Inter-Specialty Collaboration And The Peripheral Nerve Stimulator Diagnose Myasthenia Gravis In The Post-Anesthesia Care Unit: A Case Report

P L Baskin, C Soria, J Lopez

Citation

P L Baskin, C Soria, J Lopez. *Inter-Specialty Collaboration And The Peripheral Nerve Stimulator Diagnose Myasthenia Gravis In The Post-Anesthesia Care Unit: A Case Report*. The Internet Journal of Anesthesiology. 2021 Volume 40 Number 1.

DOI: 10.5580/IJA.55825

Abstract

Patients may present for general anesthesia with unrecognized myasthenia gravis. We present a case of a 59-year-old woman with a history of prolonged weakness after receiving succinylcholine in the past who later experienced profound generalized weakness after general anesthesia with rocuronium. Postoperative evaluation with a peripheral nerve stimulator showed fade of muscle contraction response with repeated stimulation suggesting an exhaustion phenomenon typical of neuromuscular disorder. Repetitive nerve stimulation tests and improvement in symptoms with pyridostigmine supported a diagnosis of myasthenia gravis. In summary, evaluation of postoperative weakness with a peripheral nerve stimulator led to a new diagnosis of myasthenia gravis.

GLOSSARY OF TERMS

MG = Myasthenia gravis
MuSK = Muscle specific tyrosine kinase
PNS = Peripheral nerve stimulator
PACU = Post Anesthesia Care Unit
NMB = Neuromuscular blockade

INTRODUCTION:

Myasthenia gravis (MG) is an autoimmune neurological disorder caused by antibodies to post-synaptic receptors in the neuromuscular junction. This leads to weakness of the voluntary muscles that worsens with repeated muscle use and improves with rest. Characteristic symptoms include ptosis and muscle exhaustion without muscle pain. A diagnosis of MG can be made from a patient's clinical history, physical exam findings, and supporting serum laboratory values and electrophysiological studies[1]. In patients with vague symptoms, MG may remain unrecognized for many years.

Most patients with MG have detectable antibodies to either the postsynaptic acetylcholine receptor (~85% of cases)[2] or muscle specific tyrosine kinase (MuSK), a receptor that stabilizes and clusters acetylcholine receptors within the neuromuscular junction (~10% of cases)[3]. Notably, a high antibody titer does not correlate with disease severity[4]. However, antibody positivity may be a risk factor for postoperative muscle weakness[5,6]. In the remaining 10% of patients without detectable antibodies, MG may develop from antibody formation to components of the neuromuscular junction that are not readily detectable with current assays[7]. For these patients, electrophysiological studies such as repetitive nerve stimulation tests demonstrating fatigability and post-exercise exhaustion can support the diagnosis[1].

Patients with MG who develop postoperative weakness are at risk of complications including pneumonia, septicemia, and bleeding[8]. Risk factors for postoperative weakness were described by Leventhal et al in 1980 (disease duration > 6 years, history of chronic respiratory disease, vital capacity < 2.9 liters, or pyridostigmine dose >750 mg daily)[9]. In a more

recent analysis, Lu et al show that antibody positivity, bulbar symptoms, use of pyridostigmine, and poor lung function correlate with weakness [6]. Similarly, Chigurupati et al identify severity of myasthenic disease, history of prior myasthenic crisis, antibody positivity, thymoma, and vital capacity < 2.9 liters[7]. In patients with unrecognized MG, these factors may be poorly characterized or unappreciated.

IRB approval was unnecessary. Written HIPAA authorization has been obtained from the patient.

CASE DESCRIPTION:

A 59-year-old female with hypertension, anxiety and obesity (BMI 36, height 170 cm, weight 105 kg) presented for elective removal of a desmoid tumor of the left chest wall. A recent hemogram and chemistry panel were unremarkable. She had taken amlodipine and sertraline (her only prescribed medications) that morning. She reported an allergy to succinylcholine ten years prior, which she described as muscle weakness after a general anesthetic for minor abdominal surgery. Her postoperative course had been complicated by surgical site infection and sepsis, which may have contributed to her weakness. Medical records were unavailable. There was no family history of anesthetic complications. She denied any formal neurological diagnoses.

