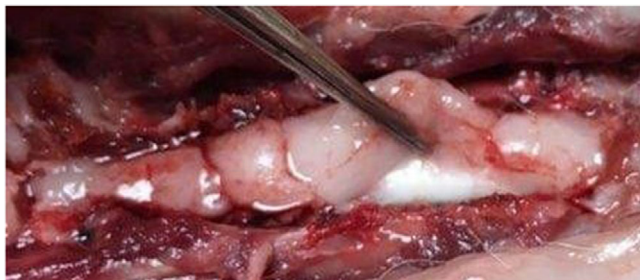


FIGURE 2 Macroscopic post-mortem finding, dorsal view at the level of T12-L1 after dorsal laminectomy. An extensive adipose mass is laterally displaced by the clamp to expose the spinal cord

density of -129 Hounsfield units and was not enhanced after injection of contrast agent (Gadoteridol (Pro Hance, Bracco) 0,5 mmol/ml, intravenous injection of 0,2 ml/kg). On MRI (MRI, Esaote Vet MR Grande 0,25 T), this material appeared hyperintense on T1- and T2-weighted images and hypointense on short T1 inversion recovery sequences, which was consistent with fat.

The dog was hospitalised and treated with buprenorphine, fluid therapy (Ringer lactate 2 ml/kg/h) and prednisolone (1 mg/kg per day). Leflunomide and cyclosporine therapies were tapered. Because of the lack of improvement after 6 days of medical management, the dog was humanely euthanised at the owner's request.

At necropsy, the mass was easily removed from the vertebral canal without adhesion to the dura mater (Figure 2). Histopathological examination with haematoxylin and eosin (H & E) staining was conducted. The tissue was composed of mature adipocytes, consisting of large polyhedral cells with abundant clear vacuoles and with eccentrically located small flattened and hyperchromatic nuclei. Adipocytes were tightly packed together and separated by thin fibrovascular tissue (Figure 3). The spinal cord was normal. The same mature adipose tissue was observed in subepithelial tissue of the tibio-tarsal synovial membrane. The synovium appeared moderately hyperplastic (Figure 4). The subepithelial tissue was richly neovascularised with few haemorrhagic areas and very scarce lymphoplasmacytic infiltrates. Overall, the histologic features were consistent with spinal epidural lipomatosis and tibio-tarsal synovial lipomatosis. Jejunum examination confirmed decidual lymphoplasmacytic enteritis. Chronic fibrous pancreatitis with hyperplasia of the pancreatic endothelium was observed. The liver examination was compatible with prolonged steroid administration.

3 | DISCUSSION

This report describes spinal epidural and synovial lipomatosis in a 3-year-old male Eurasian dog receiving chronic steroid and immunosuppressive treatment.

Pain, limb weakness and urinary incontinence are reported in people with spinal epidural lipomatosis (Fogel et al., 2005) and were also observed in this report. Long-term steroid treatment is the main factor associated with spinal epidural lipomatosis in humans (Spinnato et al.,

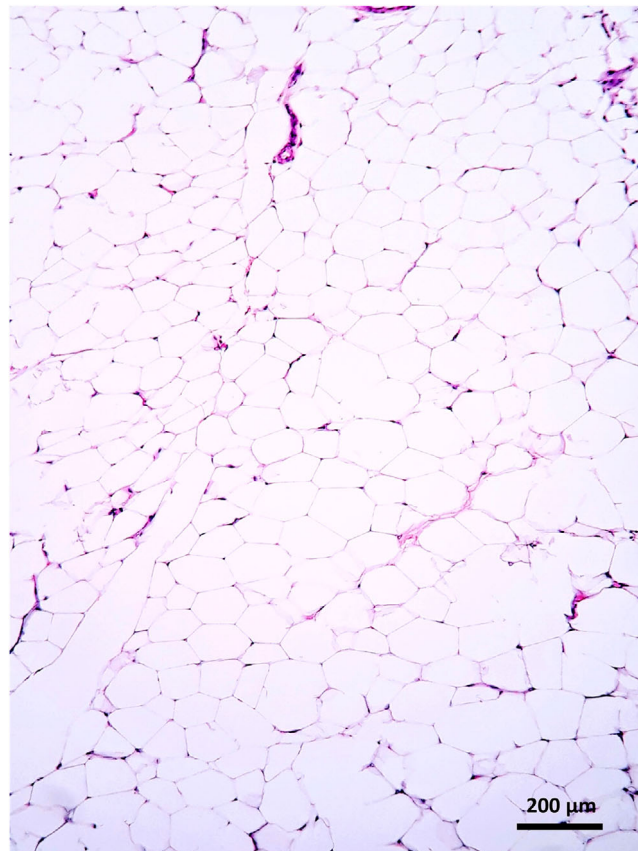


FIGURE 3 Histopathological examination of epidural lesions demonstrating lobules of mature adipose tissue (H & E, X100)

2021). It is reported in 55% (Fogel et al., 2005) to 75% (Stern et al., 1994) of cases, especially in the thoracic segment. Long-term steroid treatment, frequently reported in humans with lipomatosis, could have facilitated the overgrowth of spinal epidural fat tissue. Other associated factors, endogenous excess secretion of steroids and obesity (Fogel et al., 2005) were not suspected in our case.

