

CLINICAL VIGNETTE

A Case of Myasthenic Crisis

Lisa Zhao, M.D.

A 38-year-old Chinese female presented to the emergency room with complaints of generalized weakness and shortness of breath. Her family provided the history since she was too weak to communicate. She has had intermittent episodes of generalized weakness for the past 1.5 years. The patient's symptoms started with neck and bilateral arm weakness that has progressed. For the past few weeks, she has also felt some difficulty breathing, in addition to swallowing. She had also reported occasional double vision. She had no fever, chest pain, abdominal pain, leg swelling, vomiting, diarrhea, or recent upper respiratory illnesses or vaccinations.

She has no significant prior medical history. Her family's recent travel to China for vacation. She had visited a physician due to the onset of her symptoms and outside records included a CT scan of the thorax, which demonstrated a thymoma. The patient was started on pyridostigmine 10 days prior to her ED presentation, which family feels may have helped her symptoms.

Vital signs in the ED were Temp 36.8, HR 91, RR 20, BP 129/95, and oxygen saturations 98% on room air. The patient appeared generally ill, frail, and in mild respiratory distress. Cranial nerves appeared intact except for mild bilateral ptosis. There is diffuse 4/5 strength throughout. She had grossly normal sensation and reflexes.

Laboratory examination revealed normal CBC, BMP, and urinalysis. A CT chest did not demonstrate a thymoma, but there was near total collapse of the RLL with possible consolidation. Bedside spirometry was attempted but was unable to produce any measurement on the meter. A decision was made to intubate the patient with rocuronium and etomidate.

She was admitted to the MICU and neurology was consulted. Nerve conduction studies were consistent with post-synaptic neuromuscular junction disorder. She received IVIG for 5 days, pyridostigmine, prednisone, and empiric antibiotics for pneumonia. She remained intubated for five days and was extubated after clinical response. She was discharged on pyridostigmine and prednisone to follow-up with neurology service.

Discussion

Myasthenia gravis (MG) is a neuromuscular disorder characterized by autoimmune antibodies toward acetylcholine receptors or receptor associated proteins. The most common

antibodies implicated are anti-acetylcholine receptor antibodies or antibodies to muscle-specific tyrosine kinase (anti-MuSK). This effectively leads to a decrease of the receptors along the post-synaptic membrane along with a simplification of the post-synaptic membrane folding. The disease is characterized by muscle weakness and fatigability, where repeated usage of the muscle leads to worsening weakness. Surprisingly, muscle weakness has no correlation to the antibody load and may rather be dependent on the epitope involved.¹ Untreated or exacerbated disease may lead to myasthenic crisis, which is defined by progression of myasthenia to the point of necessitating ventilator support. This has been shown to occur in 8-27% of patients.²

Crisis usually arises from precipitating conditions. Infection, surgery, steroid use, and pregnancy are commonly implicated. Drugs such as quinidine, procainamide, beta blockers, calcium channel blockers, neuromuscular blocking agents, and antibiotics such as aminoglycosides and quinolones can also lead to crisis.² Initial testing for MG includes EMG, nerve conduction studies, and serology to detect acetylcholine receptor antibodies. However, antibodies are only detectable in approximately 85% of patients.¹ Approximately 8-10% of patients will have antibodies to muscle-specific tyrosine kinase receptor (MuSK) and not acetylcholine receptor. Computed Tomography of the chest may detect thymoma, which occurs in 10-15% of patients with MG.³ Edrophonium testing can be used if there are observable physical findings but is not specific and therefore not the preferred study.² Additionally, due to negative cardiac effects in older people, it is not the study of choice. The diagnosis of myasthenic crisis, however, depends on bedside pulmonary testing, such as a Negative Inspiratory Force < -20cm of water or a Forced Vital Capacity < 1L.⁴

