

Nervous system lymphoma with sciatic nerve involvement in two cats diagnosed using computed tomography and ultrasound guided fine needle aspiration

Diagnose van zenuwstelsellymfoom met aantasting van de nervus ischiadicus met behulp van computertomografie en echogeleide dunnenaaldaspiratie bij twee katten

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ABSTRACT

Two cats were presented with a recent history of difficulty in walking and jumping. Neurological examination was consistent with a lumbosacral or a sciatic nerve lesion in both cases with an additional C6-T2 spinal cord segment lesion in case 2. Differential diagnosis included neoplastic, inflammatory/infectious (neuritis, meningomyelitis, discospondylitis) and compressive disc disease. Computed tomography (CT) revealed an enlarged, contrast enhancing sciatic nerve from the L7-S1 intervertebral foramen, to the distal third portion of the femoral shaft. In case 2, CT also revealed an enlarged femoral nerve and an extradural mass causing mild compression of the spinal cord at T1-2 and T3-4. Ultrasonography allowed to perform fine needle aspiration of the affected sciatic nerve. Cytology was highly suggestive of indolent, small cell lymphoma in case 1, and confirmed a high-grade lymphoma in case 2, both belonging to the large granular lymphoma subtype.

SAMENVATTING

Twee katten werden aangeboden met een recente voorgeschiedenis van problemen met stappen en springen. Neurologisch onderzoek toonde in beide gevallen een lumbosacraal ruggenmergletsel of nervus ischiadicusletsel aan, met een bijkomend cervicothoracaal-spinaal letsel in het tweede geval. De differentiaaldiagnose bestond uit neoplasie, ontsteking/infectie (neuritis, meningomyelitis, discospondylitis) en compressieve aandoeningen, zoals discus hernia. In het eerste geval werd met behulp van computertomografie (CT) een verdikte nervus ischiadicus aangetoond vanaf het foramen intervertebrale L7-S1 tot aan het distale derde deel van de femur door verhoogde contrastopname. In het tweede geval toonde CT ook een verdikte nervus femoralis en een extradurale massa aan die een milde compressie veroorzaakte van het ruggenmerg ter hoogte van T1-2 en T3-4. Met behulp van echografie kon een fijnenaaldaspiraats genomen worden van de aangetaste nervus ischiadicus. Cytologisch onderzoek suggereerde een traag evoluerend en kleincellig lymfoom in het eerste geval en bevestigde in het tweede geval de diagnose van een hooggradig lymfoom. Beide lymfomen behoren tot het subtype van het grootcellige granulaire lymfoom.

INTRODUCTION

Spinal lymphoma is the most common neoplasm affecting the spinal cord in cats (Lane et al., 1994; Marioni-Henry et al., 2004; Sharp and Wheeler, 2005; Lecouteur and Withrow, 2007; Marioni-Henry et al., 2008; Marioni-Henry, 2010). Lymphoma affecting the

peripheral nervous system has rarely been reported in cats (Spodnick et al., 1992; Lane et al., 1994; Melanby et al., 2003; Higgins et al., 2008; Linzmann et al., 2009) with the brachial plexus being most commonly involved. To the authors' knowledge, involvement of the sciatic nerve has not been reported yet. The majority of peripheral nerve neoplasms described

