

Sensory Polyganglioradiculoneuritis in a Dog

Generalized reduction of nociception and conscious and unconscious proprioception were found in an approximately eight-year-old, male, Maltese mixed-breed dog presented for difficulty prehending food and experiencing ataxia of three months duration. Results of needle electromyogram, motor nerve conduction velocity, and cerebrospinal fluid analysis were normal. A diagnosis of sensory polyneuropathy was suspected. No underlying cause could be determined. Neurological signs progressed to quadriparesis over the following four months despite treatment attempts with prednisone and procarbazine. Necropsy confirmed a sensory polyganglioradiculoneuritis, but no inciting cause could be established.

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Case Report

An approximately eight-year-old, neutered male, Maltese mixed-breed dog was presented for difficulty prehending food and a progressive, generalized ataxia of three months duration. The ataxia had improved slightly on a previous one-month course of prednisolone (1 mg/kg body weight, per day, per os [PO]) therapy, but the dog was on no medication at this time. The dog had been found as a stray six years previously and had been in good health except for chronic flea allergy dermatitis and periodontal disease. Annual vaccinations (given six months prior to presentation) and frequent dentistry had been performed. Flea control was maintained with pyrethrins. No heartworm medication had been given, but he was negative for heartworm antibody.

Five months prior to presentation, the dog acutely developed an unproductive cough and ocular discharge two days after teeth cleaning and two weeks after being suspected of inhaling particles from a malfunctioning air conditioner. The particles were later analyzed and found to be silica gel. Results of a complete blood count (CBC), serum biochemistry profile, and tracheal wash cytology and culture were normal at that time. Thoracic radiographs showed a mild, right caudal lung-lobe pneumonia. Keratoconjunctivitis sicca was diagnosed, as the Schirmer's tear test was less than 4 mm in each eye. Cyclosporin 0.2% ophthalmic ointment^a was administered in each eye daily. The cough continued even after the pneumonia resolved radiographically.

Three months prior to presentation, the dog developed dysmetria of all four limbs, worse in the pelvic limbs. Bilateral conscious proprioceptive deficits of the pelvic limbs also were present. Spinal reflexes of all four limbs were normal. A diffuse encephalomyelitis was suspected, and serum titers for canine distemper virus, canine herpes virus, *Toxoplasma gondii*, *Ehrlichia canis*, *Rickettsia rickettsii*, *Borrelia burgdorferi*, and *Babesia canis* were evaluated and were negative except for a distemper virus immunoglobulin G (IgG) of 1:25, considered to be due to vaccination. An antinuclear antibody test was negative.

On presentation, the dog weighed 3.55 kg and had a mild generalized erythematous dermatitis, right otitis externa, and bilateral conjunctivitis. A cough was easy to elicit on tracheal manipulation, but there were no

increased lung sounds. Body temperature was 102° F. The dog was mentally alert and responsive, but had reduced facial nociception, evidenced by little response to needle pricking of nasal mucosa, ears, lips, and tongue. Jaw tone and swallowing appeared normal. Difficulty prehending food was observed and seemed to be due to a lack of touch sensation and proprioception of the lips and tongue. Smell and taste seemed appropriate, as the dog could find the food and would eat well once food was placed in his mouth. The tongue often protruded beyond the lips. The palpebral reflex was reduced bilaterally, although the dog could close his eyelids. Vision, hearing, and normal vestibular nystagmus were present. Other cranial nerves were normal.

The dog had extreme generalized dysmetria, worse in the pelvic limbs than the thoracic limbs. Conscious proprioception was absent in all four limbs. Limb strength was normal. The patellar reflex was absent on the left and severely depressed on the right. The sciatic notch response was depressed bilaterally, but cranial tibial, gastrocnemius, and flexor reflexes of the pelvic and thoracic limbs were normal. A crossed extensor reflex was present in all four limbs. Anal tone, defecation, and urination were normal. Although the cutaneous trunci response was present, little behavioral response was observed to pin pricking of the skin along the dorsal spinous processes of the vertebral column, suggesting reduced superficial nociception. Deep nociception, tested by the application of a hemostat forcep to the digits of all four feet, also was reduced. A diffuse disorder affecting sensory nerves carrying nociception and unconscious and conscious proprioception of the head, body, and limbs was suspected. Sensory nerves carrying the special senses of olfaction, vision, audition, and equilibrium appeared to be spared. A sensory polyneuropathy due to a metabolic disorder, endocrinopathy, toxicity, or autoimmune disease was suspected.

