Diagnosing neuromuscular disease

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Victoria Doyle discusses the considerations that need to be undertaken when assessing small animals.

NEUROMUSCULAR diseases are relatively uncommon causes of neurological disease in cats and dogs.

The clinical signs can often be vague or hard to characterise, which can make the diagnosis even more of a challenge. This article aims to discuss the clinical presentation, neurological examination and diagnostic tests that can be performed in the diagnostic investigation of neuromuscular diseases. Subsequent articles will focus on the common neuromuscular diseases.

The neuromuscular system consists of:

• the peripheral nerves – sensory, motor and autonomic;

• the muscle; and

• the neuromuscular junction.

Any part of the system can be affected, and this can be either focal or diffuse.

A full clinical history, including the signalment, is important, as a large number of breed-specific inherited diseases exist. Are the clinical signs acute or more slowly progressive?
Other important historical information includes:

• access to toxins – including organophosphates, carbamates, lead or chemotherapy drugs (such as vincristine);

• current prescribed medications;

• evidence of scavenging carrion or ingesting raw meat;

• recent skin wounds;

• recent tick infestation; and

• any signs consistent with laryngeal paralysis or megaoesophagus.

A full clinical examination is also very important to assess for any concurrent disease processes, including:

• endocrine disease (such as hypothyroidism, diabetes mellitus, insulinoma, hypo or hyperadrenocorticism);

• neoplasia (such as lymphoma, thymoma, anal sac adenocarcinoma and maybe others); and

• otitis media/interna.

It is also important to perform a full orthopaedic examination, as cases with lower motor neuron (LMN) diseases can be easily confused with orthopaedic cases. Dogs with painful orthopaedic disease or LMN disease can have a short-strided gait, may appear to have difficulty in bearing weight and may bunny hop. In addition, their limb muscles may tremble and they may shift weight from one limb to the other and try to lie down.

To localise where the lesion is likely to be, a full neurological examination is vital (Table 1). For many diseases, a degree of crossover between a neuropathy and myopathy is apparent, so the localisation may be to the neuromuscular system in general. Once the lesion has been localised, a list of differential diagnoses can be made and the diagnostic investigation can be instituted (Table 2).

Haematology and serum biochemistry are the initial diagnostic tests required for most neuromuscular diseases and to investigate the possibility of concurrent disease.

It is important to ensure that the biochemistry includes a measurement of the creatinine kinase, aspartate aminotransferase, glucose and electrolytes.
If clinical signs and the initial blood tests are consistent with endocrine disease, then specific endocrine testing should be recommended. Measurement of total thyroxine (T4) and thyroid-stimulating hormone is required where hypothyroidism is a concern.

Investigation of the adrenal axis with the use of adrenocorticotropic hormone (ACTH) stimulation tests and low-dose dexamethasone suppression tests may be required if Addison’s or Cushing’s disease are suspected. It is important to remember that peripheral neuropathies can be present before overt signs of hypothyroidism are evident.

Serology can be performed for *Toxoplasma gondii*(IgG and IgM) and *Neospora caninum* in dogs – and *Toxoplasma gondii* in cats – when protozoal disease is on the differential diagnoses list.

Many animals will show evidence of exposure to the organism. It is important to check for a two to four-fold increase in the antibody titre two to four weeks after the original sample, as this may support the diagnosis of an active infection.

If masticatory muscle myositis is suspected, blood can be submitted for type-2M antibody measurement. The test’s specificity is 100 per cent, but it only has 85 to 90 per cent sensitivity, so false negatives are possible. False negatives are more likely in the chronic stages, when muscle has been replaced with fibrous tissue or when the patient is receiving corticosteroids.

Measuring the acetylcholine receptor antibodies (AChRAb) in cases of acquired myasthenia gravis is the most accurate way of diagnosing the disease. The test’s sensitivity is 98 per cent and false negatives are more commonly seen when the patient has received corticosteroids.

Titres above 0.6nmol/L in dogs and 0.3nmol/L in cats are considered positive. False positives are rare.

In congenital myasthenia gravis, the AChRAb will be normal, as the underlying cause of the condition is the congenital lack of receptors, rather than immune-mediated destruction of the receptors.

