Chronic Hypertrophic Ganglioneuritis Mimicking Spinal Nerve Neoplasia: Clinical, Imaging, Pathologic Findings, and Outcome after Surgical Treatment

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Objective: To report the clinical, imaging, pathologic findings, surgical planning, and long-term outcome after surgery in a dog with neurologic deficits because of a hypertrophic ganglioneuritis that compressed the spinal cord.

Study Design: Clinical report.

Animal: An 8-year-old male intact Yorkshire terrier.

Methods: The dog had ambulatory tetraparesis and neurologic examination was consistent with a C1-C5 myelopathy. Magnetic resonance imaging (MRI) revealed enlargement of the left C2 spinal nerve causing compression of the spinal cord. The main differential diagnosis was spinal nerve neoplasia with compression and possibly spinal cord invasion. On ultrasonography, there was enlargement of the spinal nerve and fine needle aspiration did not show evidence of neoplasia. Fascicular biopsy of the spinal nerve was consistent with enlargement because of chronic inflammation (hypertrophic neuritis).

Results: Hemilaminectomy followed by durotomy and rhizotomy allowed resection of an intradural-extramedullary mass that was the enlarged left C2 spinal nerve. Histopathology was consistent with a hypertrophic ganglioneuritis. Thirteen months later the dog remained free of clinical signs.

Conclusion: Hypertrophic neuritis affecting the spinal nerves may be misdiagnosed as spinal nerve neoplasia that in dogs is usually malignant with a poor prognosis. Focal spinal nerve lesions with compression of the spinal cord evident on MRI may be inflammatory and are not necessarily a neoplastic condition.

Hypertrophic inflammatory neuropathy or hypertrophic neuritis is a rare clinical entity of unknown cause described in people and animals. Many cases in people are characterized by chronic demyelinating polyneuropathy accompanied by the formation of onion bulbs formed by proliferated Schwann cells, associated with focal chronic inflammation.1–3 Lesions in dogs are rare and more focal, apparently involving single nerves (BAS; unpublished) and marked by chronic lymphocytic inflammation in which onion bulb formation is not a feature.

Although the most common cause of diffuse or localized enlargement of the peripheral or spinal nerves is a neoplastic process, other causes such as inflammatory (infectious or not), metabolic, reactive processes, or inherited diseases may produce selective enlargement of the peripheral or spinal nerves.1,4,5

Focal forms of hypertrophic inflammatory neuropathy affecting the nerve root are an uncommon condition in both people and animals. There are few reports of focal inflammatory neuropathies in animals; however, information on outcome, imaging, and pathologic findings has been limited.6–8

We report a case of chronic hypertrophic ganglioneuritis mimicking neoplasia of the C2 spinal nerve in a dog with clinical signs of cervical myelopathy. The clinical signs, MRI, ultrasonographic, and pathologic findings, and successful outcome after surgical treatment are described.

CLINICAL REPORT

History and Clinical Findings

An 8-year-old, male intact Yorkshire terrier was admitted with a 3-week history of left thoracic limb monoparesis that progressed to ambulatory tetraparesis. The owners were unaware of any traumatic incident to the dog. General physical examination did not reveal abnormalities; however, on neurologic examination there was moderate ambulatory...
tetraparesis, worse on the left side. The dog had moderate proprioceptive ataxia in all 4 limbs, worse in the pelvic limbs, and was dragging the left thoracic limb. Postural reactions (paw replacement and hopping) were absent in the left thoracic limb and delayed in the other limbs. Mild neck hyperesthesia was noted upon manipulation of the cervical spine. The rest of the neurologic examination was unremarkable. On the basis of the neurologic examination, a cervical myelopathy (C1-C5 spinal cord segments) was considered most likely. The main differential diagnoses given the clinical history and neurologic findings were as follows: lateralized intervertebral disk disease, neoplastic process, and inflammatory condition. Other conditions such as syringomyelia, arachnoid diverticulum, or synovial cyst were considered less likely.

Results of complete blood count, serum biochemical profile, thoracic radiographs, and abdominal ultrasonography were unremarkable. Survey radiographs of the vertebral column under general anesthesia did not reveal abnormalities.

