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Case Report
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Magnetic Resonance Imaging Findings in a Dog with Sensory Neuronopathy

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A 3-year-old, male neutered Miniature Dachshund was presented for investigation of an acute onset, slowly progressive ataxia of 2 months' duration. Serum titers for *Toxoplasma gondii* and *Neospora caninum* evaluated before referral were negative. General physical examination was within normal limits. Neurological examination identified a "bouncy" generalized ataxia with exaggerated movements of all of the limbs, neck and head. No apparent paresis was present. The dog had proprioceptive deficits in all limbs manifested by a delay in hopping and paw placement. Clinical signs and neurological abnormalities were more severe in the pelvic limbs. The dog had bilaterally decreased menace responses and palpebral reflexes. The remainder of the neurologic examination was within normal limits. A diffuse or multifocal neuro-anatomic localization was considered most likely. Results of a CBC and serum biochemistry profile were within reference intervals. The dog was premedicated with butorphanol (0.2 mg/kg IV) and anesthesia was induced with propofol (3.5 mg/kg IV) and maintained with sevoflurane in oxygen. Magnetic resonance imaging[a] (MRI) of the brain and cervical spinal cord included T2-weighted (repetition time, [TR] [ms], echo time [TE] [ms] 3333/110) sagittal and transverse images and transverse fluid attenuation inversion recovery (TR/TE, 6000/120) images. Sagittal and transverse plane T1-weighted images (TR/TE, 515/15) were acquired before and after IV injection of gadolinium contrast material.[b] Slice thickness was 3.5 mm in all planes with an interslice gap of 0.9 mm in the sagittal and 1 mm in the transverse planes. No abnormalities were identified on MRI of the brain. In the cervical spinal cord, a linear, intra-parenchymal signal, hyperintense on T2-weighted images, delineated the dorsal funiculus (Fig 1). No contrast enhancement was observed. Differential diagnoses at this time included an inflammatory spinal cord disorder, a neurodegenerative disorder involving the cervical spinal cord, or a sensory neuronopathy. Analysis of cerebrospinal fluid, obtained by cisternal and lumbar punctures was within normal limits. Based on these findings, a sensory neuronopathy was considered the most likely diagnosis.

Abbreviations:

ERG	electroretinogram
MRI	magnetic resonance imaging

Neurologic re-examination 1 month later identified worsening of the dog's ataxia, decreased patellar reflexes and decreased nociception in the digits of all limbs. Electrodiagnostic evaluation and spinal ganglion biopsy were offered, but declined by the owner.

The dog was presented 15 months after its initial clinical presentation for assessment of perceived vision loss and further worsening of clinical signs. There was a known familial history of progressive retinal atrophy. Neurologic examination identified severe deterioration of clinical signs. Although paresis still was not apparent, the severity of the dog's ataxia impeded ambulation. Other findings included wide head and neck excursions, proprioceptive deficits in all limbs, absent bilateral menace responses, absent bilateral palpebral and corneal reflexes, bilaterally decreased responses after stimulation of the nasal mucosa, decreased pupillary light reflexes bilaterally (direct and indirect), absent patellar reflexes bilaterally and decreased nociception in the digits of all limbs. The remainder of the neurologic examination was within normal limits. A complete ophthalmic examination confirmed visual impairment and abnormalities of ocular reflexes as described above. Rudimentary corneal esthesiometry (ie, use of cotton-tipped applicator and the noncontact air-puff technique) indicated decreased corneal sensation. General anesthesia was induced and maintained by using the previously described protocol. A mixed rod-cone electroretinogram[c] (ERG) disclosed no visible ERG in the right eye and a markedly diminished ERG in the left eye with barely discernible a and b waves. Findings of the ophthalmic and ERG examinations were in agreement with

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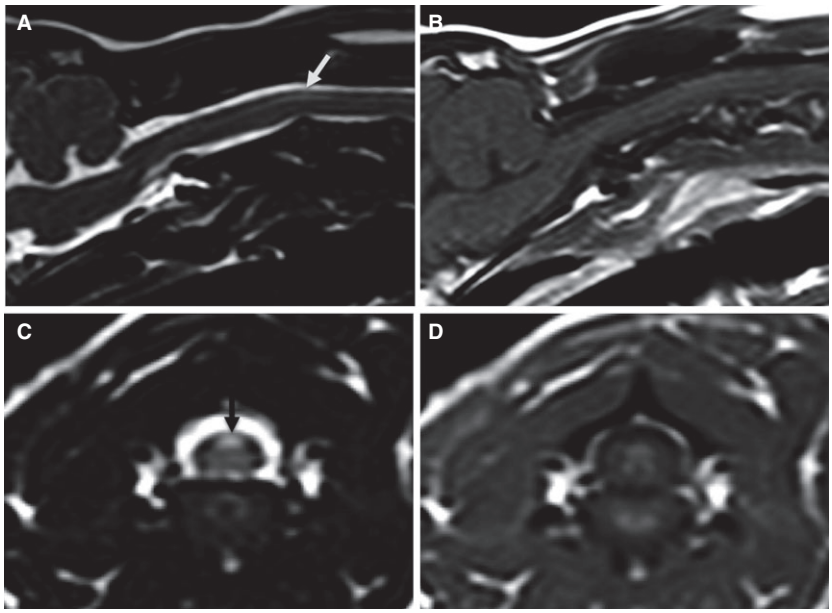

