Challenges in diagnosing a peripheral nerve sheath tumor of the ulnar nerve in a dog – a case report

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Herausforderungen bei der Diagnose eines peripheren Nervenscheidentumors des Nervus ulnaris bei einem Hund – ein Fallbericht

In diesem Fallbericht stellen wir einen seltenen Fall eines distal gelegenen peripheren Nervenscheidentumors des linken Nervus ulnaris bei einer zwei Jahre alten Rottweiler-Hündin vor. Wir beschreiben und diskutieren die klinischen und diagnostischen Befunde, sowie die Herausforderungen des Falles. Die Hündin wurde erfolgreich mit einer gliedmassenschonenden Technik (partielle Neurektomie) behandelt. Nach Chirurgie und langfristige follow-up war die Hündin Schmerz- und Lahmheitsfrei.

Schlüsselwörter: PNST, Monoparese, Lahmheit, Magnetresonanztomographie (MRI), Elektromyographie (EMG), Regionalanästhesie, medizinischer Fehler, Kognitive Verzerrung

Summary

In this case report we present the rare case of a distally located peripheral nerve sheath tumor (PNST) of the left ulnar nerve in a two-year-old female Rottweiler dog. We discuss the clinical and diagnostic findings and the challenges of the diagnosis. The dog was successfully treated with a limb sparing partial neurectomy. After surgery, the dog did not show any pain or lameness on long term follow-up.

Keywords: PNST, monoparesis, lameness, magnetic resonance imaging (MRI), electromyography (EMG), regional anesthesia, medical error, cognitive bias

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Introduction

A complete lameness examination in a dog helps to differentiate among orthopaedic or neurological disorders. Despite thorough anamnesis, general clinical, orthopaedic, and neurological examination this differentiation can still be challenging.

Peripheral nerve sheath tumors (PNST) are one possible cause of lameness/monoparesis in dogs and can arise along any part of a nerve. They are locally aggressive and tend to infiltrate the nerve along its course. Distant metastasis rate is low.[8,11,17,19,22,25,26] Based on their localization, PNSTs can be divided into three groups: root, plexus, and peripheral. The majority of PNSTs being localized in the region of the plexus or the nerve root, with the thoracic limbs being more frequently affected than the pelvic limbs.[3,5] Presented dogs are typically large-breed, middle aged dogs showing a chronic, progressive lameness with severe neurogenic muscle atrophy.[3] Discomfort is a common clinical sign and can usually be exacerbated during targeted palpation.[11,15] Neurological deficits such as lower motor neuron monoparesis or reduced spinal reflexes may become evident only late in the course of the disease. Advanced investigations described to assist in the diagnosis of PNST include ultrasound, computer tomography (CT), magnetic resonance imaging (MRI), and/or electrophysiological examinations, such as electromyography (EMG).[6,21]

If feasible, treatment of choice is wide margin (2–3 cm) surgical resection of the nerve sheath tumor.[1,7,17] Limb sparing techniques such as neurectomy have been described for distally located PNSTs. However, limb amputation is frequently required due to the proximal localization of the neoplasia.[1,24] This case report highlights, that even with all diagnostic tools available, diagnosis of distally located PNST can be challenging. Close collaboration

between different disciplines is imperative. Thus, even with delayed diagnosis satisfactory results can be reached.

Case report

A two-year-old, 43 kg, female intact Rottweiler was referred to the Clinic for Small Animal Surgery at the Vetsuisse Faculty in Zurich for re-evaluation of a progressive, moderate, left thoracic limb lameness of six months' duration. Radiographs of the affected limb, performed by the referring veterinarian, including left paw/manus, carpus, and elbow, were evaluated as unremarkable. Treatment with unspecified non-steroidal anti-inflammatory drugs (NSAID) and exercise restriction did neither alleviate pain nor lameness.

On presentation, the dog showed moderate to severe left thoracic limb lameness. The lame limb had a normal muscle mass. Spinal reflexes and proprioception of all limbs were normal. Flexion of the left carpus elicited severe pain, but no swelling, crepitus or joint instability was detected. The remaining orthopedic and neurological examination did not show any abnormality. Based on the clinical findings, lameness was localized to the carpus and a carpal sprain or an occult fracture were considered as primary differentials. Sesamoid bone disease was also considered due to the high prevalence of this pathology in Rottweilers.[10,18] A neoplastic process was considered less likely due to the young age of the dog, however, was not excluded.