Treatment of myasthenic crisis requires ventilatory support, usually with endotracheal intubation. Non-invasive positive pressure ventilation may be attempted during early stages of respiratory failure to prevent intubation but has to be done prior to development of hypercapnia.⁵ Acute therapy relies on either immunomodulation with corticosteroids, Intravenous Immunoglobulin infusion, or plasmapheresis. Plasmapheresis removes the culprit antibodies and other inflammatory mediators from the circulation.⁶ The mechanism of IVIG is unknown. It is postulated that blockade of Fc receptors on macrophages, attenuated activation of inflammatory mediators is involved.⁶ Steroids are given orally as IV formulations may increase the risk of steroid myopathy. Finally, upon discharge, other immunomodulating agents such as azathioprine, mycophenolate mofetil, and cyclosporine may be used for long-

term treatment.²

There is still some debate regarding IVIG versus plasmapheresis (PLEX). Most retrospective and prospective studies have shown less complications and shorter hospital stay with IVIG but better function outcome with PLEX at two weeks.³ The most recent Cochrane review published in 2012 evaluated seven randomized controlled trials. These studies concluded that IVIG and PLEX were both equally effective in treating short-term myasthenic crisis.^{7,8} PLEX is implemented for 5-6 days, while IVIG is administered over 2-5 days.⁴ In studies comparing IVIG treatment over 3 days versus 5 days, there was no statistical significance in improvement.⁷ Adverse events to IVIG were generally less severe than those with plasma exchange. Most commonly reported adverse events in the IVIG group included fevers, headaches, nausea, and allergic reaction. In PLEX, adverse reactions appeared to be more severe due to the requirement of central vascular access. Reported adverse reactions included arterial bleeding, septicemia, and venous thrombosis.⁸ The American Academy of Neurology's position is that they are probably equally effective in the treatment of severe myasthenia gravis and myasthenic crisis.⁹ In true crisis, PLEX should be started over IVIG due to its rapid onset. However, patient factors and availability of the intervention should be considered before deciding which route to take. For example, history of hypersensitivity to immunoglobulin and renal failure precludes IVIG while sepsis is a contraindication to PLEX.^{6,9}

In our patient, one can conclude that she carried a prior diagnosis of MG and presented with myasthenic crisis that was likely precipitated by a pneumonia. Prompt recognition of neuromuscular respiratory failure is paramount in this scenario. Initiation of ventilatory support, immunomodulating agents, and employing PLEX or IVIG would need to be employed to prevent significant morbidity and mortality.

REFERENCES

1. **Drachman DB.** Myasthenia gravis. *N Engl J Med.* 1994 Jun 23;330(25):1797-810. Review. PubMed PMID: 8190158.
2. **Lacomis D.** Myasthenic crisis. *Neurocrit Care.* 2005;3(3):189-94. Review. PubMed PMID: 16377829.
3. **Statland JM, Cifaloni E.** Myasthenia gravis. *Neurol Clin Pract.* 2013; 3:126-133.
4. **Jani-Acsadi A, Lisak RP.** Myasthenic crisis: guidelines for prevention and treatment. *J Neurol Sci.* 2007 Oct 15;261(1-2):127-33. Review. PubMed PMID: 17544450.
5. **Rabinstein AA.** Noninvasive ventilation for neuromuscular respiratory failure: when to use and when to avoid. *Curr Opin Crit Care.* 2016 Apr;22(2):94-9. doi: 10.1097/MCC.0000000000000284. PubMed PMID: 26872323.
6. **Dhawan PS, Goodman BP, Harper CM, Bosch PE, Hoffman-Snyder CR, Wellik KE, Wingerchuk DM, Demaerschalk BM.** IVIG Versus PLEX in the Treatment of Worsening Myasthenia Gravis: What is the Evidence?: A Critically Appraised Topic. *Neurologist.* 2015 May;19(5):145-8. doi: 10.1097/NRL.0000000000000026. PubMed PMID: 25970838.
7. **Gajdos P, Chevret S, Toyka K.** Intravenous immunoglobulin for myasthenia gravis. *Cochrane Database Syst Rev.* 2003;(2):CD002277. Review. Update in: *Cochrane Database Syst Rev.* 2006;(2):CD002277. PubMed PMID: 12804431.
8. **Barth D, Nabavi Nouri M, Ng E, Nwe P, Bril V.** Comparison of IVIg and PLEX in patients with myasthenia gravis. *Neurology.* 2011 Jun 7;76(23):2017-23. doi: 10.1212/WNL.0b013e31821e5505. PubMed PMID: 21562253; PubMed Central PMCID: PMC3109880.
9. **Sanders DB, Wolfe GI, Benatar M, Evoli A, Gilhus NE, Illa I, Kuntz N, Massey JM, Melms A, Murai H, Nicolle M, Palace J, Richman DP, Verschuuren J, Narayanaswami P.** International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology.* 2016 Jul 26;87(4):419-25. doi: 10.1212/WNL.00000000000002790. Review. PubMed PMID: 27358333; PubMed Central PMCID: PMC4977114.

Submitted December 5, 2016