J Vet Intern Med 2014;28:1789–1798

Electrophysiologic Confirmation of Heterogenous Motor Polyneuropathy in Young Cats

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Background: Reports of motor polyneuropathies in young cats are scarce. Further, in-depth electrophysiologic evaluation to confirm a motor polyneuropathy in young cats of various breeds other than 2 Bengal cats is lacking.

Hypothesis/Objectives: To confirm a motor polyneuropathy in young cats of various breeds.

Animals: Five young cats with heterogenous chronic or relapsing episodes of weakness.

Methods: Retrospective case series. Cats were presented for evaluation of generalized neuromuscular disease and underwent electrophysiologic examination including electromyography, nerve conduction, and repetitive nerve stimulation. Minimum database and muscle and nerve biopsy analyses were carried out. Descriptive statistics were performed.

Results: Disease onset was at 3 months to 1 year of age and in 5 breeds. The most common clinical sign (5 of 5 cats) was weakness. Additional neurologic deficits consisted of palmigrade and plantigrade posture (4/4), low carriage of the head and tail (4/4), and variable segmental reflex deficits (5/5). Motor nerve conduction studies were abnormal for the ulnar (4/4), peroneal (5/5), and tibial (2/2) nerves (increased latencies, reduced amplitudes, slow velocities). A marked decrement was observed on repetitive nerve stimulation of the peroneal nerve in 3 cats for which autoimmune myasthenia gravis was ruled out. All sensory nerve conduction studies were normal. Histologic evaluation of muscle and nerve biopsies supported heterogenous alterations consistent with motor polyneuropathy with distal nerve fiber loss.

Conclusions and Clinical Importance: Heterogenous motor polyneuropathies should be considered in young cats of any breed and sex that are presented with relapsing or progressive generalized neuromuscular disease.

Key words: Feline; Nerve conduction; Neuromuscular; Weakness.

Reports of motor polyneuropathies in young cats are few, with most limited to inherited or congenital conditions in specific breeds.[1] Among these are axonal polyneuropathy of Snowshoe cats,[2] Birman cat distal polyneuropathy,[3] glycogenosis type IV in Norwegian Forest cats,[4] alpha-mannosidosis in Persian cats,[5] Niemann-Pick disease type C,[6] hyperchylomicronemia (Siamese, Persian, Himalayan, short- and longhair domestic cats),[7,8] hyperoxaluria,[9] hypertrophic neuropathy,[10] and recurrent polyneuropathy in Bengal cats.[11,12] Inherited or congenital neuropathies usually have an early onset of clinical manifestations within weeks to a few months of age.[1] Acquired neuropathies can occur at any age secondary to exposure to pathogens, toxicants, ischemic events, nutritional deficiencies, endocrinopathies, trauma, neoplasia, immune-mediated disease, or might be of undetermined cause.[13–19]

Most polyneuropathies in cats have been reported to involve both sensory and motor components.[1,16,20] However, in-depth electrophysiologic studies for the evaluation of both components are often lacking.[2,11,17,21] Neuropathy associated with type 2 diabetes mellitus is predominantly sensory, but both sensory and motor components are affected.[15,22–25] Reports of sensory neuropathies are limited to dietary deficiency of tyrosine and phenylalanine.[13] Reports of predominantly motor polyneuropathies are limited to recurrent polyneuropathy/polyradiculoneuropathy in Bengal cats,[11,12] acute idiopathic polyneuropathy in domestic shorthair and Persian cats,[21] and axonal neuropathy in Snowshoe cats.[2] However, electrodiagnostic studies were limited and performed by different clinicians[11] or not performed at all.[21] Further, electrodiagnostic studies were restricted to motor nerve conduction studies,[2,11] with the exception of 2 Bengal cats for which sensory nerve conduction studies were performed and were normal.[11,12] Therefore, involvement of the sensory component could not be entirely excluded. The purpose of the present study was to describe a motor polyneuropathy in young cats of various breeds with signs of generalized neuromuscular disease. A major strength of this study is the performance of in-depth

Abbreviations:

AUC	area under the curve
CK	creatine kinase
CMAP	compound muscle action potential
CV	conduction velocity
EMG	electromyography
MNCV	motor nerve conduction velocity
MND	motor neuron disease
RNS	repetitive nerve stimulation
SNAP	sensory nerve action potential
SNCV	sensory nerve conduction velocity

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Submitted March 8, 2014; Revised May 6, 2014; Accepted July 23, 2014.

DOI: 10.1111/jvim.12439

electrophysiologic studies using a single standardized procedure performed by the same operator (DCW).

Materials and Methods

This retrospective case series included 5 cats diagnosed with motor polyneuropathy at the William R. Pritchard Veterinary Medical Teaching Hospital at the University of California at Davis from the years of 2005 to 2011. Medical records were reviewed. Inclusion criteria included confirmation of a polyneuropathy by neurologic examination, electrodiagnostic evaluation, and pathologic analysis of muscle and peripheral nerve biopsies. Data extracted from records included signalment, history, and results of physical and neurologic examinations. Minimum database consisted of complete blood cell count and serum biochemistry panel, serologic testing for acetylcholine receptor antibodies, serology for FIV and FeLV, urinalysis, thoracic radiographs, and abdominal ultrasound.

Electrodiagnostics

Electrodiagnostic studies were performed under general anesthesia with a similar protocol for diseased and control cats. Premedication consisted of atropine sulfate at 0.02 mg/kg subcutaneously (SC), oxymorphine at 0.05 mg/kg SC, ketamine at 5 mg/kg IV, and midazolam at 0.25 mg/kg IV. Inhalation anesthesia was maintained with isoflurane (1–2.5%) in oxygen. Lactated Ringer solution was administered at 10 mL/kg/h during the procedure. The same operator performed all electrodiagnostic testing (DCW).