An MRI of the left manus, including the carpus and metacarpal bones, was performed to further investigate the carpal region, using a 3-Tesla machine (Philips Ingenia 3,0T, Philips AG, Zurich, Switzerland) with a surface coil Micro-47 (Philips Medical Systems, Best, The Netherlands). Three-plane T2-weighted (T2w) turbo spin echo (TSE) and two-plane proton density-weighted asymmetric TSE, as well as single-plane pre- and postcontrast (0,2 mL/kg Omniscan; Gadodiamid, GE Healthcare AG, Europa-Strasse 31, 8152 Glattbrugg, Switzerland, 287 mg/mL) T1-weighted (T1w) sequences were obtained. The MRI images were reviewed by a board-certified veterinary radiologist and initially reported as unremarkable.

The dog was discharged with further symptomatic therapy consisting in NSAID (Carprofen 4 mg/kg p.o. SID: Canidryl flavour ad. us. vet, Dr. E. Graeub AG, Rehhagstrasse 83, 3018 Bern, Switzerland, 100 mg p.o.) and 10 mg/kg p.o. BID/TID Gabapentin (Gabapentin Mepha, Mepha Pharma AG, Kirschgartenstrasse 14, 4051 Basel, Switzerland, 100 mg).

Three days after initial presentation, the owner reported worsening of the clinical condition to a non-weight bearing lameness. The orthopedic and neurological re-assessment were difficult as the dog showed severe pain and aggressive behaviour when the left thoracic limb was manipulated. Pain was especially elicited by flexion of the carpus and left elbow joint. Because the initial MRI of the carpus was reported as unremarkable, bilateral CT of the elbow and shoulder joints were performed. CT failed to explain clinical signs. Due to the inconclusive diagnostic imaging studies, an elbow arthroscopy and an EMG of the muscles of the affected left forelimb were performed. Arthroscopy and EMG results were also considered unremarkable. The dog was discharged again with symptomatic therapy consisting in NSAID (Robenacoxib 1 mg/kg p.o. SID: Onsior ad us. vet., Elenco Tiergesundheit AG Mattenstrasse 24A 4058 Basel, Switzerland, 40 mg p.o.), 4 mg/kg p.o. BID Pregabalin (Pregabalin Sandoz, Sandoz Pharmaceuticals AG, Suurstoffi 14 Postfach, 6343 Rotkreuz, Switzerland, 50 mg p.o, 100 mg p.o.), and 5 mg/kg p.o. BID Amantadin (PK-Merz, Merz Pharma Schweiz AG, Hegenheimermattweg 57, 4123 Allschwil, Switzerland, 100 mg p.o.), resulting in moderate improvement.

Thirteen months later the dog was represented as the gait, after a temporary improvement, progressively worsened to a persistent, non-weight bearing lameness (part I of supplementary video 1). Hyperesthesia localized on the caudal aspect of the left forelimb and palmar aspect of paw was noted, corresponding to the median and ulnar nerve dermatome. Further manipulations in unanaesthetised condition were not possible due to severe discomfort and aggressive response of the patient. At this time, a neuropathy of the ulnar and/or median nerves was suspected. Regional anesthesia was performed with perineural injection of 0,75 mg/kg Ropivacain (Ropivacain Sintetica, Sintetica SA Via Penate 5, 6850 Mendrisio, Switzerland, 7,5mg/ml) at the level of the elbow joint. After regional anesthesia, the dog was able to walk with minimal lameness (part II of supplementary video 1). Differential diagnosis at this point were PNST, neuritis or, less likely, nerve compression. The initial MRI of the left manus was re-evaluated by a board-certified veterinary radiologist. A lesion of the left ulnar nerve in the region of the carpus could be retrospectively identified. The left ulnar nerve showed an abrupt severe and diffuse increase in diameter (up to 4,5 mm) at the level of the carpal accessory bone with distal extension of the thickening until branching of the ulnar nerve into the palmar metacarpal nerves (mid to distal metacarpal region). The margins of the thickened nerve were smooth or mildly nodular and mostly well-defined with the affected part of the ulnar nerve being hyperintense relative to skeletal muscle in T2w and proton density-weighted sequences, mixed iso- and hyperintense in pre-contrast T1w images, and showing moderate, heterogeneous contrast enhancement in post-contrast T1w images (Figure 1). Proximal to this lesion the appreciated ulnar nerve was unremarkable.