Results of a CBC, urinalysis, and serum biochemistry profile and serum cholinesterase were normal, with the exception of a serum alkaline phosphatase of 292 U/L (reference range, 8 to 56 U/L) and an alanine aminotransferase of 323.2 U/L (reference range, 15 to 58 U/L), thought to be due to the previous prednisone therapy. A low-dose dexamethasone suppression test was normal. Precortisol was 1.03 µg/dl (reference range, 0.5 to 6.0 µg/dl), and post low-dose dexamethasone (0.01 mg/kg body weight, intravenously [IV]) was 1.09 µg/dl at four hours and 0.57 µg/dl at eight hours (reference range, less than 1.2 µg/dl). A basal thyroxine (T₄) level was slightly low at 0.77 µg/dl (reference range, 0.9 to 2.6 µg/dl), but the thyroid stimulating hormone level was normal at 0.15 ng/ml (reference range, 0.03 to 0.39 ng/ml), so hypothyroidism was considered unlikely. A small liver and bronchointerstitial lung disease were seen on abdominal and thoracic radiographs, respectively. No evidence of megaesophagus or neoplasia was seen. Skull and cervi-

cal radiographs, performed under general anesthesia, were normal, except for a slight thickening and opacity in the left osseous bulla and lucency around the roots of several teeth.

No fibrillation potentials, positive sharp waves, or other abnormalities were found on electromyographic (EMG) examination of muscles of the head, body, and limbs. A sciatic tibial motor nerve conduction velocity was 59 meters per second (reference range, 55 to 75 m/sec). The evoked M responses were 5.83 and 6.75 millivolts, biphasic and considered to be normal. No decremental response to repetitive stimulation was observed. These EMG findings were indicative of normal motor nerve function. Sensory nerve stimulation was attempted but was inconclusive due to technical difficulties. An H-reflex was not performed. Analysis of cerebrospinal fluid (CSF) taken from the cerebellomedullary cistern indicated no red blood cells (RBCs), three white blood cells (WBC/µl; reference range, 0 to 6 WBC/µl), and protein less than 20 mg/dl (reference range, less than 20 mg/dl). Cytological evaluation of 50 CSF WBCs showed that 13 were small lymphocytes and 37 were reactive mononuclear phagocytes, indicating nerve root or central nervous system (CNS) disease. Serum antineuronal nuclear antibody type I and calcium channel antibodies were negative.

A diagnosis of sensory polyneuropathy of presumed autoimmune or toxic etiology was made. Since no toxicity could be established, the dog was treated for suspected autoimmune disease with oral prednisone (3 mg/kg body weight per day). Minimal improvement was seen after 23 days of treatment. Another immunosuppressive drug, procarbazine^b (50 mg/mm² per day), was added to the prednisone. The dog was maintained on the multiple vitamin and mineral supplements initiated prior to presentation. A CBC was performed every two weeks to monitor for leukopenia and anemia, which, if present, would signify bone-marrow suppression from the procarbazine. Procarbazine was discontinued after three weeks when no improvement was seen. The cough had increased, and pneumonia was suspected, but thoracic radiographs were normal. Oral amoxicillin^c (15 mg/kg body weight, q 12 hrs) and enrofloxacin^d (5 mg/kg body weight, q 12 hrs) were given, for 14 days each, in succession, but the cough continued.

Neurological deficits progressed over the next four months, despite continued oral prednisone (3 mg/kg body weight, per day). The dog developed severe depression and dyspnea and was reevaluated. Proprioceptive and nociceptive deficits remained, but now the dog had little voluntary movement of the limbs. Previously normal spinal reflexes were now depressed or absent. The left pupil was miotic. Aspiration pneumonia was suspected based on thoracic radiographs, and the peripheral WBC count of 53.70 x10³/µl (reference range, 6 to 17 WBC/µl) with 44.6 x10³/µl neutrophils (reference range,

2.5 to 12.5 $\times 10^3/\mu\text{l}$) and 3.8 $\times 10^3/\mu\text{l}$ bands (reference range, 0 to 0.3 $\times 10^3/\mu\text{l}$). Hepatomegaly was seen on abdominal radiographs. The serum alkaline phosphatase was 2,500 U/L (reference range, less than 80 U/L), and alanine aminotransferase was 167.1 IU (reference range, less than 60 IU). Due to the progression and severity of signs, the dog was euthanized.