Electromyography. A Nicolet Viking IV[a] or VikingQuest[a] was used to perform all electrophysiologic studies, including electromyography (EMG). The test was performed by use of a concentric EMG needle electrode[a] and a subcutaneous ground electrode.[b] Frequency bandwidth was 20 Hz to 10 kHz with a sensitivity of 50 μV. Multiple head, cervical, paraspinal, and appendicular muscles were examined. Insertional and spontaneous activity was examined and graded for each muscle according to a published scoring system.[26,27]

Motor and Sensory Nerve Conduction. Polyteflon-coated monopolar stainless steel electrodes[a] of various lengths were used for both stimulation and recording. A subcutaneous needle electrode was used as the ground. For both, sensory and motor nerve conduction studies, latency was measured in milliseconds (ms), duration of action potential (SNAP, sensory nerve action potential; CMAP, compound muscle action potential) in ms, amplitude in millivolts (mV) or microvolts (μV), area under the curve (AUC) in μVms or mVms, and conduction velocity (CV) in meters per second (m/s). The cats' core body temperature during recording was maintained between 37 and 37.7°C. The ulnar and peroneal nerves were selected for both sensory nerve conduction velocity (SNCV) and motor nerve conduction velocity (MNCV) studies and performed as described previously.[13,28–31] Additionally, MNCV was evaluated in the tibial nerve in 2 cats (cats 3 and 5), and SNCV in the radial nerve in 3 cats (cats 1, 2, and 4) as previously described.[29,31] Reference values used were those previously published using the same technique,[13] and 2 control neurologically normal cats (young adults [1 year of age]) from the UCD database.

Repetitive Nerve Stimulation. Repetitive supramaximal stimulation of the peroneal nerve was performed at frequencies of 1, 3, 5, 10, 20, 30, and 50 Hz. The frequency bandwidth was 2 Hz to 5 kHz, stimulus duration 0.2 milliseconds with trains of 10 stimuli used for each stimulus rate. A minimum of 1 minute of recovery time elapsed between trains of stimuli. Compound muscle action potential amplitude and AUC were compared between the first and fourth potential to assess incremental or decremental responses.[26,32] Data available from repetitive nerve stimulation (RNS) of the peroneal nerve from 2 control cats from our database were used as reference, because there are no published reference values from normal cats.

Muscle and Nerve Biopsy

Under general inhalation anesthesia, biopsy specimens were collected from the triceps brachii, vastus lateralis, and cranial tibialis muscles; and the superficial peroneal nerve at the level of the stifle joint as previously described.[13,33] Muscle biopsy specimens were snap frozen in isopentane precooled in liquid nitrogen and stored at −80°C until further processing. Fascicular nerve biopsies were either snap frozen, placed on a tongue depressor, or both, and immersion fixed in 2.5% glutaraldehyde in 0.1 M sodium phosphate buffer (pH 7.4). Semithin cross sections (1 μm) of glutaraldehyde-fixed, araldite resin-embedded nerve specimens were stained with toluidine blue-basic fuschin for light microscopy. A routine panel of histochemical stains and reactions were performed in frozen sections of muscle and nerve as previously described.[13,33]

Statistical Analysis

Data available from published nerve conduction studies using the same technique, and RNS from 2 control cats from our institution were used for reference. Because of the low number of cases and controls, descriptive statistics (mean, SD) were performed.

Results

Animals

Five young cats of both sexes (female spayed [FS], male castrated [MC]) and various breeds met the inclusion criteria. Signalments at the time of presentation were: cat 1: 11-month-old FS Bengal, cat 2: 9 month-old FS Siamese, cat 3: 2-year-old FS domestic longhair, cat 4: 1-year-old MC domestic shorthair, cat 5: 9-month-old MC Persian cat. Although the cats' age at the time of presentation ranged from 9 months to 2 years, the age at onset of first clinical manifestations ranged from 3 months to 1 year. All cats had a history of generalized weakness and decreased physical activity as the primary abnormality. Weakness started or was more noticeable in the pelvic limbs, but invariably progressed to the thoracic limbs by the time of presentation. Weakness was recurrent and appeared to resolve spontaneously between episodes in 3 cats (cats 1, 3, and 4). Two cats (cats 2 and 5) had progressive weakness of a few months' duration (3–5 months) before presentation. All cats were kept indoors, and routinely vaccinated and dewormed. Diet was balanced and met standard nutritional requirements. None of the cats were receiving any medications at the time of presentation.

Physical and Neurologic Evaluation

Physical examination showed a reduced body condition score in 4 cats (<5 of 9: 2 cats each had 3 and 4

of 9). Generalized muscle atrophy with more profound atrophy of the pelvic limb muscles was noted in 3 cats (cats 1, 3, and 4), and normal musculature in 2 cats (cats 2 and 5). All cats were bright, alert, and responsive. Four cats were weakly ambulatory and 1 nonambulatory (cat 3). All ambulatory cats had a crouched posture with palmigrade and plantigrade stance, and low carriage of the head and tail. The cats walked a few steps and sat or lay down frequently. The most severely affected cat (cat 3) rested the head on the paws of the thoracic limbs, and intermittently displayed cervical ventroflexion. Cranial nerves abnormalities included decreased menace response (cat 2), decreased palpebral reflex (cat 1), and decreased gag reflex (cat 3). Postural reactions were decreased in all limbs in 4 cats, and delayed in the thoracic limbs and absent in the pelvic limbs in 1 cat (cat 5). Segmental reflexes (biceps, triceps, patellar, gastrocnemius, cutaneous trunci) were decreased to absent in all cats. There was no apparent pain upon palpation of the musculoskeletal system, or with flexion or extension of limb joints. The neuroanatomic localization was generalized neuromuscular disease in all cats.

Clinicopathologic data

Clinicopathologic data abnormalities included hypercalcemia in 3 of 5 cats (range 11.2–12.3 mg/dL; reference range 9–10.9), hyperkalemia in 2 of 5 (both 5.3 mmol/L; reference range 3.6–4.9), low creatinine in 4 of 5 (0.5–0.9 mg/dL; reference range 1.1–2.2), elevated creatine kinase activity in all cats (497–4624 IU/L; reference range 73–260), elevated urine specific gravity in 1 of 4 (1.062; reference range 1.035–1.060), and proteinuria in 3 of 4 cats (25 mg/dL; reference range 0). Serology for FeLV and FIV was negative for all cats. Acetylcholine receptor antibody serology for the diagnosis of acquired myasthenia gravis was negative in all cats (<0.3 nmol/L). Cerebrospinal fluid from the cerebellomedullary cistern was collected in 3 cats that had total nucleated cell counts and protein levels within reference values.