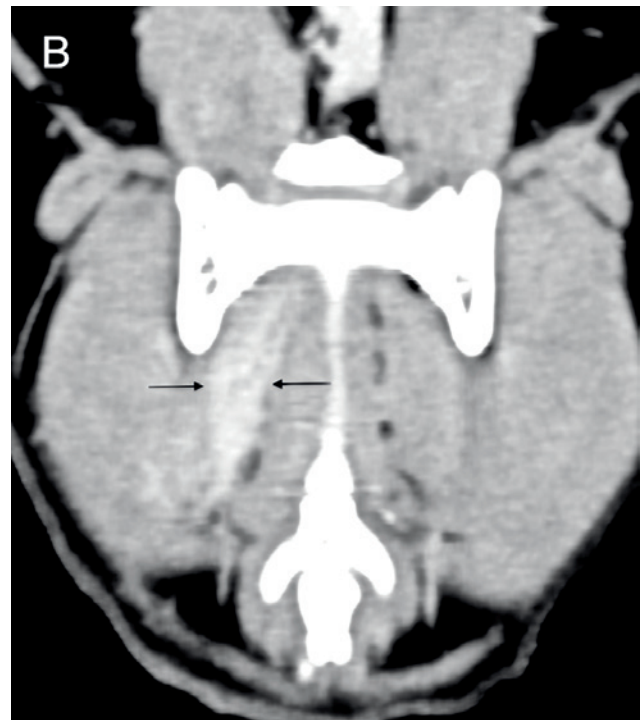
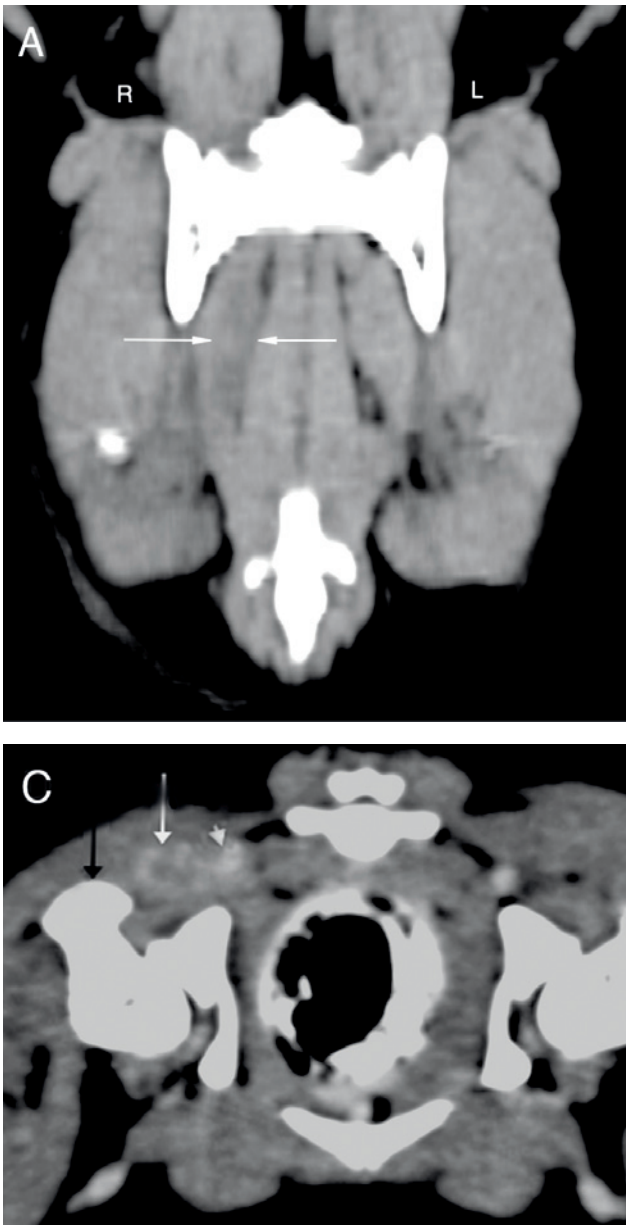


Figure 1. Computed tomography (CT) of the lumbosacral region in case 1. **A.** Dorsal multiplanar reconstruction (MPR) of the pelvic region (ventral to the sacrum and first caudal vertebrae) prior to IV contrast administration, showing a poorly delineated, hypodense, homogeneous and spindle-shaped structure following the path of the right sciatic nerve (arrow) (R: right; L: Left; cranial is on top). **B.** Same image as in A, obtained after IV contrast-fluid administration. There is marked enhancement and enlargement of the right sciatic nerve (arrow). **C.** Post-contrast, transverse CT image at the level of the coxofemoral joints showing the enlarged right sciatic nerve (white arrow) lateral to the caudal gluteal artery (arrowhead) and proximomedial to the greater trochanter of the right femur (black arrow). It appears diffusely hyperdense with a hypodense centre.

are nerve sheath tumors (NST) in both dogs and cats (Brehm et al., 1995; Kippenes et al., 1999; Platt et al., 1999; Watrous et al., 1999; Niles et al., 2001; Rose et al., 2005; Okada et al., 2007; Schulman et al., 2009; Hanna, 2013). Fine needle aspiration (FNA) is used in humans for the early diagnosis of tumors located in the spine or in the paravertebral soft tissues (Wu et al., 2005), but it has been poorly described for this condition in veterinary medicine (Hanna, 2013). In the present report, the use of combined computed tomography (CT) and ultrasonography (US), followed by US-guided FNA for the diagnosis of sciatic nerve lymphoma is described in two cats.

