Myasthenia Gravis (MG)

Classic case: 6 yr female, spayed German Shepherd, exercise intolerance and regurgitation

Presentation:

Signalment

- **Congenital** – autosomal recessive (RARE)
  - Jack Russell Terrier, Springer Spaniel, Smooth Fox Terrier, Smooth-haired Miniature Dachshund
  - Brahman cattle

- **Acquired** – most common form of MG seen
  - Mostly young and middle-aged dogs
    - Bimodal age of onset, peaking at 3 and 10 yrs
  - Many breed at risk, but German Shepherds, Golden Retrievers, Labrador Retrievers, and mixed breeds get acquired MG most often
  - Akita, German Short-haired Pointers, Chihuahua also at high risk
  - Newfoundlands, Great Danes can have inherited predisp.
  - Abyssinian & Somali most commonly affected cat breeds

Clinical signs – 3 syndromes

1. **Focal MG** – any of the following
   - Megaesophagus – regurgitation
   - Decreased swallowing reflex
   - Facial muscle weakness
   - Laryngeal paralysis
   - Very rare in cats

2. **Generalized MG**
   - Acute onset of exercise intolerance
   - Para or tetraparesis after exertion
   - Some degree of recovery after period of rest
   - During an exercise test:
     - The limbs start to tremble
     - Muscles become stiff
     - Short-strided
     - Normal proprioception and reflexes
   - Megaesophagus in the majority of dogs – regurgitation
   - Cats usually have neck ventroflexion, decreased palpebral reflex
Presentation: (continued)

Clinical signs – 3 syndromes

3. Myasthenic crisis, fulminating myasthenia gravis
   - Acute para- or tetraparesis
   - Megaesophagus is almost always present
   - Rapid progression
   - Respiratory distress
   - Occurs rarely in the cat

DDX: Hypokalemia, OPP toxicity, polyradiculoneuritis, botulism, tick paralysis, polymyositis, hypothyroidism, methimazole therapy in cats

Test(s) of choice:

- **Tensilon® (endrophonium) test**
  - Ultra-short-acting *acetylcholinesterase inhibitor* – prolongs availability of *acetylcholine*
  - Quick and practical
  - Improvement of gait disturbances w/in 1 minute and lasts 2-3 minutes in most, but not all cases
  - Risk of cholinergic crisis – rare, but be prepared
    - Respiratory disturbances, ptyalism, vomiting, miosis, tachycardia, hypotension, muscle spasms, weakness
    - Treat with atropine
  - False positive responses can occur in other myopathies or neuropathies

- **Acetylcholine receptor antibodies** – Gold Standard
  - **Acquired form only**
    - Titer can be negative early in disease or if treated concurrently with corticosteroids

- **Thoracic radiography**
  - ± Megaesophagus, ± aspiration pneumonia
  - ± Thymoma

- **Muscle biopsy**
  - Congenital form - Shows decreased acetylcholine receptors
  - Acquired form - Shows immune complexes at the neuromuscular junctions

- **Minimum data base**
  - CBC, biochemistry panel, urinalysis, T<sub>4</sub>
  - To rule out other causes of weakness and/or concurrent problems

- **Repetitive nerve stimulation**
  - Requires anesthesia and expensive electrodiagnostic equipment
  - Decremental response of compound muscle action potential
Rx of choice:
- **Cholinesterase inhibitors**
  - Inhibits the breakdown of acetylcholine
  - Dosage must be titrated to individual animal – start low
    - symptoms of overdose may mimic myasthenia!
    - Hypersalivation, vomiting, diarrhea, miosis, bradycardia, weakness
  - Pyridostigmine bromide (**Mestinon®**) – oral
  - Neostigmine – parenteral

- **Immunosuppression**
  - Use with caution – avoid if aspiration pneumonia present
  - Glucocorticoids – can exacerbate muscular weakness.
  - **Mycophenolate**
    - Azothioprine, cyclophosphamide, cyclosporine

- **Aspiration pneumonia**
  - Nebulization, coupage,
  - Antibiotics - Avoid those causing neuromuscular blockade (ampicillin, aminoglycosides)

- **Megaesophagus**
  - Improved esophageal motility – metoclopramide or cisapride
  - Elevated feedings
  - Gastroscopy tube
  - Cimetidine or ranitidine to increase pH of gastric contents and prevent esophagitis

Prognosis:
- Spontaneous resolution can occur, but **very rare**

**Congenital MG**
- Poor prognosis, EXCEPT Smooth-haired Miniature Dachshunds which have spontaneous resolution by 6 months of age

**Acquired MG**
- **Cats** – Fair prognosis because megaesophagus is rare

- **Dogs**
  - Fair – if treatment started early, **BUT 1 year mortality rate is 40-60% among all dogs**
    - Warn owners of multiple hospitalizations and high risk of aspiration pneumonia
  - Poor if dog develops aspiration pneumonia secondary to swallowing difficulties and dysphagia
  - Very poor for myasthenic crisis
Myasthenia Gravis (MG)  
Extended Version

Prevention:
• Congenital form can be prevented by adhering to good breeding practices

• Prevent aspiration pneumonia
  - Turn recumbent animals every 2 – 4 hours
  - Upright feedings, by hand
  - Gastrostomy tube

Pearls:
• **Congenital myasthenia gravis** is caused by an inadequate number of postsynaptic nicotinic acetylcholine receptors because of a **RARE** genetic defect

• **Acquired myasthenia gravis** is an autoimmune disease where antibodies bind to the postsynaptic acetylcholine receptors in striated muscle, causing them to be internalized.
  - Can be associated with other diseases: hypothyroidism, thymoma, thymic cysts, lymphoma, cholangiocellular carcinoma, anal sac adenocarcinoma, osteogenic sarcoma, methimazole therapy in cats

• Incidence of thymomas with acquired MG in cats is about 15-26%, in dogs is around 3%.


My Notes: