

Anesthetic Implications of Myasthenia Gravis: A Case Report

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Myasthenia gravis is an autoimmune neuromuscular disorder that causes the destruction and overall decrease in functional acetylcholine receptors at the neuromuscular junction. The resultant respiratory and cardiovascular implications are a primary cause of mortality; therefore, a complete and comprehensive understanding of this disorder is vital for the anesthesia provider. The case presented demonstrates

the anesthetic challenges involved, with a focus on the overall approach, pharmacologic considerations, physiological changes, and an emphasis on preoperative optimization.

Keywords: Anesthesia, myasthenia gravis, neuromuscular disorder.

The incidence of myasthenia gravis (MG) is cited as 50 to 142 cases per 1 million or 0.25 to 2.0 per 100,000 population.^{1,2} Gender discrepancy is present, and women 20 to 30 years of age are most often affected, followed by men who are often older than 60 years of age when their disease presents.¹ The disease is a chronic autoimmune disorder characterized by a decrease in acetylcholine receptors at the neuromuscular junction secondary to their destruction or inactivation by circulating antibodies.¹ Muscular weakness, fatigability, and rapid exhaustion especially after repetitive voluntary muscle use, as with exercise, are the hallmark signs of the disorder. Four types of the disease have been classified based on the severity of muscular involvement and range from self-limiting extraocular muscle involvement (type 1) to severe whole-body generalized muscular weakness (type 4).³ Patients are at an increased risk of pulmonary aspiration because of pharyngeal and laryngeal muscle weakness, and they may present with dysphagia, dysarthria, and an overall difficulty of handling secretions. Cardiovascular involvement usually occurs and manifests in atrial fibrillation, heart block, and cardiomyopathy, with the presented case having hypertension as the only known cardiovascular manifestation.

Myasthenia gravis has historically been a challenging disease for the anesthetist to manage because of its involvement in the pulmonary, muscular, and cardiovascular systems as well as with drug interactions. This case report describes a patient with MG undergoing parathyroidectomy and examines the related anesthetic implications.

Case Summary

An 80-kg, 158-cm, 56-year old woman with an ASA physical status of 3 presented for parathyroidectomy. The patient's medical history included MG with an age

at onset of 25 years, rheumatoid arthritis, primary hyperparathyroidism, and hypertension. At the time of the procedure, she was in remission from a prior exacerbation 6 months earlier. Her current treatment involved oral pyridostigmine. The patient denied any anesthetic complications during her prior surgical procedures.

Preoperatively, the blood pressure reading was 146/78 mm Hg, pulse rate was 71 beats/min, respiratory rate was 16 breaths/min, oral temperature was 37.1°C, and oxygen saturation was 98% on room air. The patient denied any generalized pain or discomfort. The review of systems revealed a normal pulmonary and cardiovascular status and mild generalized weakness that the patient expressed was her baseline. The neck range of motion was slightly limited because of mild pain on extension and flexion but without paresthesia. A Mallampati score of 3 was assigned along with a thyromental distance greater than 7 cm. The sternomental distance was greater than 12 cm, and dentition was natural, without any loose, chipped, or missing teeth. The patient furthermore denied any shortness of breath, chest pain, or dysphagia. The complete blood cell count and chemistry laboratory values were within normal limits except for an elevated calcium level. The chest radiograph was clear, and the electrocardiogram demonstrated normal sinus rhythm.

The choice of anesthetic was decided on with the collaboration of the surgeon and patient, and a general anesthetic with a laryngeal mask airway (LMA Unique) was chosen. A peripheral 20-gauge intravenous (IV) catheter was inserted in the left hand in the preoperative holding area. The patient was given midazolam, 2 mg IV, and ranitidine (Zantac), 50 mg IV, before transporting her into the operating room. Once in the operating room, the patient was placed supine and preoxygenated with 100% fraction of inspired oxygen for 3 minutes. Induction of anesthesia was conducted with lidocaine, 1 mg/kg (80 mg) IV, followed by a propofol bolus of 2

mg/kg (160 mg) IV. Mask ventilation was accomplished with an oral airway because of the limited range of motion of the neck, and the LMA was placed without trauma. Maintenance of anesthesia was accomplished by sevoflurane inhalation to a minimum alveolar concentration (MAC) of 1.3 throughout while the patient maintained spontaneous ventilation. Blood pressure was maintained at 20% of the baseline. Total surgical time was 35 minutes. During emergence from anesthesia, the LMA was discontinued without event after it was concluded that there was no bleeding in the airway and an oral airway was placed while ensuring that spontaneous ventilation was adequate.

