Case Report Rapport de cas

Ultrasound-guided fine needle aspiration in the diagnosis of peripheral nerve sheath tumors in 4 dogs

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Abstract — Ultrasound-guided fine needle aspiration was used in establishing the diagnosis in 4 cases of malignant peripheral nerve sheath tumor. Sonographic and cytologic characteristics are discussed. Because of its availability and ease of use, axillary ultrasonography with fine needle aspiration can be an initial diagnostic step for suspected brachial plexus tumors.

Résumé — Aspiration à l'aiguille fine guidée par échographie dans le diagnostic des tumeurs de la gaine des nerfs périphériques chez 4 chiens. L'aspiration à l'aiguille fine guidée par échographie a été utilisée pour établir le diagnostic de 4 cas de tumeurs malignes de la gaine des nerfs périphériques. Les caractéristiques échographiques et cytologiques sont présentées. À cause de sa disponibilité et de sa facilité d'utilisation, l'aspiration à l'aiguille fine par échographie axillaire peut constituer une première étape dans le diagnostic de tumeurs suspectées du plexus brachial.

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Dog 1

A 7-year-old, spayed female, Labrador retriever was presented to the Ontario Veterinary College (OVC) with a complaint of progressive left thoracic limb lameness of 2 months' duration. The dog had been treated with meloxicam (Metacam; Boehringer Ingelheim, Burlington, Ontario), 0.1 mg/kg body weight (BW), PO, q24h for 3 wk with no improvement.

Case description

The physical and orthopedic examinations, aside from the evidence of nonlocalized lameness, and the survey radiographs of the affected limb were unremarkable. Neurological examination revealed left thoracic limb lameness with decreased muscle tone and flexor reflex, as well as pronounced muscle atrophy, mainly over the scapula. Proprioceptive positioning was intact in all limbs. Neither a mass nor pain could be detected by deep axillary palpation or limb manipulation. Based on the protracted history and physical, orthopedic, and neurological examination findings, a neurogenic lameness was suspected. Results from the initial diagnostic procedures, including a complete blood (cell) count (CBC), biochemical profile, and 3-view thoracic radiographs [left lateral (LL), right lateral (RL), and ventrodorsal (VD)], showed no significant abnormalities.

Magnetic resonance imaging (MRI) of the cervicothoracic spine was carried out; the findings indicated the presence of a mass in the brachial plexus and, thus, an ultrasound-guided fine needle aspiration (US-FNA) from the ventral aspect of the axilla was used in order to characterize the mass and plan treatment. The patient was sedated with butorphanol (Torbugesic; Wyeth Animal Health, Guelph, Ontario), 0.2 mg/kg BW, IV, and acepromazine (Atravet; Ayerst Veterinary Laboratories, Guelph, Ontario), 0.05 mg/kg BW, IV, and positioned in dorsal recumbency. Ultrasonographic images of the left axilla were obtained by using a broad-band 8/5 MHz transducer with color Doppler (Phillips ATL 3000; Phillips Electronics, Markham, Ontario). An echogenic homogeneous mass, 1.1 cm in diameter, was easily detected with the transducer (Figure 1). The right axilla was used for comparison. The fine needle aspiration (FNA) of the left axillary mass was done by using a 22 G, 8.5-cm (3.5-in) spinal needle. The stylette was not removed from the needle until the tip reached the surface of the mass. The aspiration was collected by using multiple thrusts of the needle into the mass. Direct smears of the aspirated material were air dried and then stained with Wright's stain (Wright's Stain Solution; Fisher Scientific, Ottawa, Ontario). Cytological examination of the smears revealed a proteinaceous, mildly hemorrhagic background containing a large population of stromal cells (Figure 2). These fusiform to slightly oval cells

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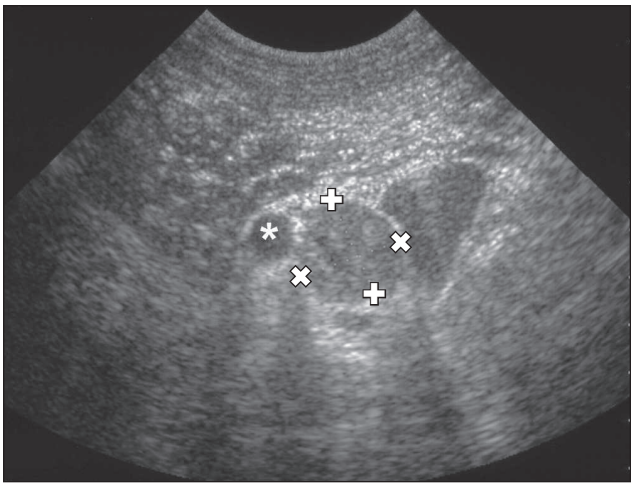