In cases where centronuclear myopathy – previously referred to as Labrador myopathy – is suspected, there is a genetic test available (via www.aht.org.uk/genetics_tests.html) that looks for the PTPLA (protein tyrosine phosphatase-like member A) mutation on cheek swabs.

Conscious thoracic radiographs are required to assess for megaoesophagus, which can be present in a number of neuromuscular diseases. The use of sedation or general anaesthesia is generally contraindicated for the accurate diagnosis of megaoesophagus. During sedation, or in anaesthetised patients, air may be present within the oesophagus – which can be confused with megaoesophagus.
Radiographs are also useful to assess the presence of primary neoplasia (such as thymoma, bronchogenic carcinoma) or for metastatic disease. Imaging of the abdomen with radiographs and ultrasound is also recommended to assess for the presence of neoplasia.

It is important to remember that some neuromuscular diseases can be seen as a paraneoplastic condition, which can present before overt evidence of a tumour (such as polymyositis in boxers and other breeds, as a paraneoplastic syndrome with lymphoma developing within one year). It is important to remember that some neuromuscular diseases can be seen as a paraneoplastic condition, which can present before overt evidence of a tumour (such as polymyositis in boxers and other breeds, as a paraneoplastic syndrome with lymphoma developing within one year).

Electrodiagnostic tests are extremely important to fully characterise the neuromuscular lesion. Electromyography is useful to assess the presence of a myopathy or denervation (Figure 1).

Motor nerve conduction velocity is important to characterise a motor neuropathy (Figures 2 and 3). It can suggest whether the neuropathy is primary due to myelin or axonal loss. Sensory nerve conduction velocity can be used to assess for the presence of a sensory neuropathy (such as breed-specific sensory neuropathy).

F waves are used to evaluate the function of the motor nerve roots and are a useful test in patients with suspected polyradiculoneuritis (Figure 4).

Repetitive nerve stimulation repeatedly stimulates one nerve; this is a useful test for patients suspected to have myasthenia gravis or botulism (Figure 5).

Lumbar cerebrospinal fluid analysis is indicated, especially when diseases of the nerve roots are suspected (such as polyradiculoneuritis), as an increase in protein is often evident.

Magnetic resonance imaging can also be utilised in a variety of neuromuscular disorders, including cases with myositis (Figures 6a and 6b), and may help to guide where muscle biopsies should be taken from. It can also be useful in diagnosing peripheral nerve diseases, such as nerve sheath tumours, neuritis and trauma (Figure 7).

The next stage in the diagnosis for many neuropathies or myopathies is a nerve and muscle biopsy. The site where the biopsies are taken depends on the region that is affected – in effect, the temporalis muscle is biopsied in cases with suspected masticatory muscle myositis.

However, if the lesion is more diffuse, then sampling standard muscles and nerves can improve the chances of a diagnosis being made.

Standard muscles that are commonly biopsied include (Figure 8):

• lateral head of the triceps;

• vastus lateralis; and
• cranial tibial.

Standard mixed nerves (motor, sensory and autonomic fibres) that are biopsied include (Figure 9):

• common peroneal nerve;

• tibial nerve; and

• ulnar nerve.

Sensory nerves that can be biopsied, if appropriate, include:

• caudal cutaneous antebrachial nerve (thoracic limb); and

• caudal cutaneous sural nerve (pelvic limb).

It is very important that the samples are processed and transported correctly, as incorrect handling will adversely affect the results.

It is advisable to check with the laboratory to find out how it would like to receive the samples before performing the biopsy.

In general, the morbidity associated with the biopsy is low. However, extreme care should be taken when taking the nerve biopsy to ensure that only one third of the width of the nerve is sampled.

An extremely large number of neuromuscular diseases can affect cats and dogs. It is important that the lesion is accurately localised (nerve, muscle or neuromuscular junction) and that a systematic approach towards the diagnosis is instituted.

Treatment and prognosis is closely linked with the underlying cause of the neuromuscular lesions, but can range from good (idiopathic polyradiculoneuritis) to poor (paraneoplastic neuromuscular disease).

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References


