Severe polymyositis and neuritis in a cat

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Case Description—A 4-year-old domestic shorthair cat was evaluated for a 1-week history of shifting limb lameness that progressed to tetraparesis.

Clinical Findings—Physical examination revealed generalized muscle atrophy and signs of discomfort when the muscles of the appendicular skeleton were palpated. Neurologic examination revealed diminished myotatic and withdrawal reflexes in all 4 limbs. Results of a CBC indicated mild neutrophilia, and serum biochemical analysis revealed mild hyperalbuminemia and high creatine kinase activity. The cat was anesthetized, and an electromyogram (EMG), CSF sample, and nerve and muscle biopsy specimens were obtained. The EMG revealed positive sharp waves and fibillation potentials; CSF analysis revealed albuminocytologic dissociation, and histologic examination of muscle and nerve specimens revealed severe myositis and neuritis. Immune-mediated polymyositis and neuritis were suspected.

Treatment and Outcome—With physical therapy and long-term corticosteroid drug treatment, the cat recovered complete motor nerve function.

Clinical Relevance—The severity and rapid progression of clinical signs, combined with the EMG abnormalities and histologic findings, could have led to inappropriate euthanasia for this cat. Veterinarians should be aware that immune-mediated polymyositis and neuritis in cats can have an excellent prognosis with appropriate, long-term treatment. (J Am Vet Med Assoc 2009;235:172–175)

A 4-year-old neutered male domestic shorthair cat weighing 4.8 kg (10.6 lb) was evaluated at the Iowa State University Veterinary Teaching Hospital for a 1-week history of lameness that had progressed to tetraparesis. The cat initially had weight-bearing lameness in the left pelvic limb, which progressed to lameness in the left thoracic limb and then to generalized weakness. It had been treated with meloxicam* (dose unknown) by the referring veterinarian, with no clinical improvement. The cat had no history of prior medical problems, trauma, or known exposure to toxicants. It was housed strictly indoors and had been routinely vaccinated.

Physical examination revealed the cat was bright, alert, and responsive, and its rectal temperature, pulse rate, and respiratory rate were unremarkable. No overt physical abnormalities were detected other than generalized muscle atrophy. Palpation of the vertebral column did not elicit a pain response from the cat; however, palpation of the muscles of the appendicular skeleton yielded signs of mild to moderate discomfort. Neurologic examination revealed the cat had normal mentation and cranial nerve function but a crouched gait and generalized weakness that was more evident in the thoracic limbs than in the pelvic limbs. Myotatic and withdrawal reflexes were diminished in all 4 limbs, but conscious proprioception was intact. On the basis of these findings, a diffuse motor-unit disease was suspected.

A CBC was performed, revealing neutrophilia (13.0 × 10^3 cells/µL; reference range, 3.2 × 10^3 to 12.5 × 10^3 cells/µL). A differential count revealed 60% neutrophils, 25% lymphocytes, 10% monocytes, 3% eosinophils, and 2% basophils. A platelet clumping score of 2 was assigned. A platelet count of 246,000 cells/µL (reference range, 150,000 to 450,000 cells/µL) was measured. The WBC count was 1.5 cells/µL (reference range, 0.4 to 1.1 cells/µL). A clinical chemistry panel revealed a total protein concentration of 6.8 g/dL (reference range, 2.1 to 3.5 g/dL), a serum albumin concentration of 3.8 g/dL (reference range, 2.1 to 3.5 g/dL), and high creatine kinase activity (785 U/L; reference range, 50 to 250 U/L). Results of a urinalysis were unremarkable.