**Imaging Findings**

Magnetic resonance imaging (MRI) of the cervical spinal cord was performed using a 1.0-tesla (T) superconducting magnet system (Intera 1.0T, Philips Healthcare, Surrey, UK; Fig 1). MRI of the cervical spine revealed severe enlargement of the trunk and ventral branch of the left C2 spinal nerve within the paraspinal musculature. The enlarged segment of the nerve passed through the C1-C2 intervertebral foramen into the vertebral canal with marked thickening of tissue in the dorsal and ventral nerve rootlet regions and invasion into the left dorsal and ventral lateral aspects of the spinal cord. The spinal cord was severely compressed at this level by the mass of abnormal tissue. The nerve and spinal cord components of the mass were isointense on T1-weighted images (WI) and hyperintense on T2-WI to paraspinal muscle. On T1-WI after contrast gadolinium administration (Magnevist, Bayer Healthcare Pharmaceuticals, Newbury, UK) there was marked and homogeneous contrast enhancement. The peripheral portion of the enlarged nerve extended from the intervertebral foramen into the peripheral soft tissues for approximately 1.5 cm and was 0.5 cm at the level immediate exterior to the intervertebral foramen. Within the spinal cord the contrast enhancing portions of the mass encompassed approximately 50% of the transverse diameter of the spinal cord. The left dorsal paraspinal musculature showed increase in signal intensity on T1-WI and T2-WI consistent with fat replacement secondary to a likely neurogenic atrophy of the muscle.

Cerebrospinal fluid (CSF) analysis obtained from a lumbar puncture was unremarkable (total protein, 35 mg/dL [reference interval, <45 mg/dL]; total nucleated cell count 1 cell/μL [reference interval, <5 cells/μL]; cytology showed some mononuclear cells. Polymerase chain reaction (PCR) for *Neospora caninum* and *Toxoplasma gondii* on blood were negative. On the basis of the MRI findings, the main differential diagnosis was neoplasia of

![Figure 1](image)

**Figure 1** Initial MRI (A–C) T2-weighted sagittal and transverse images, (D–F) precontrast and (G–I) postcontrast T1-weighted sagittal and transverse images of the cervical spinal cord. Note the markedly enlarged portions of the left C2 spinal nerve including peripheral, foraminal, and nerve rootlet components (yellow arrows). Distinguishing the specific location of the mass relative to the spinal cord is challenging. On the T2 images the mass is located extradurally, but also appears intradural/extramedullary with spinal cord compression ([A–C] yellow arrows). On postcontrast images, the contrast-enhancing portions of the nerve mass extend and compress markedly the spinal cord ([G–I] yellow and white arrows). Atrophy of the regional musculature is present.
the C2 spinal nerve with extension into the spinal cord. The primary differential was a malignant nerve sheath tumor (MNST) followed by spinal nerve lymphoma. Although less likely, an inflammatory or reactive process such as hypertrophic neuropathy was also considered.

Ultrasound examination (Logiq e Vet GE Medical, Milwaukee, WI) of the C1-C2 intervertebral foramina on both sides of the neck was performed. At the level of the caudal cervical vertebrae, a 10 MHz 12L-RS linear probe and Power Doppler were used to distinguish the C2 spinal nerve from surrounding vessels. The normal C2 spinal nerve on the right side was seen as a hypoechoic band about 2 mm wide exiting the intervertebral foramina between the hyper-echoic pedicles of the C1 and C2 vertebrae. On the left side, the C2 spinal nerve was swollen and appeared as a hypoechoic band 5 mm wide with well-defined margins (Fig 2). Ultrasound-guided fine needle aspirates (FNAs) were obtained from the spinal nerve on the left side as described for peripheral nerve sheath tumors. Samples were collected using negative pressure as well as multiple thrusts of the needle through the spinal nerve. Ultrasound-guided FNAs of the left C2 spinal nerve revealed only a few mononuclear scattered cells in a basophilic background. Because of the guarded prognosis, a fascicular biopsy of the left C2 spinal nerve was offered to the owners before attempting a more aggressive surgical approach.

Surgical Incisional Biopsy

After premedication with methadone (0.2 mg/kg intravenously [IV]) and acepromazine (0.02 mg/kg IV), anesthesia was induced with diazepam (0.5 mg/kg IV) and propofol (3 mg/kg IV) and maintained with isoflurane in oxygen. The dog was positioned in sternal recumbency with the head gently flexed in a neutral position. A dorsal approach to the cranial cervical spine was performed. Upon identification of the body of the axis, fibrotic muscles (likely secondary to atrophy) were noted and a swollen and reddish structure, consistent with the left C2 spinal nerve, was seen ventral to the body of the axis. A fascicular biopsy of the spinal nerve was taken as well as a biopsy of the muscles surrounding the C2 spinal nerve. The muscles, subcutaneous tissues, and skin incision were apposed in layers.