Fig 1. MRI at initial clinical presentation. (**A**) Mid-sagittal T2-weighted image of the cranial cervical spinal cord discloses a linear hyperintensity in the dorsal funiculus (white arrow). (**C**) Transverse T2-weighted image at the level of C2-C3 discloses hyperintensity of the dorsal funiculus (black arrow). (**B** and **D**) T1-weighted mid- sagittal (B) and transverse (D) images at the corresponding levels as (A) and (C), respectively.

a presumptive diagnosis of progressive retinal atrophy. Electromyography[d] of the left pelvic and thoracic limbs and epaxial musculature identified no abnormalities. Sciatic-tibial motor nerve conduction velocity was within normal limits (57 m/s; reference interval, 55–75 m/s). Tibial sensory nerve conduction velocity was decreased (31 m/s; reference interval, 63.4 $\pm$ 5.3 m/s).[1] Magnetic resonance imaging of the cervical spinal cord confirmed the previous findings and additionally, identified a hyperintensity on T2-weighted images delineating bilaterally the caudal cerebellar peduncles and cerebellar white matter (Fig 2). Cerebral cortical atrophy also was evident (Fig 2). These findings were considered suggestive for progression of the previously diagnosed presumptive sensory neuronopathy. Based on the findings in a previous case report on sensory neuronopathy in a dog,[2] medical treatment was started with cyclosporine (5 mg/kg PO q12h for 6 weeks). Serial neurologic examinations, by the same examiner (SDD), documented continued progression of the dog's clinical signs and development of difficulties prehending food. Because of concerns regarding the dog's quality of life, euthanasia was advised but declined by the owners.

Thirty-three months after the initial clinical presentation, at age 5 years and 9 months, the dog died suddenly at home and was presented immediately for a post-mortem examination. The owners reported stabilization of the dog's condition until death after the last visit to our referral institution. Post-mortem examination disclosed poor body condition with decreased muscle mass. Additional abnormalities indicated left-sided congestive heart failure as the most likely cause of death. The spinal cord appeared grossly normal. Histopathologic examination of cervical and thoracic spinal cord sections disclosed a sparsely cellular appearance of the dorsal funiculus. Staining with luxol fast blue identified diffuse myelin loss throughout the dorsal funiculus of the cervical, thoracic and lumbar spinal cord segments (Fig 3A,B) with contracted myelin sheaths and axonal atrophy. Detailed examination of selected spinal ganglia (Fig 3C) identified a decreased number of neuronal cell bodies with a small population of round cells with large dark nuclei and scant cytoplasm. Immunohistochemistry for CD3 and CD79A of the spinal ganglia was largely negative, indicating that the population of round cells most likely represented perineural satellite cells with only rare T lymphocytes (CD3-positive cells). Examination of the brainstem disclosed focally extensive loss of myelin in the lateral cuneate nucleus, the nucleus gracilis, and the medial cuneate nucleus. No other abnormalities were detected in the brainstem. Examination of the cerebellum identified bilateral symmetrical marked demyelination of the cerebellar white matter (Fig 3D) and neuronal cell loss of cerebellar nuclei. Mild lymphoplasmacytic perivascular cuffing also was seen. Examination of the cerebrum confirmed cerebrocortical atrophy with mild enlargement of the lateral ventricles. No other abnormalities were identified in the forebrain or thalamus. Detailed examination of the sciatic nerves, eyes, and optic nerves did not disclose any abnormalities. Detailed examination of the retina unfortunately was not possible because of the presence of postmortem artifacts. Examination of the trigeminal ganglion was not performed. These abnormalities were considered suggestive for neuronal cell loss in the spinal ganglia with secondary axonal and myelin loss in the dorsal funiculus; myelin loss in the nucleus gracilis, medial and lateral cuneate nuclei, cerebellar white mat-

