Sensory and motor neuropathy in a Border Collie

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- In Border Collies, sensorimotor neuropathy develops as a result of progressive depletion of peripheral nerves; typically, sensory dysfunction is evident early in the disease.
- In affected dogs, motor nerve dysfunction can be detected electrophysiologically but apparently develops at a slower rate than sensory nerve dysfunction.
- The hereditary characteristic of this disease is not known.

A 5-month-old 8.2-kg (18-lb) female Border Collie was evaluated at the Kansas State University Veterinary Medical Teaching Hospital because of hind limb incoordination. Clinical signs were first noticed by the owner 3 weeks prior to evaluation at the hospital and had progressively worsened. The dog continued to be active and eat and drink normally and was fed a commercial dry dog food; its vaccination status was current. This puppy was from a litter of 6, of which 1 additional puppy was affected with similar clinical signs. That other puppy was euthanatized, and no necropsy was performed.

On physical examination, the dog was thin with prominent spinal processes and pelvic bones. The dog was active and alert and had a rectal temperature of 39°C (102.3°F), pulse rate of 132 beats/min, and respiratory rate of 24 breaths/min. Findings of thoracic auscultation and abdominal palpation were unremarkable. On both hind limbs, there were erosions of the footpads that would bleed when the dog was active. Hind limb ataxia was prominent with intermittent knuckling of the feet and hyperextension of the limbs. Neurologic evaluation revealed that conscious proprioception was reduced in the forelimbs and absent in the hind limbs. The flexion reflexes were absent in all limbs except for stimulation of 2 areas: the medial dorsal surface of digit 2 of the hind limbs and the dewclaws of the forelimbs. Patellar reflexes were normal in both hind limbs, but all other spinal reflexes of the forelimbs and hind limbs were considered absent or markedly diminished. Superficial and deep pain responses were absent in all limbs. There was muscle atrophy in the hind limbs but not in the forelimbs. Results of cranial nerve evaluation indicated no deficits, and the panniculus reflex was normal. Anal tone was considered normal. The urinary bladder was easily expressed, and during the dog's hospitalization, it was noted that the dog was pollakiuric but did not empty the urinary bladder completely.

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A CBC, serum biochemical analyses, and urinalysis were performed. No clinicopathologic abnormalities were detected. Thoracic radiographs were obtained and were interpreted as normal; there was no radiographic evidence of esophageal dilatation. The presumptive diagnosis was diffuse sensory neuropathy, similar to that which has been previously reported[1] in this breed.

The following day, the dog underwent **electromyography (EMG)**, sensory and motor **nerve conduction velocity (NCV)** evaluation, and muscle and nerve biopsy procedures. The dog was premedicated with midazolam (0.025 mg/kg [0.011 mg/lb], SC) and hydromorphone (0.0125 mg/kg [0.006 mg/lb], SC); anesthesia was induced with thiopental (9.6 mg/kg [4.36 mg/lb], IV) and maintained with isoflurane. Electrophysiologic assessments were performed on the left side, and muscle and nerve biopsy specimens were obtained from the right side of the dog. The sensory NCV evaluation revealed no conduction in the tibial, common peroneal, and radial nerves and decreased conduction (42.7 to 43.3 m/s; reference range,[2] 69.4 ± 6.9 m/s) in the ulnar nerve (the conduction was not polyphasic). Evaluation of motor NCV revealed decreased conduction velocity in the tibial nerve (41.1 m/s; reference range, 53.0 ± 2.8 m/s); conduction was polyphasic with decreased amplitude (0.5 mV; reference range, 23.3 ± 2.3 mV).[3,4] Motor NCV evaluation revealed decreased conduction velocity in the common peroneal nerve (32 m/s; reference range,[4] 79.8 ± 1.8 m/s); conduction was polyphasic and of normal amplitude. Furthermore, motor NCV evaluation revealed decreased conduction velocity in the ulnar nerve (44.5 m/s; reference range,[4] 58.9 ± 1.0 m/s); conduction was not polyphasic but was of normal amplitude. The EMG was considered to be within normal limits, other than reduced recruitment from the pectineus muscle. These findings supported a diagnosis of sensory and motor neuropathy.