The patient was then transported to the postanesthesia care unit on oxygen administered via a nasal cannula of 2 L/min. The procedure was uncomplicated, and the patient complained of minimal postoperative pain.

Discussion

• **Epidemiology and Background.** Myasthenia gravis is believed to be the most common progressive autoimmune disorder involving the postsynaptic junction.¹ It has a varying degree of involvement ranging from the ocular or other localized regions to a global involvement. As is evident in the presented case, many patients are absent of active symptoms or are in remission throughout their unique course of the disease. With the chronic and progressive destruction of the postsynaptic acetylcholine receptors (AChR), inadequate depolarization occurs at the neuromuscular junction (NMJ) to trigger a muscular action potential, which leads to an overall decrease in neuromuscular transmission. Initially, muscle strength is strongest with voluntary movements but quickly decreases as acetylcholine release tapers. Significant portions of MG cases are associated with an IgG antibody against the AChR.¹ These antibodies reduce the number of functional receptors by several mechanisms. First, cross-linking of receptors with the IgG antibodies increases receptor destruction.¹ Second, the antibody-receptor complex directly causes damage to the NMJ membrane.¹ Another portion of the MG cases that are negative for IgG antibodies have antibodies against the muscle-specific receptor kinase at the NMJ.² Destruction of this kinase leads to developmental abnormalities of the NMJ, which results in the functional lack of AChR. The presented case was not tested for antibodies of either type because this patient had long-standing MG.

Even though a definitive trigger of MG remains to be discovered, patients with MG tend to have some abnormality of their thymus gland, which may include thymic hyperplasia or a thymoma.¹ Ptosis is often a predisposing symptom that may stay confined and be self-limiting or convert to a generalized form in the latter course of the disease. Distal limb muscular involvement occurs less frequently than in proximal muscles.² Respiratory com-

promise is rarely present in isolation but may affect some patients and is termed a *myasthenic crisis* when control of the airway is necessary (ie, tracheal intubation and mechanical ventilation).¹ The patient in this case lacked apparent signs and symptoms of active pulmonary compromise at the time of evaluation.

• **Anesthetic Implications.** When beginning to manage a patient with MG, it is important to evaluate the patient's current treatment modalities. Patients treated with anticholinesterase agents should hold this dose the morning of the surgery to avoid interactions with neuromuscular blocking agents.¹ In the presented case, the morning dose of pyridostigmine was held preemptively in the event the anesthetic had to be emergently or otherwise inadvertently converted to a general anesthetic with tracheal intubation where the use of muscle relaxation would be required. The length of time from the last exacerbation and the severity of the overall disease (with and without serologic studies) should be investigated. Furthermore, respiratory function should be evaluated by obtaining forced vital capacity (FVC) measurements before surgery to assess the need for postoperative mechanical ventilation.¹ A poor FVC is a strong indicator of the need for postoperative ventilation. The presented patient obtained normal values of FVC performed preoperatively as per an internal medicine consult.

Patients with MG have a higher incidence of heart disease because the antibodies have a high affinity for β_1 and β_2 adrenergic receptors.⁴ Consequently, a thorough and complete cardiovascular assessment is crucial in the preoperative phases. The patient described in this case report revealed long-standing hypertension with a normal electrocardiographic finding and otherwise stable hemodynamics.

