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FELINE NEUROMUSCULAR DISORDERS

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Feline neuromuscular diseases may be classified according to their location as (1) those involving peripheral nerves and/or nerve roots, (2) those involving the neuromuscular junction, and (3) those that involve muscle. Each of these neuromuscular diseases will produce lower motor neuron (LMN) disease, however significant variation in clinical signs may occur. Peripheral nerve and muscle diseases result in varying degrees of paresis, muscle atrophy, hyporeflexia, and hypotonia. Hyporeflexia, hypotonia, ataxia and proprioceptive positioning deficits are most characteristic of peripheral nerve disease. Some primary muscle disorders may be characterised by muscle hypertrophy rather than atrophy. Neuromuscular junction disorders ("junctionopathies") result in a variety of clinical signs, that range from flaccid paralysis to exercise-induced weakness.

Cervical ventroflexion is a dramatic sign of generalised neuromuscular weakness in cats. The chin usually rests near the thoracic inlet, with the eyes positioned dorsally to maintain a straight-ahead gaze. Other common physical examination findings are a slight protrusion of the dorsal aspects of the scapulae when weight is placed on thoracic limbs, and a stiff thoracic limb gait. A crouched, wide-based stance is often seen in pelvic limbs. Possible causes to consider for this posture are: subacute or chronic organophosphate toxicity, potassium-depletion myopathy, thiamine-responsive neuromuscular weakness, hyperthyroidism, immune-mediated (idiopathic) polymyositis, myasthenia gravis, polyneuropathy, hypernatraemic polymyopathy, ammonium chloride toxicity, hereditary myopathies (Burmese, Devon rex), hypocalcaemia, and portosystemic encephalopathy.

Megaoesophagus has rarely been reported in cats, although a predisposition has been noted in Siamese and Siamese-related breeds. In most cats the cause of acquired megaoesophagus is unknown; however, the condition has been associated with several systemic neuromuscular disorders, such as myasthenia gravis, botulism, polymyositis, polyradiculoneuritis, tick paralysis, lead toxicosis, feline muscular dystrophy-like conditions, laryngeal paralysis/polyneuropathy complex, and glycogen storage diseases.

Diagnosis of feline neuromuscular diseases requires a complete neurological examination, minimum data base (full blood count, serum biochemistry panel, urinalysis, thoracic radiographs), electrophysiological evaluation, and muscle/nerve biopsies.

NEURONOPATHIES

1. Feline Dysautonomia

Feline dysautonomia (Key-Gaskell syndrome) is a generalised disorder of autonomic ganglia recognised in cats in the United Kingdom in 1981, and more recently in other countries. There is no age or breed predilection for this disease. The disorder is a neuronal disorder; however, clinical signs relate more to autonomic dysfunction, and are largely gastrointestinal in nature. The most common signs are depression, anorexia, constipation, dry external nares and oral mucosa, reduced tear production, regurgitation, protrusion of the membrana nictitans, mydriasis, and bradycardia. These signs usually occur acutely, but may progress insidiously over a week or more.

2. Tetanus

Although cats are supposedly resistant to the effects of the *Clostridium tetani* exotoxin, several cases of tetanus have been reported in this species. The toxin interferes with release of neurotransmitters from inhibitory interneurons in the spinal cord. Local tetanus has been reported in cats, where the disease is characterised by tonic rigidity of a single limb.

3. Feline Motor Neuron Disease

Motor neuron disease (MND) is a term used to describe a group of disorders that have principal clinical and pathologic features related to degeneration and loss of lower motor neurons. The cause of MND in cats remains undetermined. Diagnosis is confirmed at necropsy by the detection of neuron loss and gliosis in the ventral horn of the spinal cord, with secondary degeneration of nerve fibers in ventral nerve roots and peripheral nerves

INHERITED POLYNEUROPATHIES

1. Sphingomyelinase-Deficiency Polyneuropathy

Niemann-Pick disease (NPD) is an autosomal-recessive lysosomal-storage disease characterised by a deficiency of sphingomyelinase.

2. Hyperchylomicronemia-Associated Neuropathy

Inherited primary hyperchylomicronemia is a suspected autosomal-recessive disease characterised by fasting hyperlipemia, lipemia retinalis, and peripheral neuropathy. Clinical signs are usually not seen prior to 8 months of age. Compression by lipid granulomas of peripheral, cranial, and sympathetic nerves, especially at the level of the intervertebral foramina, results in neurological signs. Resolution of neurological signs and decrease in blood-lipid levels occurs following 2-3 months of dietary management.

3. Hyperoxaluric Peripheral Neuropathy

Primary hyperoxaluria is a suspected autosomal-recessive disease of domestic short-hair cats in Great Britain. Acute renal failure, in cats between 5 and 9 months of age, results from renal tubular deposition of oxalate crystals. Severe generalised LMN weakness accompanies the renal failure. Weakness is attributed to accumulation of neurofilaments in ventral nerve roots, proximal axons, and intramuscular nerves. All reported cats died before 12 months of age. The pathogenesis of peripheral nerve lesions is unknown.