Electrodiagnostics

Electromyography. Generalized spontaneous activity, consisting of fibrillation potentials and positive sharp waves, was identified in nearly all of the muscles examined. These abnormalities varied from 1+ to 3+ (mild to severe) according to a published grading scale in all 5 cats.[26]

Motor and Sensory Nerve Conduction. Motor nerve conduction was abnormal for the ulnar and peroneal nerves in all cats as shown in Table 1. In all cats, CMAPs were characterized by increased latencies, decreased amplitudes, prolonged durations (dispersed, polyphasic, or both), decreased AUCs, and slow CVs (Table 1, Figs 1, 2). Conduction block as defined by more than 50% reduction of CMAP amplitude when stimulating proximally as compared to distally, was observed in the peroneal nerve of 2 cats (Fig 2). The tibial motor nerve conduction studies in 2 cats were also abnormal (data not shown). Sensory nerve conduction velocity studies were similar to data available

Table 1. Motor nerve conduction (ulnar, peroneal). Number of cats shown (affected, controls), Malik 1989 and Tuler 1990 correspond to published data for ulnar nerve[39] and peroneal[28] nerves, respectively, with identical techniques to those of this study.

	Lat (ms)	Dur (ms)	Amp (mV)	Area (mVms)	CV (m/s)
Ulnar (motor)					
			Carpus		Carpus-elbow
Cats (4)	1.65 (0.39)	3.98 (2.36)	2.45 (2.47)	3.51 (2.76)	55.75 (4.5)
Controls (2)	1.1 (0)	1.6 (0.1)	21.5 (0.86)	19.7 (0.71)	84.7 (0.98)
Malik 1989	NR	NR	18.8 (4.7)	11.2 (3.1)	88.3 (17.8)
			Elbow		
Cats (4)	3.55 (0.52)	3.88 (2.89)	1.63 (2.14)	2.16 (2.67)	
Controls (2)	2.45 (0.07)	1.7 (0)	21.86 (0.91)	19.69 (2)	
Malik 1989	NR	NR	15.7 (4.8)	9.8 (2.9)	
Peroneal (motor)					
			Hock		Hock-stifle
Cats (5)	2.3 (1.26)	3.52 (1.9)	3.57 (4.11)	4.69 (4.56)	48 (18.15)
Controls (2)	1.05 (0.07)	2.1 (0.14)	24.21 (6)	30.76 (6.62)	90.5 (6.36)
No reference	NR	NR	NR	NR	NR
			Stifle		Stifle-hip
Cats (5)	4.26 (1.84)	4.26 (2.92)	2.97 (3.66)	4.24 (4.34)	59.8 (17.24)
Controls (2)	2.05 (0.07)	2.15 (0.21)	25.66 (3.57)	32.75 (3.07)	97.5 (6.36)
Tuler 1990	NR	NR	NR	NR	89 (10)
			Hip		Hock-hip
Cats (5)	6.24 (2.4)	4.98 (3)	2.51 (3.3)	3.52 (4.4)	53.6 (17.13)
Controls (2)	3.3 (0.14)	2.1 (0.07)	23.98 (5.03)	28.03 (7.36)	94.5 (6.36)
Tuler 1990	NR	NR	NR	NR	78 (4)

Lat, latency; Dur, duration (measured from onset of upward deflection to return to baseline as shown); Amp, amplitude; Area, area under the curve (automatically calculated by Viking software[a]); CV, conduction velocity, mean (SD); NR, not reported or available.

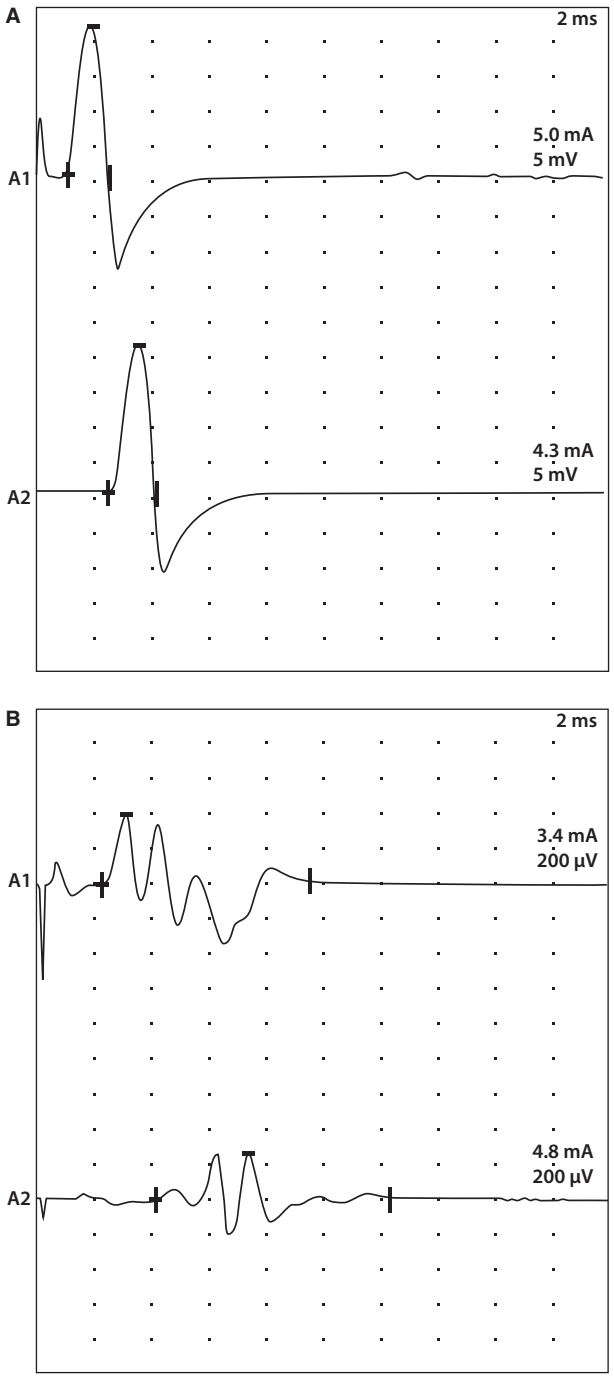

Fig 1. Motor nerve conduction study of the ulnar nerve. Stimulating sites at A1 = carpus, A2 = elbow, CMAP is shown, time (ms), amplitude (mV or µV) as shown. **(A)** Normal cat. Note amplitude in mV. **(B)** Cat 3. Note increased latency, amplitude in µV, polyphasic CMAP, and temporal dispersion.

from 2 control cats from our database (Table 2, Fig 3A,B).

