Proceedings of the 34th World Small Animal Veterinary Congress
WSAVA 2009

São Paulo, Brazil - 2009

Next WSAVA Congress:

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INVESTIGATION OF NEUROMUSCULAR COLLAPSE

Signalment & History
The signalment is often helpful in diagnosing diseases of the lower motor neuron system. A detailed history is also important in identifying neuromuscular diseases and may often provide insight into specific differential diagnoses. Important historical information includes questions aimed at systemic signs of disease. In addition, if the owners report vomiting, it should be determined if the episodes are truly vomiting or regurgitation. Knowledge of the diet can be helpful information, especially in case where the owners are making homemade diets, as these diets can be deficient in essential nutrients. The vaccination history is also vital information, especially in younger animals. Recent travel history should be determined because of the differing prevalence of certain infectious diseases in various geographic locations. Potential for exposure to toxins, although rare, should also be explored. This is true in the younger animals that have a greater propensity for dietary indiscretion. Likewise, certain products used to treat or prevent ectoparasites have pharmacologic agents that may cause diffuse neuromuscular signs in small animals.

Neurologic Examination
A careful and complete neurologic examination is paramount in all patients suspected of having a neuromuscular disease. The goal of the neurologic examination is to determine the correct anatomic diagnosis. Mentation is usually unaffected in cases of neuromuscular disease. Nevertheless, some neuromuscular diseases may be secondary to a systemic disease, which may alter the level of consciousness or may have a multifocal disease, with damage to the brain being a feature of the disease. For proper gait evaluation, the patient should be observed walking on surfaces that provide adequate traction. To understand gait evaluation, it is important to distinguish the difference between ataxia and paresis. This is paramount to correctly localizing the disease process to the muscular system or within the nervous system. Ataxia refers to incoordination alone and does not typically accompany neuromuscular disease. On the other hand, paresis is defined as a weakness or inability to generate a gait, and the term paralysis refers to a more severe paresis where there is no voluntary movement. Although, the decreased voluntary function can be due to CNS disorder, it is one of the signs of muscle disease. Paresis due to nerve disease is usually, but not always, a flaccid paresis. The quality of the paresis is determined through observation in the tone in the limbs as well as the reflexes. The gait typically is characterized by short, sometimes stiff strides, which may get worse with the length of the exercise. The animals may appear lame, can have muscle tremors or fasciculations or may ‘bunny hop’ in the pelvic limbs.

Minimum Data Base
A complete blood cell count, serum biochemistry panel (including creatine kinase levels and electrolytes), and urinalysis should be evaluated in every animal with suspected neuromuscular disease. Other tests to consider would include: (i) A thyroid panel – as hypothyroidism can cause primary nerve disease; (ii) CSF tap – to rule out associated or primary CNS disease; (iii) Infectious disease titers; (iv) ACTH stimulation (+/- low dose dex. Suppression test) – as Cushing’s and Addison’s can cause neuromuscular weakness; (v) Serum Acetylcholine receptor antibody titers

COMMON NEUROMUSCULAR CONDITIONS CAUSING COLLAPSE
Acute Polyradiculoneuritis (Coonhound Paralysis)
Acute polyradiculoneuritis produces acute flaccid quadriplexes or quadriplegia in any breed of dog or cat. In dogs the condition was originally called "Coonhound paralysis" as it was first described in Coonhounds 7-10 days after exposure to an antigen in raccoon saliva. The inciting cause is often unknown although recent vaccination or illness can be documented in some cases. There has been some evidence to suggest the involvement of Clostridial organisms in the intestine as a source of antigen. These external antigens are apparently similar to proteins comprising part of the ventral nerve roots and motor nerves, and clinical signs are caused by an immune-mediated attack of these structures with the invasion of inflammatory cells. Animals are presented with an acute, progressive, flaccid quadriparesis that often ascends from the pelvic limbs to the thoracic limbs over a 12-24 hour period. On rare occasions the thoracic limbs are more involved than the pelvic limbs. The palpebral reflex may be depressed or absent in both eyes due to involvement of the facial nerve (CN 7) and dysphagia may be present due to vagus nerve (CN 10) dysfunction. If respiratory involvement is severe, abdominal respirations, hypoventilation and hypoxia occur. Hyporeflexia or areflexia with hypotonicity is usually present in all four limbs. Some tail movement may be preserved. Sensation remains intact, and some animals have generalized hyperesthesia. Affected dogs should be closely monitored as they may worsen over a seven-day period before they stabilize and begin to slowly improve. Paresis then paralysis of intercostal and diaphragmatic muscles can occur so respiration should be monitored to detect hypoventilation and hypoxia. Blood gas determinations should be evaluated if possible to detect increased pCO2 and decreased pO2. Oxygen therapy or assisted ventilation may be necessary for a few days in some cases. Severe generalized muscle atrophy may occur making physical therapy essential. The prognosis is usually good with adequate support and most dogs recover in 4-12 weeks. Avoidance of known antigenic stimuli such as vaccinations should be considered to prevent recurrence of signs. Recurrences with no known stimulus have been documented in some dogs and cats.