Figure 1. Transverse sonographic image of the left axilla of a 7-year-old, spayed female, Labrador retriever presented with a complaint of chronic left thoracic limb lameness. An echogenic homogeneous mass is seen delineated by the markers (+). The axillary artery is labeled (*).

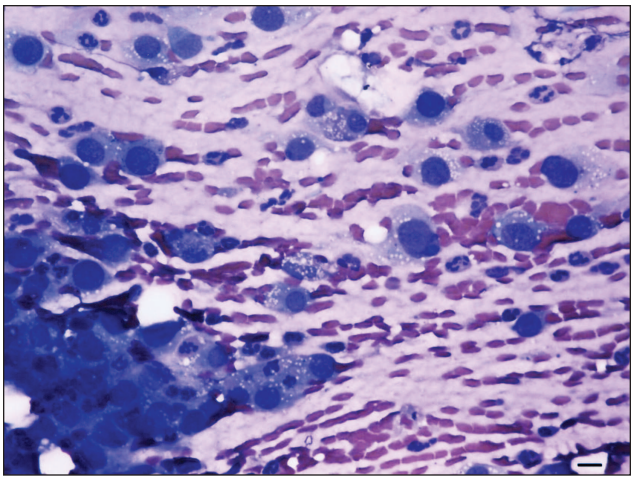

Figure 2. Fine needle aspirate of a left axillary mass from a 7-year-old, spayed female, Labrador retriever. The slide contains a proteinaceous, hemorrhagic background with moderate numbers of fusiform to rounded stromal cells. These stromal cells exhibit a moderate amount of basophilic, often finely vacuolated cytoplasm, and round to oval nuclei with frequent evidence of single to multiple, prominent nucleoli. Moderate anisokaryosis and anisocytosis are present along with rare multinucleated stromal cells. A cytological diagnosis of sarcoma was made. Wright's stain. Bar = 10 μm.

were found both individually and in loosely cohesive clusters. The cells contained a moderate amount of basophilic, occasionally vacuolated, cytoplasm. Nuclei were round to oval, with a clumped chromatin pattern and contained evidence of single to multiple, prominent nucleoli. Multinucleation, as well as moderate anisokaryosis and anisocytosis, was observed. A small amount of eosinophilic extracellular matrix was found in association with some stromal cell clusters. A cytological diagnosis of sarcoma was made. The patient was readmitted 2 wk later for left thoracic limb amputation. At surgery, a round mass associated with the nerves of the left brachial plexus was found. A malignant peripheral nerve sheath tumor was confirmed by histological evaluation of the mass.

Dog 2

A 14-year-old, castrated male, miniature schnauzer was presented to the OVC with a complaint of progressive left thoracic limb lameness of 8 months' duration. He had been treated with cage rest and meloxicam (Metacam; Boehringer Ingelheim, Burlington, Ontario), 0.1 mg/kg BW, PO q24h, intermittently for several weeks with little or no improvement.

Case description

On physical examination, the only abnormality was a grade IV/VI systolic murmur, with no concurrent signs of cardiac failure. Orthopedic examination identified diffuse muscle atrophy of the left thoracic limb. No other abnormalities were observed on orthopedic examination and in survey radiographs, both left and right thoracic limbs appeared to be normal.

On neurological examination, there was little usage of the left thoracic limb, which showed decreased muscle tone and flexor reflex. No evidence of pain or of a mass was observed on deep axillary palpation. Based on the protracted history and physical, orthopedic, and neurological examination findings, a neurogenic lameness was suspected. A peripheral nerve sheath tumor was the primary differential diagnosis. Results from the initial diagnostic procedures, including a CBC, biochemical profile, 3-view thoracic radiographs (LL, RL, VD), and abdominal ultrasonography, were unremarkable.