CASE REPORTS

Case 1

A seven-year-old, spayed, female Persian cat, weighing 2 kg, was presented with a ten-day history of

progressive difficulty in walking and jumping. There was no improvement with non-steroidal anti-inflammatory treatment. Blood analysis was unremarkable. Radiographic examination of the lumbosacral region did not reveal any significant abnormalities, except for mild vertebral spondylosis deformans at the level of L7-S1.

Neurological examination revealed marked right pelvic limb paresis with partial plantigrade gait. Paw replacement was absent and the hopping response was decreased in the right pelvic limb. Furthermore, in the affected limb, the withdrawal reflex was reduced and the patellar reflex was increased, which were consistent with patellar pseudohyperreflexia. Muscle tone was decreased and marked muscle atrophy was evident in the territory of sciatic nerve innervation (biceps femoris, semimembranosus, semitendinosus and cranial tibial muscles) in the right pelvic limb. The rest of the neurological examination was within normal limits.

A focal, right-sided L6-S1 spinal cord lesion or a lesion in the proximal part of the right sciatic nerve was suspected. The differential diagnosis included neoplastic, inflammatory (neuritis, focal myelitis, discospondylitis) and compressive lesions (disc disease with foraminal involvement). CT examination of the lumbosacral region was recommended.

Under general anesthesia, CT images were acquired with a four-slice, multidetector helical CT unit (Aquilion Multi 4; Toshiba Medical System, Tochigi, Japan). The patient was placed in dorsal recumbency. The lumbosacral spine and pelvic region were evaluated before and after intravenous administration of 2 mL/kg sodium-meglumine-ioxithalamate (Telebrix 35; Guerbet France, Villepinte, France). Slice thickness was 0.5 mm. Multiplanar reconstructions (MPR) were performed. The bony structures were smooth and regular (except for mild spondylosis deformans at L7-S1). There was no enlargement of the intervertebral foramina. Pre-contrast examination revealed a hypodense, homogeneous and spindle-shaped structure in the path of the right sciatic nerve, with loss of peripheral fat, poorly defined margins, and increased thickness when compared to its left counterpart (Figure 1A). Post-contrast images (Figure 1B) showed marked, peripheral enhancement of the lesion, with a hypoattenuated centre and an enlargement in the region of the right sciatic nerve pathway. This enlargement could be followed from the vertebral canal at the level of L7-S1, through the right L7-S1 intervertebral foramen, then ventrolateral to the sacrum, dorsolateral to the right coxofemoral joint and finally, along the caudal aspect of the right femur to the distal third of the femoral shaft (Figures 1C). Furthermore, there was moderate atrophy of the right biceps femoris, semimembranosus, semitendinosus, cranial tibial and gluteus muscles. Lumbar cerebrospinal fluid (CSF) was collected via lumbar puncture at L5-L6. CSF cell count revealed 3 cells/microL (ref-

erence range < 5 cells/microL). The protein concentration in the CSF was not measured.

US examination was performed using an Esaote ultrasound machine (MyLab60; Esaote, Firenze, Italy) with a multifrequency (9-5 MHz) microconvex-array transducer. The sciatic nerve was identified in the pelvic region, dorsal to the right coxofemoral joint, by positioning the probe on the skin as described in a previous report (Haro et al., 2011). It appeared as a large, hypoechoic cord, slightly heterogeneous and outlined by two hyperechoic, linear interfaces. No abdominal abnormalities were noticed on the US. US and US-guided FNA were performed by a board-certified veterinary radiologist (DR). Cytological examination revealed a highly cellular and purely lymphoid sample of monotonous, mature lymphocytes, with fine, azurophilic cytoplasmic granules (Figure 2A, B). This severe, lymphocytic infiltration of the sciatic nerve was highly suspicious of an indolent, small cell lymphoma. After these procedures, neurological examination was not performed. The owner declined feline leukemia virus search. The owners declined chemotherapy, and only corticosteroid treatment was instituted. Two months later, no improvement was noticed, the animal continued to deteriorate and was euthanized at the owners' request. The owners refused post-mortem examination.

Case 2

A thirteen-year-old, castrated, male domestic shorthair cat was referred for a three-week history of progressive paralysis of the left pelvic limb and a Horner's syndrome.

