Fall 2014

Myasthenia Gravis: A closer look

Erin L. Ricker
Otterbein University, erin.ricker@otterbein.edu

Myasthenia Gravis: A closer look

Erin L. Ricker, BSN, RN
Otterbein University, Westerville, Ohio

Introduction

Myasthenia gravis (MG) is a rare, chronic autoimmune disease that affects the neurotransmitter acetylcholine and the acetylcholine receptors at the neuromuscular junction (Mestecky, 2013). MG causes fluctuating skeletal muscle weakness and fatigue. According to the Myasthenia Gravis Foundation of America (MGFA) (2010), 20 per 100,000 patients are diagnosed with MG, although researchers believe several more patients are misdiagnosed or missed entirely.

Several neurological disorders have similar clinical presentations to MG making it difficult for inexperienced practitioners to identify and properly diagnose patients. Patients are often misdiagnosed and delayed proper treatment for one to two years after initial presentation of symptoms (Koch, Steele, & Koch, 2013). Remissions and exacerbations make MG difficult for practitioners to diagnose (Weeks, 2012).

Other possible differential diagnoses include:

- Guillian Barré
- Bell's palsy
- Multiple Sclerosis
- Amyotrophic lateral sclerosis
- Polymyositis
- Stroke

As an Advanced Practice Nurse (APN), it is important to understand the variable clinical presentations that can occur with this disease. The purpose of this presentation is to discuss an individual case study and review the pathophysiology of MG in order to assist the APN in recognizing symptoms early.

Case Study

A 59-year-old Caucasian male was seen by his primary care provider (PCP) with complaints of blurred vision and increased difficulty raising his eyelids. Upon further evaluation, the PCP learned the patient had recently returned home from a one week long trip to Utah. While in Utah, the patient stated he developed a bad cold with symptoms of extremely sensitive, watery eyes and severe headaches. Symptoms progressed throughout the week with continued complaints of double vision and weakness in raising bilateral eyelids. Weakness was noted in both eyes, although the patient stated his right eye was worse than the left eye. Upon returning home, the patient was first seen by his optometrist who recommended further evaluation by his primary care provider (PCP).

Case Study Cont'd

The patient was sent for an immediate magnetic resonance image (MRI) with suspicions of an aneurysm or stroke. Results of the MRI were normal. The patient was then referred to a neurologist for additional testing. After an ophthalmic catheterization to rule out blockages and several neurological examinations, results were inconclusive. A tensilon test was performed to confirm suspicions of MG. Following the positive tensilon test, the patient was checked for acetylcholine receptor antibodies (AChR-Abs) which were present in the patient's blood serum. AChR-Abs are detected in approximately 50% of patients with ocular MG, although AChR-Abs are present in 80-90% of patients with generalized MG (Azeem, Law, & Arora, 2014).

Epidemiology

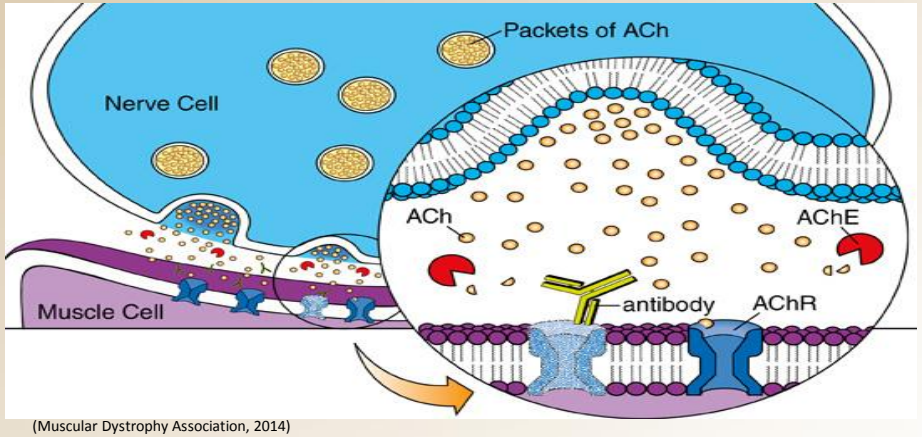
- MG occurs in all races and affects both males and females (MGFA, 2010).
- Asians, compared to other ethnic groups, have a slightly more common onset of MG at a younger age (Weeks, 2012).
- MG can occur at any age although most patient affected are over fifty years of age (Abbott, 2010).
- Women are often affected more than men during the first five decades, where as men are more commonly affected between the sixth and eighth decade (Koch et al., 2013).
- Approximately 20,000 to 70,000 people in the United States are affected by MG (McCance, Huether, Brashers, & Rote, 2014).
- Advances in treatment options such as plasmapheresis, immune therapy, and thymectomy are believed to have increased patient's longevity (Abbott, 2010).
- Although MG is not hereditary, 5% of cases show a familial predisposition for acquiring the disease (Weeks, 2012).