Tick Paralysis
Tick paralysis is caused by a neurotoxin secreted by female ticks of the genus *Dermacentor* (North America) or *Ixodes* (Australia). The toxin causes inhibition of acetylcholine release at the neuromuscular junction or impairs depolarization of the distal lower motor neuron, and is released as long as the tick is embedded and feeding. Dogs are most frequently affected. This disease is rarely seen in cats except in Australia. An acute, ascending flaccid quadriparesis develops over a 12-24 hour period and looks clinically identical to acute polyradiculoneuritis. Severely depressed or absent spinal reflexes in all four limbs with preserved sensation is typically found on the neurologic examination. Some tail movement may be preserved. Respiratory distress from paresis of intercostal muscles and the diaphragm can be seen in advanced cases. Reduced or absent palpebral reflexes due to facial nerve (CN 7) dysfunction may be present but involvement of other cranial nerves is rare in North America. Laryngeal and pharyngeal paresis may occur in cases in Australia. Any dog or cat with acute flaccid quadriplegia should be carefully examined for an engorged tick including in and around the ears and in between the toes. The EMG can be used to differentiate tick paralysis and acute polyradiculoneuritis. Care should be taken to remove the whole tick if found. The use of topical pesticides to remove possible ticks should be used with caution as organophosphates may further compromise neuromuscular function. Respirations should be monitored as a few cases may require oxygen therapy or ventilatory assistance.

Botulism
Ingestion of toxin from the organism *Clostridium botulinum* is a rare cause of flaccid quadriplexes or quadriplegia in dogs. Cases documented in dogs have been associated with type C toxin. Natural occurring botulism has not been documented in the cat. The most common source of infection is probably through the ingestion of carrion although Clostridial infections may play a role. The toxin interferes with the release of acetylcholine from the endplates of motor neurons, resulting in failure of
neuromuscular transmission. Acute, progressive quadriparesis develops over a 12-24 hour period and varies in severity depending on the amount of toxin ingested. All limb spinal reflexes are depressed or absent and muscle tone is reduced. Facial paralysis, dysphonia, dysphagia and megaesophagus from cranial nerve involvement are often seen. Constipation and urinary retention have also been documented. As the toxin only affects the motor endplates, sensation remains intact. The EMG changes are similar to tick paralysis and coral snake envenomation. The toxin can be identified in the serum, feces, vomitus or carrion by a mouse neutralization test, although this must be done early on in the disease process to be useful. Although a Type C antitoxin is available, to be effective it must be administered before entry of the toxin into the nerve endings and most cases already have neurologic signs on presentation. Many affected dogs recover fully within 2-3 weeks.

Myasthenia gravis
Myasthenia gravis commonly presents as episodic or exercise-induced weakness due to impaired transmission of acetylcholine at the neuromuscular junctions (NMJ) of skeletal muscles. Other clinical presentations of myasthenia gravis include: dysphagia, laryngeal paresis, regurgitation, paraparesis and quadriparesis. Myasthenia gravis may be congenital or acquired associated with an immune mediated or paraneoplastic process. Congenital myasthenia gravis occurs in Jack Russell terriers, Smooth Fox terriers, Samoyeds and various breeds of cats. Acquired myasthenia gravis may occur in some cats 2-4 months following initiation of methimazole (Tapazole) therapy for hyperthyroidism. The weakness resolves following discontinuation of the methimazole. In immune-mediated myasthenia gravis, antibodies are formed against the acetylcholine receptors (AchR) of skeletal muscles and interfere with normal muscle contraction. Affected animals will develop a progressive shortened stride with exercise, which progresses to total fatigue and inability to walk. Strength returns with a brief rest and they are again able to ambulate for short distances. The palpebral reflex will fatigue with repeated testing and sometimes facial nerve paresis is present. Despite profound weakness, conscious proprioception and spinal reflexes are usually normal. Megaesophagus and dysphagia are common and can result in excessive salivation, regurgitation, aspiration pneumonia and death. Intravenous administration of the short-acting anticholinesterase, edrophonium chloride (Tensilon) 1-5 mg in dogs and 0.2-1 mg in cats may cause a dramatic improvement in strength during an episode of collapse. If higher doses are given, a cholinergic crisis of bradycardia, profuse salivation, dyspnea, cyanosis and limb tremors may result which can be reversed with intravenous atropine 0.05 mg/kg. Both false-positive and false-negative Tensilon tests can occur. Other causes of weakness like polymyositis commonly improve with edrophonium chloride. A definitive diagnosis can be made with serology documenting elevated AchR antibodies in the serum. As some cases may be falsely seronegative, re-testing is important in all weak animals suspected to have myasthenia gravis. The severity of clinical signs may not correspond with the degree of elevation of AchR antibody titers. Megaesophagus and aspiration pneumonia may be seen on thoracic radiographs. In paraneoplastic myasthenia gravis a thymoma may be seen as a cranial mediastinal mass on thoracic radiographs. A thorough physical and radiographic examine including abdominal ultrasonography should be performed to search for neoplasia. Some dogs with myasthenia gravis have concurrent hypothyroidism and weakness will not improve until both disorders are treated. The serum total T4 or free T4 levels are usually reduced and TSH levels are usually elevated in hypothyroidism. Myasthenia gravis and polymyositis may also occur concurrently and serum CK levels may be elevated. EMG is often normal except for a decremental evoked muscle response on repetitive nerve stimulation of 5/second. Initial therapy usually consists of the administration of oral pyridostigmine bromide (Mestinon) 0.5-3 mg/kg every 8-12 hours with food. A liquid formulation of pyridostigmine bromide is recommended so that the dose can be easily adjusted to the level needed to control the clinical signs. With high doses, weakness may occur as a result of a cholinergic crisis and therefore a low dose of pyridostigmine is initially given then slowly increased until weakness is resolved. Oral famotidine 5 mg/kg/day may reduce the nausea and gastrointestinal irritation from the pyridostigmine bromide. Resolution of clinical signs can be seen in many dogs on a spontaneous basis.
Hypokalemic polymyopathy
Hypokalemia in cats may cause an acute onset of generalized weakness, persistent ventral flexion of the neck and occasionally muscle pain.