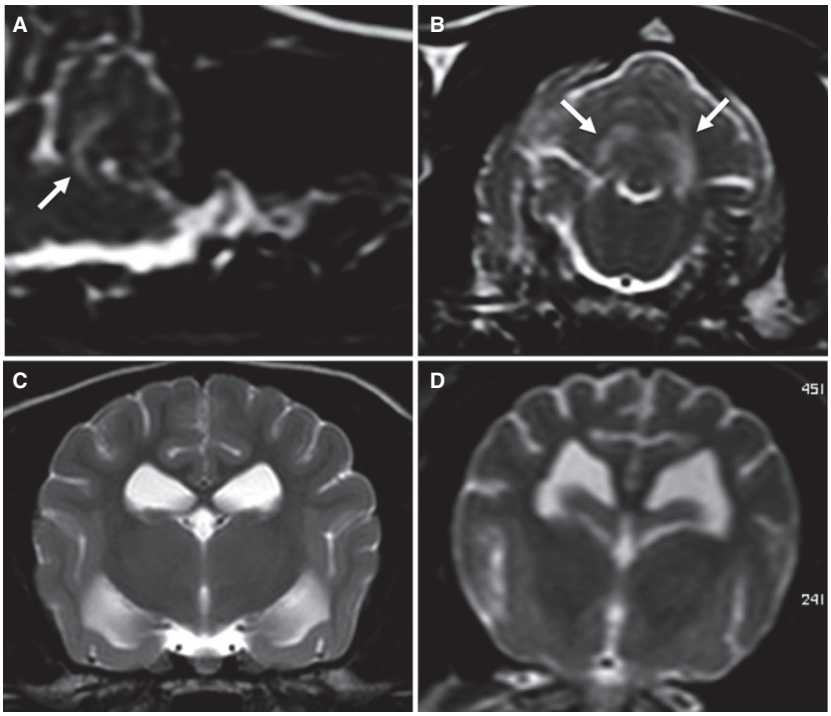

Fig 2. MRI studies at the time of initial presentation (**C**) and 15 months later (**A**, **B** and **D**). (A) T2-weighted sagittal image at the level of the cerebellum discloses hyperintensity of the caudal cerebellar peduncle (white arrow). (B) T2-weighted transverse image at the level of the cerebellum discloses bilateral hyperintensity of the caudal cerebellar peduncles (white arrows). (D) T2-weighted transverse image at the level of the forebrain discloses widened sulci compared with the initial (C) study.

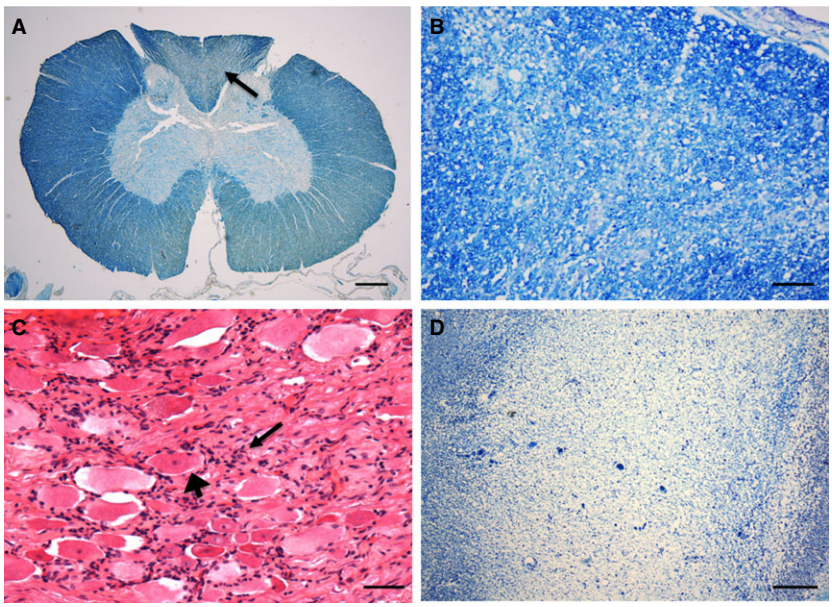

Fig 3. Histopathology of the cervical spinal cord (**A**), cervical spinal cord dorsal funiculus (**B**), cervical dorsal root ganglion (**C**), and cerebellum (**D**). (A) Focal, V-shaped extensive myelin loss in the dorsal funiculus (arrow; luxol fast blue, 20×). Scale bar 200 μm. (B) V-shaped extensive myelin loss in the dorsal funiculus (luxol fast blue, 200×). Scale bar 50 μm. (C) Diffuse neuronal loss and increased perineural satellite cells (arrow). A relative well-preserved neuron can be seen in the center of the image (arrowhead; hematoxylin and eosin, 400×). Scale bar 25 μm. (D) Extensive myelin loss in cerebellar white matter (luxol fast blue, 100×). Scale bar 100 μm.

ter; and neuronal cell loss in the cerebellar nuclei. The dog's visual impairment most likely was not related to these findings and was attributed to a presumptive diagnosis of progressive retinal atrophy.