Lipomatosis has been reported less commonly in the synovium in humans (Howe & Wenger, 2013) and recently in the stifle of a dog (Orehkova & Schwarz, 2021). Clinical features of synovial lipomatosis include pain and swollen joints (Rao et al., 2011), which was described by the referring veterinarian at the time of polyarthritis suspicion. Histological diagnosis of synovial lipomatosis is difficult, as the subcellular connective tissue of the synovial membrane can be adipose depending on the location in the joint (Eurell & Frappier, 2013). We can therefore not strictly conclude synovial lipomatosis. Examination of other synovial membranes or comparison with the control sample should have been done. One case of synovial lipomatosis associated with short bowel syndrome has been described in a human patient. It was speculated that excessive fat deposition led to the development of synovial lipomatosis (Siva et al., 2002). A link with an increase in triglycerides in intestinal malabsorption could be suspected (Thompson, 1989). A similar association between chronic inflammatory enteritis and spinal epidural and synovial lipomatosis development could be considered possible in the dog described in this report. However, normal albumin,

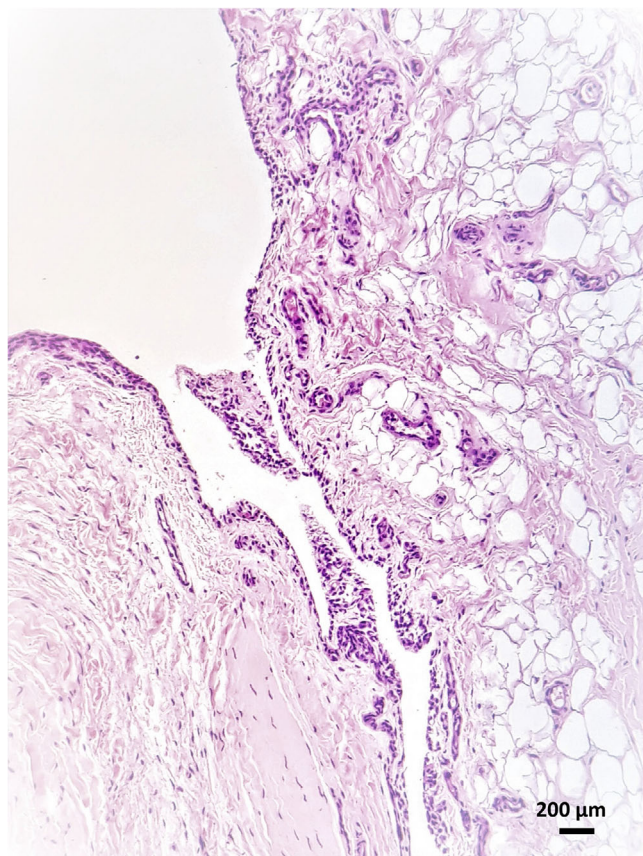


FIGURE 4 Histopathological examination of a tarsal synovial lesion demonstrating the synovial membrane overlying mature well-differentiated adipose tissue (H & E, X100)

folates and cobalamin values in our dog ruled out a malabsorption disorder.

A moderate chronic inflammatory infiltrate can be present in synovial lipomatosis in humans (Rao et al., 2011). In dogs, pain and synovial inflammation associated with lipomatosis might have led to an erroneous diagnosis of immune-mediated polyarthritis by the previous veterinarian. This could also explain the poor response to immunosuppressive therapy and the normal serum C-reactive protein concentration. Alternatively, lipomatous changes could have developed secondarily to chronic synovial inflammation (Howe & Wenger, 2013).

The association of several forms of lipomatosis is rarely described. In humans, multifocal lipomatosis has been linked to benign symmetric lipomatosis (Nielsen et al., 2001), metabolic disorder (Ishihara et al., 2019) and peculiar syndromes of aberrant adipose metabolism. We could therefore raise the hypothesis of metabolic trouble to explain the association of synovial and spinal epidural lipomatosis rather than steroid treatment. However, spinal epidural and synovial forms have not been described together in these syndromes.

Surgical and conservative treatment have been described in humans with variable success for spinal epidural lipomatosis (Fogel et al., 2005). In the present report, surgical treatment was declined by the owner due to the extensive nature of the lesion (from T8 to

L3). Medical treatment of lipomatosis in humans includes progressive steroid withdrawal, weight loss, analgesia and rest. Steroid tapering was not initiated in this dog at the owner's request and based on his concern that the dog had refractory immune-mediated polyarthritis. Retrospectively, since synovial lipomatosis was eventually diagnosed without clear evidence of immune-mediated polyarthritis, progressive steroid withdrawal might have been beneficial.

In conclusion, spinal epidural lipomatosis should be considered in dogs with clinical signs of myelopathy and receiving long-term immunosuppressive steroid therapy, especially if an extradural mass resembling fat tissue is found on MRI or CT examination.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualisation, investigation, writing—original draft: Marion Signoret. *Writing—review and editing:* Lucille Gros. *Investigation* *writing—review and editing:* Claire Dally. *Supervision, writing—review and editing:* Kevin Le Boedec. *Investigation, writing—review and editing:* Renaud Dumont. *Writing—review and editing:* Laurent Cauzinille.

ETHICS STATEMENT

All relevant legal and ethical requirements have been met with regard to the humane treatment of the animal. Owners' consent and confidentiality were respected.

DATA AVAILABILITY STATEMENT

The data that support this case report are available from the corresponding author, [M.S.], upon request.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1002/vms3.842>.

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