Neuropathies, myopathies and neuromuscular junction disorders

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Dogs and cats presenting with peripheral neuromuscular disease are often confusing for the clinicians, especially in the early phase when it is often mistaken for lameness. This lecture will focus on the tetraparetic/paralytic patient suffering from generalized peripheral neuromuscular disease.

Hallmarks for peripheral neuromuscular disease:

- Weakness (no ataxia if only motor neurons are affected – sensory neurons can be intact).
- Altered sound of voice/bark, loss of "voice"/ability to bark.
- Muscle atrophy (occurs quickly, within days, and can be profound).
- Flaccid paresis/paralysis with reduced to absent muscle tone.
- Hypo reflexia to absent reflexes, patella reflexes are usually the first to be diminished.
- Proprioception is generally intact (if the animal is strong enough to weightbear).
- The gait pattern is characterized by a short stepping gait (as if the animal is walking on broken glass).
- Weakness – generally of the flexor muscles.
- Tremors while standing still.

In case of a generalized polyneuropathy, the clinical signs are usually first evident in the longer neurons such as the recurrent nerve (leading to altered sounding bark, "loss of voice"), Sciatic and femoral nerves (weakness of the pelvic limbs) and the lateral thoracic nerve (loss of panniculus/cutaneous trunci reflex).

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Differential diagnoses for acute tetraparetic/paralytic patients with generalized peripheral neuromuscular disease in the Netherlands:

- Polyradiculoneuritis
- Botulism
- Organophosphate intoxication
- Blue-Green algae (anatoxin intoxication)
- Lead toxicity
- Carbamate intoxication
- Fulminant Myasthenia Gravis
- Aminoglycoside antibiotics (Ca antagonist)
- Autoimmune Polymyositis
- Hypokalemic myopathy
- Endocrine polyneuropathy (Diabetes or Cushing's)
- (Tick Paralysis) not seen in Europe.

Diseases	Cranial Nerve deficits	Megaesophagus	Electro diagnostics	Spinal reflexes
Polyradiculoneuritis	Can have	No	EMG abnormal after 5-7 d. (denervation)	Weak to absent
Botulism	Most often	Can have	EMG normal Repetitive nerve stim. abnormal	Weak to absent
Fulminant Myasthenia Gravis	No (blink reflex "wears out")	Can have 50% of dogs 15% of cats	EMG normal Repetitive nerve stim. abnormal	Mostly normal
Organophosphate intoxication	Can have	Can have	Normal/abnormal	Weak to absent
(Polymyositis)	Most often	Can have	EMG severely abnormal!!	Weak to absent

The most common complication of these patients are:

- Respiratory dysfunction/hypoventilation.
  - Always monitor oxygenation.
  - Give O2 supplementation if needed.
- Dysphagia and aspiration pneumonia.
  - Always feed small amounts at a time in an upright position.
  - Place feeding tubes if needed.

Polyradiculoneuritis (Coonhound paralysis)
This is a disease affecting mainly the motor nerve roots in the ventral aspect of the spinal cord. It is believed that the mechanism of disease is based on "molecular mimicry", meaning that the immune system is wrongly triggered to attack the animals own motor neurons. A number of underlying causes for this molecular mimicry has been suggested where the first described was a reaction to racoon saliva after hunting dogs being bitten (hence the name Coon hound paralysis). Other suggested underlying causes/triggers are: Toxoplasma gondii and Campylobacter jejuni.

Onset of disease is often acute where the animal becomes progressively worse over a period of a few days. Despite the severity of this disease, most dogs tend to make a complete recovery although it often takes many weeks to months before the animal is ambulatory again.

Diagnosis is made based on clinical presentation and by excluding other underlying causes. A conclusive diagnosis can be made on electrodiagnostic examination (EMG and motor nerve conduction velocity studies) in combination with muscle and nerve biopsies.

The treatment is exclusively supportive where physiotherapy holds an important role. Soft bedding, placing a urinary catheter and feeding a nutritious diet is what is known to help. Other, novel treatments described in the literature are IV immunoglobulins and Plasmapheresis/Plasma exchange, which both showed promising results with faster recovery times. Prednisolone has been associated with more complications and should not be used for these patients.

Organophosphate intoxication
There are a large number of different organophosphates in the world, mostly different types of pesticides. Organophosphates exerts their toxic effect by inhibiting acetylcholinesterase, causing an excess of ACh in the synapsis which can lead to different clinical signs mainly:

- *Muscarinic effects* - Hypersalivation, miosis, frequent urination, GI problems and dyspnea
- *Nicotinic effects* - Muscle fasciculations, cramping, weakness, and diaphragmatic failure
- *CNS effects* - Confusion, Tremors, Seizures, Coma

Three types of paralysis may result from organophosphate poisoning:

- Acute LMN paralysis secondary to continued depolarization at the neuromuscular junction
- Organophosphate-induced intermediate syndrome, acute paralysis and weakness of several cranial motor nerves, neck flexors, and facial, extraocular, limb and respiratory muscles 24–96 h. after poisoning
- Delayed polyneuropathy occurs 2-5 weeks after exposure. Mostly affecting the hind limbs causing distal muscle weakness

Diagnosis is made on clinical presentation in combination with measuring the cholinesterase activity.

Treatment for organophosphate intoxication is mainly supportive care but some clinical signs can be targeted directly such as *Muscarinic effects* can be treated with Atropine. *Nicotinic effects* are treated with Pralidoxime (2-PAM) and the *CNS effects/Tremors* are treated with Benzodiazepines.

Myasthenia gravis
Is a relatively common disease where the Acetyl choline receptors, in the post synaptic membrane, are lacking. Although often referred to as one disease, there are actually a number of different diseases ranging from congenital defects where animals are born without ACh receptors or to little production of ACh, to the more common, acquired form where auto anti-bodies are formed against a specific protein in the ACh receptor.

The classic presentation of myasthenia patients is exercise intolerance where the animal needs to sit down to rest after walking only a shorter stretch. These dogs are mostly completely normal on a clinical and neurological examination. Only in the extreme cases these patients can develop what is called a fulminant Myasthenia gravis causing a tetraparalysis.
50% of dogs and 15% of cats with Myasthenia gravis will also have a megaesophagus.

Treatment of Myasthenia gravis:

- Anti ACh-esterase treatment – Neostigmine or Pyridostigmine, start with a low dose to prevent the risk of causing a cholinergic crisis.
- Immunosuppression (prednisolone) may be needed but should not be given in case of a fulminant myasthenia.
- Supportive therapy – feeding upright, stimulate gastric motility, prevent aspiration pneumonia are essential parts of the treatment.