Repetitive Nerve Stimulation. The baseline CMAP amplitude was markedly decreased in diseased cats (4.3 ± 5.91 versus 28.86 ± 17.8 mV in controls, Fig 4A). Cats 3 and 5 had substantial decrements (>35%) in both, amplitude and AUC, across all stimulus frequencies (Fig 4B). At high rates (30 and 50 Hz), cat 1 had decrements of 38 and 25% for amplitude and AUC, respectively. Cats 2 and 4 had decrements of <16% at all stimulus rates. In control cats, mild increment to no variation was observed in CMAPs at low rates of stimulation. One control cat had an increment of 18% in amplitude with unchanged AUC at 50 Hz.

Muscle and Nerve Biopsy

All muscle biopsies from all 5 cats had moderate to marked myofiber size variation throughout cryosections from all muscle specimens. Using the myofibrillar ATPase reaction, angular atrophy involving both muscle fiber types was noted in numerous myofibers (>100 myofibers/fascicle, muscle fascicles counted 10) (Fig 5). Fiber type grouping was observed in 3 cats in all muscles examined. Intramuscular nerve branches were evident in biopsies from all cats and showed apparent nerve fiber loss and occasional myelin ovoids in all muscles examined (Fig 5). Motor end-plates were identified with the esterase reaction (Fig 5). Diseased cats had 0–15 motor end-plates per muscle fascicle compared to 2–20 in 2 control cats with normal muscle biopsies. Staining for in situ antibodies against motor end-plates using the *Staphylococcus* protein-A horseradish peroxidase reaction was negative in all muscle specimens examined. Frozen sections of the superficial peroneal nerve of all cats showed normal nerve fascicles adjacent to abnormal nerve fascicles (Fig 5). The abnormalities were profound and included extensive nerve fiber loss and endoneurial fibrosis, myelin ovoids and subperineurial edema.

Semithin resin-embedded peripheral nerve biopsy sections of the superficial peroneal nerve were available for 4 affected cats (Fig 6). For cat 1, only a single normal appearing fascicle was available for evaluation with a subjectively appropriate density of myelinated fibers. No axonal degeneration, demyelination, or fiber loss was noted. For cat 3, 3 nerve fascicles were present with variable severity of lesions (Fig 6A,B). Scattered nerve fibers had inappropriately thin myelin sheaths for the axon diameter, supernumerary Schwann cells surrounding thin and small myelinated fibers (presumptive onion-bulb formations), and nerve fiber loss. In cat 4, regional nerve fiber loss was evident. Scattered small thinly myelinated fibers were present suggesting attempts at regeneration (presumptive regeneration sprouts) (Fig 6C). Acute axonal degeneration including swollen and dark staining axons, forming myelin ovoids and foamy macrophages were evident in the biopsy from cat 5 (Fig 6D).

Follow-Up

Cats 1, 2, and 4 were lost to long-term follow-up. Cat 3 was unable to stand, eat, or drink unassisted at