Neurological examination revealed mild ambulatory tetraparesia with plegia of the left pelvic limb. Paw replacement was absent and the hopping response was markedly decreased in the left pelvic limb, while slightly reduced in the other limbs. Muscle

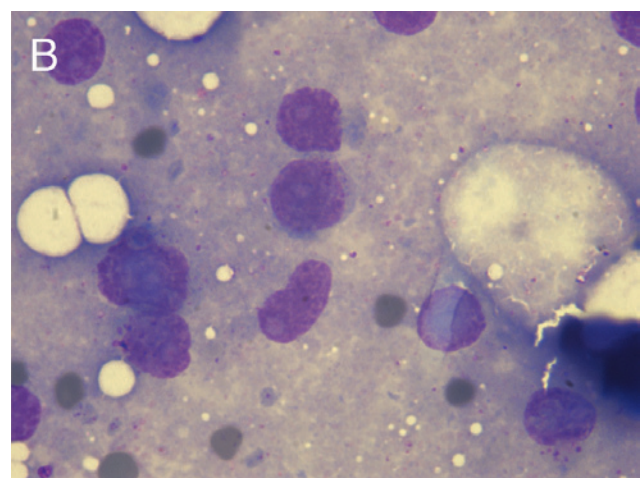
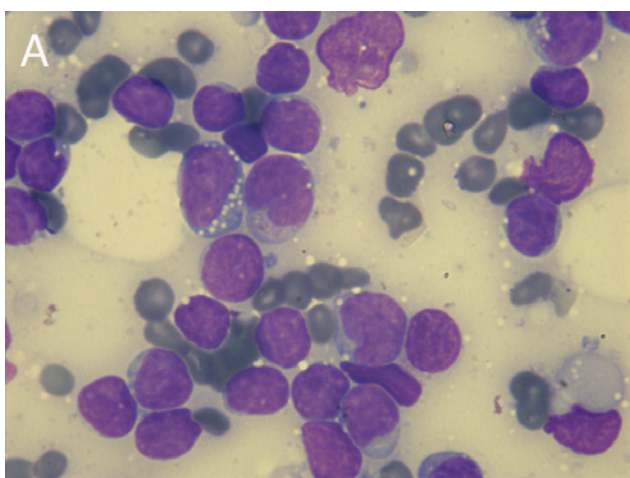


Figure 2. Cytology smear of the sciatic nerve lymphoma in case 1 (A) and in case 2 (B). A. There is a purely lymphoid population of small cells with lymphocytic features: mature, clumped chromatin without nucleolus and pale cytoplasm containing fine, azurophilic granules (x100). B. Large cells with fine chromatin, a prominent nucleolus and obvious azurophilic granules (x100).

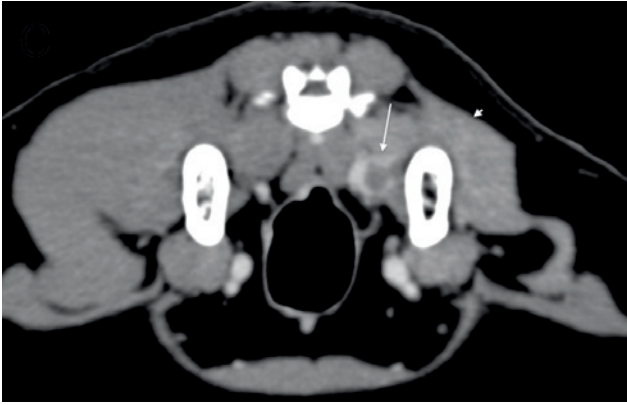


Figure 3. Computed tomography (CT) of the lumbosacral region in case 2. Post-contrast transverse CT image at the level of the pelvic canal showing the left sciatic nerve to be markedly enlarged, hypoattenuating and surrounded by a hyperdense, contrast enhanced halo (arrow). Muscle atrophy is visible (arrowhead).

tone was decreased, withdrawal and patellar reflexes were absent in the left pelvic limb. Muscle tone and spinal reflexes were normal in the right pelvic limb. Muscle tone was reduced in both thoracic limbs but withdrawal reflexes were normal. Marked muscle atrophy was noticed in the territory of the left sciatic nerve innervation. The cranial nerve examination showed a left-sided Horner's syndrome. The rest of the neurological examination was normal. Multifocal nervous system involvement was suspected, including a left-sided L4-S1 spinal cord lesion and a C6-T2 lesion with left-sided ocular sympathetic system involvement.