Magnetic resonance imaging indicated the presence of a mass in the left brachial plexus. Ultrasound-guided FNA of the left axilla was done by using the same preparation and a similar technique to Dog 1. An echogenic homogeneous mass, 2.0 cm in diameter, was easily detected with the transducer (Figure 3). The right axilla was used for comparison. Cytological smears of the fine needle aspirates were prepared as for Dog 1. Cytological examination revealed a large population of stromal cells with cytological features similar to those of Dog 1 (Figure 4). The cytological diagnosis was a sarcoma. Following amputation of the left thoracic limb, a 2.0 cm diameter mass was observed arising from the brachial plexus. A malignant peripheral nerve sheath tumor was the histological diagnosis.

Dog 3

A 9-year-old, spayed female, German shepherd was presented to the OVC with a complaint of left thoracic limb lameness for 3 mo. There was no history of trauma and she had been treated with various nonsteroidal anti-inflammatory drugs and rest without improvement.

Case description

On gait examination, the dog exhibited a partial weight-bearing lameness of the left thoracic limb with marked muscle atrophy of all its muscles. The flexor reflex of the left thoracic limb was decreased. The spinal reflexes of the other limbs were normal. Proprioceptive positioning was intact in all limbs. A mass was not detected on deep axillary palpation.

Results from a CBC and biochemical profile were unremarkable. The patient was anesthetized for electromyography

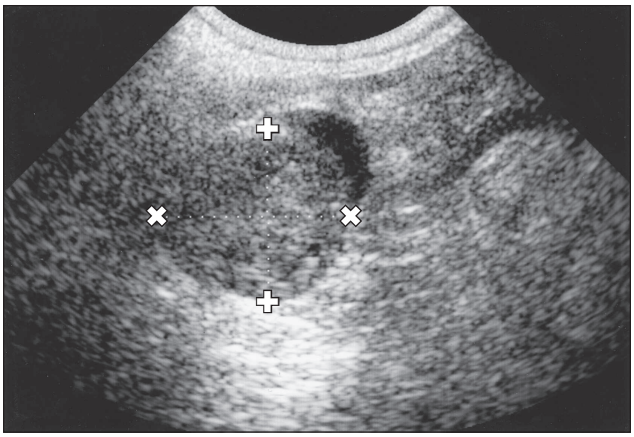

Figure 3. Transverse sonographic image of the left axilla of a 14-year-old, castrated male, miniature schnauzer presented with a complaint of chronic left thoracic limb lameness. An echogenic mass is observed delineated by the markers (+).

(EMG) and motor nerve conduction velocity testing. The EMG results indicated denervation atrophy involving the m. biceps brachii and m. extensor carpi radialis on the left thoracic limb. Motor nerve conduction velocity was normal. Ultrasonographic examination of the left axilla indicated the presence of a rounded hypoechoic to isoechoic mass, 2.0 cm in diameter. Fine needle aspiration of the left mass was prepared for and carried out as in the other dogs. The cytological features of this mass differed somewhat from those of Dogs 1 and 2; the most remarkable difference was the abundant, eosinophilic, extracellular matrix in which the malignant stromal cell population was admixed. Individual cytological features of the stromal cell population again included moderate anisokaryosis and anisocytosis, and the presence of occasional cytoplasmic vacuolation. A cytological diagnosis of a sarcoma with possible chondroid differentiation was made. Further diagnostic and therapeutic interventions were refused, so histological evaluation of this mass was not possible.

Dog 4

A 9-year-old, neutered male, golden retriever was presented to the OVC with a complaint of a right thoracic limb lameness of 2 months' duration. Radiographic examination of the shoulder, humerus, and elbow did not reveal abnormalities. The dog had been treated with meloxicam (Metacam; Boehringer Ingelheim), 0.1 mg/kg BW, PO, q24h for 6 wk, with minimal improvement. In the week before presentation, limb pain and marked wasting of the right thoracic limb muscles had been observed.

Case description

Physical and neurological examinations revealed a right non-weight-bearing thoracic limb lameness; exaggerated motion of the right pelvic limb, marked muscle atrophy over the right scapula and humerus; anisocoria, with the right pupil smaller than the left; and decreased flexor reflex of the right thoracic limb. Orthopedic examination did not elicit pain in the right thoracic limb. A mass was not identified upon deep axillary palpation, but discomfort was elicited.