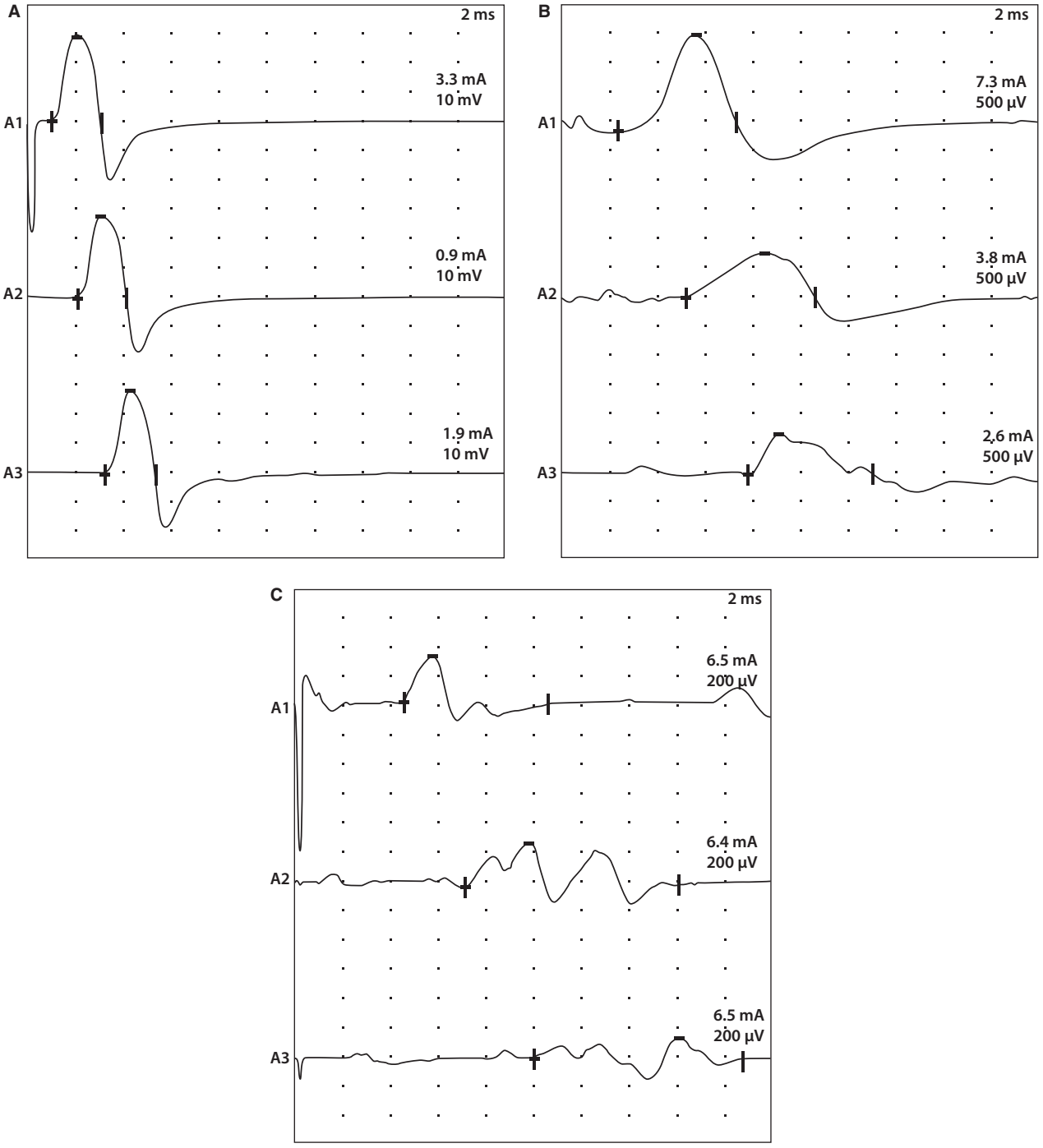

Fig 2. Motor nerve conduction study of the peroneal nerve. Stimulating sites at A1 = hock, A2 = stifle, A3 = hip, CMAP shown, time (ms), amplitude (mV or µV) as shown. **(A)** Normal cat. Note amplitude in mV. **(B)** Cat 1. Note increased latency, amplitude in µV, temporal dispersion, and conduction block (A2, A3). **(C)** Cat 3. Note amplitude in µV, multiphasic CMAP, temporal dispersion, and conduction block (A3).

18 months of age and was euthanized. No necropsy was performed in this cat. Cat 5 recovered fully 6 months after the initial presentation with no specific treatment. The cat has remained active with no gait deficits and regained normal muscle mass over the 2-year follow-up.

Discussion

This study highlights the importance of performing an in-depth electrophysiologic examination in cats with generalized neuromuscular disease. Despite this effort, the underlying cause(s) of the presented motor

Table 2. Sensory nerve conduction (ulnar, radial, peroneal). Number of cats shown (affected, controls), Dickinson 2004 corresponds to published data for peroneal nerve[13] with identical technique to that of this study.

	Lat (ms)	Amp (μV)	CV (m/s)
Ulnar (sensory)			
	Elbow		Carpus-elbow
Cats (3)	1.23 (0.31)	24.66 (20.22)	85.33 (18.01)
Controls (2)	1.15 (0.07)	14.41 (15.62)	83.5 (2.12)
	Cd Cervical		Elbow-Cd
Cats (3)	2.63 (0.35)	8.83 (9.05)	115 (8.54)
Controls (2)	2.45 (0.21)	6.62 (5.26)	126.5 (0.71)
	Cr Cervical		Cd-Cr Cerv
Cats (3)	3.57 (0.4)	2.27 (1.04)	84 (8.66)
Controls (2)	3.3 (0.28)	3.16 (2.08)	84.5 (6.36)
Radial (sensory)			
	Elbow		Carpus-elbow
Cats (3)	1.57 (0.21)	13.47 (7.97)	77.33 (10.02)
Controls (2)	1.25 (0.21)	29 (22.63)	83.5 (2.12)
	Cd Cervical		Elbow-Cd
Cats (3)	3.07 (0.4)	5.43 (4.34)	107.67 (6.81)
Controls (2)	3 (0.28)	4.6 (1.41)	110.5 (4.95)
	Cr Cervical		Cd-Cr Cerv
Cats (3)	3.9 (0.53)	1.74 (0.7)	90.33 (19.14)
Controls (2)	3.8 (0.42)	3.7 (1.84)	94.5 (7.78)
Peroneal (sensory)			
	Hock		Paw-hock
Cats (5)	0.82 (0.15)	72.45 (58.32)	57.8 (8.29)
Controls (2)	0.65 (0.07)	54.03 (49.48)	59 (22.63)
Dickinson 2004	1.1	34.92	53
	Stifle		Hock-stifle
Cats (5)	1.84 (0.25)	13.79 (11.61)	82.6 (7.23)
Controls (2)	1.65 (0.21)	14.49 (3.12)	95.5 (14.85)
Dickinson 2004	2.2	7.29	67
	Hip		Stifle-hip
Cats (5)	3.2 (0.79)	6.65 (4.41)	90.6 (20.53)
Controls (2)	2.95 (0.04)	8.67 (2.61)	91.5 (2.47)
Dickinson 2004	3.9	14.61	84
	L4-L5		Hip-L4-L5
Cats (5)	4.18 (0.76)	7.69 (5.68)	108.75 (9.11)
Controls (2)	3.85 (0.07)	5.33 (0.24)	116 (15.56)
Dickinson 2004	5.3	8.79	89

Lat, latency; Amp, amplitude; CV, conduction velocity, mean (SD).

polyneuropathy remained undetermined, but are suspected to be heterogenous. Electrodiagnostic testing ruled out a sensory component in these cats and confirmed a predominantly motor polyneuropathy. Although motor end-plates were not morphologically or functionally evaluated, the observed distal nerve fiber loss and damage (intramuscular nerve branches, Fig 5) could result in injury to neuromuscular junctions and cause a decremental response to repetitive nerve stimulation. Decremental responses of 10% or more have been typically associated with myasthenia gravis,[20] an autoimmune disorder in which autoantibodies cause destruction of end-plate AChRs.[34] This study also highlights that predominantly motor polyneuropathies do occur in young cats of various breeds and not exclusively in young Bengal cats.