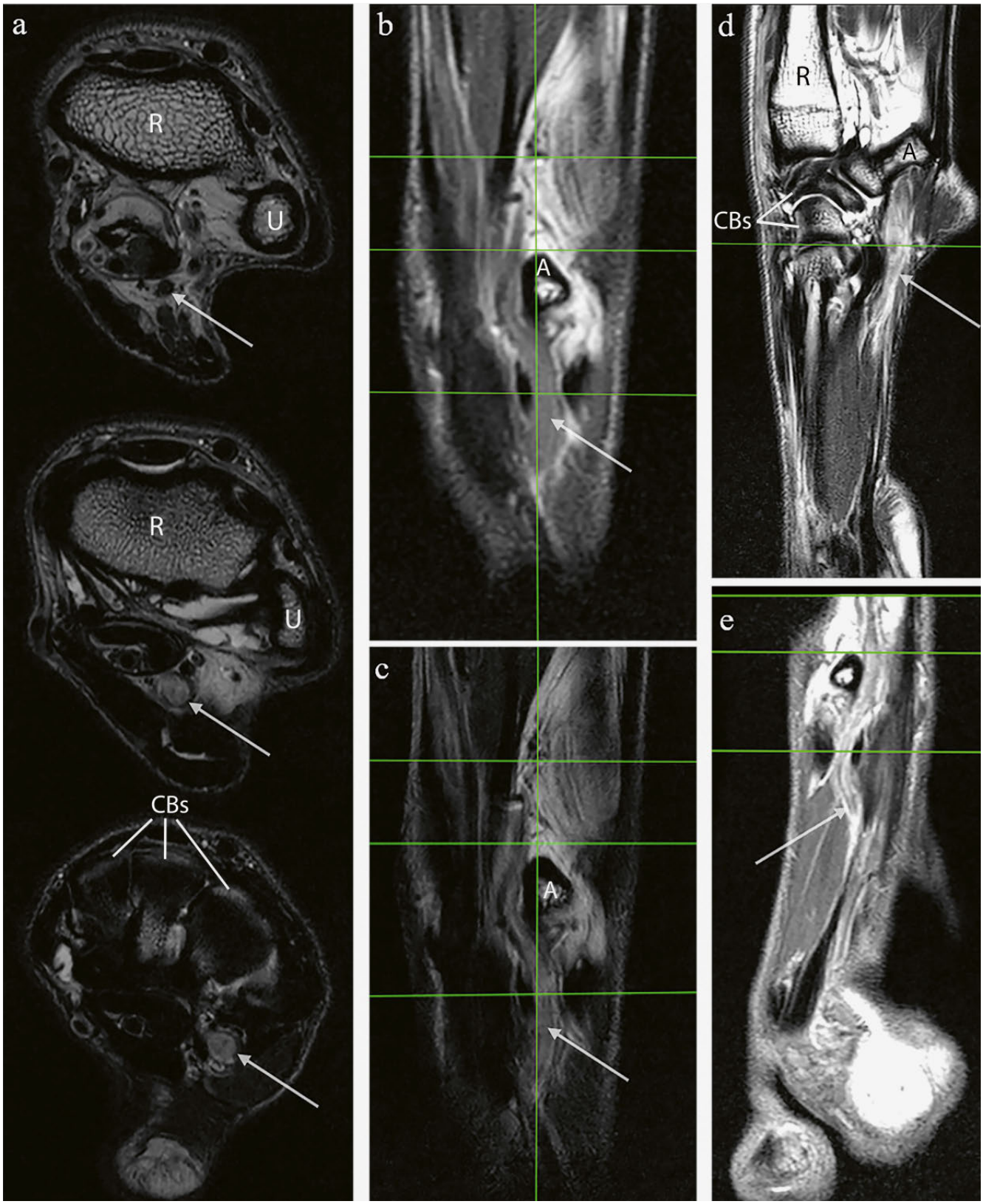

Figure 1: Transverse T2w (a), dorsal T1w (b) and T2w (c), sagittal T2w (d), and sagittal T1w post contrast (e) images of the left front limb of the affected dog. The green lines represent the regions of the transverse (horizontal lines) and sagittal (vertical line) sections. The green line in picture (d) represent the most distal transverse section (bottom image in (a)). The ulnar nerve (white arrow) is unremarkable in the most proximal transverse section (top picture in (a)). Distal to this location the ulnar nerve is severely thickened and is mixed iso- to hyperintense in T1w, hyperintense in T2w, and displays moderate heterogeneous contrast enhancement in postcontrast T1w images (e). R: radius; U: ulna; CBs: carpal bones; A: accessory carpal bone.