Table 1. A summary of myasthenia gravis (MG) subtypes*

	AChR-MG without thymoma	AChR-MG with thymoma	MuSK-MG	Seronegative-MG
Age of onset	Usually <40 years (EOMG) Less often >40 years (LOMG)	Usually >40 years (LOMG)	Usually <40 years (EOMG)	Usually <40 years (EOMG)
Sex	Predominantly women	Men more than women	Predominantly women	Predominantly women
Presentation	Ocular onset but gradually progresses to generalised	Generalised with or without bulbar involvement	Generalised MG with bulbar involvement and frequent crisis	Ocular onset but gradually progresses to generalised

*Cavalcante et al (2012). AChR, acetylcholine receptor; EOMG, early-onset MG; LOMG, late-onset MG; MuSK, muscle-specific tyrosine kinase.

(Mestecky, A., 2013, p.111)



(Muscular Dystrophy Association, 2014)

Pathophysiology

MG is an autoimmune disease caused by autoantibodies that target skeletal muscles (Cufi et al., 2012). Researchers believe a virus or bacteria is responsible for triggering the body's autoimmune response (Weeks, 2012). Once the immune system is triggered, activated B cells, or plasma cells, begin producing immunoglobulin G (IgG). Synthesis of anti-AChR antibodies require activated CD4+ T cells to interact with and stimulate B cells (Cufi et al., 2012). The thymus gland, suspected in developing autoantibodies that block receptor sites for acetylcholine (ACh), stores T cells and is a common target organ for infectious diseases. (Cufi et al., 2012).

ACh is a neurotransmitter responsible for producing voluntary muscle contraction. Voluntary muscles are controlled by nerve impulses sent from the brain to motor neurons that stimulate one or more muscle cells within the neuromuscular junction (NMJ) (McCance, et al., 2014).

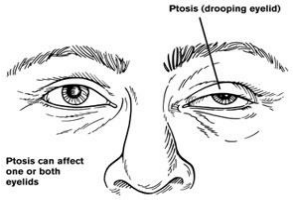
NMJs are formed as axons divide and enter skeletal muscles (Weeks, 2012). When stimulated, ACh is released from the axons (Weeks, 2012). Voluntary skeletal muscle contractions occurs from the binding of ACh to the nicotinic acetylcholine receptors (AChR) (Mestecky, 2013). The NMJ also consists of a synaptic cleft which contains acetylcholinesterase (AChE), an enzyme responsible to hydrolyze ACh and terminate signal transmission (Trouth, Dabi, Solieman, Kurukumbi, & Kalyanam, 2012).

Anti-AChR antibodies affect neuromuscular transmission through complement binding and activation, antigenic modulation, or complete blockage of the AChR (Cufi et al., 2012). This blockage causes a defect in nerve impulse transmission at the NMJ (McCance et al., 2014). Over time, functional loss of AChRs occurs and affected muscles become inadequately stimulated resulting in weakness and fatigability (Mestecky, 2013). Antibodies destroy receptor sites faster than the body can replace them, reducing receptor sites by approximately 80% (MGFA, 2010).