Postoperative Care

The dog recovered well after surgery with no neurologic deterioration. Methadone (0.2 mg/kg subcutaneously every 4 hours) was administered during the first 24 hours after surgery. A transdermal 50 µg/h fentanyl patch (Durogesic; Janssen-Cilag, UK) was placed to manage pain during the first 3 days. Cephalexin (20 mg/kg IV every 8 hours) was administered for 3 days. The dog was discharged 3 days after surgery with instructions to administer prednisone (0.5 mg/kg orally every 12 hours for 3 weeks), ranitidine (1 mg/kg orally every 12 hours for 3 weeks), and cephalexin (20 mg/kg orally every 12 hours for 3 days).

Histopathology

Formalin fixed, paraffin-embedded sections were stained with hematoxylin and eosin. Microscopic examination of the abnormal spinal C2 nerve revealed the endoneurium to be expanded by a variable proportion of myxoid stroma and proliferated cells with fusiform nuclei that seemed to be Schwann cells or endoneural fibroblasts (Fig 3). Multifocal perivascular lymphocytes and neutrophils were observed infiltrating the supporting soft tissue and a moderate lymphocytic infiltrate was also found within the nerve fibers. The skeletal muscle was characterized by degenerative changes with variation in muscle fiber size, increased interstitial cells (neutrophils, lymphocytes, and macrophages), a focus of small angular fibers, suggesting denervation atrophy, and occasional internal nuclei. The histopathologic findings were consistent with chronic inflammatory condition rather than a neoplastic process. A diagnosis of hypertrophic neuritis with neurogenic muscular denervation was made.

Given the histopathologic findings, more invasive surgery to excise the mass was offered to the owners;
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**Figure 3** Hematoxylin and eosin stained section of the incisional biopsy of the abnormal C2 spinal nerve. Overview of the peripheral nerve showing an inflammatory infiltrate (A), myxoid changes (B), and cell proliferation within the endoneurium (C). Inset A (detail of the inflammatory infiltrate). Inset B (myxoid change within the nerve. Inset C (cell proliferation within the endoneurium. Hematoxylin and eosin ×40, scale bar 1 cm = 160 microns.

However, they declined surgery and treatment with prednisone (0.5 mg/kg orally every 12 hours) was continued. Mild improvement was noticed during the first 2 weeks, but over the next 2 months the dog’s neurologic status deteriorated progressively to a nonambulatory tetraparesis. At this time recheck MRI of the cervical spine revealed an increase in the size of the affected nerve (Fig 4) and the owners elected to perform surgery.

**Surgical Excisional Biopsy**

The dog was premedicated with methadone (0.2 mg/kg IV) and acepromazine (0.02 mg/kg IV), induced with diazepam (0.5 mg/Kg IV) and propofol (3 mg/kg/ IV), and maintained with isoflurane in oxygen. The dog was positioned in sternal recumbency with the neck ventroflexed. Cephalexin (20 mg/kg IV) was given intraoperatively every 2 hours and methadone (0.2 mg/kg IV every 4 hours) to reduce pain. A dorsal median skin incision was made extending from the occipital protuberance to the middle of C4 caudally. The subcutaneous fascia was incised to expose the superficial cervical musculature (occipitalis, cervicoscutularis, and cervicoauricularis and platysma). The superficial cervical musculature was separated on the midline fibrous raphe allowing the exposition of the paired biventer cervicis muscles. The paired biventer cervicis muscles were separated exposing the rectus capitis dorsalis muscle. The cranial and caudal aspects of the rectus capitis dorsalis were removed from the bone by combined blunt and sharp dissection and periosteal elevation to expose the cranial half of C2 and the arch of the atlas on the left side. At this stage, a firm white to grayish mass consistent with the left C2 spinal nerve was seen (Fig 5A).

A dorsolateral left-sided hemilaminectomy was performed using a high-speed air drill at the level of C1-C2 intervertebral space. The hemilaminectomy extended over the caudal half of the dorsal lamina of the atlas and the cranial half of the axis. The interarcuate ligament was carefully incised to expose the spinal cord and the spinal root. Durotomy was performed and exposed a firm grayish mass located along the left dorsal aspect of the spinal cord, apparently originating from the left C2 spinal nerve that seemed to be involving both dorsal and ventral roots. The mass did not seem to infiltrate the spinal cord parenchyma. Durotomy and rhizotomy allowed a complete gross resection of the abnormal nerve root based on the surgeons’ assessment. Tissue was submitted for histopathologic evaluation. The

**Figure 4** Postcontrast T1-weighted sagittal (A) and transverse (B) images of the cervical spinal cord. Note the contrast enhancing portions of the nerve mass causing severe compression of the spinal cord (white arrows).
laminectomy was covered with a fat graft and cervical musculature, subcutaneous tissues and skin were apposed in layers.