A nerve biopsy of the altered region of the left ulnar nerve was performed with an open surgical approach. The biopsy was evaluated by a board-certified pathologist. The neoplastic proliferate displayed a dense population of expanding and infiltrating spindled neoplastic cells arranged in streams, interwoven bundles, and whorls sorted by a fibrous stroma. Tumorous cells showed mild anisokaryosis and anisocytosis with a moderate amount of cytoplasm, central oval nuclei with finely stippled chromatin and inconspicuous nucleoli. No mitotic figures were observed. The axons entrapped by the neoplastic proliferate displayed multifocal dilation and Wallerian degeneration. The histopathologic changes were confined within the epineurium. One surgical margin was infiltrated with neoplastic cells. Histologic diagnosis was incompletely resected benign PNST with high suspicion of Schwannoma.

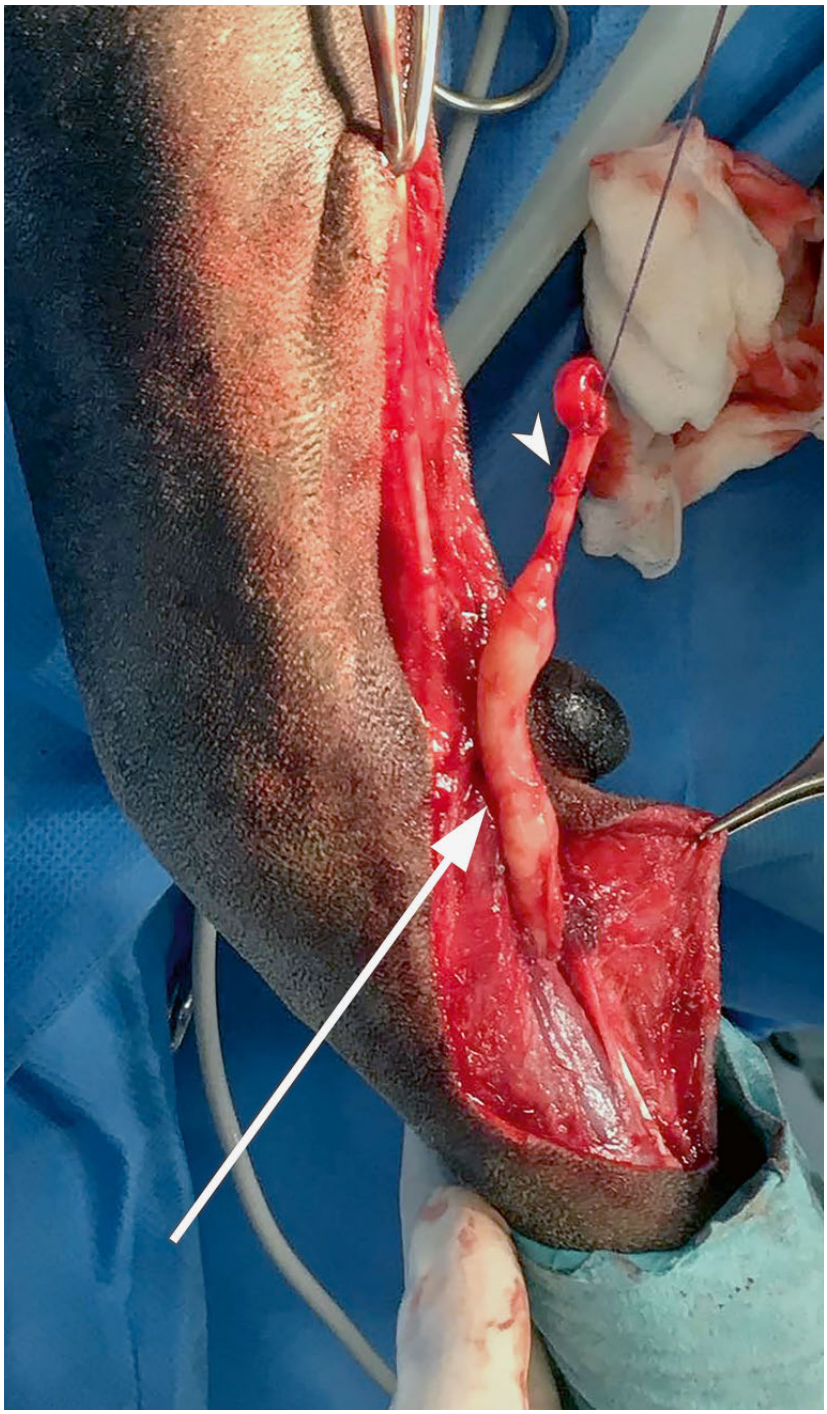

Figure 2: Intraoperative image of the segmentally thickened left ulnar nerve (arrow) due to a distally located peripheral nerve sheath tumor. Note the normal size of the proximal part of the left ulnar nerve (arrowhead).

Surgical therapy was discussed with the owner, which opted for a limb-sparing technique. Partial neurectomy of the ulnar nerve with wide margins (2–3 cm) was performed. The ulnar nerve was exposed through a palmar approach extending from the distal metacarpal region up to the proximal third of the antebrachium. Multiple well-circumscribed, firm, round nodules were identified intraoperatively along the course of a segmentally thickened ulnar nerve (Figure 2).

Histopathology findings were comparable with the presurgical biopsy. Histologic diagnosis was in toto removal with clean surgical margins of a benign PNST most likely originating from Schwann cells.

On a short term follow up control two weeks after surgery, the dog was able to walk with minimal lameness, was cooperative and did not show any sign of discomfort or aggressive behaviour. On long term follow-up, eight months after surgery, the dog was in good clinical condition and according to the owner and to the referring clinician the dog was pain-free and had no lameness.

Discussion

Establishing a diagnosis of PNST can be challenging, especially in the early stage of the disease when the clinical presentation may be almost indistinguishable from an orthopedic disorder. Months can pass between the appearance of more specific clinical signs and diagnosis of PNST.[21] Brehm et al. reported a statistically significant longer duration of clinical signs before diagnosis a PNST belonging to the peripheral group compared either to the plexus or root group.[3]

