Imaging and histopathologic features of reversible nerve root and peripheral nerve edema secondary to disc herniation in a cat

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Abstract
Nerve root enlargement with increased contrast uptake has been reported in dogs and humans secondary to nerve root compression. In cats, nerve root enlargement and contrast uptake only have been reported in association with inflammatory and neoplastic diseases, but not as a sequela to nerve root compression. An 8-year-old oriental short hair cat was presented with acute neurologic deficits consistent with left-sided sciatic nerve deficit and possible L6-S1 myelopathy. Magnetic resonance imaging (MRI) was performed and identified compression of the cauda equina and L7 nerve root associated with intervertebral disc herniation (IVDH) at L6-L7 as well as widespread sciatic nerve enlargement with moderate rim enhancement. A hemilaminectomy was performed to evacuate herniated disc material. The nerve root was biopsied and submitted for histological evaluation. Interstitial nerve edema was diagnosed. Follow-up MRI 3 months postoperatively showed complete remission of the changes. Nerve root thickening together with contrast enhancement may represent nerve edema in cats secondary to IVDH.

Keywords
feline, MRI, rim enhancement, sciatic nerve

INTRODUCTION

Intervertebral disc herniation (IVDH), a common neurological condition in dogs, occurs less frequently in cats, with a recently estimated prevalence of 0.24%.1 Thickening of nerve roots and spinal ganglia secondary to IVDH mimicking peripheral nerve sheath tumors (PNST) has been described in dogs2,3 and humans.4-10 Disc material extruded into the vertebral canal or foramina can cause compression and inflammation of the dorsal root ganglion and spinal nerves.3

Common magnetic resonance imaging (MRI) features of PNST in cats and dogs include thickening of the nerve, with associated increased T2 and mildly decreased or unaltered T1 signal intensity.11,12 These imaging characteristics are nonspecific and observed with other conditions including lymphoma and neuritis.13,14 Neural enhancement after contrast administration is considered a critical feature in the diagnosis of PNST12, but it is not pathognomonic and also can be found in primary7 inflammatory processes13 or inflammation secondary to mechanical nerve impingement.3,15
similar enhancement pattern has been described after experimentally induced peripheral nerve compression in rodent models.\textsuperscript{16}

To date, thickening of nerve roots and peripheral nerves in cats has been reported only in neoplastic disorders, most commonly peripheral nerve lymphoma,\textsuperscript{17-25} and rarely in nerve sheath tumors,\textsuperscript{11,26-30} suspected immune-mediated\textsuperscript{13,31} and infectious neuritis,\textsuperscript{32} and hyperchylomicronemia.\textsuperscript{33} In contrast, nerve root thickening has not been reported in IVDH in cats.\textsuperscript{34-41}

Differentiation of neoplastic and nonneoplastic causes of nerve root thickening by MRI is challenging and may impact clinical decision making.\textsuperscript{5-6,8}

We describe the MRI features of a histologically confirmed peripheral nerve edema secondary to disc extrusion in a cat and its subsequent resolution after surgical treatment.

\section{CASE HISTORY}

An 8-year-old 5-kg male neutered oriental shorthair indoor cat was referred to the neurology service of the small animal clinic of the University of Zurich with a history of acute onset of hind limb lameness 10 days before admission. Despite medical treatment with 0.1 mg/kg meloxicam (Metacam 0.5 mg/mL ad us. vet., oral suspension, Boehringer Ingelheim Animal Health) PO q24h, clinical signs did not improve. Physical examination disclosed bilateral popliteal lymphadenomegaly and a systolic heart murmur (grade I/VI). During a neurological examination, left hind limb monoparesis with plantigrade stance and bilateral decreased proprioceptive placing were noticed. Tibialis cranialis and withdrawal reflexes were decreased on the left side. Behavioral reactions suggesting pain during paravertebral palpation could not be reliably elicited. Therefore, the neuroanatomical localization was L6-S1. Neoplasia (eg, lymphoma, PNST) or inflammation were considered the most likely differential diagnoses. Hematology and serum biochemistry results including serum creatine kinase activity and serum amylloid A concentration were unremarkable. Feline leukemia virus antigen and feline immunodeficiency virus antibody tests were negative. The popliteal lymph nodes were aspirated, but results were not diagnostic.

Magnetic resonance imaging of the lumbar spine was performed under general anesthesia using a 3 Tesla scanner (Philips Ingenia, Philips AG, Zurich, Switzerland). Imaging protocol consisted of T2-weighted (T2W) turbo spin echo sequences in sagittal (echo time [TE] 100 ms; repetition time [TR] 3487 ms; slice thickness, 2.5 mm) and transverse planes (TE, 100 ms; TR, 4562 ms; slice thickness 2.5 mm), T2W spectral presaturation with inversion recovery (SPIR) sequences in dorsal (TE, 55 ms; TR, 1700 ms; slice thickness, 2.5 mm) and transverse planes (TE, 55 ms; TR, 3710 ms; slice thickness, 2.5 mm), T1-weighted (T1W) turbo spin echo sequence in the transverse plane (TE, 8 ms; TR, 520 ms; slice thickness, 2.5 mm) and T1W SPIR sequence in the transverse plane (TE, 8 ms; TR, 597 ms; slice thickness, 2.5 mm) after IV administration of gadolinium-based contrast agent (0.1 mmol/kg; Omniscan, GE Healthcare AG, Opfikon, Switzerland).

