Myasthenia Gravis

Julie A. Koch, DNP, RN, FNP-BC; Marlee R. Steele, DNP, RN, FNP-BC; and Logan M. Koch

ABSTRACT

Myasthenia gravis (MG) is a chronic neuromuscular disorder characterized by fluctuating skeletal muscle weakness and fatigue. This rare autoimmune condition can present a diagnostic challenge for the advanced practice nurse (APN). Because of its low incidence in clinical practice and frequently unrecognized symptoms, a delay of 1 to 2 years prior to diagnosis is not uncommon. Recognition of the clinical features is a key component of prompt diagnosis. To avoid delay in treatment, APNs should be aware of variations in MG symptoms and the tools used to confirm a suspected diagnosis. Because patients benefit from the care of neuromuscular specialists, APNs are not expected to be experts within MG treatment. But knowledge of general treatment principles affords the APN an opportunity to collaborate with the neuromuscular specialist to provide care for patients with MG. Using an individual example, this article reviews the experience of an older adult with MG from clinical presentation through treatment. [Journal of Gerontological Nursing, 39(12), 11-15.]
Myasthenia gravis (MG) is a chronic neuromuscular disorder characterized by varying degrees of fluctuating skeletal muscle weakness and fatigue. Recognition of the clinical features of MG is a key component of prompt diagnosis. Because older adults with MG benefit from the care of neuromuscular specialists, advanced practice nurses (APNs) are not expected to be experts in disease treatment. Yet, to avoid delay in therapy, all providers should be aware of the variation in MG symptoms and the tools used to confirm a suspected diagnosis. Knowledge of general MG treatment principles affords primary care APNs an opportunity to collaborate with neuromuscular specialists to promote optimal health care.

**INDIVIDUAL EXAMPLE**

A 71-year-old man is seen with complaints of intermittent weakness and muscle fatigue progressively worsening over the past month. A previous long-distance runner, he now has difficulty ambulating the 100-foot driveway to get his mail. His symptoms of profound leg weakness and fatigue have been attributed to age and his underlying history of coronary artery disease and atrial fibrillation. However, over the past few months, he also reports having noted “eye strain” when working at the computer for long periods of time. He associated that with the aging process, as his symptoms always resolved after a “good night’s rest.” Most recently, he has developed intermittent double vision that seems to be worse when reading at bedtime.

Because the patient’s clinical presentation was consistent with a neuromuscular disorder, a detailed evaluation was performed. He denied any recent changes in weight, no fever, chills, and shortness of breath or chest pain. He denied any allergies. He stopped smoking in 2004; alcohol intake was limited to two beers per month. His medications included warfarin (Coumadin®), atorvastatin (Lipitor®), and amiodarone (Cordarone®).

Vital signs, including pulse oximetry (98% at room air), were within expected parameters. Despite his history of atrial fibrillation, his heart rhythm was regular. Peripheral pulses were 3+. No carotid bruit was detected. Cognition, sensation, and cerebellar function were intact. Gait was coordinated and even. Pupils were equal, round, and reactive to light and accommodation. There was an absence of Lhermitte’s sign; no radicular pain was elicited with neck flexion. No weakness was noted on initial closing of the eyelids, but repetitive opening and closing revealed slight weakness on the right. The patient was asked to gaze laterally and slightly upward to check for fatigability in lid movement. Within 1 minute notable ptosis of the right eyelid and mild nystagmus developed; the patient also began to report diplopia. The ice test was performed; after 2 minutes of application, marked improvement of the ptosis was noted. He was able to open and close his jaw for 100 repetitions. His gag reflex was intact. The patient was asked to read an extensive passage aloud, and no speech abnormalities were elicited within 3 minutes. Initial strength of the upper extremities was noted to be 4+/5; no atrophy was apparent. Deep tendon reflexes of upper and lower extremities were 2+. Upper extremity weakness, with mild fasciculation, became apparent after 30 seconds of 90° arm abduction. The patient was given 1 minute to complete 45° straight leg raises, but was only able to sustain this activity for 15 seconds. The patient was asked to rise from a seated position 20 times, and was only able to complete eight repetitions.