4. Hypertrophic Polyneuropathy

Hypertrophic polyneuropathy has been described in 2 unrelated 12-month-old cats. Affected cats had intention tremors, decreased postural reactions, hyporeflexia, and mild sensory loss.

5. Birman Cat Distal Polyneuropathy

A degenerative polyneuropathy has been reported in several litters of Birman cats bred from the same parents.

ACQUIRED PERIPHERAL NEUROPATHIES

1. Diabetic Polyneuropathy

A distal polyneuropathy has been reported in cats with uncontrolled or poorly controlled type 2 diabetes mellitus. Neurological abnormalities include a plantigrade stance, progressive paraparesis, muscle atrophy, and patellar hyporeflexia. The cause of this polyneuropathy is incompletely understood.

2. Ischemic Neuromyopathy

Ischemic neuromyopathy occurs in cats with cardiomyopathy, subsequent to thrombosis of the caudal aorta or its principal branches. The ischemic injury to both muscle and peripheral nerve is produced by collateral-circulation vasoconstriction induced by substances such as serotonin and thromboxane A2 released by platelets trapped in the thrombus.

3. Trauma

Brachial plexus avulsion produced by severe thoracic limb abduction with secondary stretching or tearing of nerve roots is a commonly occurring peripheral nerve injury of cats. Sacroiliac fracture/dislocation, sacral fracture, or caudal vertebral fracture/luxation may result in damage to the sixth and seventh lumbar and the first two sacral nerve roots. Mononeuropathies of radial nerve and sciatic nerve occur in cats following mechanical blows, gunshot wounds, fractures, pressure and stretching.

4. Neoplasia

Feline malignant lymphoma, often associated with FeLV-infection, may involve nerve roots or peripheral nerves. Other primary peripheral nerve neoplasms rarely are seen in cats.

5. Toxic Neuropathies

Drug-induced neuropathies are not well defined in cats. It is likely that as chemotherapeutic treatment of neoplasia becomes more aggressive, more drug-induced neuropathies will be recognised (e.g. vincristine). A delayed neurotoxicity may occur in cats days or weeks after minimal exposure to organophosphates. Lesions are associated with distal degeneration of motor nerves that begins in the periphery (dying-back axonopathy). Peripheral neuropathy may occur sporadically with spontaneous lead-poisoning. Megaesophagus and partial laryngeal paralysis, believed to be due to lead-associated neuropathy, have been reported in a cat. Othe toxins related to neuropathies in cats are salinomycin, acrylamide and pyrethrins. thalium,

6. Laryngeal Paralysis

Acute laryngeal paralysis was diagnosed in 3 cats with signs of upper airway obstruction, including dysphonia, absence of purring, and progressive inspiratory dyspnea. Varying degrees of paralysis of vocal folds and arytenoid cartilages were noted. One cat was positive for FeLV. Underlying responsible mechanisms were not defined.

7. Miscellaneous Peripheral Polyneuropathies

Single case reports exist of a variety of peripheral neuropathies in cats. These include: 2 cats with histologically-confirmed inflammatory polyneuropathy (a chronic relapsing polyradiculoneuritis) and an acute polyneuritis, an idiopathic chronic relapsing polyneuropathy responsive to immunosuppressive glucocorticoid therapy and an acute brachial plexus neuropathy with a suspected relationship to a previous vaccination. It is reasonable to expect that there will be future reports regarding FeLV and FIV infections and their association with neuromuscular diseases of cats, particularly polyneuropathies. Paraneoplastic neuropathies and radiation-induced neuropathies of cats are likely to be reported in the future. Polyneuropathy has been described in experimental black cats with chronic dietary restriction of phenylalanine and tyrosine.

DISORDERS OF THE NEUROMUSCULAR JUNCTION

1. Myasthenia Gravis

Myasthenia gravis is a condition that results from either a congenital or an acquired reduction of acetylcholine receptors of neuromuscular junctions. Both forms have been reported to occur in cats. Two of the acquired cases were associated with thymoma, and another with a cystic thymus. Acquired myasthenia gravis has been reported frequently in Abyssinians and Somalis (closely related to Abyssinians), which may suggest a possible association with the major histocompatibility complex, as in humans. The most consistent signs in cats include tremors, initial stiffness with progression to generalised weakness on exercise,

cervical ventroflexion, dysphagia, dysphonia, ptyalism, facial weakness, and dyspnea. Overt megaesophagus or esophageal hypomotility is common.

2. Miscellaneous "Junctionopathies"

Abnormalities in neuromuscular junction function may also result from tick paralysis, administration of certain drugs, selected toxins, or from envenomation. Botulism has not been reported as a clinical entity in cats, however, it may be produced experimentally in cats. Paraneoplastic junctionopathies are likely to be reported in cats in the future. The association of acquired myasthenia gravis and thymoma in cats is a good example of a paraneoplastic junctionopathy.