Under general anesthesia, CT was performed using a similar protocol as in case 1. Moreover, the cervical spine and the head were also evaluated. Regarding the lumbosacral and pelvic regions, the bony structures were smooth and regular. Severe muscle atrophy was observed in the biceps femoris, semimembranosus,

semitendinosus, cranial tibial and gluteus muscles. After IV contrast administration (Telebrix 35; Guerbet France, Villepinte, France), the 5th, 6th and 7th lumbar nerve roots were found to be enlarged, hypoattenuating and surrounded by a hyperattenuating halo on the left side. The left 5th lumbar nerve (femoral nerve root) was slightly enlarged compared to its right counterpart, and it could be followed alongside the psoas muscles until it was lost in the cranial thigh muscle mass. The 6th and 7th lumbar nerves (sciatic nerve roots) were markedly enlarged from the intervertebral foramina; they joined ventrolateral to S1, forming a tubular structure running along the ventrolateral aspect of the sacrum, over the sciatic notch of the left ilium, then dorsolateral to the left coxofemoral joint and finally caudal to the left femur (Figure 3). In the cranial thoracic vertebral column, contrast enhancement was noticed in meningeal tissue on the left side of the spinal cord and in the intervertebral foramina between T1-T2 and T3-T4. It was associated with a slight mass effect on the spinal cord.

US was performed with a multifrequency microconvex transducer (11-8 MHz) (Aplio400; Toshiba Medical System, Tochigi, Japan). The same approach was used as in case 1. The left sciatic nerve appeared as a broad, hypoechoic cord, outlined by two hyperechoic interfaces (Figure 4A). It was located adjacent to the gluteal artery and vein that could be identified with color-Doppler ultrasound. US-guided FNA of the sciatic nerve was performed dorsomedial to the left coxofemoral joint (Figure 4B). Cytological examination revealed a dense lymphoid sample with numerous naked nuclei, large cells with immature fine chromatin, single prominent nucleoli and clear cytoplasm with obvious azurophilic granules (Figure 2B). It was in favor of an aggressive lymphoma affecting the sciatic nerve. The cat was euthanized a few days after these examinations, and the owners declined necropsy.

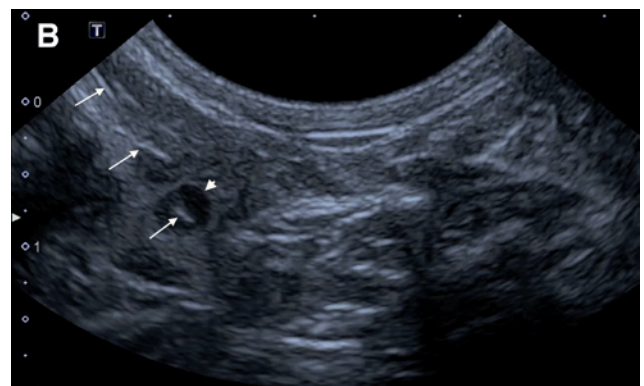
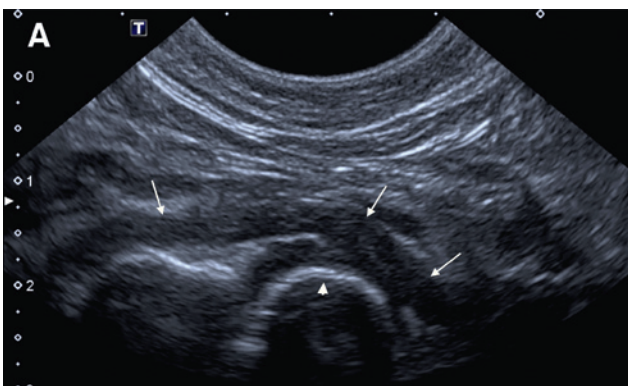


Figure 4. Ultrasonographic images of case 2. A. Longitudinal image of the left sciatic nerve (arrows), dorsal and craniodorsal to the left coxofemoral joint (arrowhead). The cat was placed in sternal recumbency and a dorsolateral approach was performed. The sciatic nerve is delineated by two hyperechoic, linear interfaces and appears as a large, hypoechoic and slightly heterogeneous band (cranial is to the left, dorsal is to the top). B. Transverse view of the left sciatic nerve (arrowhead) dorsal to the coxofemoral joint, where a fine needle aspiration is being performed. The tip of the needle (arrows) appears as a hyperechoic, linear structure within the sciatic nerve.