After reviewing the patient’s medical history and physical examination, it was determined that his extremity weakness and fatigability, accompanied by eye fatigue and diplopia, without pupillary involvement, were consistent with MG. The gradual onset of his symptoms, which included ocular and generalized manifestations, essentially ruled out botulism, Guillain-Barré syndrome, polymyositis, retro-orbital tumor, and cranial nerve palsies. The worsening, as opposed to improvement, of symptoms upon repetitive movement ruled out Lambert-Eaton myasthenic syndrome. Despite the presence of prolonged symptoms, asymmetric muscle weakness and atrophy were not present; thus, amyotrophic lateral sclerosis was determined to be unlikely.

**ETIOLOGY AND EPIDEMIOLOGY**

Within MG, antibodies against acetylcholine (ACh) nicotinic post-synaptic receptors form at the neuromuscular junction of peripheral nerves (Gilhus, 2012; Goldenberg, 2013). The antibody-antigen immune complexes and their associated inflammation result in the dysfunction that inhibits normal neuromuscular transmission (Armstrong & Schumann, 2003). In the majority of patients, immunoglobulin G antibodies attack acetylcholine receptors (AChRs), but they may also be directed toward muscle specific kinase (MuSK) (Abbott, 2010; Armstrong & Schumann, 2003; Blum et al., 2011). T lymphocytes have also been implicated in the pathogenesis of MG, as specific subsets of T cells are known to respond to antigenic stimulation and activate AChR-specific B cells (Blum et al., 2011; Turner, 2007). This breakdown of immune tolerance is thought to involve the thymus, as thymic abnormalities (hyperplasia or thymomas) are present in the majority of patients with MG.

Although it is a relatively rare autoimmune disorder, MG is now thought to affect approximately 36,000 to 60,000 Americans (Kutzin, 2012; Myasthenia Gravis Foundation of America [MG Foundation], 2010). Although women are more
commonly affected than men during the first five decades of life, men are more often diagnosed between ages 60 and 80 (Abbott, 2010).

**CLINICAL FEATURES OF MG IN OLDER ADULTS**

The clinical features of MG are characterized by painless striated muscle weakness that worsens after repeated or sustained activity and improves with rest (Conti-Fine, Milani, & Kaminski, 2006; Meyer & Levy, 2009). The extent of symptoms can vary from day to day or even specific hours within any given day, but clinical features usually become more pronounced in the hours before bedtime. In addition to physical activity or exercise, the weakness of MG may become more apparent with several exacerbating factors: emotional stress, hot environments, rapid changes in body temperature, infection, hyperthyroidism, surgery, trauma, and specific medications (i.e., aminoglycosides, beta adrenergic blockers, calcium channel blockers, chloroquine, fluoroquinolone, haloperidol, iodinated contrast, lidocaine, macrolides, magnesium, muscle relaxants, phenytoin, procainamide, quinidine, quinine, and tetracycline) (Abbott, 2010; Goldenberg, 2013; Kutzin, 2012; Meyer & Levy, 2009).

Ocular manifestations (i.e., diplopia and ptosis) are the primary symptoms in the majority of patients (Meyer & Levy, 2009; MG Foundation, 2010). Extraocular muscle weakness may occur asymmetrically, resulting in diplopia. Older adults with diplopia may seek care from their optometrist; visual convergence and the presence of an upward gaze