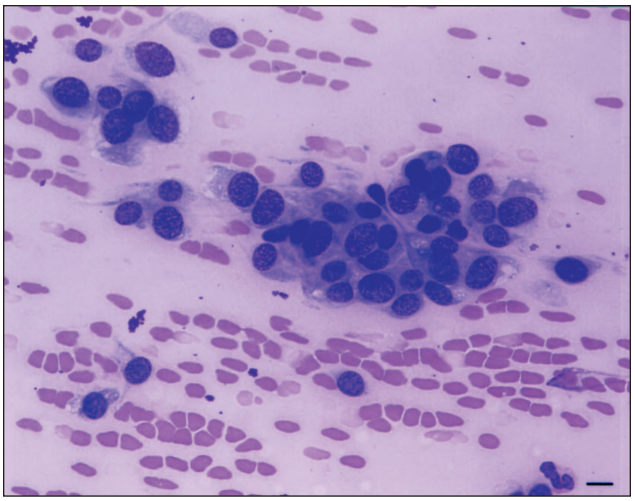

Figure 4. Fine needle aspirate of a left axillary mass from a 14-year-old, castrated male, miniature schnauzer. The slide exhibits a lightly hemorrhagic, proteinaceous background with moderate numbers of individual and clustered stromal cells. Nuclei are round to oval with a clumped chromatin pattern and exhibit single to multiple, prominent nucleoli. The cytoplasm is lightly basophilic and occasionally finely vacuolated. Moderate anisokaryosis and anisocytosis are noted. A cytological diagnosis of sarcoma was made. Wright's stain. Bar = 10 μm.

Results from a CBC, biochemical profile, and urinalysis did not reveal significant abnormalities. Ultrasonography revealed a large hypoechoic mass (4 × 6 cm) in the caudal aspect of the right axillary region. Fine needle aspiration was prepared for and performed as previously described. The cytological sample was highly cellular and revealed a pleiomorphic population of individual and clustered stromal cells with cytological features similar to those in Dogs 1 and 2. Occasionally, a small amount of eosinophilic, extracellular matrix could be detected in association with cell clusters. A cytological diagnosis of a soft tissue sarcoma was made. Due to the extensive nature of this mass revealed on ultrasonography and the dog's clinical signs, which suggested both peripheral and central nervous system involvement, further diagnostic and therapeutic interventions were declined.

Discussion

Malignant peripheral nerve sheath tumors (MPNST), previously called schwannomas or neurofibromas, are a principal cause of chronic neurogenic lameness in dogs (1). The clinical presentation of MPNST is indistinguishable from that of other causes of lameness in the early stages of the disease. The diagnosis of MPNST has evolved over time from survey radiographs, myelography, and surgical exploration of the brachial plexus, to computed tomography (CT) and, more recently, ultrasonography and magnetic resonance imaging (2–8). Some of these diagnostic methods are either expensive or invasive and others are not widely available to practitioners, thereby delaying the diagnosis of MPNST. Ultrasound-guided fine needle aspiration does not require general anesthesia and is widely available. Cytological evaluation can allow distinction between different brachial plexus neoplasms, which can have a large impact on therapy and prognosis.

To the authors' knowledge, this is the 1st description of combined ultrasonographic and cytological features of MPNST in dogs. It is important to emphasize that the identification of an axillary mass does not equate with the diagnosis of MPNST. Even though MPNST is the most common neoplasm at that location, other tumors also occur. The authors have seen both lymphoma and histiocytic sarcoma located in the brachial plexus of dogs, and other tumors have also been reported (9,10). Inflammatory conditions may also be present in the region of the brachial plexus. It is important to differentiate primary tumors (MPNST), from other brachial plexus neoplasms.

Malignant peripheral nerve sheath tumors of the thoracic limb are difficult to diagnose. Clinically, most patients are presented with chronic progressive thoracic limb lameness, indistinguishable from musculoskeletal lameness. A palpable axillary mass has been reported as a common clinical sign for some (3,11), but not for others (2,9). Reviewing 112 cases of MPNST from 6 different reports where axillary palpation had been performed (2–4,7,9,11), a mass was found in 33 dogs (29.4%). Therefore, one should not rely on this clinical finding to diagnose nerve sheath tumors in dogs. Other clinical signs commonly listed are pain on palpation or manipulation of the limb, hypotonia, hyporeflexia, muscle atrophy, proprioceptive positioning deficits, Horner's syndrome, and abnormalities in the reflex of the m. cutaneous trunci (12). Proprioceptive ataxia and paresis can be seen if the tumor compresses the spinal cord (12). Only Dog 4 had evidence of Horner's syndrome (miosis) and abnormal gait in the right pelvic limb, suggesting tumor involvement of the T1-3 spinal nerves and ipsilateral spinal cord.