A complete necropsy was done within a few hours after euthanasia. At necropsy, the cranioventral lung lobes were consolidated and mottled tan and red. The liver was enlarged with an accentuated reticular pattern. The CNS was removed and fixed by immersion in 10% neutral buffered formalin. Selected peripheral nerves, skeletal muscles, and ganglia, as well as other organs were collected in 10% formalin. All tissue samples were embedded in paraffin, cut into 5- μm thick sections, and stained with hematoxylin and eosin (H&E) stain. Sections of the CNS also were stained with luxol fast blue (LFB) and Bodian's method for axons. Additionally, gluteraldehyde-fixed samples of the sciatic nerve were postfixed in osmium tetroxide and dehydrated in serial alcohol solutions and propylene oxide prior to embedding in araldite resin. Sections (1 μm) were stained with toluidine blue for light microscopy. A sample of the biceps femoris muscle was flash frozen in isopentane, precooled in liquid nitrogen, and 8- μm thick sections were evaluated with standardized histochemical stains and enzyme reactions.

Histological examination of the lung tissue revealed suppurative bronchopneumonia compatible with aspiration. Under polarized light, sections of lung revealed a few birefringent crystals in areas of inflammation that were interpreted as silica particles. Nodular collagenous scars or granulomas, suggestive of chronic silicosis, were not present in the lung. Vacuolar degeneration of hepatocytes was consistent with steroid hepatopathy.

Coronal sections of formalin-fixed spinal cord revealed a "V-shaped" area of white discoloration corresponding to the dorsal funiculi that was more prominent in the lumbar and cervical spinal cord. The most remarkable histological lesions were present in the white matter of the spinal cord and consisted of severe, diffuse loss of axons and demyelination in the dorsal funiculi (i.e., fasciculus cuneatus and gracilis) and the dorsal nerve roots. Longitudinal sections of the spinal cord revealed marked wallerian degeneration with linear chains of digestion chambers in the dorsal columns. The dorsal roots and spinal ganglia had perivascular and diffuse interstitial infiltrates of predominantly lymphocytes with fewer macrophages and plasma cells; the lumbar region was affected more severely [Figure 1]. This ganglionitis was accompanied by mild to marked loss of neuronal cell bodies and proliferation of satellite cells. Histomorphology of the ventral roots and trigeminal nerve was normal. The right and left sciatic nerves had some fascicles with axonal loss, dilated myelin sheaths,

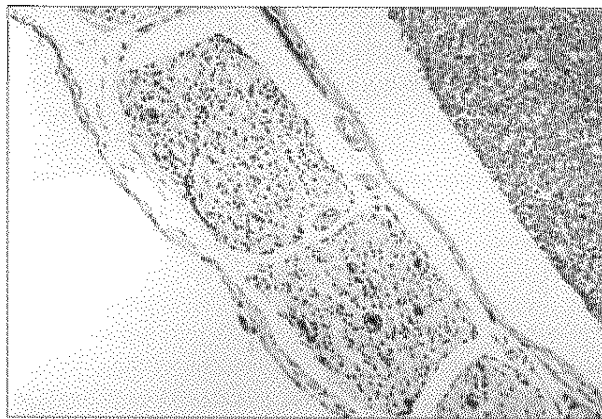


Figure 1—Dorsal nerve roots from a dog diagnosed with a sensory polyganglioradiculoneuritis, showing infiltrates of lymphocytes and marked loss of axons and myelin (Hematoxylin and eosin stain, 180X).

intramyelin infiltration by large lipid-laden macrophages, and focal areas of mononuclear cell (primary lymphocytes) infiltration. Muscle innervated by the sciatic nerve was histologically normal, supporting the diagnosis of a primary sensory neuritis. No lesions were observed in any part of the brain, multiple skeletal muscles, or enteric ganglia (Meissner's or Auerbach's).