The MRI findings indicated severely decreased T2 signal intensity of the L6-L7 intervertebral disc. Furthermore, immediately dorsally, severe extradural compression of the conus medullaris was caused by a moderate amount of homogeneous material, T2 hypointense relative to spinal cord signal intensity. The compressive material was located at the left ventrolateral aspect of the vertebral canal, causing a partial focal narrowing of the cerebrospinal fluid and epidural compartments, and extended into the left intervertebral foramen at L6-L7. Moderate peripheral enhancement surrounding the extradural material was identified after contrast medium injection. Moreover, the left L7 nerve root was severely thickened compared to the right root and displayed moderately increased T2 signal intensity with a slightly heterogeneous appearance associated with moderate homogeneous contrast enhancement. Likewise, the left sciatic nerve was moderately thickened, homogeneously increased in T2 signal intensity, and could be followed to the level of the medial aspect of the distal third of the femoral diaphysis. Moderate associated rim enhancement also was identified (Figure 1).

The imaging diagnosis was severe extradural compression of the conus medullaris associated with IVDH at L6-L7 and severe thickening of the left L7 nerve root and sciatic nerve. Differential diagnoses for the thickened nerve root and sciatic nerve included an inflammatory process secondary to disc extrusion or a concomitant neoplastic disease such as lymphoma or PNST.

After the MRI, the owner elected surgical treatment. A left-sided hemilaminectomy was performed at the level of L6-L7. Material that grossly resembled extruded nucleus pulposus and hemorrhage was removed from the epidural space immediately adjacent to the left intervertebral foramen and between the cauda equina nerve roots. The left L7 dorsal root ganglion, dorsal nerve root, and proximal L7 spinal nerve were markedly enlarged, and a partial thickness biopsy specimen was collected from the dorsal root ganglion. The cat recovered uneventfully. The plantigrade stance and gait disappeared during the 5 days of hospitalization.

The sampled tissue was submitted to the Clinical and Comparative Neuropathology Lab, University of Munich, for histopathological analysis. Histopathological examination identified marked myxoid endoneurial edema with separation of nerve fibers, individual myelinated fiber degeneration and focal perineuronal satellite cell hyperplasia in the associated ganglion (Figure 2). Interstitial edema caused by nerve root compression or in response to extrafocal epiradicular inflammation was suspected. Endoneurial and periradicular infiltrative disorders, such as radiculitis and neoplasia, and fibroblastic nerve root remodeling were histologically excluded.

The cat was presented for follow-up examination 3 months after hospital discharge, and at this time no neurologic deficits were recognized. A follow-up MRI of the lumbar spinal cord was performed using the same image acquisition protocol as described above. Slight irregularly contoured left epaxial muscles were observed at L6-L7. The epaxial muscles had normal T2 and T1 signal intensity and mild diffuse enhancement after contrast medium administration. A well-defined and regularly margined defect at the left side of the laminae, consistent with the reported hemilaminectomy, was present. The extruded
disc material was not evident at follow-up, suggesting complete decompression after surgery, and the L7 nerve roots were symmetrical and displayed normal signal intensity. The sciatic nerves were symmetrical and had normal mild T2 hyperintensity and T1 iso-intensity relative to muscle signal intensity, with no enhancement evident after contrast agent injection (Figure 3). The remaining structures were unchanged in comparison to the first scan, and the findings were consistent with complete regression of the previously reported L7 segmental neuropathy.

Nerve and nerve root thickening in cats has been described in neoplastic (eg, PNST, lymphosarcoma) or inflammatory diseases and is associated with a guarded prognosis. Common imaging features include enlargement of the nerve, hyperintensity in T2-weighted sequences and in T2-weighted sequences with additional fat suppression, as well as contrast enhancement. In cats affected by peripheral nerve lymphoma, widening of the neuroforamen also may be found, likely because of bone atrophy secondary to chronic compression and slow growth of the tumor.

Neither nerve or nerve root thickening nor contrast enhancement has been described in cats with IVDH, likely because its prevalence is approximately 10 times lower than in dogs. Although several studies have described imaging findings in dogs with intervertebral disc diseases, little attention has been paid to associated nerve root pathology. Even in dogs, clinical reports describing nerve root pathology secondary to disc extrusion or chronic compression are rare. Descriptions of nerve root thickening after IVDH in dogs indicate increased signal intensity on T2-weighted sequences with and without fat suppression, as well as homogenous contrast uptake in T1-weighted sequences. In the human medical literature, mechanisms of abnormal contrast enhancement on MRI have been hypothesized to reflect a breakdown in the blood-nerve barrier (BNB) caused by injury, ischemia, inflammation, demyelination, or axonal degeneration, and increased vascular permeability with accompanying vasodilatation. In dogs, histologically lymphocytic ganglionitis has been identified after IVDH. This inflammatory change in nerve roots secondary to disc herniation is thought to be induced by entry of the nucleus pulposus into the spinal canal. It is supported by the fact that peripheral contrast enhancement of
Herniated disc material more often is found in disc extrusions as compared with protrusions in dogs and humans. Especially in dogs, the presence of calcified disc material and hemorrhage in the epidural space seems to trigger inflammatory processes with monocytes and macrophages.