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<td><strong>Symptomatic therapy (AChE inhibitors)</strong></td>
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| Pyridostigmine (Mestinon®) | • Initial: 30 mg every 4 to 6 hours  
• Maintenance: 60 mg four times daily (180 mg sustained release)  
• Maintenance doses up to 1500 mg per day may be needed in severe cases. Titrate dose to minimize risk for cholinergic crisis. Correlate largest dose with time of most prominent weakness. | Common dose-dependent cholinergic side effects include nausea, vomiting, diarrhea, abdominal or muscle cramping, and increased production of tears, saliva, and bronchial secretions. |
| **Immune-directed therapy** | | |
| Steroids | | |
| Prednisone (Deltasone®) | • Initial: 60 to 100 mg per day  
• Maintenance: 5 to 15 mg per day  
• Dosing gradually tapered, after 2 to 4 weeks, as symptom improvement noted | Commonly initiated during hospitalization. Temporary worsening of muscle weakness may occur. Often used in conjunction with AChE inhibitors. |
| **Non-steroid immunomodulators** | | |
| Azathioprine (Imuran®, Azasan®) | • Initial: 1 mg/kg per day (50 mg)  
• Maximum: 2.5 mg/kg per day  
• Monitor CBC and LFT | Often needed when unable to taper to low maintenance doses of steroids. May take months for apparent response. Severe adverse effects, including malignancies (e.g., lymphoma) and opportunistic infections may occur. |
| Mycophenolate mofetil (CellCept®) | • Initial: 250 mg twice daily  
• Maximum: 3 g per day  
• Monitor CBC and CMP | |
| Cyclosporine (Neoral®, Sandimmune®) | • Initial: 25 mg twice daily  
• Maximum: 3 to 6 mg/kg per day divided twice daily  
• Monitor BP, renal function, drug levels | |
| Cyclophosphamide (Cytoxan®) | • Initial: 25 mg daily  
• Maximum: 2 to 5 mg/kg per day  
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*Note. AchE = acetylcholinesterase; CBC = complete blood cell count; LFT = liver function tests; CMP = complete metabolic profile; BP = blood pressure; BMP = basic metabolic profile; UA = urinalysis.*

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may be detected during an eye examination. Unilateral or bilateral ptosis may be noticeable while working at a computer, reading, or during long periods of driving (Kothari, 2004); older adults may find themselves tilting their heads back to extend the visual field beneath their ptosis.

In approximately 10% to 40% of cases, symptoms remain limited to the extraocular muscles (ocular MG) (Conti-Fine et al., 2006; MG Foundation, 2010; Weeks, 2012). Yet, muscular weakness more commonly progresses to generalized MG, which may affect oropharyngeal, skeletal, and/or respiratory muscles (Conti-Fine et al., 2006). Speech patterns may reflect weakness of the soft palate (prominent nasal intonation), tongue, lips, and supportive facial muscles (slurring of words) (Kothari, 2004). Muscle weakness and fatigability may also result in changes in expression, chewing fatigue, difficulty swallowing, and the inability to maintain jaw closure after chewing. In those with mild generalized MG, neck flexor weakness may be the only clinical finding, and patients may hold their jaw and neck up with their hand. More commonly, patients will complain of profound fatigue and variable weakness of the extremities. In general, upper extremity weakness is a more common presenting symptom than lower extremity weakness. Limb weakness tends to be proximal and symmetric; however, the weakness should not be limited to the distribution of any single nerve root or level of the central nervous system (Smith & Stickler, 2012). Patients may have difficulty maintaining their arms in an abducted position. This weakness may result in difficulty brushing teeth, combing hair, or steering a motor vehicle. When fine motor movement of the hands is impaired, difficulty with handwriting may become apparent (Weeks, 2012). Those with lower extremity involvement often complain of difficulty rising from a seated position, going up and down stairs, or ambulating what they would consider “normal” distances. In individuals with advanced generalized MG, bladder function may also be affected. In more advanced cases, generalized MG can also involve the respiratory muscles and may lead to respiratory distress or failure.

DIAGNOSTIC TESTING

In most MG cases, the neuromuscular history and physical examination are used to establish a preliminary diagnosis. Initial diagnostic studies are often ordered by the primary care APN while awaiting a neuromuscular referral.

Because pharmacological therapy can be complex and a number of commonly prescribed medications may exacerbate muscle weakness, it is often wise to include a pharmacist within the collaborative MG management team.

Laboratory Studies

With the availability of tests to evaluate AChR antibodies, laboratory studies have replaced pharmacological studies (i.e., edrophonium challenge) as the standard for diagnosing MG. The presence of AChR antibodies in a symptomatic patient virtually confirms the diagnosis. Titers may be falsely negative when drawn early in the disease process or in those with mild disease (Meyer & Levy, 2009). Those with generalized symptoms who are anti-AChR negative should undergo testing for anti-MuSK antibodies.