It is well documented that patients with MG are extra sensitive to the effects of nondepolarizing agents and are resistant to the effects of depolarizing agents.^{2,5,6} In general, when nondepolarizing agents are used, the onset is shorter and duration is longer, suggesting an increased sensitivity.¹ The presence of anticholinesterase therapy further complicates this clinical picture. If anticholinesterase is administered on the morning of surgery, the dose of nondepolarizing agent, specifically vecuronium, needs to be increased as resistance is seen.⁵ However, if anticholinesterase is omitted on the day of surgery, sensitivity to vecuronium is seen.⁵ To avoid handling resistance of a neuromuscular blocking agent and possibly encountering a residual blockade at the end of the surgery because of increased doses, it is recommended to omit the anticholinesterase the morning of the surgery. When succinylcholine is used, MG patients are at a higher risk of developing phase 2 blocks, especially with repeated doses.² To circumvent the complications with nondepolarizing and depolarizing agents, it has been suggested that because of the unique metabolism of atracurium, it

may be the neuromuscular agent of choice.¹ Additionally, because of the similarities in metabolism of atracurium and cisatracurium, it may be safe to assume that cisatracurium is also safe and a preferred agent. There were no contraindications for the use of an LMA; therefore, the patient in this case received an anesthetic that avoided neuromuscular blocking agents altogether.

Because volatile anesthetics enhance the effects of nondepolarizing agents, it is important to be aware of their impact on patients with MG.⁷ When comparing the volatile anesthetics, sevoflurane was shown to potentiate the effects of nondepolarizing agents to the greatest degree of all the volatile anesthetics in patients with MG.⁷ This was an important consideration for this patient because in the event that muscular relaxation was required, an approach that avoided or minimized the use of volatile anesthetics would have been considered. Overall, the IV agents appear to be relatively uneventful. Barbiturates, propofol, etomidate, and ketamine have all been used without event.³ Opioids appear to be safe but may have an untoward effect of central nervous system depression that in high doses impair the NMJ.^{2,5} Furthermore, it has been demonstrated that β -adrenergic antagonists and corticosteroids exacerbate MG.²

When evaluating the choice of anesthetic, there has been some controversy regarding neuraxial use in the patient with a neuromuscular disease. Ester local anesthetics may provide some problems because of their metabolism and especially in the patients with MG being treated with an anticholinesterase.⁸ It is therefore recommended that neuraxial anesthesia be performed, with reduced doses of amide local anesthetics.² There is a greater risk of respiratory compromise when an epidural anesthetic is administered, and a spinal technique has the advantage of smaller overall local anesthetic dosages. The local anesthetic of choice should be the one with the weakest concentration and least motor involvement.⁹

Several proposed techniques avoid the pitfalls of having to manage neuromuscular blocking agents. The use of propofol or sevoflurane with opioids without the use of any neuromuscular blocking agents has been used with success.¹⁰ Both of these approaches allowed for the successful and uneventful extubation of patients in the operating room at the end of the procedure.¹⁰ The successful and uneventful outcome of the presented case with propofol and sevoflurane further reinforces this technique. Additionally, the use of the LMA in the presented case avoided the use of neuromuscular blocking agents. Consequently, the need for postoperative mechanical ventilation is higher in patients with MG when neuromuscular blockers are used.¹⁰ Propofol alone for induction and maintenance of anesthesia was adequate in a number of MG cases that also allowed for early extubation and no need for postoperative mechanical ventilation.¹⁰

Perhaps the most important consideration for the patient with MG is determining which anesthetic agents to use that avoid any possible depression in muscular function. The current literature supports a thorough preoperative evaluation to gauge the extent of disease, current treatment, and the involvement of other systems, especially cardiovascular and respiratory systems. The patient in the presented case had a thorough investigation of all systems to evaluate extent of the present disease. Perhaps, the most important are the cardiovascular and pulmonary systems, which proved to be normal in this case. The anesthetic of choice may be the one that avoids neuromuscular blocking agents and uses short-acting induction agents. Perhaps, vigilant peripheral neuromuscular monitoring is of more importance if neuromuscular blocking agents must be used. This is an important note because close monitoring of the NMJ by a peripheral nerve stimulator better allows for reduced dosages to achieve the same degree of muscular relaxation. The presented case avoided the use of neuromuscular blocking agents and used an LMA that helped avoid the overuse of anesthetic agents that depress neuromuscular transmission.

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