The anesthesiologist suspected pseudocholinesterase deficiency. A pseudocholinesterase level was drawn. Results would not be available for several days. The patient received fentanyl 100 mcg, midazolam 2mg, propofol 200 mg, lidocaine 60 mg, and rocuronium 50 mg at induction. She was intubated uneventfully. She received sevoflurane for 80 minutes. No additional neuromuscular blockers were administered. Cefazolin 2000 mg, dexamethasone 4mg and ondansetron 4mg were administered for infection and nausea prophylaxis, respectively. Neuromuscular blockade (NMB) was reversed with sugammadex 2 mg/kg. Depth of NMB was not assessed prior to reversal. After reversal, train-of-four stimulation with a peripheral nerve stimulator (PNS) at the left ulnar nerve at the wrist revealed four visible muscle contractions of the adductor pollicis brevis and five seconds of sustained muscle contraction in response to 100 Hz tetanic stimulation. A quantitative monitor was not used.

After reversal, the patient opened her eyes and mouth on request and swallowed spontaneously. Tidal volumes were 300 cc with spontaneous ventilation. She was extubated to six liters of oxygen via simple face mask. Shortly after, she had rapid, shallow breathing and supraclavicular retractions with inhalation. When asked if she felt weak, she nodded yes.

The differential diagnosis for weakness included iatrogenic exacerbation of NMB (e.g. aminoglycosides, fluoroquinolones, tetracyclines, macrolides, antispasmodics, lithium, antipsychotics, steroids, magnesium, or IV contrast – the patient had received none apart from 4mg dexamethasone), electrolyte derangements (e.g. potassium, magnesium, phosphorus, or calcium abnormalities), or neurological pathologies (e.g. MG, Lambert Eaton myasthenic syndrome, myotonia congenita, muscular dystrophy, Guillain Barre, amyotrophic lateral sclerosis, or periodic paralysis). An electrolyte panel was drawn. The patient maintained > 95% oxygen saturation with 6L oxygen via simple facemask. She was transferred to the post-anesthesia recovery unit (PACU) for continued observation.

In the PACU, physical exam revealed moderate bilateral ptosis, mild weakness of the orbicularis oculi, and 2/5 strength in all extremities (able to move extremities but unable to lift against gravity). An electrolyte panel resulted with normal values (sodium 141 mmol/L, potassium 4.2 mmol/L, calcium 9.3 md/dL, glucose 119 mg/dL, magnesium 2.2 mg/dL, phosphorus 3.1 mg/dL). An arterial line was placed to quantitatively assess ventilation and gauge the need for reintubation. Arterial blood gas demonstrated carbon dioxide 48 mmHg, pH 7.36, oxygen 148 mmhg, and bicarbonate 26 mmol/L. Given symptoms concerning for residual NMB, a PNS was applied to the left wrist with the patient's permission. Train of four stimulation of the ulnar nerve revealed one visible muscle contraction of the adductor pollicis brevis (previously, the patient had four visible muscle contractions at this site). A second dose of sugammadex at 4 mg/kg was administered (for a total of 6 mg/kg). Subsequently, train-of-four stimulation with a PNS at the left wrist showed no muscle response at all. However, application of the PNS to the right ulnar nerve (new laterality) at the wrist showed four visible muscle contractions in the right adductor pollicis. The anesthesiologist then suspected a neuromuscular disorder.

A neurologist was consulted to diagnose suspected neuromuscular disease. The patient was interviewed and described symptoms that had not been mentioned preoperatively: Extreme exhaustion at the end of the day, repeated falls at the end of the workday, and extreme difficulty keeping her eyes open while driving home after