Other Studies

Although individuals older than 50 often have a normal or atrophic thymus, it is generally recommended that every MG patient be screened for thymic disorders (thymoma or hyperplasia) via contrasted computed tomography (CT) or magnetic resonance imaging at the time of diagnosis (Goldenberg, 2013; MG Foundation, 2010; Skeie et al., 2010). Single-fiber electromyogram is able to reveal variations in neuromuscular transmission in 95% to 99% of patients with MG (Conti-Fine et al., 2006). Patients with MG who report shortness of breath should be evaluated with spirometry; vital capacity or peak flow will decrease after repeated testing efforts. The ice pack test has reported high sensitivity rates (which may exceed 80%) in patients with prominent ptosis. The test is positive if ptosis clears or measurably decreases when an ice pack is placed over the ptosis-affected eyelid for 2 minutes.

TREATMENT

In the past, MG, if left untreated, had mortality rates as high as 40% (MG Foundation, 2010; Weeks, 2012). However, the prognosis has improved markedly; those living with MG now have a near-normal life expectancy. Conventional pharmacological treatment (Table) has included the use of acetylcholinesterase (AChE) inhibitor agents for symptomatic relief and a range of immune-directed therapeutic agents (i.e., immunomodulators and immunosuppressives) to modify the disease process (Blum et al., 2011). Monoclonal antibodies and tumor necrosis-factor-alpha have been used in those with more severe disease who have not responded to other treatment (Gilhus et al., 2011). Nonpharmacological therapy can also be helpful for MG patients. In cases in which rapid response is needed (e.g., myasthenia crisis), plasma exchange or intravenous immunoglobulin infusion may be used.
Thyrectomy is not usually indicated for older adults, but is helpful for those with young-onset MG, those younger than 60 with moderate to severe muscle weakness, and all those with thymoma. Conservative measures (i.e., lid crutches or Fresnel prisms) can be useful for the older adult with refractory ptosis and diplopia. Strabismus or blepharoptosis surgery may benefit those who do not respond to conservative therapy.

**INDIVIDUAL EXAMPLE UPDATE**

Based on clinical presentation, a diagnosis of MG was presumed. A consultation with a neuromuscular specialist was undertaken; an appointment was scheduled. In the interim, initial laboratory analyses were performed to rule out other causes. Complete blood cell count, thyroid function studies, and a comprehensive metabolic profile were all within normal limits. A chest CT ruled out thymic abnormalities. Because of the patient’s vascular history, a CT scan of the head and carotid doppler study ruled out stroke, brain tumor, and significant carotid stenosis. AChR/MuSK reflexive antibody testing was also performed. The patient’s AChR binding antibody testing was reported as “positive: elevated”; thus, MuSK antibodies were not evaluated.

Based on the relatively mild symptom manifestation, the neuromuscular specialist elected to initiate therapy on an outpatient basis. Corticosteroid therapy was initiated with prednisone (Deltasone®) 30 mg twice per day. Pyridostigmine (Mestinon®) was also prescribed at a dose of 30 mg every 6 hours to improve his current symptomatology and minimize the risk of worsening his condition during prednisone initiation. The patient and his wife were advised to call if symptoms worsened during titration, and they were provided education on when and how to seek emergent medical care. Subsequently, the patient has been titrated down to prednisone 5 mg daily and has been converted to 180 mg of sustained-release pyridostigmine.

**CLINICAL IMPLICATIONS**

Due in part to its relatively rare incidence and variable clinical presentation, diagnosing MG in the older adult can present a clinical challenge for APNs. Older adults with mild weakness may initially attribute their symptoms to the aging process; therefore, a delay of 1 to 2 years prior to diagnosis is not uncommon. Primary care providers need to be aware of the variations in MG presentation and the tools used to confirm the diagnosis. Because pharmacological therapy can be complex and a number of commonly prescribed medications may exacerbate muscle weakness, it is often wise to include a pharmacist within the collaborative MG management team. Although initial treatment is effective for most patients, there is a need to balance long-term therapy against potential side effects, and patient education is imperative. Once educated, patients can take a more active role in selecting treatment options.

**SUMMARY**

Diagnosing and treating MG in older adults poses several challenges. Fortunately, within this individual example, the APN recognized initial symptoms, provided a thorough examination, and promptly sought assistance from a neuromuscular specialist. The patient has tolerated his combination of symptomatic and disease-modifying treatment well. He has noted that he is able to read at bedtime without developing double vision. And, although he has no plans of returning to long-distance running, he now has no difficulty retrieving his mail or taking the dog for a 1-mile walk twice per day.

**REFERENCES**


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