Generally patients over 50 years of age have normal or atrophic thymus glands (Koch et al., 2013). Approximately 70% of patients with MG continue to produce antibodies as a result of thymus hyperplasia or tumors, called thymomas (Weeks, 2012).

Thymomas are usually benign, thymic epithelial tumors. Approximately 30-50% of patients with thymomas develop MG (Priola & Priola, 2014). Thymectomy is generally recommended for patients with thymoma and reduces symptoms in approximately 70% of patients (Weeks, 2012). The patient presented in this case study later discovered he did not have a thymoma. Koch et al. (2013) recommend all patients with MG have a computed tomography or magnetic resonance imaging to detect presence of thymomas.

In addition to those who produce AChR antibodies, two other subtypes of MG exist: seronegative-MG and muscle-specific tyrosine kinase (MuSK) MG (Mestecky, 2013). No antibodies are identified in patients with seronegative-MG. Patients with MuSK-MG produce antibodies that attack a different protein, the muscle-specific tyrosine kinase, in the NMJ (Mestecky, 2013).



(Drachman, 2007, p.1)

Clinical Features

- There are two main clinical categories of MG: generalized AChR myasthenia and ocular myasthenia.
- Ocular myasthenia symptoms are limited to the eyelids and extraocular muscles (Azeem et al., 2014).
- Generalized AChR myasthenia includes generalized symptoms in which bulbar, limb, and respiratory muscles are affected (Azeem et al., 2014).
- Patients who experience generalized symptoms typically present with ocular symptoms first (Weeks, 2012).
- Fluctuating muscle weakness in ocular, bulbar, respiratory, and limb muscles is a hallmark sign of MG (Khan & Bennett, 2014).
- Muscle weakness is often less in the morning when ACh stores are highest (Abbott, 2010).
- Emotional stress, heat, infections, surgery, and hyperthyroidism can exacerbate symptoms and cause muscle fatigue (Koch et al., 2013).
- In the majority of patients, initial presentations of ptosis and diplopia are the primary symptoms (Koch et al., 2013).
- Ptosis and diplopia occur from extraocular muscle (EOM) weakness.
- Other common presentations include slurred speech, dysphagia, dysarthria and limb weakness (MGFA, 2010).
- Muscle weakness is typically exacerbated with prolonged or provoked muscle use and improves with periods of rest (Abbott, 2010).
- Detailed review of systems is imperative to uncover symptoms patients may believe are insignificant, such as decreased weakness in the evening or after strenuous activities (Abbott, 2010).
- Include muscle strength testing and attempt to provoke muscle fatigue by asking patients to maintain an upward gaze. Fluctuating muscle strength is commonly seen in the ocular and oropharyngeal muscles (Abbott, 2010).

Common Signs and Symptoms

- Ptosis (most common early sign)
- Blurred or double vision
- Slurred speech
- Difficulty chewing or swallowing
- Weakness and fatigue in arms and legs
- Respiratory weakness

Implications

APNs must recognize symptoms of MG early to begin proper treatment. As seen in this case study, symptoms of MG are variable making MG difficult to diagnose. The patient developed ocular symptoms rapidly without fluctuations in muscle weakness. Typically MG is gradual with periods of exacerbation and remission. Patients generally experience increased muscle fatigue in the evening, unlike the patient in the case study. The patient stated he experienced heightened muscle fatigue often in the morning and at different times throughout the day. The patient's MG was believed to be triggered by a virus causing the body to produce anti-AChR antibodies that began blocking receptors in the extraocular muscles. The patient's case is also rare in that clinical presentation was limited to ocular symptoms and did not progress to other skeletal muscles. According to Koch et al. (2013), only 10% to 40% of symptoms are limited to extraocular muscles (EOMs). Because the patient sought medical assistance rapidly and physicians were able to confirm a diagnosis of MG, the patient was treated properly and overall outcomes were improved. It is unknown whether symptoms would have progressed beyond the EOMs if diagnosis and treatment were delayed.