In the presented case, at initial presentation a PNST was considered unlikely due to young age of the dog, absence of neurological deficits, and absence of muscle atrophy. Furthermore, discomfort and aggressive behaviour of the patient complicated the clinical assessment.

EMG initially failed to detect any abnormalities, most likely because early neoplastic infiltration of the fascicles did not yet compromise axon activities. Additionally,

the PNST in our case was located distally, where the ulnar nerve provides only motor innervation to the palmar interosseus muscle. These findings diverted differentials further from a PNST.

On MRI examination the PNST in this dog was initially overlooked despite evaluation from an experienced boarded radiologist with more than 20 years of experience. Definitive diagnosis was set retrospectively only 14 months after first presentation and re-evaluation of the same MRI study.

PNSTs typically display characteristic MRI features, with mass like or diffuse thickening of the affected nerve, which usually appears T2-hyperintense and T1-isointense to the surrounding skeletal musculature showing a varying degree of contrast enhancement. However, signal intensity of PNSTs in T2w and T1w sequences is not uniform and mixed T2w signal, as well as hypointense to mixed T1w signal are also described in PNSTs in the root and plexus group.[9,13,21,27] In addition, there is lack of literature in veterinary medicine describing the anatomical appearance and MRI features of distal PNSTs (peripheral group of PNSTs), which are less common and less investigated than the other forms like brachial PNSTs (root group of PNSTs) or trigeminal PNSTs.

In the present case we opted for a limb sparing partial neurectomy considering the favourable results obtained in the study of van Stee et al.[24] Due to the distal location of the PNST we speculated that wide margin resection on both side of the PNST was possible. Thus, allowing in toto removal of the neoplasia and good prognosis with mean survival time comparable to limb amputation.[24] In this dog non-infiltrated margins were histopathologically confirmed and if this would have not been the case limb amputation could still have been subsequently undertaken.