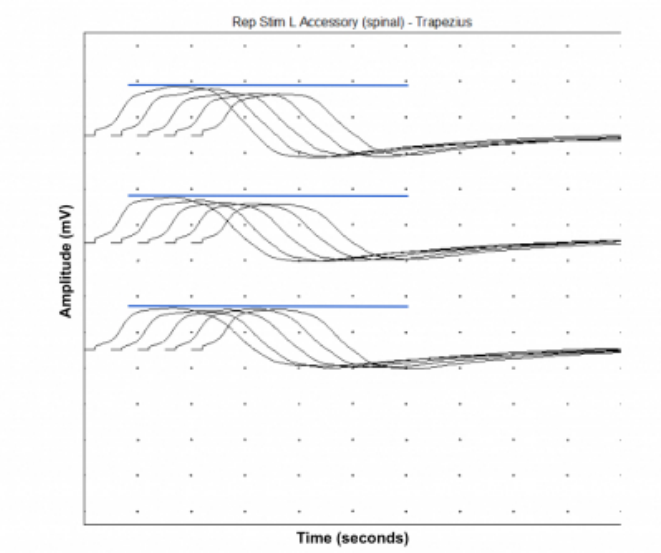
work. She revealed that she had seen an optometrist for frequent episodes of blurred vision. She had also been evaluated by cardiology for extreme fatigue, but when a Holter monitor and echocardiogram revealed no abnormalities, she was referred to psychiatry, diagnosed with anxiety, and prescribed sertraline. She noted that psychiatric characterization of her symptoms may have caused her to under-report her weakness preoperatively. Based on this history and physical examination, she was clinically diagnosed with MG. An acetylcholine receptor antibody and MUSK antibody titer were drawn.

After four hours of rest in the PACU, the patient returned to her baseline neurological function (no ptosis, unlabored respiration, and ambulation without assistance). Apart from rest, she did not receive treatment for MG. She expressed a strong preference to be discharged home with her caretaker. She was discharged with a follow-up appointment with a neurologist.

At the neurology appointment, the previously-drawn acetylcholine receptor and MUSK antibody titers were undetectable. Repetitive nerve stimulation tests showed exhaustion phenomenon in the left spinal accessory nerve (Figure 1), which supported a diagnosis of seronegative MG. A trial of pyridostigmine resulted in a significant improvement in symptoms, further supporting a clinical diagnosis of MG. Immunomodulating treatment was deferred due to stability of symptoms. Additional studies were recommended. The patient reported satisfaction with her medical treatment.

Figure 1

Low frequency (3 Hz) repetitive nerve stimulation test showing 12-14% decrement of amplitude in the left spinal accessory nerve. The blue horizontal lines are provided for reference and indicate the peak amplitude achieved with initial stimulation.



DISCUSSION:

This patient previously sought medical attention for symptoms of fatigable weakness with multiple sub-specialties. Her clinical diagnosis was only made after her encounter with anesthesiology. This highlights the ability of general anesthesia to unmask neuromuscular disease. Anesthesiologists are well suited to diagnose previously unrecognized neuromuscular disorders and have the ability to bridge gaps in patient care[10] via close observation and interdisciplinary collaboration. The postoperative complications of this patient underscore the importance of a thorough preoperative interview and the benefit of a careful evaluation of postoperative weakness.

The use of PNS is inconsistent within anesthesiology. Although evidence has shown that incomplete reversal of NMB is a risk factor for death, pneumonia, and postoperative complications[11], 40% of anesthetics do not document depth of NMB[12]. In the US, most anesthesiologists do not have access to quantitative monitors of NMB and approximately 10% of anesthesiologists never use monitors of NMB[13]. In 2015, the FDA approved sugammadex, which is highly efficacious in reversing NMB and is associated with improved clinical outcomes[14]. An unfortunate consequence may be that the PNS is perceived as less necessary than before, since the likelihood of ineffective

reversal is quite low. Nonetheless, the PNS is an inexpensive and valuable tool. In this case, repeated stimulation with a PNS illustrated fatigability similar to what can be found with a formal electrophysiological repetitive nerve stimulation test; progressively weaker muscle contractions at repeatedly stimulated nerves (left ulnar) and paradoxically strong muscular responses when a new nerve (right ulnar) is chosen.

Of note, this patient reported weakness after succinylcholine, which is not classically consistent with MG[15]. We may speculate that her weakness was due to an exacerbation of MG from perioperative stress and is unrelated to succinylcholine itself.

In summary, anesthesiologists are well suited to diagnose neuromuscular disorders. In this case, multidisciplinary evaluation of postoperative weakness and utilization of the PNS led to a new diagnosis of MG.