Postoperative Care

Methadone (0.2 mg/kg, subcutaneously every 4 hours) was administered for the initial 24 hours after surgery. A fentanyl patch (50 μg/h) was placed on the dorsum. Gabapentin (7 mg/kg orally every 12 hours), cephalaxin (20 mg/kg/IV every 8 hours), ranitidine (1 mg/kg IV every 12 hours) and prednisone (0.5 mg/kg orally every 12 hours) were administered for 5 days.

The dog recovered uneventfully from surgery and 3 days later the dog was able to walk unassisted and was discharged 5 days after surgery. At discharge, the dog had ambulatory tetraparesis with moderate proprioceptive ataxia in all 4 limbs and mild discomfort upon manipulation of the cervical spine. Postoperative medications included, gabapentin (7 mg/kg orally every 12 hours for 1 week) and a 3-week tapering course of prednisone (starting dose 0.5 mg/kg orally every 24 hours).

The excised tissues were formalin fixed, embedded in paraffin, and sections were stained with hematoxylin and eosin. Histopathology of the abnormal C2 nerve root revealed an expanded endoneurium with clusters of whorled cells in a myxoid stroma, lymphocytic infiltrates, and considerable collagen deposition in the nerve and sensory ganglion (Fig 5B). As the second biopsy specimen included the spinal ganglion with the C2 nerve, a diagnosis of chronic hypertrophic sclerosing lymphocytic ganglioneuritis was made.

Outcome

On recheck examination 2 weeks later, the dog had only mild ambulatory tetraparesis worse on the left side. Recheck MRI of the cervical spine 2 months after surgery did not reveal relapse of the condition (Fig 6), at that time the neurologic examination was unremarkable. Thirteen months after surgery there was no recurrence of clinical signs and the neurologic examination was still unremarkable.

DISCUSSION

Spinal cord compression secondary to inflammatory neuropathies invading the vertebral canal is rarely described in people or dogs. Hypertrophic neuritis or hypertrophic inflammatory neuropathy is a rare non-neoplastic condition described in people, dogs, and cats. Hypertrophic neuritis is an unusual chronic inflammatory demyelinating neuropathy of unknown origin that mainly affects the brachial plexus unilaterally or bilaterally and can be focal or multifocal. Brachial plexus neuritis as a cause of a multiple mononeuropathy is a rare inflammatory disorder limited to the brachial plexus that has been reported in people, dogs, and cats.

Focal chronic inflammatory neuropathies affecting the spinal nerves are a rare condition in human and veterinary medicine. Most common causes of spinal nerve enlargement in dogs are neoplasms such as nerve sheath tumors or peripheral nervous system (PNS) lymphomas. However, non-neoplastic tumor-like conditions (inflammatory and/or degenerative hypertrophic neuropathies) are increasingly being reported in both human and veterinary literature as a cause of focal spinal nerve enlargement.

MRI is the modality of choice for the diagnosis of spinal cord diseases in humans and is becoming more widely available in veterinary medicine. The major advantages of MRI compared with other imaging modalities is obtaining images in multiple planes and the superior resolution for imaging soft tissues, such as the spinal cord, nerve roots, skeletal muscle, brachial plexus region, or intervertebral discs.

There are a few reports on use of MRI in animals with inflammatory neuropathies. In people, MRI is useful for detection of non-neoplastic hypertrophy of spinal nerve roots, particularly in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). MRI findings of brachial plexus neuritis have been described in 2 dogs and 1 cat. Hypertrophy of the cervicothoracic nerve
Figure 6  T2-weighted sagittal (A) and transverse (B) and T1-weighted sagittal (C) and transverse (D) images after gadolinium administration of the cervical spinal cord showing no evidence of relapse of the mass. Mild contrast enhancement can be observed in laminectomy site indicating probably postoperative scarring from the previous surgery.

roots in a dog has been reported in a dog with CIDP.\textsuperscript{22} To our knowledge, there have been few reports in animals of focal hypertrophic neuritis of the nerve roots with compression of the spinal cord diagnosed by means of MRI and confirmed histopathologically; published reports have been abstracts.\textsuperscript{6,7} In our dog, on MRI, there was marked thickening of the C2 spinal nerve that was likely secondary to the cellular inflammation, myxoid stromal deposits, and sclerosis. Further, MRI allowed identification of an intradural extramedullary spinal cord mass arising from the second cervical spinal nerve. However, the first differential diagnosis based on MRI findings was spinal nerve neoplasia with an inflammatory condition of the spinal nerve being less likely.