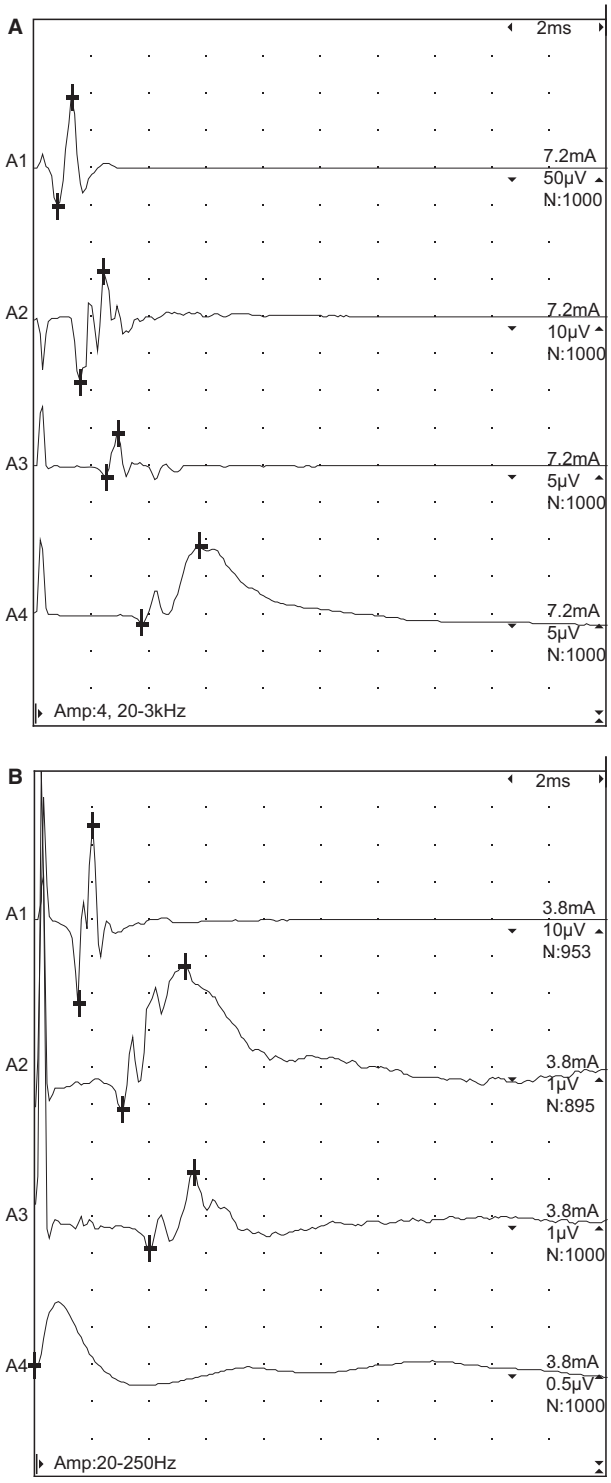

Fig 3. Sensory nerve conduction study. Time is in ms, amplitude in μV as shown for each recording area. **(A)** Normal SNAPs of the peroneal nerve in cat 3. Recording sites at A1 = hock, A2 = stifle, A3 = hip, A4 = L4-L5. **(B)** Normal SNAPs of the ulnar nerve in cat 4. Recording sites at A1 = elbow, A2 = C6, A3 = C1, A4 = frontal.

Correction made after online publication September 17, 2014: Figure 3 legend has been updated.

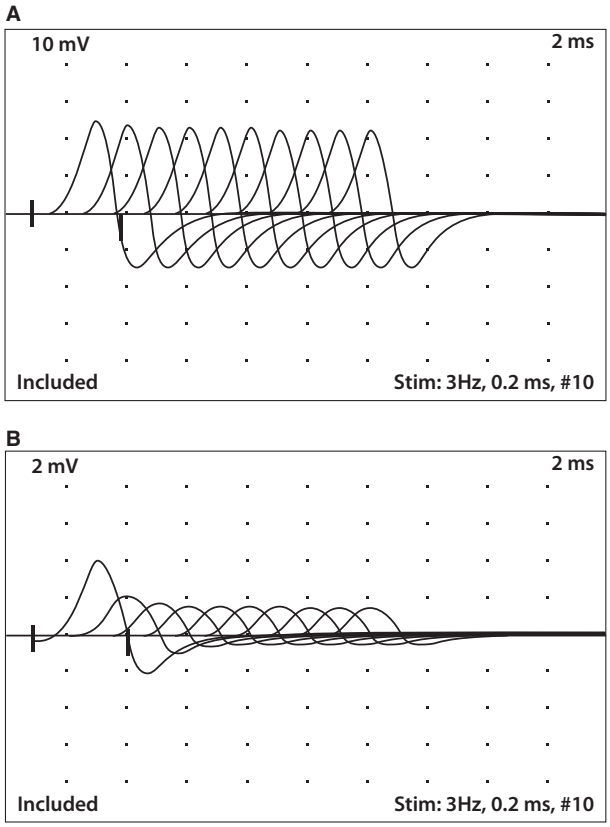

Fig 4. Repetitive nerve stimulation of the peroneal nerve. **(A)** Control cat at stimulation rate of 3 Hz. Note amplitude at 10 mV per division. **(B)** Cat 5 at stimulation rate of 3 Hz. Note decreased CMAP and decrement over subsequent trains of stimulation. Amplitude at 2 mV per division.

Further, in-depth electrodiagnostic testing was not performed in all reported Bengal cats (n = 38) except for 2 cats.[11,12] Therefore, conclusive exclusion of a sensory component in those cats was not possible. Even though all cats in this study had a similar clinical presentation, early onset of disease (<1 year of age), and electrodiagnostic findings consistent with a motor polyneuropathy, the different course of disease (relapsing in 3 cats with apparent clinical resolution in between episodes, and progressive in 2 cats) along with different pathologic patterns within resin-embedded fascicular nerve biopsies would suggest different etiologies for these motor polyneuropathies. The apparent clinical resolution in 3 cats (cats 1, 3, and 4) was supported by the presence of fiber type grouping in muscle biopsies consistent with chronicity, denervation, and reinnervation. Further, onion-bulb formations in nerve biopsies of cat 3 (domestic longhair) were consistent with recurrent demyelination and remyelination similar to Bengal cats.[11]

Neuromuscular diseases can represent a diagnostic challenge in cats because dysfunction in the various regions of the neuromuscular system (peripheral nerve, neuromuscular junction, muscle) can present with similar clinical signs.[16] Electrodiagnostic testing is essential in the investigation of motor, sensory, or mixed neuropathies.[13,28,29] Based on the involvement of the motor component of the neuromuscular system, motor polyneuropathy and motor neuron disease (MND) were considered in the cats of the current study.[12,35] Both inherited and acquired MND have been reported in cats.[35–38] In the veterinary literature, polyneuropathies with predominant motor involvement based on full diagnostic evaluation of motor and sensory components are limited to 2 young Bengal cats (1 cat each study).[11,12] In this study of 5 cats, one of the cats was a Bengal (cat 1) and did not have sensory deficits. Certainly, additional Bengal cats with relapsing polyneuropathy should be evaluated for sensory deficits.