Medical errors have long been established in the human literature and in 2016 these have been estimated to be the third leading cause of death in the United States.[2,4,12,16] Medical errors can be broadly categorized as diagnostic, treatment, preventive, and other errors.[4] In human diagnostic radiology the average daily error rate is approximately 4 %.[23] Cognitive biases are the major cause of diagnostic errors in radiology and the classification revised by Kim and Mansfield in 2014 with 12 types of errors is to date the most widely accepted classification in human medicine.[12] The most common cognitive error type is underreading (type 4 error), where the finding is simply missed.[12] This also happened in our case report where an experienced radiologist missed the finding in the MRI study and encountered the most common cognitive error. As possible cause of the error we could consider system-related sources such as workplace interruptions, shift length and timing, pace of reading images, and lighting conditions. Which all may affect the psychophysical process of visual diagnosis due to increased mental and visual fatigue.[14] Inattentional, availability, and framing biases should also be considered.[4,20] Inattentional biases are characterized by missing a finding because of unusual appearance or location. In availability bias diagnoses not recently seen, such as rare conditions like in our case, are not considered and therefore are underdiagnosed. Scarce literature about carpal MRI and features of distally located PNST in veterinary medicine may also have played a role in this case. Framing biases reflect the situation in which the radiologist is influenced by the clinical question.[4,20] In our case report, at initial presentation, neurological conditions were considered unlikely and this may have influenced imaging assessment. Structured reporting and the use of diagnostic checklists should also be considered, as they have been shown to reduce errors in medicine.[14] Furthermore, it should not be forgotten that effective communication between radiologists, radiology technicians, and clinicians is paramount in reducing errors.[20]

In conclusion, we report the challenging case of a young Rottweiler dog with a distally located PNST affecting the left ulnar nerve. After delayed diagnosis, the dog was successfully treated with limb sparing neurectomy 14 months after initial presentation. This case report is clinically significant as it represents one of the few reported cases of PNSTs belonging to the peripheral group and treated with limb sparing neurectomy. In addition, the present case report highlights the paramount impor-

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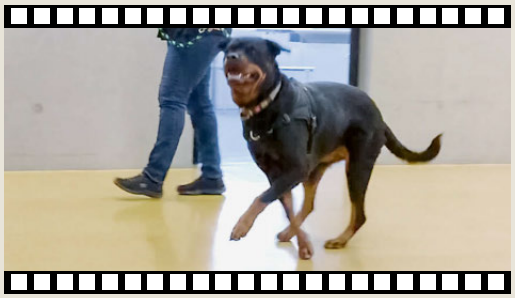

Online-Video

Video 1: Gait of a Rottweiler dog with a distally located peripheral nerve sheath tumor before and after regional anesthesia.

tance of analysing and understanding diagnostic errors so that appropriate measures can be taken to decrease future mistakes. Errors are unavoidable hazards of the human condition and we should learn from them. The philosopher Aurelio Agostino d'Ippona once said "*errare humanum est*", meaning "to err is human", but he also added "*perseverare autem diabolicum*", "but to persist in the error is diabolical".

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Défis dans le diagnostic d'une tumeur de la gaine du nerf ulnaire chez un chien – un rapport de cas

Dans ce rapport de cas, nous présentons le rare cas d'une tumeur périphérique de la gaine du nerf ulnaire/cubital gauche chez une chienne Rottweiler de deux ans. Nous discutons les résultats cliniques et diagnostiques et les défis liés au diagnostic. Le chien a été traité avec succès par une neurectomie partielle. Après la chirurgie, lors du suivi à long terme, le chien n'a plus présenté ni de douleur ni de boiterie.

Mots clés: PNST, monoparése, boiterie, imagerie par résonance magnétique (IRM), électromyographie (EMG), anesthésie régionale, erreur médicale, biais cognitif

Insidie della diagnosi di un tumore della guaina nervosa del nervo ulnare in un cane – un case report

In questo rapporto vi presentiamo il raro caso di un tumore periferico della guaina del nervo ulnare sinistro in un cane Rottweiler femmina di due anni. Discutiamo i risultati clinici e diagnostici e le sfide legate alla diagnosi. Il cane è stato trattato con successo con una neurectomia parziale. Dopo l'intervento, a lungo termine il cane non ha più mostrato alcun dolore o zoppia.

Parole chiave: PNST, monoparesi, zoppia, risonanza magnetica, elettromiografia (EMG), anestesia regionale, errore medico, bias cognitivo

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