DISCUSSION

Lymphoma affecting the peripheral nervous system has rarely been reported in cats (Spodnick et al., 1992; Lane et al., 1994; Mellanby et al., 2003; Higgins et al., 2008; Linzmann et al., 2009) with the brachial plexus being most commonly involved. These two cases are of particular interest because to the authors' knowledge, involvement of the sciatic nerve has not been reported yet.

In the current cases, the CT features of the sciatic nerve lesion were similar to those previously described for the brachial plexus (Linzmann et al., 2009). The involved nerves were abnormally enlarged, hypodense in pre-contrast study with a marked, peripheral enhancement of the lesion, with a hypoattenuated centre after contrast injection. In case 2, the additional lesion seen at T1-T2 and T3-T4 was not sampled. The authors could therefore not confirm its histological nature. Nevertheless, given the presence of the sciatic nerve lesion yielding a diagnosis of lymphoma, and the similar CT features, there was a high probability that the two lesions were related.

Ultrasonographic features of the normal feline sciatic nerve have recently been described (Haro et al., 2011) as a thin hypoechoic tubular structure outlined by two hyperechoic lines. The use of ultrasonography and US-guided FNA has been recently described in three cats with schwannoma in the brachial plexus (Hanna, 2013). These cases appeared as a mass. In the cases of lymphoma presented here, the sciatic nerves kept the usual hypoechoic tubular appearance, but they were markedly and diffusely enlarged.

FNA is safer and less invasive than biopsy and was performed without any complication such as hemorrhage in the patients of the present cases. Nevertheless, no neurological examination was performed after general anesthesia in these two animals to assess the potential risks associated with FNA of the sciatic nerve.

In humans, lymphoma affecting primarily peripheral nerves is very rare, and few cases of sciatic nerve involvement have been reported (Descamps et al., 2006; Liang-Hong et al., 2009). Interestingly though, this nerve appears to be the most common site of peripheral nerve lymphoma (Liang-Hong et al., 2009). The diagnosis is usually obtained using magnetic resonance imaging (MRI) and surgical biopsy. It has been shown to be difficult to differentiate peripheral nerve sheath tumors from peripheral nerve lymphoma on CT or MR imaging (Roncaroli et al., 1997), because the appearance of the involved sciatic nerve is not specific for lymphoma, i.e. homogeneous contrast enhancement and thickening. Histopathology is therefore necessary to confirm the diagnosis.

In humans, FNA is commonly used. In a study addressing paraspinal masses, FNA yielded a definitive diagnosis in 66% of the cases (Wu et al., 2005). Sensitivity and specificity of FNA of paraspinal masses were 88% and 75% respectively, based on 59 cases

(including 5 non-Hodgkin's lymphomas and 2 NST) (Wu et al., 2005). These results have to be nuanced in the particular case of NST, as FNA has been shown not to be reliable for the early diagnosis of this type of tumors. It is, however, very accurate in the follow-up of NST, and also to confirm metastases or local recurrence (Jimenez-Heffernan et al., 1999; Wakely et al., 2012). The authors have encountered four cases of sciatic masses diagnosed by CT in cats in the last 18 months. US-guided FNA and cytology were in favor of lymphoma in only two cases, and it was inconclusive in the other two cats. As biopsies were denied in all of the animals, the reasons for the two negative results are unclear. This could be due to the technique (small sample size) or to the nature of the tumor (lymphoma versus NST, or a specific subtype of lymphoma).

In the present two cases, FNA allowed the authors to distinguish a particular subtype of lymphoma: the large granular lymphoma. The relative frequency of this subtype has been well recognized in feline medicine (Wellman et al., 1992; Darbes et al., 1998). It most frequently affects the gastrointestinal tract (Franks et al., 1986; Krick et al., 2008; Barrs and Beatty, 2012). In one published case, there was systemic and brain involvement (Tsuboi et al., 2010). These lymphomas may be either indolent small cell (low grade) lymphomas or aggressive (high grade) large cell lymphomas. Whereas the cytological diagnosis of aggressive large cell lymphoma, as in case 2, is easy on FNA, the diagnosis of indolent small cell lymphomas, as in case 1, is more challenging on FNA.

Further multicentre, prospective studies are needed to compare FNA/cytology and histology to evaluate the sensitivity and specificity of cytology for tumors affecting peripheral nerves in cats.

In conclusion, this report describes the CT and US features of two cases of feline lymphoma with sciatic nerve involvement and the use of US-guided FNA to confirm the diagnosis.

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