Discussion

From the clinical signs and necropsy findings, a sensory polyganglioradiculoneuritis affecting all spinal nerves was confirmed. Involvement of the trigeminal nerve was suspected because of absent facial nociception and lip and tongue proprioception, but this was not confirmed histologically. Sensory polyganglioradiculoneuritis has been rarely reported in dogs, and the lymphocytic neuritis extending along the length of the sciatic nerve, as in this case, has not been reported previously. In the previously reported eight cases, three were males and five were females of varying large and small breeds with an age of onset ranging from 1.5 to nine years.¹⁻⁴ All animals were ataxic. Conscious proprioception was examined in six cases and was reduced. The patellar reflex was examined in eight affected dogs and was reduced or absent in seven. Nociception of the face was evaluated in eight dogs and was reduced in six dogs, increased in one dog, and normal in one dog. One other dog had anisocoria. Other abnormalities seen that did not occur in the case reported here were megaesophagus, head tilt, voice loss, urinary and fecal incontinence, and hearing loss. Crossed extensor reflex was not reported in the other cases. The cause of the crossed extensor reflex, usually associated with upper motor neuron disease, was not determined in this dog. All dogs progressively worsened, and although necropsy confirmed sensory ganglioradiculitis, the underlying cause was not determined in any case.

Underlying causes of sensory polyneuropathies in humans include infectious diseases such as leprosy, human immunodeficiency virus, and Lyme disease.⁵ An attempt to rule out infectious diseases by evaluating serum titers to specific organisms was performed in this dog. Metabolic and endocrine disturbances associated with diabetes mellitus, uremia, and hypothyroidism can produce primary sensory neuropathies in humans.⁵ Serum tests to evaluate these disorders also were normal in this dog. Inherited sensory polyneuropathy seemed unlikely in this case, because he was a mixed-breed dog with an onset of signs at nine years of age and the lesion was inflammatory in nature. Paraneoplastic sensory polyneuropathies occur in humans, but no neoplastic condition was found in this dog. Antineuronal antibody (ANA) tests are often positive in humans with paraneoplastic sensory polyneuropathies, but they were negative in this dog.⁵ No response was seen after 21 days of the anticancer drug, procarbazine.

This dog had no exposure to toxic substances, such as vincristine, thallium, and hexocarbons, known to produce sensory neuropathies in humans.⁵ Although a specific history of exposure to organophosphates was lacking, a serum acetylcholinesterase level was obtained in this case due to the occasional environmental use of these substances.

By process of elimination, an autoimmune process was suspected even though the ANA was negative. A positive ANA supports an autoimmune disease diagnosis in dogs, but a negative ANA does not rule it out. Xerostomia, xerophthalmia, and severe sensory neuropathy with prominent sensory ataxia have been reported in humans with the immune-mediated disorder, Sjogren's syndrome.⁵ One of the pathological processes in these patients can be dorsal root ganglionitis with infiltrates of T-lymphocytes and macrophages. Humans with Sjogren's syndrome test positive for antibodies to extractable nuclear antigens such as ro (SS-A) and la (SS-B).⁵ These antibodies were not evaluated in this dog, because the appropriate reagents could not be located.

The role of silica gel inhalation causing immune-mediated disease in this dog is questionable. Silicosis in humans is associated with a hyperactivity of humoral-mediated immunity, and systemic lupus erythematosus has been associated with silicosis.^{6,7} Silica crystals were present in the lung tissue of this dog, so it is possible that silica exposure may have resulted in immune stimulation and clinical sensory polyganglioradiculoneuritis in this dog.

Conclusion

Although rare, sensory polyganglioradiculoneuritis should be considered in any dog that has multiple sensory deficits of the head and limbs with normal motor functions. The diagnosis might be confirmed by histo-

logical examination of a spinal nerve dorsal root ganglion biopsy antemortem. In this and previously reported cases, the diagnosis was confirmed at necropsy.

^a Optimune; Schering-Plough, Kenilworth, NJ

^b Matulene; Roche, Pfizer Animal Health, Exton, PA

^c Amoxi-tabs; SmithKline Beecham, Pfizer Animal Health, Exton, PA

^d Baytril; Miles, Bayer Co., Shawnee Mission, KS

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