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Note

Full title: Hypertrophic neuritis causing tetraparesis in a cat

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Running head: HYPERTROPHIC NEURITIS IN A CAT
ABSTRACT

An 8-year-old castrated male cat presented with acute ataxia and paresis in all four limbs. The cat also exhibited signs of autonomic nervous system impairment. Magnetic resonance imaging revealed swelling of the brachial plexuses bilaterally. Despite treatment, the cat died after 10 days of treatment. A postmortem examination revealed swollen radial nerves and cervical nerve roots in which infiltration of inflammatory cells was histologically confirmed. Additionally, lymphocytic infiltration was found around the blood vessels of the sciatic nerve bundle and the vagus nerve. Histological features were comparable to previously reported brachial plexus hypertrophic neuritis in a cat. Our case was unique in that the autonomic nerves were also involved in addition to the somatic nerves in all four limbs.

KEY WORDS

brachial plexus, feline, hypertrophic neuritis, polyneuropathy, tetraparesis
Enlargement of the peripheral nerves is a feature of various peripheral neuropathies, for which the term “hypertrophic neuritis” usually indicates the unique pathological changes associated with onion bulb formation [10]. Hypertrophic neuritis is a non-neoplastic condition, mainly causing demyelinating neuropathy in humans and dogs [7, 10, 12, 13]. Many cases in humans are characterized by chronic inflammatory demyelinating polyneuropathy (CIDP) accompanied by the formation of onion bulbs composed of proliferated Schwann cells and chronic focal inflammation [1, 10, 13]. There is currently only a single report of a cat with hypertrophic neuritis of the brachial plexuses [3]. We described herein a cat with hypertrophic neuritis mainly involving the brachial plexuses, similar to the previously reported case, but which additionally had involvement of the sciatic nerve and the autonomic nervous system.

An 8-year-old castrated male domestic shorthair cat was referred to us with a 5-day history of paresis in all four limbs and anorexia. The cat was initially lifting his left thoracic limb. Within 5 days, clinical signs progressed to severe knuckling in the left thoracic limb followed by the right thoracic limb. Previous serological tests for feline leukemia virus antigen and feline immunodeficiency virus (FIV) antibodies were negative and positive, respectively. The cat had no history of exposure to toxins or trauma. On physical examination, heart rate, body temperature and lymph nodes were unremarkable. The cat was tachypneic, and bronchovesicular breath sounds were detected. Neurological examination revealed that the cat was tetraparetic and non-ambulatory. Postural reactions were reduced in all four limbs and were worst on the left thoracic limb. Spinal reflexes were reduced in all four limbs. On cranial nerve examination, the right eye exhibited miosis. Based on these findings, multifocal spinal cord lesions involving at least the C6-T2 and L4-S3 spinal cord segments and/or multiple peripheral nerve lesions were suspected. Complete blood count and serum biochemistry profile findings were within normal limits. The anti-toxoplasma antibody test was negative. Thoracic
radiographs revealed esophageal dilatation, gas in the digestive tract, and a mixed alveolar and interstitial lung pattern, which was most likely related to aspiration pneumonia. Abdominal ultrasound examination was unremarkable.

We performed magnetic resonance imaging (MRI) (0.4-Tesla APERTO Eterna; Hitachi, Tokyo, Japan) in order to evaluate the spinal cord and the brachial plexus. Anesthesia was induced with propofol (propofol for animal; Mylan Inc., Canonsburg, PA, U.S.A.) and maintained with isoflurane (isoflurane for animal; Mylan Inc.). T2-weighted images (TR=1,600 msec and TE=105 msec), fluid-attenuated inversion recovery (FLAIR) images (TR=9,000 msec, TE=100 msec), and pre- and post-contrast (following intravenous injection of 0.1 mmol/kg of gadodiamide hydrate) (Omniscan; Daiichisankyo, Tokyo, Japan) T1-weighted images (TR=450 msec and TE=18 msec) of the cervical and thoracic spinal cords were obtained. T2-weighted images and FLAIR images depicted severe swelling of the brachial plexuses bilaterally. The swollen cervical spinal nerves were hyperintense to surrounding muscles on T2-weighted images and FLAIR images, and isointense on T1-weighted images (Fig. 1A-C). The brachial plexuses were remarkably enhanced on post-contrast T1-weighted images (Fig. 1D). Fine needle aspiration of the swollen brachial plexus was performed under ultrasonographic guidance; however, cytology was not diagnostic due to an insufficient number of cells obtained.

Based on the suspected immune mediated etiology of the disease, the cat received prednisolone (Predonine; Shionogi & Co., Ltd., Osaka, Japan) orally at 1 mg/kg twice daily. Enrofloxacin (Baytril; Bayer Yakuhin, Ltd., Osaka, Japan) was given orally at 5 mg/kg once daily for suspected aspiration pneumonia. Three days later, recovery of postural reactions was noted in the hindlimbs, but not in the thoracic limbs and there were no improvements in breathing or appetite. Severe pain in the thoracic limbs and respiratory deterioration were observed after 7 days of treatment. Gabapentin (Gabapen; Pfizer Inc., New York, NY, U.S.A.)
was administered orally at 3 mg/kg three times a day, and had a mild analgesic effect.