The cat was anesthetized, and an EMG, CSF sample, and nerve and muscle biopsy specimens were obtained. The EMG included evaluation of the appendicular and epaxial musculature. Positive sharp waves and fibillation potentials were most marked within the supraspinatus, biceps brachii, triceps brachii, and extensor carpi radialis muscles bilaterally and were mild to moderate in the quadriceps femoris, vastus lateralis, semimembranosus, and gastrocnemius muscles bilaterally. These findings were consistent with a diagnosis of diffuse myopathy or, less likely, neuropathy. Analysis of a CSF sample collected from the lumbar subarachnoid space revealed hyperproteinemia (122.1 mg/dL; reference range, 10 to 27 mg/dL), high CK activity (113 U/L; reference range, 0 to 5 U/L), an RBC count of 11,150 cells/µL (reference range, 0 to 30 cells/µL), and a WBC count of 3 cells/µL (reference range, 0 to 5 cells/µL). Cytologic evaluation of the CSF sample revealed low cellularity with few RBCs and rare, intact, small lymphocytes. No etiologic agents or neoplastic cells were detected.

Platelets were clumped but appeared adequate in number. Serum biochemical abnormalities included hyperalbuminemia (3.8 g/dL; reference range, 2.1 to 3.5 g/dL) and high CK activity (785 U/L; reference range, 50 to 250 U/L). Results of serologic tests for FeLV antigen, anti-FIV antibody, and anti-Toxoplasma gondii IgG and IgM (at 1:40 dilution by use of indirect immunofluorescence assay) were negative. Findings on thoracic radiographs were unremarkable.

The severity and rapid progression of clinical signs, combined with the EMG abnormalities and histologic findings, could have led to inappropriate euthanasia for this cat. Veterinarians should be aware that immune-mediated polymyositis and neuritis in cats can have an excellent prognosis with appropriate, long-term treatment. (J Am Vet Med Assoc 2009;235:172–175)

Abbreviations

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<tr>
<td>CK</td>
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fixed but chilled immediately following collection or immersed in neutral-buffered 10% formalin. An ulnar nerve biopsy specimen was similarly fixed in formalin. Biopsy specimens were shipped refrigerated by an overnight service to the Comparative Neuromuscular Laboratory, University of California. Once received, the chilled muscle specimens were flash frozen in isopentane precooled in liquid nitrogen and stored at −80°C until further processed. Formalin-fixed muscle specimens were paraffin embedded, and the fixed ulnar nerve specimen was embedded in araldite resin.

Mixed mononuclear cell infiltration of variable severity was detected within all 3 muscle specimens. In triceps brachii muscle, areas of mild mononuclear cell infiltration and areas of extensive myofiber loss, atrophy, and fibrosis were detected within the same sections (Figure 1). Multifocal areas of cellular infiltration with an endomysial and perimysial distribution as well as variable fiber atrophy and loss were also present within the other muscle specimens. Scattered mononuclear cell infiltrations were evident under the perineurium and within the endoneurium in the ulnar nerve biopsy specimen (Figure 2). On the basis of these findings, a diagnosis of inflammatory myopathy (myositis) and neuropathy (neuritis) was made.

While results of serologic testing for antibodies against *T gondii* and histologic examination of biopsy specimens were pending, the cat was treated empirically with clindamycin (12 mg/kg [5.5 mg/lb], PO, q 12 h) and physical therapy, including range-of-motion exercises. Clindamycin administration ceased once the negative results of the anti-*T gondii* antibody tests became available. On the basis of the results of evaluations of muscle and nerve biopsy specimens and the absence of an identifiable infectious disease or neoplasia, treatment was initiated with an immunosuppressive dosage of prednisone (1.5 mg/kg [0.7 mg/lb], PO, q 12 h). Range-of-motion exercises were continued.

The cat was reassessed at the hospital 2 weeks, 6 weeks, and 10 weeks after the initial evaluation. Within 6 weeks, muscle mass in the pelvic limbs and the right thoracic limb had increased and mobility had considerably improved. However, the left thoracic limb still had muscle atrophy and was not consistently used for walking. When weight was placed on the left thoracic limb, the cat walked on the dorsomedial aspect of the paw, although without apparent discomfort. All other aspects of the physical examination were unremarkable. Neurologic examination revealed normal mentation and cranial nerves as well as improved reflexes and overall strength in all limbs. The prednisone dosage was decreased (to 1.5 mg/kg, PO, q 24 h), and range-of-motion exercises were continued. The cat continued to steadily improve and, after 12 weeks of treatment, was considered fully recovered. The prednisone dosage was consequently steadily tapered.