References

1. Shin JO. Distinguishing Features of the Repetitive Nerve Stimulation Test Between Lambert–Eaton Myasthenic Syndrome and Myasthenia Gravis, 50-Year Reappraisal. Journal of Clinical Neuromuscular Disease. 2017;2: 66-75.
2. Lindstrom, J., Seybold, M.E., Lennon, V.A., Whittingham, S. & Duane, D.D. Antibody to acetylcholine receptor in myasthenia gravis: prevalence, clinical correlates and diagnostic values. Neurology 26, 1054–1059 (1976).
3. Hoch, W., McConville, J., Helms, S. et al. Auto-antibodies to the receptor tyrosine kinase MuSK in patients with myasthenia gravis without acetylcholine receptor antibodies. Nature Medicine. 2001;7:365–368.
4. Aurangzeb S, Tariq M, Irshad M, Badshah M, Khan RS. Relationship between anti-acetylcholine receptor antibody titers and severity of myasthenia gravis. J Pak Med Assoc. 2009;59(5):289-292.
5. Lu W, Yu T, Longhini F, Jiang X, Qin X, Jin X. Preoperative risk factors for prolonged postoperative ventilation following thymectomy in myasthenia gravis. Int J Clin Exp Med. 2015;8(8):13990-13996. Published 2015 Aug 15.
6. Chigurupati K, Gadhinglajkar S, Sreedhar R, Nair M, Unnikrishnan M, Pillai M. Criteria for Postoperative Mechanical Ventilation After Thymectomy in Patients With Myasthenia Gravis: A Retrospective Analysis. J Cardiothorac Vasc Anesth. 2018;32(1):325-330. doi:10.1053/j.jvca.2017.06.045
7. Thanvi BR, Lo TCN. Update on myasthenia gravis. Postgraduate Medical Journal. 2004;80:690-700.
8. Chang YW, Chou YC, Yeh CC, et al. Outcomes after major surgery in patients with myasthenia gravis: A nationwide matched cohort study. PLoS One. 2017;12(6):e0180433. Published 2017 Jun 30. doi:10.1371/journal.pone.0180433
9. Leventhal SR, Orkin FK, Hirsh RA. Prediction of the need for postoperative mechanical ventilation in myasthenia gravis. Anesthesiology. 1980;53(1):26-30. doi:10.1097/00000542-198007000-00006
10. Amalbert R, Benhamou D, Auroy Y, Degos L. Adverse events in medicine: Easy to count, complicated to understand, and complex to prevent. Journal of biomedical informatics. 2011;44(3):390-394.
11. Kirmeier E, Eriksson LI, Lewald H, et al. Post-anaesthesia pulmonary complications after use of muscle relaxants (POPULAR): a multicentre, prospective observational study [published correction appears in Lancet Respir Med. 2018 Nov 6;:]. Lancet Respir Med. 2019;7(2):129-140.
12. Thomsen JL, Nielsen CV, Palmqvist DF, Gätke MR. Premature awakening and underuse of neuromuscular monitoring in a registry of patients with butyrylcholinesterase deficiency. Br J Anaesth. 2015;115 Suppl 1:i89-i94. doi:10.1093/bja/aev103
13. Naguib M, Kopman AF, Lien CA, Hunter JM, Lopez A, Brull SJ. A survey of current management of neuromuscular block in the United States and Europe. Anesth Analg. 2010;111(1):110-119. doi:10.1213/ANE.0b013e3181c07428
14. Kheterpal S, Vaughn MT, Dubovoy TZ, et al. Sugammadex versus Neostigmine for Reversal of Neuromuscular Blockade and Postoperative Pulmonary Complications (STRONGER): A Multicenter Matched Cohort Analysis. Anesthesiology. 2020;132(6):1371-1381.
15. Eisenkraft JB, Book WJ, Mann SM, Papatestas AE, Hubbard M. Resistance to succinylcholine in myasthenia gravis: a dose-response study. Anesthesiology 69:760-763, 1988. doi: https://doi.org/10.1097/00000542-198811000-00021

Author Information

Paola L. Baskin, MD
Resident Physician in Anesthesiology, University of California, San Diego
San Diego, CA

Claire Sampankanpanich Soria, MD
Assistant Clinical Professor of Anesthesiology, Assistant Residency Program Director for Anesthesiology, University of California, San Diego
San Diego, CA

Jose Angel Soria Lopez, MD
Assistant Clinical Professor of Neurology, University of California, San Diego
La Jolla, CA