MYASTHENIA GRAVIS

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Congenital Myasthenia Gravis

Congenital myasthenia gravis of cats and dogs is characterized as a post-synaptic defect with a deficiency of acetylcholine receptors (AchR) at the neuromuscular junction, in the absence of evidence of autoimmunity.

In animals with AchR deficiency, anticholinesterase drugs should be beneficial. However, full return of strength rarely is seen. Long-term treatment of congenital MG usually is unsatisfactory. Intensive supportive care is essential. Some affected animals may survive up to several years. In some breeds of dog, spontaneous remission of congenital MG may occur (e.g., miniature Dachshund).

Acquired Myasthenia Gravis

Acquired myasthenia gravis (MG) of dogs and cats is a well-characterized autoimmune disease affecting the neuromuscular junction. However, the inciting auto-antigen remains undefined. Muscular weakness and excessive fatiguability result from autoantibody mediated destruction of nicotinic AchRs of the neuromuscular junction.

Optimal therapeutic approaches for dogs or cats with acquired MG have not been established. One confounding factor in the assessment of treatments for acquired MG is the frequent occurrence of spontaneous remissions. Up to 87.7% of affected dogs will go into spontaneous remission at an average of 6.4 months after diagnosis (range: 1 to 18 months).

Early and accurate diagnosis is an essential aspect for obtaining a good clinical outcome in most cases of acquired MG. Experienced clinical judgment and cooperative, dedicated owners also are essential considerations. Recognition of esophageal dilation and/or pharyngeal weakness prior to institution of therapy is mandatory.

Supportive Care

Aspiration pneumonia

Prevention and treatment of aspiration pneumonia is an essential consideration in animals with acquired
MG. Frequent turning of recumbent animals, antibiotic therapy, nebulization and coupage are examples of treatment considerations for aspiration pneumonia.

**Fluid therapy**

Maintenance of adequate hydration is essential in animals with acquired MG. Intravenous fluid therapy may be necessary in animals that regurgitate liquids.

**Nutritional support**

Special feeding procedures (e.g., feeding food and water from elevated feed bowls or holding an animal in a vertical position for 20 minutes after feeding), placement of a gastrotomy tube, and in some cases parenteral nutrition, must be considered. Placement of a gastrotomy tube also may facilitate delivery of oral medications.

**Respiratory support**

Intensive care and ventilatory support may be required in animals with severe aspiration pneumonia or severe generalized weakness.

**Modification of gastrointestinal tract function**

Management of dysphagia and megaesophagus, with associated complications of aspiration pneumonia, regurgitation and esophagitis, is an essential consideration. Drugs that may improve esophageal motility (e.g., metoclopramide), increase lower esophageal sphincter tone (e.g., cisapride), or increase the pH of gastrointestinal contents (e.g., cimetidine or ranitidine) should be considered.

**Specific Therapy**

Specific therapy for acquired MG is based on the severity of the disease in a specific animal. To facilitate treatment decisions, a classification system that addresses the heterogeneous and variable clinical signs of acquired MG has been introduced for use in dogs and cats:

- Group 1: Mild or focal MG
- Group 2: Moderate generalized MG
- Group 3: Severe generalized or acute fulminating MG.

**Anticholinesterase agents**

Anticholinesterase agents, that act to enhance neuromuscular transmission by prolonging the action of acetylcholine at the neuromuscular junction, are used in all the above patient groups. Dosage must be adjusted for each dog or cat depending on individual tolerance of adverse effects and response to treatment. Drugs available include pyridostigmine bromide (Mestinon®, 1-3 mg/kg, orally BID or TID) and neostigmine bromide (Prostigmin®, 2 mg/kg/d, orally in divided doses to effect). Pyridostigmine bromide is available in four dosage forms syrup, conventional tablets, slow release tablets and injectable forms.

**Immunosuppressive therapy**

Should an optimal response to therapy not be achieved with supportive care and anticholinesterase drugs, immunosuppressive drugs may be used. Use of immunosuppressive drugs is controversial, particularly as a
“first line” treatment, due to the high incidence of aspiration pneumonia (particularly in dogs) and the potential for glucocorticoids to exacerbate muscle weakness.

- **Glucocorticoids.** Low dose prednisone therapy (0.5 mg/kg every other day) has been recommended in mildly (Group 1) and moderately (Group 2) affected animals. Contraindications for glucocorticoid therapy include ongoing infections or aspiration pneumonia, diabetes mellitus, severe obesity, uncontrolled hypertension, and gastrointestinal ulcerations.

- **Other immunosuppressive agents** (e.g., azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil) may be recommended for animals in Groups 1 and 2 where use of glucocorticoids is contraindicated, or should adverse effects of glucocorticoids become difficult to manage.

- **Azathioprine.** The onset of clinical effect of azathioprine is delayed, and therefore its use should be combined with prednisone. Adverse effects of azathioprine include bone marrow suppression, hepatotoxicity, pancreatitis and gastrointestinal tract irritation. Use of azathioprine is not recommended in cats, as the adverse effects on bone marrow are more common than in dogs.

**Aphoresis**

When available, plasma exchange is an easily applicable technique for rapid and massive removal of antibodies, and its beneficial role is well established in the management of acquired MG.

**Concurrent neoplasia**

Should a concurrent thymic mass or other neoplasia be present, then surgical removal, with or without radiation therapy, should be considered. As a majority of dogs with thymoma and acquired MG also have megaesophagus and aspiration pneumonia, and because mortality rate after thymectomy in these dogs is high, it is recommended to delay thymectomy until clinical signs of MG are controlled by means of medical management.

**Treatment of Acute Fulminating Myasthenia Gravis**

Management of severe generalized acquired MG (Group 3) is difficult. Affected animals should be managed in an intensive care unit. Anticholinesterase therapy and ventilatory support provide the basis for therapy. Ventilatory support usually is required due to weakness of intercostal muscles and diaphragm, or due to concurrent pulmonary infection (often resulting from aspiration pneumonia). Where possible, culture and sensitivity testing of material obtained by means of tracheal wash should be done, and broad-spectrum intravenous antibiotic therapy instituted. Aminoglycosides and ampicillin should be avoided due to their possible adverse effects on neuromuscular transmission. Immunosuppressive agents should be used with care in patients with aspiration pneumonia. Plasmapheresis and intravenous immunoglobulin have been used to treat people with acute fulminating MG.

**Monitoring the Response to Treatment**

In the absence of immunosuppression, determination of serial AchR antibody titers may aid in determination of both disease status and duration of treatment. Treatment should be continued in the presence of positive AchR antibody titers.
Feline Myasthenia Gravis

A high incidence of thymoma has been reported in association with acquired MG of cats. Drug induced (acquired) MG has been reported in hyperthyroid cats following initiation of methimazole treatment. While cats with acquired MG may be managed successfully using anticholinesterase therapy, glucocorticoids may be used as a “first line” treatment, as exacerbation of muscle weakness and induction of other adverse effects of glucocorticoids, seen in dogs, do not appear to be a problem.

General Considerations

1. Confirm a diagnosis of acquired MG as rapidly as possible. Trial therapies should be avoided.
2. Be aware of those drugs that adversely affect neuromuscular transmission and whose use is contraindicated in animals with acquired MG (e.g., ampicillin, aminoglycosides, anti-arrhythmic agents, phenothiazines, anesthetics, narcotics and muscle relaxants).
3. Advise owners to neuter cats or dogs with acquired MG.
4. Do not “over vaccinate” animals with acquired MG.

Reference