When the prednisone dosage was decreased from 0.5 mg/kg (0.23 mg/lb) every 24 hours to 0.5 mg/kg every 48 hours 6 months after the initial evaluation, the cat’s physical condition deteriorated but improved again when the prednisone dosage was increased. Within 6 weeks after the relapse, the prednisone dosage was successfully tapered to 0.5 mg/kg every 24 hours; at that time, owners described the cat as almost fully recovered. At the last follow-up evaluation 14 months after initial diagnosis, results of ambulation and neu-
rologic examinations were unremarkable. Muscle atrophy was still evident in the left thoracic limb, but the limb was consistently used for walking, although at times the paw would flip dorsally. The prednisone dosage was further tapered to 0.25 mg/kg (0.1 mg/lb) every 24 hours at that time. One month later, the cat was described by the owners as remaining fully recovered; therefore, the prednisone dosage was tapered to 0.125 mg/kg (0.06 mg/lb) every 24 hours. Additional gradual tapering with the ultimate goal of discontinuing prednisone administration was planned.

**Discussion**

The history and clinical presentation of the cat of this report were consistent with a diagnosis of neuromuscular disease. Although neuromuscular diseases in cats can have a narrow range of clinical signs, numerous inherited and acquired disorders can affect the feline neuromuscular system. Disorders affecting motor neurons and nerve roots, peripheral nerves, neuromuscular junctions, and muscles can have a similar clinical appearance.

We ruled out readily treatable causes of weakness, including hypokalemia, hypotension, hypercaldemia, hypoglycemia, and hyperglycemia, in the cat of this report. Electromyography revealed diffuse changes in the thoracic and pelvic limb muscles consistent with myopathy or neuropathy. Measurement of motor nerve conduction velocity could potentially have provided additional insight into the ongoing pathologic process in this cat but was not performed. The diagnosis of myositis, with variable severity within and between muscles, was reached by detection of infiltrations of mixed mononuclear cells within multiple muscle biopsy specimens. Concurrent neuritis was also diagnosed because of the detection of mononuclear cell infiltration within the ulnar nerve biopsy specimen. Because there was no evidence of neoplasia or infection with FIV, FeLV, or *T gondii*, immune-mediated myositis (polymyositis) and neuritis were considered most likely. The cat’s response to corticosteroid drug treatment supported this diagnosis. A preneoplastic form of myositis could not be ruled out; however, neoplasia was not evident at up to 14 months after the original diagnosis.

The total protein concentration within the CSF sample was markedly high in the absence of cytologic abnormalities, which is a condition referred to as albuminocytologic dissociation. The degree of blood contamination evident within the CSF sample would not be expected to considerably alter CSF protein concentrations. Reported reasons for albuminocytologic dissociation include inflammatory, degenerative, compressive, or neoplastic disease. In addition, albuminocytologic dissociation has been associated with viral nonsuppurative encephalomyelitis, increased permeability of the blood-brain barrier, local necrosis, ischemic myelopathy, seizures, fever, intervertebral disk extrusion, degenerative myelopathy, myelomalacia, granulomatous meningoencephalitis, and intrathecal globulin production as well as interruption of usual CSF flow and absorption. In the cat of this report, the albuminocytologic dissociation could have been attributable to increased production of protein within the CNS resulting from an inflammatory process or albumin leakage through an incomplete blood–spinal cord barrier at the dorsal root ganglion. Protein electrophoresis of the CSF sample could have helped to determine whether the protein consisted of albumin or globulins, but this was not performed. The high CSF CK activity was nonspecific finding; however, a breach in the blood-brain barrier could have contributed to the increase, particularly given that serum CK activity was also high. High serum CK activity is consistent with muscle damage but is not necessarily diagnostic for myositis. An increase in serum CK activity can develop with necrotizing myopathies, dystrophic myopathies, and other muscle diseases as well as in inflammatory myopathies.