We describe serial MRI findings in a dog with clinical, electrodiagnostic and pathologic evidence of a disorder selectively affecting some parts of the sensory nervous system. To the best of our knowledge,

MRI findings in this type of disorder has not been reported previously. Disorders that selectively affect primary sensory pathways can anatomically be divided into sensory neuronopathies, in which the primary changes occur in the nerve cell bodies or spinal ganglia[3] and sensory neuropathies, in which the more distal axon or myelin sheath primarily is affected. Although dogs with sensory neuronopathies and sensory neuropathies can have similar clinical signs, the clinical presentation of dogs with sensory neuronopathies is characterized by an obvious gait abnormality, consisting of a generalized "bouncy" ataxia,[3–8] where dogs with pure sensory neuropathies often present predominantly with signs of auto-mutilation.[9–15] The dog of this report suffered from a neuronopathy: histopathologic examination revealed abnormalities predominantly in the spinal ganglia. Although no histopathologic abnormalities were found in the sciatic nerves, electrodiagnostic evaluation indicated at least functional involvement of the sensory components of the peripheral nervous system. Sensory neuronopathies rarely occur in dogs, the most common cause being ganglioradiculitis.[3–8] Ganglioradiculitis is a disease of unknown etiology affecting adult dogs of several breeds. Histopathologically, it is characterized by mononuclear inflammation of craniospinal sensory ganglia, autonomic ganglia and dorsal nerve roots with secondary Wallerian-like degeneration of the dorsal spinal funiculus.[2–8] Clinical signs typically are acute in onset and slowly progressive, consisting of an unusual "bouncy" ataxia that most resembles cerebellar ataxia, generalized proprioceptive deficits, facial and peripheral hypalgesia, decreased patellar reflexes and difficulties prehending food.[6] Masticatory muscle atrophy, megaesophagus, dysphagia, loss of vision and loss of hearing also have been reported in dogs with ganglioradiculitis.[3–5,7,8] Although dogs can present with characteristic clinical signs, reaching a definitive diagnosis of a sensory neuronopathy requires post-mortem evaluation.[3–5,7,8]

Magnetic resonance imaging has been used in people with sensory neuronopathies for diagnosis and assessment of clinical severity.[16] Similar to the dog presented here, MRI findings in people with sensory neuronopathies also are characterized by a linear intraparenchymal hyperintensity on T2-weighted images delineating the dorsal funiculus of the cervical spinal cord.[16,17] These selective MRI abnormalities of the dorsal spinal cord columns have been associated with a primary lesion located in the spinal ganglia and dorsal nerve roots.[17] The distribution of MRI findings in the dog of this report corresponded well with our histopathologic findings and previously reported pathology reports of dogs with sensory neuronopathies.[3–5,7,8] A consistent pathologic finding in dogs with sensory neuronopathies is a V-shaped discoloration in the dorsal funiculus of the cervical spinal cord. This finding can be explained by Wallerian-like degeneration throughout the ascending dorsal spinal cord columns secondary to a primary disease process in the spinal ganglia.[6] After entering the spinal cord, the general proprioceptive axons concerned with conscious proprioception enter the dorsal funiculus without synapsing and course cranially in the fasciculus gracilis and fasciculus cuneatus, transmitting proprioceptive information respectively for the pelvic and thoracic limbs. The general proprioceptive pathways for cerebellar transmission, however, have a less uniform anatomy. Although most axons synapse near the spinal gray column before coursing cranially in 1 of the spinocerebellar tracts, axons forming the cuneocerebellar tract, similarly to the pathways for conscious proprioception, enter the dorsal funiculus without synapsing and course cranially in the fasciculus cuneatus.[6] The linear hyperintense lesion on T2-weighted images restricted to the dorsal funiculus of the cervical spinal cord therefore is likely to represent Wallerian-like degeneration of the dorsal funiculus secondary to a primary disease process affecting the spinal ganglia and dorsal nerve roots. The second MRI study demonstrated hyperintensity on T2-weighted images delineating the caudal cerebellar peduncles. Although it cannot be excluded that the dog presented here suffered from a disorder independently affecting specific parts of the sensory nervous system, this imaging finding can be explained by considering the specific anatomy of the general proprioceptive pathways and the concept of trans-synaptic degeneration. The proprioceptive axons traveling cranially in the dorsal funiculus synapse in the caudal medulla. More specifically, the proprioceptive axons for conscious proprioception synapse in the nucleus gracilis and medial cuneate nucleus, whereas axons of the cuneocerebellar tract synapse in the lateral cuneate nucleus. Axons of neuronal cell bodies in the lateral cuneate nucleus finally enter the cerebellum via the caudal cerebellar peduncle.[6] Neurons form interconnected networks, whereby axon terminals of a neuron synapse with other neurons. When a neuron degenerates, afferent and efferent synaptic contacts also degenerate. This process is commonly referred to as trans-synaptic degeneration.[18] Considering this neuropathological concept the findings of hyperintensity in the caudal cerebellar peduncles may represent trans-synaptic degeneration caused by progression of the disease process. This hypothesis is supported by the observed histopathologic abnormalities in the nucleus gracilis, medial cuneate nucleus, lateral cuneate nucleus and cerebellar white matter. Histopathologic examination at the light microscopic level, however, identified no distinct abnormalities in the more rostral ascending proprioceptive pathways, such as the medial lemniscus, thalamus and cerebral white matter, explaining the cerebrocortical atrophy apparent on MRI and pathologic examination as a result of trans-synaptic degeneration.