Neurological conditions and breathing deteriorated, followed by the development of flaccid tetraplegia and dyspnea. The cat died of respiratory failure after 10 days of the treatment after which necropsy was performed with the owner’s consent.

Postmortem macroscopic examination revealed marked enlargement of the brachial plexuses bilaterally and the lumbosacral nerve roots (Fig. 2A, B). No abnormalities were noted grossly at multiple transverse sections of the spinal cord. Pulmonary edema was found in the lung. For light microscopy, tissue samples were fixed in 10% formalin, and paraffin-embedded sections were stained with hematoxylin and eosin. Microscopic examination showed infiltration of lymphocytes, macrophages and plasma cells in the swollen cervical nerve roots (Fig. 2C) and radial nerves (Fig. 2D). Axon fragmentation with macrophage invasion was observed in radial nerves. In sciatic nerve bundles, lymphocytes mainly infiltrated around the blood vessels (Fig. 2E). The peripheral nerve in the coronary adipose tissue was infiltrated by a small number of lymphocytes and macrophages. The vagus nerve innervating the stomach showed mild accumulation of lymphocytes and plasma cells. Infectious pathogens were not detected by histopathological examination of peripheral nerves; however, polymerase chain reaction (PCR) of the seventh cervical nerve tissue for FIV was positive. In the parenchyma of the spinal cord, no abnormalities were observed. Obstructive edema without bacteria was detected in the lung, which was considered to be the direct cause of death.

Differential diagnosis of polyneuritis includes infectious [2, 5, 9, 11] and immune-mediated [4, 6] causes. In our case, immune-mediated etiology was suspected as histopathological examination detected no infectious pathogens. Postmortem examination by PCR demonstrated the presence of FIV antigens in the peripheral nerves of our case. Although we did not directly demonstrate a relationship between FIV and polyneuritis in the present
case, these two diseases may have been related as a previous experimental study reported that
FIV induced immune compromises and dysfunction of the peripheral nervous system [8].
Severely enlarged peripheral nerves of the brachial plexus were characteristic in our case and
a previously reported case of hypertrophic neuritis [3], in which the affected nerves were
limited to the brachial plexuses. In contrast, in our case, inflammatory changes were found
not only in the brachial plexuses, but also in the sciatic nerve and autonomous nerves.
Inflammatory changes in sciatic nerve bundles were milder than in the radial nerve.
Considering the clinical signs, it is thought that the disorders in the sciatic nerve were of an
early stage.
In humans, hypertrophic neuritis is a rare clinical entity of unknown cause that
mainly affects the brachial plexus unilaterally or bilaterally and can be focal or multifocal [13].
A histopathological feature of the affected peripheral nerves in humans is chronic
inflammatory demyelination accompanied by onion bulb formation, resulting from Schwann
cell proliferation after repeated episodes of demyelination and remyelination [13, 14]. In our
case, onion bulb formation was not observed, similar to the previously reported cases of
hypertrophic neuritis of the brachial plexus that described chronic lymphocytic inflammation
in the absence of onion bulb formation [3]. Therefore, hypertrophic neuritis may be a different
pathological entity in humans and cats.
We speculate that dysfunction of the somatic nervous system produced
non-weight-bearing protraction of the limbs. Although megaesophagus can result from
somatic nerve dysfunctions, the miosis, gas in the digestive tract and megaesophagus found in
our case may suggest impairments of the autonomic nervous system.
Our case emphasized the notion that various nerves can be impaired by
hypertrophic neuritis in cats. Hypertrophic neuritis should be taken into consideration as a
differential diagnosis of tetraparesis and signs of autonomic dysfunctions in cats.
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**Figure legends**

Fig. 1. Magnetic resonance images of the brachial plexus at the level of the C7-T1 intervertebral disk space. T2-weighted images (A), fluid-attenuated inversion recovery images (B), and T1-weighted pre- (C) and post-contrast images (D) are shown. A bilateral symmetrical abnormality was due to the severely swollen eighth cervical nerve and brachial plexus (white arrows). The swollen cervical nerves were hyperintense on T2-weighted images and FLAIR images and isointense on T1-weighted images. The lesion was enhanced using gadodiamide hydrate.

Fig. 2. Macro- and microscopic views of the brachial plexuses and lumbosacral spinal cord. A ventral view of the brachial plexus (A) showed swelling with notable thickening of the sixth, seventh, and eighth cervical nerve roots (white arrowheads). A dorsal view of the lumbosacral spinal cord also showed swelling with notable thickening of the seventh lumbar nerve root and first sacral nerve root (black arrowheads; B). A microscopic view (hematoxylin and eosin) of longitudinal sections of the eighth cervical nerve root (C) and radial nerves (D) showed infiltration of lymphocytes, macrophages, and plasma cells. Axon fragmentation (black arrow) with macrophage invasion (black arrowheads) was observed on the radial nerve. Furthermore, in sciatic nerve bundles (E), lymphocytes were mainly infiltrated around the blood vessels. Scale bar in C = 100 μm and D = 50 μm (applies to D and E).
Fig. 1