Conclusion

As seen in this case study, MG can have presentations similar to other neurological diseases. Because MG is relatively rare with variable clinical presentations, it is important for the APN to understand the subtypes and characteristics. To avoid misdiagnosis, APNs should consider MG when patients report fluctuating muscle weakness (Abbott, 2010). Understanding variations of MG can assist the APN in confirming a diagnosis and avoid delays in treatment (Koch et al., 2013). A thorough review of symptoms along with a complete physical and neurological examination is vital to diagnose MG. MG should also be included in the differential diagnosis for any patient who reports fluctuating muscle weakness and complaints of ophthalmic, neurologic, or gastrointestinal issues (Abbott, 2010). Although there is currently no cure for MG, recognizing symptoms early can improve patient outcomes. Early diagnosis and treatment can improve patient outcomes and decrease disease progression. With proper treatment, patients with MG can lead relatively normal lives.

References

Abbott, S. A. (2010). Diagnostic challenge: Myasthenia gravis in the emergency department. *Journal of the American Academy of Nurse Practitioners, 22*(9), 468-473. doi:10.1111/j.1745-7599.2010.00541.x

Azeem, N., Law, R. J., & Arora, A. (2014). 73-year-old man with recent-onset dysphagia. *Mayo Clinic Proceedings, 89*(6), 845-849. doi:10.1016/j.mayocp.2013.07.022

Cufi, P., Dragin, N., Weiss, J. M., Martinez-Martinez, P., De Baets, M. H., Roussin, R., ... Le Panse, R. (2012). Implication of double-stranded RNA signaling in the etiology of autoimmune myasthenia gravis. *American Neurological Association, 73*(2), 281-293. doi:10.1002/ana.23791

Drachman, D. B. (2007). *Myasthenia gravis.* Retrieved from www.dana.org./Publications/GuideDetails.aspx?id=50029

Khan, K. A., Bennett, J. D. (2014). Undiagnosed myasthenia gravis owing to a very unusual primary presentation. *Oral and Maxillofacial Surgery, 118*(4), e101-e104. doi:10.1016/j.oooo.2014. 02.027

Koch, J.A., Steele, M. R., & Koch, L. M. (2013). Myasthenia gravis. *Journal of Gerontological Nursing, 39*(12), 11-15. doi:10.3928/00989134-20131108-01

McCance, K. L., Huether, S. E., Brashers, V. L., & Rote, N. S. (2014). *Pathophysiology: The biological basis for disease in adults and children.* (7th ed.). St. Louis, MO: Elsevier/Mosby

Mestecky, A. (2013). Myasthenia gravis. *British Journal of Neuroscience Nursing, 9*(3), 110-112.

Muscular Dystrophy Association (2014). *What causes Myasthenia Gravis?* Retrieved from: mda.org/disease/myasthenia-gravis/causes/inheritance

Myasthenia Gravis Foundation of America, Inc. (2010). *What is Myasthenia Gravis?* Retrieved from http://myasthenia.org/WhatisMG.aspx

Priola, A. M., & Priola, S. M. (2014). Imaging of thymus in myasthenia gravis: From thymic hyperplasia to thymic tumor. *Clinical Radiology, 69*, e230-e245. doi:10.1016/j.crad.2014.01.005

Trouth, A. J., Dabi, A., Solieman, N., Kurukumbi, M., & Kalyanam, J. (2012). Myasthenia gravis: A review. *Autoimmune diseases, (2090-0422),* 1-10. doi:10.1155/2012/874680

Weeks, B. (2012). Myasthenia gravis: Helping patients have better outcomes. *The Nurse Practitioner, 37*(9), 30-36.