In agreement with previous reports, electromyography and motor nerve stimulation studies were within normal limits,[4] whereas sensory nerve stimulation identified decreased sensory nerve conduction velocity.[5] Although sensory neuronopathies in dogs are characterized by a primary disease process affecting the spinal ganglia and dorsal nerve roots, progression of the disease is expected to result in Wallerian-like degeneration of the more distal portions of the sensory peripheral

nerves. Previous reports have identified mild degenerative abnormalities of mixed motor and sensory nerves, such as the sciatic nerves. These abnormalities included axonal loss, dilated myelin sheaths, and infiltration of mononuclear cells.[2,4,5,7] In the case presented here, examination of both sciatic nerves identified no abnormalities, making it more difficult to explain the abnormal sensory nerve conduction velocity. The electrodiagnostic evaluation and post-mortem examination, however, were separated by a period of 18 months. Although we cannot exclude that more sensitive diagnostic techniques, such as teased fiber preparations or electron microscopy,[5] would have identified abnormalities in the peripheral nerve sections, it is also possible that morphological abnormalities present during the electrodiagnostic evaluation were no longer present at the time of histopathological examination.

Although the clinical presentation of the dog of this report was similar to previously reported cases of ganglioradiculitis in dogs, the histopathological findings differed. Mononuclear inflammation of craniospinal ganglia and dorsal nerve roots, considered a histopathologic hallmark in dogs with ganglioradiculitis, was not present in the dog presented here.[7] Two possibilities are considered to explain this difference: First, compared to most previously reported cases of ganglioradiculitis in dogs, the dog of this report had an exceptionally long duration of clinical signs before it was presented for post-mortem examination. Inflammation may only be present in the more acute stages of ganglioradiculitis, which subsequently subsides in the chronic stages of the disease, which may result in decreased numbers of neuronal cell bodies without an inflammatory infiltrate. We are aware of only 1 reported case of sensory neuronopathy in a dog with a comparably long duration of clinical signs before a post-mortem examination was performed.[3] Interestingly, mononuclear infiltration of the spinal ganglia and dorsal nerve roots was almost nonexistent in this previous case. Secondly, neuronal cell loss without inflammation is a hallmark of neurodegenerative conditions. Therefore, the case described here could represent a novel neurodegenerative condition selectively affecting some parts of the sensory nervous system.

In summary, this report described serial MRI findings in a dog with a sensory neuronopathy. Although the clinical signs were similar to ganglioradiculitis, the histopathologic findings differed. It is unclear if this discrepancy was caused by the chronicity of the dog's condition or if these findings are indicative of a novel, most likely neurodegenerative, disease.

Footnotes

[a] 1.5 tesla Intera, Philips Medical System, Eindhoven, The Netherlands

[b] 0.1 ml/kg gadoterate meglumine, Dotarem, Guerbet, Milton Keynes, UK

[c] Visio System Mobile ERG, Siem Bio Medicale, France coupled to an SLE CPS-20 Photic Stimulator, UK

[d] Viking Quest EMG, Nicolet Biomedical, Madison, WI

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