Although a few published clinical reports include descriptions of myopathies in cats associated with electrolyte disturbances, hyperthyroidism, infectious agents, neoplasia, muscular dystrophies, and other congenital myopathies, most descriptions of idiopathic (autoimmune) inflammatory myopathy (polymyositis) in cats are in book chapters, review articles, and meeting proceedings. To the authors’ knowledge, the basis for these descriptions has not been established in peer-reviewed veterinary journals. Clinical signs of polymyopathy and polyneuropathy in cats are similar regardless of the underlying cause and include generalized weakness, ventroflexion of the neck, and, from time to time, dysphagia. Thus, the diagnosis of polymyositis and polyneuritis is a diagnosis of exclusion after ruling out infection and obvious neoplasia and confirmation of inflammation within biopsy specimens.

The true prevalence of polymyositis in cats is not known, but the disease is likely uncommon. From 2001 through 2007, 624 diagnostic muscle biopsy specimens from cats were submitted to the Comparative Neuromuscular Laboratory at the University of California for histologic examination. This is an international reference laboratory devoted to the study of neuromuscular diseases in companion animals. The biopsy specimens were all interpreted by the same muscle pathologist (GDS). Of these muscle specimens, 17 (2.7%) had evidence of an inflammatory myopathy. Of the 17 specimens, 2 were from cats with thymoma associated with concurrent myasthenia gravis and 2 others were from cats in which lymphoma was diagnosed several months after an inflammatory myopathy was diagnosed. Although specimens of peripheral nerve were not received for all 17 cats, concurrent neuritis was diagnosed in 2 cats.

In human medicine, the term polymyositis is reserved for diffuse inflammatory myopathies in which an identifiable cause is not found. Criteria for the definitive diagnosis of idiopathic polymyositis in cats are not well-defined. In a review article, it was suggested that a definitive diagnosis of idiopathic polymyositis can be made when any 3 or more of the following criteria are confirmed: appropriate clinical signs, high serum CK activity, generalized EMG abnormalities, negative results of serologic testing for autoimmune and infectious diseases, and results of histologic evaluation of muscle biopsy specimens suggestive of inflammatory myopathy.
According to these criteria, the cat of the present report had idiopathic polymyositis. Recently, the diagnosis of polymyositis in humans was extended to include invasion of non-necrotic fibers by CDB+ lymphocytes and upregulation of major histocompatibility complex class I activity on myofibers.29 Immunohistochemical detection of T-cell phenotypes of cellular infiltrates would have provided additional information regarding the cause of disease in the cat reported here but was not performed.

Serum CK activity is reportedly moderately to markedly increased, compared with the upper reference limit in cats with polymyositis.31,26–28 In the present case, the serum CK activity could be interpreted as only mildly high (785 U/L; reference range, 50 to 250 U/L). Therefore, serum CK activity values that are within the reference range or that are only mildly high should not be interpreted as ruling out the possibility of an inflammatory myopathy. Evaluation of muscle biopsy specimens is critical to reaching a correct diagnosis.

Although an inciting cause of polymyositis and neuritis was not identified in the cat described here, it is possible that an infectious agent could have acted as a trigger for an autoimmune reaction or that occult neoplasia could become evident later in the course of the disease. The improvement of the cat with corticosteroid drug treatment and the relapse after dosage tapering are most consistent with the diagnosis of an immune-mediated disease. Because of the relapse, multimodality immunosuppressant treatment could have been used if increasing the dosage of prednisone did not result in improvement of clinical signs. Other drugs used for immunosuppression in cats include cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil, and leflunomide30 or cytotoxic drugs such as cyclophosphamide, azathioprine, chlorambucil, and methotrexate.31 However, potential adverse effects of these drugs need to be considered, and to the authors’ knowledge, the usefulness of immunosuppressive drugs in the treatment of cats with inflammatory myopathies and neopathies has not been scientifically evaluated.

In the present report, the rapid progression, severity of clinical signs, EMG abnormalities, and histologic findings could have led to inappropriate euthanasia. However, because the correct diagnosis was made and the appropriate treatment (physical therapy and long-term corticosteroid drug treatment) was administered, the cat recovered completely.

References