Additional similarities between some of the cats of this study and the Bengal cats with relapsing polyneuropathy included early onset of disease (mean age 10.6 months), with weakness as the most common clinical sign, and neurologic examination consistent with neuromuscular disease.[11,12] Similar to our study, clinicopathologic data did not support systemic illness or endocrinopathies.[11,12] Serum creatine kinase activity was mildly elevated in 21 of 29 Bengal cats (146–7,888 U/L),[11] and in all cats from this study (497–4,624 U/L). In both studies, fibrillation potentials were the most common alteration on EMG examination.[11] Fibrillation potentials and positive sharp waves (also commonly observed in our cats) were thought to be the result of denervation.[26] Fibrillation potentials and positive sharp waves typically develop 2–3 weeks after the onset of injury, which is consistent with the history of these cats.[26]

In the study of Bengal cats, nerve conduction measurements were performed in 23 cats for motor and 2 cats for sensory assessment.[11,12] When reported, the MNCVs for the sciatic, peroneal, or tibial nerves were decreased.[11,12] Motor CV of the ulnar nerve was evaluated and found decreased in 3 of 4 cats,[11] and in one case report.[12] Factors such as age, size, and limb temperature[20] affecting nerve conduction were not considered responsible for the altered results in these cats. Late potentials, such as F waves, were only evaluated in 1 Bengal cat case report, and supported a polyradiculoneuropathy.[12] In our study, late wave recordings were attempted for the peroneal nerve, but potentials were unable to be consistently obtained as reported[39]; therefore, the data were not presented. There is similar difficulty in obtaining late waves for the peroneal nerve in humans.[26]

The decremental response of the CMAP to RNS of the peroneal nerve in 3 of 5 cats in this study (cats 1, 3, and 5) is clinically relevant. This is an important finding because a decrement of 10% or more of baseline at low stimulation rates is typically attributed to myasthenia gravis.[20,26,27,40] In our study, a decremental response of 10% or more was identified at low stimulation rates (1 and 3 Hz) in 3 cats. In 2 of these 3 cats, the decrement was profound at 1 Hz (decrement >35%) and 3 Hz (>50%). However, decremental responses can be observed with any disorder that compromises neuromuscular transmission including other junctionopathies and polyneuropathies.[32] Therefore,

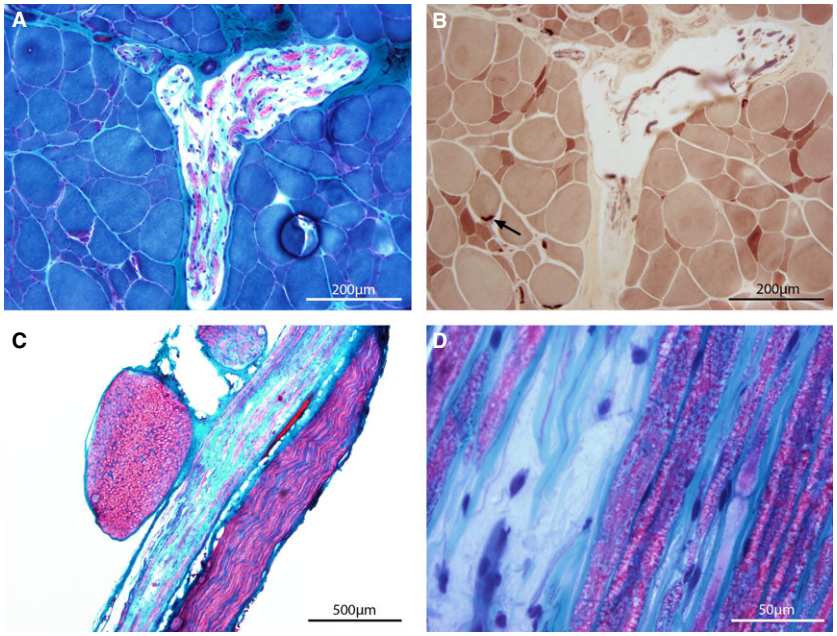

Fig 5. Histochemical evaluation of muscle and nerve. **(A, B)** Intramuscular nerve branch in the triceps muscle of cat 3 on Modified Gomori trichrome (A) and esterase reaction (B). Note angular myofiber atrophy intermixed with hypertrophic fibers, lack of nerve fibers, and darkly stained motor end-plates (arrow) at the periphery of a few myofibers (bar = 200 µm). **(C, D)** Superficial peroneal nerve. Note normal nerve fascicle adjacent to abnormal nerve fascicle on cross sections and longitudinal sections with reduced visible axons and myelin on modified Gomori trichrome (bar = 500 µm [A], 50 µm [B]). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

this finding is not disease specific.[32] A decremental response on RNS because of a motor polyneuropathy has not been previously described in the veterinary literature. Further, autoimmune myasthenia gravis was ruled out based on the negative acetylcholine receptor antibody titers.[34] At high stimulation rates of 30 and 50 Hz, the 3 cats had decrements of 38–69% and 25–73% for CMAP amplitude and AUC, respectively. This was different from our control cats, which had minimal variations and in one, pseudofacilitation was observed at 50 Hz (increment in amplitude of 18% without change in AUC).[26,32] Repetitive nerve stimulation was reported as normal in 1 Bengal cat in the large study.[11]

In the previously reported study of Bengal cats, 26 cats had nerve biopsies collected from the peroneal nerve, and less frequently from the tibial and caudal cutaneous sural nerves.[11] Similar descriptions of normal nerve fascicles adjacent to abnormal nerve fascicles were made.[11] However, the study did not specify which nerves had such finding.[11] The peroneal and tibial nerves are mixed nerves (motor, sensory), whereas the sural nerve is purely sensory.[16] It would have been helpful to know if the sural nerve was affected and to what extent compared with the peroneal and tibial nerves in this cohort of cats, because histologic evaluation of the sural nerve would have added further information on any sensory involvement. The prognosis for Bengal cats with relapsing polyneuropathy has been reported to be good.[11,12] Because of lack of follow-up in 3 cats (including the Bengal cat), the prognosis for all cats could not be determined. Cat 3 had recurrent signs, but signs rapidly progressed on last episode requiring euthanasia. Cat 5 had progressive signs of disease, but recovered after 6 months with no specific treatment and remained normal on last follow-up 2 years later.

