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Case Report

Myasthenia Gravis Crisis Treatment Modalities

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Abstract

Myasthenia Gravis is a rare disorder, with an incidence rate of approximately 20 per 100,000 people in the US. It is characterized by muscle weakness that worsens with exertion and improves with rest [1]. Often, the first presenting manifestation is involvement of extrinsic ocular muscles. Myasthenia can progress to other limb musculature as well as other bulbar muscles. The etiology of this disorder is unknown, but it is caused by circulating antibodies directed against acetylcholine receptors at the neuromuscular junction (NMJ). This disease process is highly treatable, especially with prompt recognition. A few of the main treatments involve immunoglobulins and plasma exchange. Here, we report a case of the complex nature of myasthenia crisis and the efficacy and length of appropriate treatments. A 79-year-old female with a past medical history of myasthenia gravis, presented with worsening shortness of breath that started the previous day. Chronically on pyridostigmine, she had an exacerbation of symptoms and entered into a crisis which involved extensive support such as intubation, ventilation, aggressive medical therapy, and use of intravenous immunoglobulins (IVIG) and plasma Exchange (PLEX). The patient was subsequently extubated and finished PLEX and IVIG courses. She continued to exhibit marked dysphagia, however, which required speech therapy and enteral feeding. Unfortunately, patient opted for discharge home with hospice care, as she no longer wanted to be treated despite her persistent dysphagia. This case highlights the importance of recognizing myasthenic crisis, the potency and efficacy of treatments, and associated complications.

Keywords: Myasthenia Gravis; Immunoglobulins; Plasma Exchange; Acetyl Choline Receptor; Intravenous Immunoglobulins

Abbreviations

PLEX: Plasma Exchange; NMJ: Neuromuscular Junction; IVIG: Intravenous Immunoglobulins; SIADH: Syndrome of Inappropriate Diuretic Hormone

Introduction

Myasthenia Gravis is an autoimmune disorder affecting the neuromuscular junction. It occurs due to antibodies against the acetylcholine receptors at the NMJ. It manifests as generalized muscle weakness which can involve the respiratory muscles, distal and proximal extremities, eyes, and throat [1]. Effects on the respiratory muscles can lead to a myasthenic crisis, which is a medical emergency. The reduced transmission of impulses due to the antibodies affecting acetylcholine receptors engenders progressive muscle weakness on exertion. As a patient rests, muscle weakness ameliorates. Mainstay treatment for myasthenia gravis includes pyridostigmine which is an acetylcholine esterase inhibitor; this allows for more acetylcholine to be available at the NMJ instead of being degraded which can lead to a reduction in symptoms. Other treatments include steroids, IVIG and PLEX which are typically used in a myasthenic crisis. Herein, we report a case of Myasthenia Gravis crisis.

Case Presentation

A 79-year-old female, with a past medical history of paroxysmal atrial fibrillation, nonischemic cardiomyopathy, heart failure with preserved ejection fraction, history of pacemaker hypertension, syndrome of inappropriate diuretic hormone (SIADH), hypothyroidism, and myasthenia gravis, presented with worsening short-

ness of breath on exertion that had started the day prior. Initial presentation was at first attributed to an acute on chronic diastolic heart failure exacerbation. On physical exam, she was alert & oriented to self, place and time. Her pupils were equal and reactive to light bilaterally. Ocular movements were intact without signs of nystagmus or weakness. The patient had no lower por upper extremity weakness with 5/5 strength. Sensation to light touch was symmetrical and intact bilaterally. Finger to nose testing was negative bilaterally. Deep tendon reflexes were +2/4 throughout both upper and lower extremities. Pacemaker noted on exam of the chest. She was not in respiratory distress, and lung sounds were clear and equal bilaterally with no adventitious breathing sounds. Lab findings included wbc at 14.3 X $(10)^3$/uL and Hgb at 14.5 g/dL. Treatment for heart failure exacerbation was initiated with diuretics and goal directed medical therapy as tolerated. However, her respiratory status worsened and the patient was subsequently admitted to the ICU and placed on BiPAP. During her ICU admission, she was found to be in myasthenic crisis with worsening respiratory depression. Patient was intubated and was first treated with high dose steroids of prednisone 60mg daily. Neurology was consulted for concern of acute on chronic hypercapnic respiratory failure secondary to myasthenic crisis. Patient was started on IVIG and was continued on her home pyridostigmine.

As time progressed in the ICU, the patient was not able to be weaned off the ventilator and required more extensive support. Negative inspiratory force continued to worsen. The patient underwent 5 courses of IVIG, but she did not have significant improvement in respiratory status. The decision was made to start PLEX to help with the patient's myasthenic crisis. While undergoing PLEX, the patient had a significant improvement in symptoms, NIF improved to a satisfactory level from a previous -15cm to 26cm, and she was able to be extubated. The patient completed 5 courses of IVIG and was on PLEX for 7 days post IVIG. Once extubated, she did not pass swallow evaluation at bedside or by repeated evaluations from speech therapy due to severe dysphagia affecting safety with oral intake.