Sections of fresh frozen biopsy specimens from the gastrocnemius muscle were evaluated by use of a standard panel of histochemical stains and enzyme reactions.[5] There was notable generalized myofiber atrophy without fiber type grouping. Biopsy specimens were obtained from the distal caudal cutaneous sural nerve (mixed sensory and motor), the lateral superficial radial nerve (sensory), the dorsal branch of the ulnar nerve (sensory), and the superficial peroneal nerve (mixed sensory and motor). All biopsy specimens were fixed in neutral-buffered 10% formalin. The nerve specimens were embedded in epoxy resin, sectioned (1 µm thick), and stained with toluidine blue. Histologically, the predominant abnormality in both the sensory and motor nerves was severe nerve fiber depletion with myelin ovoids, foamy macrophages, and axonal degeneration in the remaining fibers in some sections (**Figures 1 and 2**). No regenerating fibers were observed. Given the

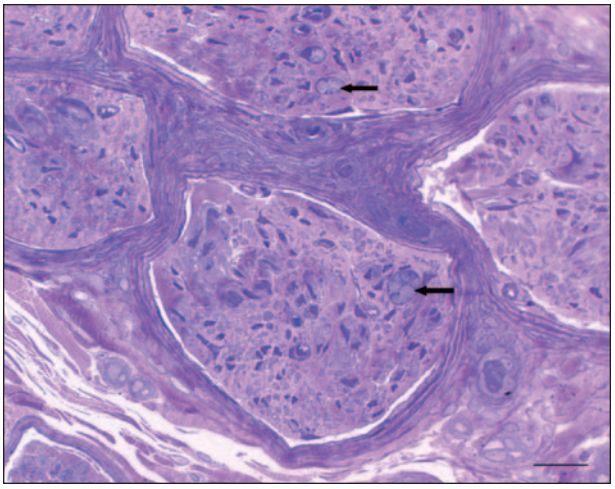

Figure 1—Photomicrograph of a resin-embedded 1-µm section from the lateral superficial radial nerve of a 5-month-old female Border Collie with progressive hind limb ataxia. Notice that nerve fascicles have marked nerve fiber loss. Myelin ovoids (arrows) are indicative of previous axonal degeneration. Toluidine blue stain; bar = 400 µm.

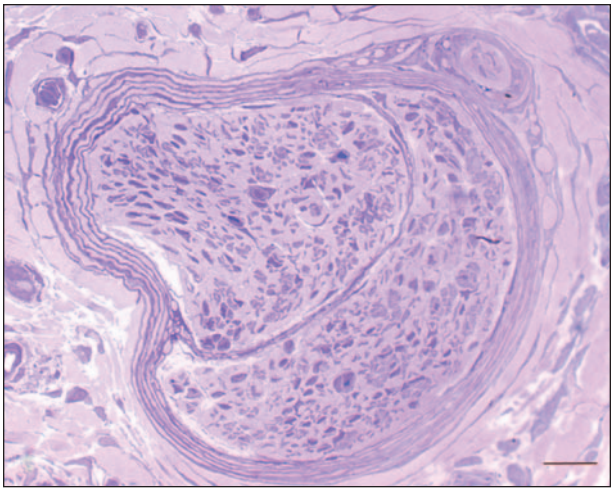

Figure 2—Photomicrograph of a resin-embedded 1-µm section from the peroneal nerve of a 5-month-old female Border Collie with progressive hind limb ataxia. Similar to findings in the sensory nerve specimen from this dog (illustrated in Figure 1), there is marked nerve fiber loss in the peroneal nerve. Endoneurial fibrosis is present, and only scattered Schwann cells and fibroblasts remain. Toluidine blue stain; bar = 400 µm.

marked depletion of most myelinated fibers within the peroneal nerve (a mixed nerve), a diagnosis of mixed motor and sensory neuropathy was made.

The dog was discharged, and a recommendation was made to the owners that booties should be used to cover the dog's feet for protection of the footpads. At 18 months after the initial evaluation, the dog could no longer support its weight and had only gross motor function in the hind limbs, which was restricted by tendon contracture that held the legs in extension. Conscious proprioception was absent in the left forelimb and decreased in the right forelimb. Urinary and fecal continence had continued normally since the time of discharge, and the initial signs of pollakiuria were attributed to poor training. Twelve months after discharge, regurgitation was first observed and occurred every other day; however, radiography was not performed to evaluate for esophageal dilatation. Laryngeal paralysis was not clinically evident. The dog had marked muscle atrophy of the hind limbs and pelvic and lumbar areas. Since the dog's discharge from the hospital, there had been no weight gain and no appreciable change in overall body size. The dog was euthanatized 1 month later because of severe regurgitation, and a necropsy was not permitted.

On evaluation of the pedigrees of the dam and sire of the dog of this report, 1 common relative was identified. The pedigrees of the dam and sire of another Border Collie puppy in which sensory neuropathy (with no apparent motor component) was diagnosed at the University of Tennessee College of Veterinary Medicine were also evaluated.[a] Common relatives were not identified in the pedigrees of the dam and sire of that puppy, and there did not appear to be any relatives in common between that puppy and the dog of this report. At the Royal Veterinary College, London, severe sensory and motor neuropathy has been diagnosed in 4 additional Border Collies (2 of which were littermates).[b] Nerve biopsy specimens from one of these puppies were evaluated histologically by one of the authors (GDS), and findings were similar to those in the dog of this report. Pedigrees of these additional 4 dogs were not available.

