How To...
The Facts of
Myasthenia Gravis

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How Does Bonnie Present?

Bonnie, 34, developed severe double vision two years ago that gradually worsened. Her right eyelid subsequently started drooping, more so towards the end of the day. Bonnie also noted some difficulty lifting heavy objects with her right arm.

What should be done? Go to page 101.

More than 80% of MG patients experience fluctuating double vision and/or eyelid drooping.

How do I recognize MG?

The hallmark of myasthenia gravis (MG; an autoimmune disorder caused by antibodies directed against acetylcholine receptors) is painless, fluctuating muscle weakness. More than 80% of patients present with eye muscle weakness, which leads to double vision and/or drooping of the eyelids. Symptoms fluctuate and worsen as the day goes on. MG should be particularly suspected if these symptoms are variable.

Fluctuating symptoms can be confirmed with repeated observations during an eye examination. Only in about 10% of patients do symptoms remain confined to eye muscles (ocular MG). In 85% to 90% of cases, other muscles are also involved (generalized MG).

Weakness of oropharyngeal musculature manifests as:

- nasal voice,
- difficulty chewing and swallowing, and
- altered facial expression.

If respiratory muscles are involved, the patient will experience shortness of breath during minimal exertion or even while talking. Limbs and neck muscles are commonly affected in MG. The deltoid, neck, and finger extensors are commonly involved.

How do I know MG is unlikely?

Symptoms not consistent with the diagnosis of MG include:

- numbness/paresthesias with weakness,
- muscle pain,
- bowel or bladder disturbances, and
- muscle wasting.

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Table 1

Management options for MG

Cholinesterase inhibitors (Mestinon®)	• First line of therapy for symptomatic relief in a majority of MG patients since they do not have long-term side-effects
Steroids:	• Mainstay of immunosuppressive therapy due to their predictable and rapid response in 75% of MG patients • Main advantages are lack of need for blood monitoring, low cost, and a simple dose regimen • In patients with severe disease, steroids should be initiated under close surveillance while the patient is hospitalized
Immunosuppressants	• Azathioprine and cyclosporine are the two most commonly used agents, producing a sustained and marked improvement in symptoms, which may be delayed for several months • Associated with serious hematologic side-effects; close blood monitoring is required
Plasma Exchange (PEX)	• Most potent and rapidly effective treatment for MG and is reserved for severe symptoms or refractory patients • Almost all MG patients improve rapigly with PEX, though the effect wears off over several weeks unless PEX is combined with other immunosuppressive therapy
Intravenous Immunoglobulin (IVIG)	• Role of IVIG is similar to PEX in that it provides rapid, albeit transient, symptomatic improvement in most MG patients (> 50%) that begins within a week and may last several months
Thymectomy	• Recommended treatment in most MG patients • Can produce long-lasting improvement though the response is unpredictable and may take several years • Younger patients and early thymectomy are the best predictors of a good response • Definitely indicated in MG patients who are found to have a thymoma

How is MG aggravated?

Infections, stress, or excessive heat can aggravate MG weakness. Several commonly used drugs can also worsen patients' symptoms, including:

- antibiotics (gentamycin, erythromycin),
- beta blockers (propranolol),
- calcium-channel blockers,
- magnesium salts,
- d-penicillamine, and
- curare and related drugs used during surgery.

How do I diagnose MG?

A small intravenous dose of Tensilon leads to a rapid and dramatic improvement in patients with significant diplopia or ptosis. In appropriately selected patients, the sensitivity of this test approaches 90%.

Although a normal result does not exclude MG, AchR antibody level in the serum must be obtained.

Thymoma should be excluded by a computed tomography scan of the chest. Autoimmune conditions (*i.e.*, thyroid abnormalities) must also be ruled out through testing.

How do I know when to refer?

Patients should be referred to an electromyography (EMG) laboratory if the diagnosis remains uncertain. The sensitivity of repetitive nerve stimulation testing and single-fiber EMG is about 60% to 70% and > 95%, respectively.[1]

Patients should also be referred to a neurologist for management decisions and regular followup.

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How Do I Test Bonnie?

A Tensilon test was negative. Testing for acetylcholine receptor antibodies and a chest computed tomography (CT) scan were normal. Her symptoms did not respond to a therapeutic trial of cholinesterase inhibitors.

Repetitive nerve stimulation studies were normal. Single-fiber electromyography showed abnormal neuromuscular transmission, suggesting the diagnosis of myasthenia gravis.

How should Bonnie be treated?

Go to page 102.

How Do I Treat Bonnie?

Bonnie was started on high-dose prednisone, with which she rapidly became asymptomatic. She is currently doing well, taking a maintenance dose of prednisone. Due to her plans for pregnancy, other immunosuppressants are being avoided.

Take-home message

- Most patients with MG present with fluctuating diplopia and ptosis.
- Acetylcholine receptor antibodies may be absent in a patient with MG.
- EMG is the most sensitive test for diagnosing MG.
- Long term immunosuppression is required for most patients with MG.
- Due to their potential for rapid deterioration, MG patients need to be closely followed by general practitioners and treating specialist.

How do I treat MG?

Table 1 outlines various management options. MG should be managed on an individual basis, taking into consideration:

- the severity of the patient's symptoms,
- age,
- gender,
- functional limitations, and
- financial limitations.[2]

Delaying definitive therapy may be reasonable, as about 10% of MG patients may spontaneously remit during the first year.

The fluctuating nature of the condition and the propensity for symptomatic patients to rapidly progress to respiratory failure necessitate close followup. Regular communication between the general practitioner and specialist is crucial, as the condition can worsen rapidly into crises during infection or stress, particularly when the disease is not well-controlled.

Since MG patients usually take an immunosuppressant, general practitioners should be on the lookout for any adverse effects of these drugs.

How is MG changing?

A new antibody directed against muscle-specific tyrosine kinase has been detected in the sera of 30% to 70% of patients with seronegative MG.[3]

Recent studies have shown the efficacy of mycophenolate mofetil (CellCept®) in MG, with up to 70% of patients reporting sustained symptomatic improvement with CellCept, some of whom were refractory to other drugs.[4] A clinical trial to assess the efficacy of CellCept in MG patients is currently enrolling patients at the University of Alberta. CME

References

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