Interestingly, the presence of hemorrhage and extruded disc material was identified surgically in the cat of this report without inflammatory changes and cell infiltration and with the presence of edema identified in the nerve root biopsy sample. In both experimental studies in rodents and clinical studies in humans, more severe edema was associated with rapid onset of compression. Furthermore, occurrence of nerve root edema and its extent seem to be greater when compression and contact with nucleus pulposus occur together, compared with compression of nerve root or nucleus pulposus contact alone. The acute onset of clinical signs in our case could be consistent with rapid onset of nerve compression and therefore could explain the massive and widespread intraneural edema.

In contrast to the focal nerve root changes associated with IVDH in dogs, the lesion within the nerve in our cat extended much farther distally. Although no MRI anatomical studies of the pelvic plexus in healthy cats have been performed, in healthy dogs no contrast enhancement in the pelvic plexus is observed. Contrast enhancement along the peripheral nerve indicates breakdown of the BNB. Especially in traumatic cases, increased contrast enhancement is consistent with more severe nerve injury. The intact BNB represents a complex of endoneurial endothelial cells forming specialized tight junctions, increasing intraneural edema and contrast uptake under increasing pressure. Intraneural edema caused by mechanical compression is vasogenic in origin, induced by congestion of venous blood flow. The BNB is maintained in arterial blood flow, but after congestion of the vulnerable venous system, perfusion in capillaries (feeding nerve roots directly) and venules is impaired leading to ischemia and intraneural edema by breakdown of the BNB. In experimental rodent models, increased BNB permeability in the entire nerve distal to the injury could be found as early as 3 days after induced contusion, with maximal BNB permeability after 7 days. The MRI features described here and associated with the acute onset of clinical signs mirror the experimental model and suggest sudden onset of severe pressure on the nerve root. Thickening of the nerve root and contrast uptake have not been reported to influence outcome in dogs with IVDH. Similarly, in humans reversibility of these findings after decompressive surgery has been demonstrated. The overall outcome in IVDH in cats is considered good to excellent after decompressive surgery, but the relevance of concomitant thickening and contrast enhancement of the nerve or nerve root in cats is unknown. The cat described here showed complete neurological recovery and reversibility of nerve and nerve root changes on MRI within 4 months after surgery, suggesting that, similar to IVDH in dogs, thickening and increased contrast uptake of the nerve root may not be an indicator of negative outcome.

The mechanism underlying the lack of focal inflammatory response in the nerve root remains unclear and contrasts with previous reports in dogs with IVDH. To our knowledge, no study has described inflammatory cell infiltration after disc extrusion in cats or the absorption of disc material, which is considered an indicator for inflammation. Inflammatory reactions in degenerated or herniated disc material may be different in cats compared to dogs and people.

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FIGURE 3
Comparison of the preoperative and 3 months postoperative time points. Sagittal T2-weighted (T2W), A-B, and transverse T1-weighted (T1W) spectral presaturation with inversion recovery (SPIR) images at the level of S2-3, indicated by the yellow line. C, At presentation; D, At follow-up. Complete regression of the contrast uptake and thickening of the sciatic nerve was present at follow-up. D. Images displayed in radiological convention: cranial and right sides of the patient are to the left of the image.
other hand, inflammatory changes may have been missed in histopathology because of very small sample size and sample location in the dorsal root ganglion rather than in the distal portion of the affected segmental nerve. More distal biopsies of the affected nerve could have increased the sample size and allowed visualization of inflammatory cell infiltration. Nevertheless, sampling of the nerve root was performed surgically during hemilaminectomy in a segment of the nerve root that showed not only representative changes on MRI, but also macroscopic changes during surgery and is therefore considered representative. Histologic findings from benign nerve root pathologies are rarely reported in veterinary medicine and include a wide spectrum of changes and possible species-specific responses have yet to be described.

This case documents complete neurological recovery in a cat with severe, distally extending nerve thickening as well as increased contrast enhancement secondary to IVDH. Severe nerve root thickening together with increased contrast enhancement may be present in nerve edema in cats secondary IVDH and should be a differential diagnosis in addition to neoplasia or chronic neuritis.

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CONFLICT OF INTEREST DECLARATION
Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION
Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION
Authors declare no IACUC or other approval was needed. We report a clinical patient that received standard of care treatment. Therefore no ethical approval is required.

HUMAN ETHICS APPROVAL DECLARATION
Authors declare human ethics approval was not needed for this study.

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