Ultrasonography in the diagnosis of disorders of the peripheral nervous system has been reported in dogs.\textsuperscript{23,24} Ultrasound examination has been reported as a useful tool in the diagnosis of peripheral nerve tumors in people and animal. Reports describing ultrasonographic diagnosis of nerve sheath tumors in dogs have been limited to tumors located in the brachial plexus.\textsuperscript{10,23} To our knowledge, the ultrasonographic characteristics of hypertrophic inflammatory neuropathy affecting either the brachial plexus or the spinal nerves have not been described in animals. Detection of cervical nerve root hypertrophy by means of ultrasonography in people with CIDP has been reported\textsuperscript{21} and there was an excellent capability for detecting hypertrophy of the cervical nerve roots. The authors suggested that ultrasound examination might become the method of first choice in the diagnosis of hypertrophy of cervical nerve roots in patients with chronic CIDP.\textsuperscript{21} Ultrasonography could be useful in animals for detecting hypertrophy of the nerve roots when co-localizing signs exist such as focal neurogenic atrophy or previous imaging findings as occurred in this dog. Ultrasound examination revealed moderate hypertrophy of the cervical spinal root in our dog, which was consistent with MRI findings, and facilitated FNA of the swollen spinal nerve. However, ultrasound FNA revealed only a few scattered mononuclear cells, excluding a definitive diagnosis. Since FNA yields smaller tissue fragments than samples obtained by incisional or excisional biopsy, many of the morphologic criteria used by pathologists in the diagnosis of tumors are not present.\textsuperscript{25} One of the main limitations of ultrasound-guided FNA is the possibility of false negative results, especially if the mass is small or if nondiagnostic aspirates are taken.\textsuperscript{10} In our dog, a neoplastic process could not be ruled out on the basis of the normal FNA cytologic features. Further studies are necessary to evaluate the potential usefulness of ultrasound and ultrasound-FNA in identifying inflammatory or neoplastic conditions affecting the nerve roots of animals.

The histopathologic findings were consistent with hypertrophic neuritis affecting the spinal nerve in which chronic inflammation and matrix deposition within the nerve were the major features. Onion bulb formation, a feature of some chronic hypertrophic neuropathies in people, resulting from Schwann cell proliferation after repeated episodes of demyelination and remyelination, was not evident in this dog.\textsuperscript{26,27} Other differential histopathologic diagnoses of a focal spinal nerve enlargement include localized hypertrophic neuropathy (LHN) which is now known as intraneural perineuroma. When first identified, LHN
Corticosteroid treatment is usually in-annual; 85:251–260
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or neoplasms.
Acta Neuropathol (Berl.)
may have a benign cause such as inflammation that can be
as a reminder that focal spinal nerve enlargement in dogs
nerves may be misdiagnosed as spinal nerve neoplasia, par-
ticulary nerve sheath tumors and it appears that standard
nerves as in this case is advocated based on the similar
MRI appearance of neoplastic and more benign processes
such as hypertrophic neuritis or ganglionneuritis. In people,
fascicular biopsy of the peripheral or spinal nerves has
been proven of great value to make the correct histopatho-
logic diagnosis and optimal treatment in patients with either
hypertrophic inflammatory neuropathies or neoplasms.
Limited data are available regarding prognosis of hyper-
trophic neuritis and secondary compression of the spinal
cord in dogs, however it seems that hemilaminectomy, duro-
tomy, and resection of the affected spinal nerve results in
favorable prognosis. Corticosteroid treatment is usually in-
effective in cases of chronic hypertrophic neuritis. In this
dog, treatment with corticosteroids led to mild improve-
ment during the first 2 weeks; however, the dog’s neuro-
logic condition subsequently deteriorated. Hemilaminec-
tomy and durotomy followed by rhizotomy of the nerve
root and spinal nerve allowed complete resection of the af-
fected cervical spinal nerve and the dog was free of clinical
signs 13 months after surgery.

Summarily, hypertrophic neuritis affecting the spinal
nerves may be misdiagnosed as spinal nerve neoplasia, par-
ticularly nerve sheath tumors and it appears that standard
MRI sequences are not able to discriminate between inflam-
matory and neoplastic nerve enlargement. This case serves
as a reminder that focal spinal nerve enlargement in dogs
may have a benign cause such as inflammation that can be
managed surgically with a favorable clinical outcome.

REFERENCES