To our knowledge, there is 1 previous case report[1] of sensory neuropathy in a Border Collie puppy that was also 5 months of age at the time of evaluation. Similar to the dog of this report, that puppy had severe hind limb ataxia with loss of conscious proprioception in all limbs, loss of superficial and deep pain responses in the limbs, lack of flexor reflexes in all limbs, normal patellar reflexes, no conduction of sensory nerve action potentials, and no abnormalities detected via EMG. However, in that puppy, the panniculus reflex was absent, facial sensory response was absent, and motor NCVs were considered within reference ranges (although motor NCVs for the sciatic, tibial, and ulnar nerves were at the lower limit of their respective reference ranges). The described histologic findings in the sensory nerves were similar in that puppy and the dog of this report. Although that puppy was described as not having motor nerve involvement, motor or mixed sensory and motor nerve biopsy specimens were not evaluated. In the dog of this report, examination of sensory and mixed sensory and motor nerves revealed similar nerve fiber depletion.

Pure sensory neuropathies have been reported[6-8] in long-haired Dachshunds, English Pointers, and a Jack Russell Terrier. Other sensory and mixed sensory and motor neuropathies have also been reported. Polyneuropathies involving the motor and sensory nerves in dogs include giant axonal neuropathy of Alsatians, inherited hypertrophic neuropathy of Tibetan Mastiffs, progressive axonopathy in Boxers, distal sensorimotor polyneuropathy in Rottweilers, progressive myelopathy and neuropathy in New Zealand Huntaway dogs, and inherited polyneuropathy in Leonbergers.[9-15]

In the dog of this report, the initial sensory nerve dysfunction with progressive motor nerve dysfunction was consistent with a mixed motor and sensory neu-

ropathy. The presence of the slowed motor NCV, generalized muscle fiber atrophy, and generalized nerve fiber loss within the peroneal nerve was consistent with this assumption. The peroneal nerve is a mixed motor and sensory nerve, and the generalized loss of nerve fibers would indicate that both sensory and motor fibers were depleted. The absence of EMG changes in association with a motor neuropathy was unusual, although several of the previously mentioned polyneuropathies were accompanied by delayed changes in NCVs and EMG characteristics. In dogs with giant axonal dystrophy, EMG does not reveal evidence of denervation at 11 months of age, despite obvious clinical signs; the first EMG abnormalities are typically detected at approximately 16 months of age, and widespread EMG changes are generally recorded at 20 months of age.[9] In a retrospective study[11] of hypertrophic neuropathy, 5 of 6 affected puppies had an abnormal EMG and progressive decreases in motor and sensory NCVs were determined over time. Likewise, in a retrospective study[15] of inherited polyneuropathy in Leonbergers, 1 of 12 affected dogs had a normal EMG, despite histologic confirmation of chronic nerve fiber loss. It is possible that the nerve degeneration in the Border Collie of this report was not widespread or severe enough to result in EMG changes at the time of initial evaluation, and EMG abnormalities may have been identified had the test been repeated later during the progression of the disease.

An early, rapid loss of sensory nerves and a slow progressive loss of motor nerves may have been responsible for the assessment in the earlier report[1] that the disease in the Border Collie is a sensory neuropathy. Reevaluation of affected dogs later during the course of the disease may reveal both sensory and motor nerve involvement. The laryngeal paralysis-polyneuropathy complex of Rottweilers and Dalmatians may represent the opposite end of the spectrum in sensorimotor neuropathies, with early, rapid loss of motor nerves and slow progressive loss of sensory nerves.[16,17] Although these 2 polyneuropathies are associated with development of laryngeal paralysis and motor neuropathy, axonal degeneration has been identified in sensory nerves in Rottweilers and a decrease in sensory NCV has been detected in 1 Dalmatian.[16,17]

The lack of pedigrees relating to most of the aforementioned affected Border Collies makes it impossible to evaluate the hereditary character of this sensorimotor neuropathy. Of the 2 pedigrees available, only the dam and sire of the dog of this report had a relative in common. Of note, however, is that the sire of the common relative was a Great Britain International Champion.[c] The popularity of that line of Border Collies may result in an increase in the prevalence of this sensorimotor neuropathy in that breed. It would be incumbent on veterinarians that evaluate Border Collies with signs of this sensorimotor neuropathy to obtain pedigrees and inform the breeders of the possible hereditary nature of this disease.

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b. Capello R, The Royal Veterinary College, North Mymms, Hatfield, UK: Personal communication, 2003.
c. International Sheep Dog Society, Clifton House, Bedford, UK.

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