INHERITED MYOPATHIES

1. Muscular Dystrophy

Muscular dystrophy-like disorders of cats have been reported in the Netherlands and the U.S.A. To date all affected cats have been males, which suggests an X-linked inheritance. Clinical signs may first be seen in cats at 5-6 months of age, and include generalised skeletal muscle hypertrophy, excessive salivation, reduced exercise tolerance, stiff gait and "bunny-hopping" when running, difficulty in jumping, adducted hocks, cervical rigidity, vomiting/regurgitation, and partial protrusion of the tongue.

2. Hereditary Myopathy of Devon Rex Cats

This is a congenital myopathy of Devon rex cats. Characteristic clinical signs, including ventroflexion of the head and neck, protrusion of the scapulae, and esophageal weakness, all reflect dysfunction of striated muscle, while skeletal muscle pathology is suggestive of a muscular dystrophy.

3. Nemaline Myopathy

An apparently inherited myopathy, characterized by the presence of large numbers of nemaline rods in skeletal muscle fibers, has been investigated in cats.

4. Myositis Ossificans

Clinical, radiographic, electromyographic, and pathological findings in cats with fibrodysplasia ossificans progressiva have been described. This disorder affects young adult to middle-aged cats of both sexes. Characteristic clinical features include progressive stiffness of gait, with enlargement of proximal limb musculature.

5. Miscellaneous Inherited Myopathies

Glycogen storage diseases (or glycogenoses) are rare disorders of cats. Deficient activity of one of the enzymes involved in glycogen degradation or synthesis results in inadequate glycogen utilisation, and in glycogen accumulation within various tissues, including muscle. There are several reports of glycogenoses in cats. Glycogen storage disease Type IV has been reported in 3 young related Norwegian forest cats.

6. Myotonia Congenita

Myotonia refers to a state of prolonged contraction or delayed relaxation of a muscle after voluntary movement or following mechanical or electrical stimulation. This disorder is characterized by muscle spasm (stiffness) and temporary inability to initiate movement. A block in chloride conduction in the muscle fiber membrane is thought to be the underlying mechanism responsible for congenital myotonia. Myotonia congenita has been reported in domestic cats, although the mode of inheritance and molecular defect have not yet been elucidated.

ACQUIRED MYOPATHIES

1. Infectious Polymyositis

Infectious myositis may occur in association with bacterial infection, migrating parasites, or protozoan disease. Whilst cats are the only definitive hosts for *Toxoplasma gondii (*and a majority of cats may have serum antibodies to this organism) muscle involvement is not an outstanding feature of *Toxoplasma* infection of cats. Experimental inoculation of cats with the protozoan *Neospora caninum* may produce fatal, necrotising encephalomyelitis, polymyositis, pneumonia and hepatitis. Naturally-occurring feline neosporosis has not been reported to date.

2. Immune-Mediated (or Idiopathic) Polymyositis

Polymyositis occurs sporadically in cats, occasionally in association with thymoma. Inflammatory infiltrates are predominantly mononuclear with small lymphocytes and macrophages. Neutrophils are seen infrequently. Eosinophils are rarely seen. Clinical signs are characterised by a persistent cervical ventroflexion, appendicular weakness, painful muscles, and exercise intolerance. Serum levels of creatine kinase and aldolase are elevated. A report of polymyositis in a cat in association with myasthenia gravis and thymoma further supports an immune-mediated aetiology.

3. Potassium-Depletion Polymyopathy

This acute feline polymyopathy, resulting from a severe total body potassium depletion, is usually secondary to a reduced potassium intake and increases in the fractional excretion of potassium in urine (due to renal dysfunction). Clinical signs include muscle weakness, cervical ventroflexion, stiff and stilted gait, and muscle pain. A similar syndrome with a suspected hereditary basis has been reported to occur in Burmese cats.

4. Miscellaneous Myopathies

There are a number of case reports of muscle-related diseases of cats. Descriptions include: nutritional myopathy secondary to vitamin E deficiency myositis secondary to *Clostridium chauvoei* and *Clostridium septicum* infections fibrotic myopathy of the semitendinosus muscle and quadriceps contracture secondary to trauma. Episodic weakness and signs of

depression have been noted in young domestic short-hair cats (less than 1 year of age) with hypernatraemia secondary to hypodypsia. The most common clinical sign of hypernatraemic myopathy is ventral flexion of the neck. Causes of hypodypsia include lesions of the hypothalamus, and mechanical inability to swallow - a potentially serious complication of hypertrophic feline muscular dystrophy. The association between myositis and malignant neoplasia (paraneoplastic myopathy) is likely to be reported in the future. Myopathies in cats may occur in association with FeLV or FIV infections (e.g. FeLV-associated immunosuppression may enable encystment of *Sarcocystis* spp. in muscle).

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