Although congenital or acquired MND could not be entirely ruled out in the absence of histologic evaluation of lower motor neuron cell bodies, MND was thought to be less likely. MND is chronic and progressive with no recurrent episodes of normalcy.[36,37] According to the revised El Escorial criteria for the diagnosis of MND in humans, EMG, MNCV, and SNCV must aid in ruling out other neuromuscular disorders and have findings supportive of clinical MND.[41] These findings consist of acute denervation in the form of fibrillation potentials, positive sharp waves and fasciculation potentials; and reinnervation as seen as giant motor unit action potentials in specific body segments.[41] In addition, there should be no conduction block or evidence of demyelination on MNCV, and sparing of sensory nerves (normal SNCV).[41] Features of MND include normal or reduced CMAP amplitude (subject to the number of neurons lost), normal or decreased MNCV (depending on whether the fastest motor neurons are spared or not), but not less than 75% of the lower limit of normal, and normal F wave latencies.[41] The cats in this study had fibrillation potentials and positive sharp waves on EMG supportive of acute denervation, sparing of sensory nerves on SNCV studies, and findings consistent with both axonal loss (markedly decreased CMAP), and demyelination (increased latency, decreased CV, temporal dispersion [±polyphasia], and conduction block) based

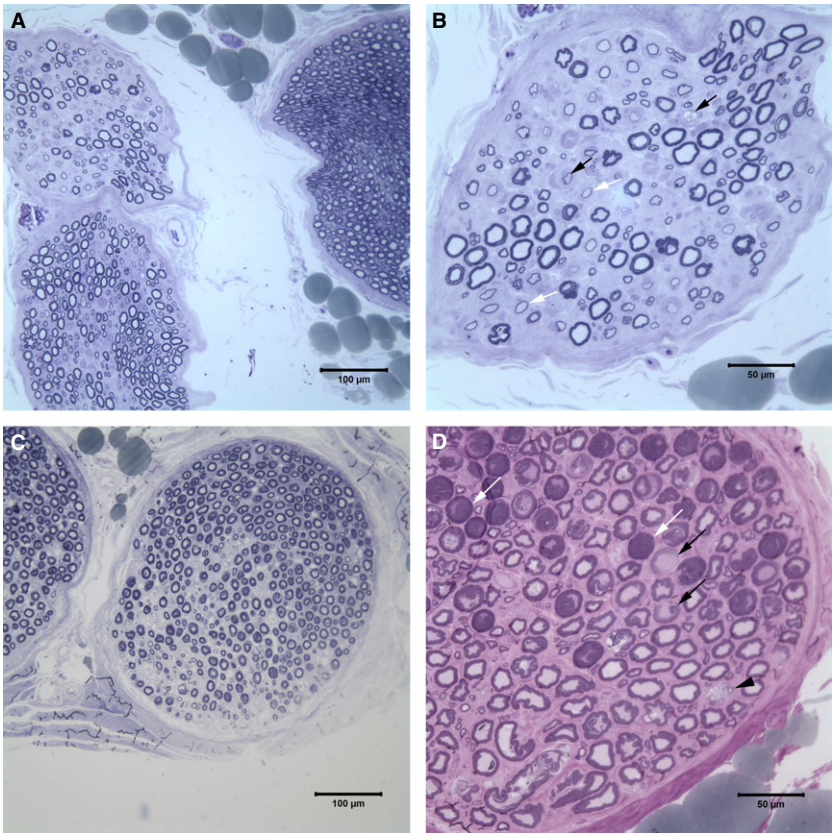

Fig 6. Evaluation of resin-embedded superficial peroneal nerve biopsies from cats with motor polyneuropathy. **(A)** Low-power image of resin-embedded sections of peroneal nerve from cat 3 showing variable nerve fiber loss in 3 fascicles. Fiber loss was evident in the 2 fascicles on the left, and a subjectively normal density of myelinated fibers was evident in fascicle on the right (bar = 100 µm). **(B)** Higher power image shows numerous inappropriately thinly myelinated fibers (white arrows) and onion-bulb formations (black arrows) (bar = 50 µm). **(C)** Low-power image of the peroneal nerve from cat 4 showing regional nerve fiber loss and small-caliber nerve fibers consistent with regenerative sprouts. (bar = 100 µm). **(D)** Image from the peroneal nerve of cat 5 showing swollen and dark staining axons consistent with axonal degeneration (white arrow), forming myelin ovoids (dark arrow) and a foamy macrophage (arrowhead) (bar = 50 µm). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

on MNCV studies. Additionally, neurogenic muscle atrophy in the absence of substantial nerve pathology is seen in MND.[36,37] In these cats, one of the most striking findings was histologic evidence of neuropathy in nerve fascicles and intramuscular nerve branches.

In conclusion, predominantly motor polyneuropathies might occur in young cats of any sex and breed. Based on clinical presentation, electrodiagnostic testing, and histologic evaluation of nerve biopsies, motor polyneuropathies can be relapsing or progressive. Regardless of a relapsing or progressive course of disease, severely compromised distal motor nerves can affect neuromuscular transmission resulting in decremental responses on RNS testing as shown in this study. Therefore, clinicians should be aware that a decremental response on RNS is not an exclusive finding of myasthenia gravis. A specific cause(s) for motor polyneuropathy was not determined in these cats. However, despite the similarities on age at onset of disease and clinical presentation in these cats, different etiologies are possible given the differences in course of disease and pathologic findings. Motor polyneuropathy should be considered in young cats of any breed and sex that present with relapsing or progressive generalized neuromuscular disease.

Footnotes

[a] Nicolet Biomedical Inc, Madison, WI
[b] Grass Medical Instruments, Quincy, MA

Acknowledgments

The authors thank John Doval for technical assistance. The study was performed at the University of California at Davis and the University of California San Diego. No financial support provided for the study.

Conflict of Interest Declaration: The authors disclose no conflict of interest.

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