As the patient had been in the ICU for an extended period of time, plan for a nasogastric tube or gastronomy tube was made for medication administration and nutritional support. Unfortunately, patient was not able to tolerate the nasogastric tube and went into transient ventricular tachycardia. The gastronomy tube was held due to the risk of reintubation. Although her respiratory status had markedly improved, the dysphagia persisted. She later became adamant on not having any further interventions. The patient did not want to proceed with possible gastronomy tube placement and opted for home hospice as her wish was to return home with no further aggressive measures. The patient was discharged home with home hospice.

Discussion

Myasthenia gravis is a very rare disorder that requires prompt recognition and treatment, the lack of which can lead to a medical emergency. When a patient is experiencing myasthenic crisis, they may require more aggressive therapy. This can include steroids, IVIG, or PLEX. Choosing the correct therapy is often a dilemma. The contrast of steroids versus the other therapies is that it reduces the autoimmune response. By blunting the immune response to the patient's own acetylcholine receptor's antibodies, clinicians hope to achieve remission of symptoms and an alleviation of the patient's crisis. Unfortunately, steroids can lead to concurrent increase in muscle weakness which can lead to an even greater exacerbation of the crisis. This occurs especially due to diaphragm weakening which in turn affects respiration and increases the work of breathing. What a clinician must do is to delicately balance the therapeutic use of steroids versus how the patient is doing clinically and adjust therapy as needed.

IVIG is another form of therapy used in myasthenic crisis. IVIG are immunoglobulins that combat the antibodies which affect acetylcholine receptors. This mainstay treatment is the first treatment usually used by clinicians in a crisis. Dosing is usually 2g/kg per day for two to five days. 1g/kg can be used, but there is limited data directly comparing different doses for the treatment of myasthenic crisis [10]. Utilizing IVIG treatments for patient with renal failure or heart failure is also preferable [10]. While IVIG and PLEX are both available, there is not sufficient evidence to suggest which treatment is more effective [9]. Some studies have suggested PLEX to be faster and superior [9]. For PLEX, 5 exchanges are usually performed every other day for 10 days [3]. PLEX allows for the exchange of plasma that contains a patient's antibodies for plasma without the antibodies that are against the acetylcholine receptors. This in turn helps reduce a patient's crisis and hopefully resolves their medical emergency.

Recently, an unmasked study compared a short course of PLEX with IVIG and showed no significant difference between treat-

ments [9]. Other smaller studies have also suggested PLEX on the other hand to be much faster and superior when compared to IVIG [9]. Since IVIG is very costly, it becomes important to determine which therapy is most effective and efficacious for patients. In this case, both IVIG and PLEX were implemented. One of the main problems that many clinicians struggle with is whether to do IVIG and PLEX together and which one to do first. The problem with doing IVIG first is that it is very costly. Another issue to consider is when to switch to PLEX if IVIG therapy shows limited improvement in a patient?

This problem is further exacerbated in that IVIG, and its therapeutic potential, is removed with PLEX since it is a plasma exchange. It can be said that we are going backwards on treatment due to removing all of the IVIG which may, in the first day or two, worsen a patient's crisis. Although, clinicians may see this as of little concern due to insufficient response to IVIG [3]. Our patient's findings were consistent with an acute myasthenic exacerbation with an insufficient response to IVIG. Once on PLEX, the patient did seem to get worse transiently but did thereafter improve to the point of extubation and being able to breathe on their own with minimal oxygen support or ancillary therapies such as BiPAP.

In general, the prognosis of patients in an myasthenic crisis is good if detected and treated promptly. Clinical improvement can be seen with both PLEX and IVIG [3]. The outcome is based on response to the IVIG or PLEX. Both can be done and in either order. PLEX can be done after IVIG but it has to be noted that a patient has an insufficient response to treatment before moving on with PLEX. Our patient had a complex course, long hospital stay, and multiple comorbidities which may have also factored into the response the patient had to treatments.

Conclusion

In conclusion, clinicians should be efficient in recognizing the signs and symptoms of myasthenia gravis and appreciating when a patient is in a crisis. It is very important to start prompt treatment to have a better prognosis. Unfortunately, there is still ambiguity regarding the efficacy or superiority of various treatments. The medical community, as of now, has come to a general consensus to treat patients first with IVIG, and, if there is not a sufficient response to treatment, then the clinician would switch to PLEX. We know that PLEX will undo any treatment done by giving IVIG, and it must be noted that the patient does not have an adequate response in order to start PLEX. This should not be taken as a rule but as more of a guideline.

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Conflict of Interest

The author has no financial interest or any conflict of interest to declare.

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