Ultrasonography is a useful procedure in the diagnosis of distal MPNST in dogs (12). The reported ultrasonographic characteristics of these tumors have ranged from hypoechoic (8,13) to a mixed echogenicity (6). We noted similarly variable ultrasonographic features; in 2 of the dogs, these were homogeneous and echogenic in relation to the surrounding soft tissue, while in the other 2 dogs cases, they were predominantly hypoechoic. The Doppler examination did not reveal vascularization in any of the 4 cases. In humans, schwannomas and neurofibromas (both considered benign tumors) are usually well-defined, solid, hypoechoic soft tissue masses with faint distal acoustic enhancement that may not always be distinguishable from other soft tissue masses (14). Indistinct margins are more frequent in MPNST of humans as a result of their more infiltrative growth (15–17). It may be difficult to differentiate a peripheral nerve sheath tumor from a normal or abnormal lymph node on the basis of ultrasonography. The most reliable method of differentiation is identification of the nerve associated with the MPNST, which is normally hyperechoic relative to the surrounding tissue. Examination with an ultrasound beam positioned at 90° to the surface of the tumor and nerve, reveals the nerves as echogenic (17). One should preferably rely on the relationship of the mass to the surrounding neural structures and not solely on its ultrasonographic echogenicity when attempting to diagnosis an MPNST. Nevertheless, in this series of cases it was not possible to confidently associate the mass with a neural structure. Ultrasonography was, for all of our cases, a superior technique to axillary palpation for detection of a mass. Despite the positive finding of a mass on ultrasonography, the authors were unable to palpate a tumor in any of the 4 dogs.

Cytological descriptions of canine MPNSTs are scant within the veterinary literature (18), although the histological and immunohistochemical characteristics of these tumors have been reviewed (19,20). Individual tumor cell morphology within histological and cytological samples from both canine and human MPNSTs has been described as ranging from interwoven pleiomorphic stromal to round to epithelial cells, with occasional evidence of cartilaginous and osseous metaplasia (17,20–24). The 4 dogs presented in this series exhibited cytological features similar to those reported in the literature. Three of the FNA samples yielded a predominance of pleiomorphic stromal cells, while 1 sample contained abundant eosinophilic matrix in addition to malignant stromal cells. The matrix may be related to cartilaginous or osseous metaplasia of the tumor, but this was not confirmed histologically. Although all of the FNA samples contained stromal cells with features of malignancy, a definitive diagnosis of a MPNST was not possible on the basis of cytology alone. However, the additional ultrasonographic findings of peripheral nerve association with the aspirated mass allowed a diagnosis of MPNST to be made in the 2 dogs for which histological tumor evaluation was not obtained. Additional clinical evidence of peripheral nerve involvement in included in Dog 3, electromyographic evidence of neurogenic denervation, and in Dog 4, evidence of Horner's syndrome and spinal cord involvement.

In dogs, nerve sheath tumors have an affinity for the brachial plexus. Based on the reported location of nerve sheath tumors, more than 50% of tumors are located in the plexus area or distally (2,4,10) and, in fact, the majority of the tumors may be accessible to ultrasonography. Limitations to the diagnosis of US-FNA are the possibility of false negative results, if the mass is small or located proximally, and nondiagnostic aspirates. This technique should not be seen as a single diagnostic tool but, rather, as being complementary to other diagnostic methods, such as CT and MRI, that allow evaluation of proximal nerve structures and the spinal cord. Its main advantage relies on its simplicity and the fact that it can be performed under sedation, contrary to CT, MRI, or electrodiagnostic techniques. Currently, the prognosis for dogs having an MPNST is guarded to poor. Most studies describe a short-term survival. This is likely because the cases tend to be considered as musculoskeletal disorders before a neurological diagnostic work-up is performed, usually several months after the onset of clinical signs (4). The technique of US-FNA may provide earlier detection of MPNST and other brachial plexus tumors in dogs, potentially positively influencing the survival of these patients.

Authors' contributions

All authors, except Dr. Ruotsalo, were involved with the clinical management of the patients. Dr. Ruotsalo examined the cytologic samples and made the cytologic diagnoses. All authors contributed to the preparation of the manuscript. CVJ

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