Myasthenia Gravis and Pericarditis in a Patient with Thymoma

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Keywords: *myasthenia gravis, pericarditis, myocarditis, cardiac involvement*

Introduction

Cardiac involvement in myasthenia gravis (MG) is rare but has been described in the literature.[1] Manifestations of cardiac involvement in MG are varied but include (and are not limited to) pericarditis[2], giant cell myocarditis[3], Takotsubo cardiomyopathy[4], and a variety of arrhythmias[5]. The exact pathogenesis of cardiac involvement in MG is unclear and is likely dependent on the specific cardiac manifestation. However, there has been an association with the production of antibodies against striated muscle in these patients, especially in those with thymoma[6]. In fact, anti-striational antibodies have been described in 97% of patients with thymoma with cardiac involvement.[7] Specific antibodies that have been implicated in the literature include anti-Titin, anti-Ryanodine, anti-Mitochondrial 7, anti-Smooth muscle alpha, anti-Citrate acid extract.[8] The prognosis of cardiac involvement in MG is varied and it is unclear whether the presence of specific antibodies is predictive of disease course. Myocarditis associated with MG can be rapidly fatal.[9] In this report, we describe a case of pericarditis in a patient with MG and thymoma with no prior cardiac history.

Case Report

Patient Presentation

A 27-year-old African American male presented to our Emergency Department with dyspnea, fatigable weakness, and an inability to hold his head up. He had been diagnosed at an outside hospital with MG two weeks prior after an episode of respiratory failure requiring intubation. There, he was found to have a large anterior mediastinal mass on imaging concerning for thymoma, and he was anti acetylcholine receptor antibody positive. He was treated with intravenous immunoglobulin as per protocol and discharged home on pyridostigmine. Aside from his new diagnosis of MG, his past medical history was unremarkable. He was given a course of doxycycline for suspected Lyme disease 2 months prior, which on rare occasions is known to unmask symptoms of MG. He was not taking any medications at the time aside from the pyridostigmine after being diagnosed with MG. There was no family history of malignancy or autoimmune disease.

At time of presentation to our hospital, about two weeks after initial diagnosis, he was noted to have respiratory distress and generalized weakness with fatigue. He was afebrile, his heart rate was in the mid-90's, his blood pressure was 132/74, and his respiratory rate was 34. Pulse oximetry revealed an O_2 saturation of 86%. On physical exam, he displayed decreased air movement without wheezes or rales. His cardiac exam was unremarkable aside from tachycardia. His neurologic exam showed marked facial weakness, ptosis worse on the left side, 2/5 strength in his proximal upper extremities, 3/5 strength in his proximal lower extremities, and no distal weakness. Deep tendon reflexes and sensation were intact. Due to his hypoxia and respiratory distress, an arterial blood gas (ABG) was performed which showed respiratory acidosis. A presumptive diagnosis of acute hypoxic respiratory failure due to myasthenic crisis was made, and the patient was intubated and sent to the Intensive Care Unit. His serum was *positive* for anti-acetylcholine receptor antibodies (binding +, blocking +, modulating -) and *positive* for anti-striational antibodies.

Hospital Course

The patient was started on an increased dose of pyridostigmine. Initially, his ptosis and weakness were slow to resolve. On the third day of his hospitalization, he developed a fever of 38 and tachycardia to the 110's. An echocardiogram was obtained out of concern for infective endocarditis and was negative for vegetations but did show an ejection fraction of 40-45% with global diffuse hypokinesis. Due to concern for myocarditis associated with thymoma, a cardiac MRI was ordered. A creatine kinase (CK) was ordered to rule out concurrent polymyositis and was 63 IU/L (Normal reference range 29-168 IU/L). The cardiac MRI showed constrictive pericarditis with pericardial effusion and mild subepicardial enhancement of the lateral wall (Figure 1).

The patient was started on metoprolol and lisinopril. On hospital day 5, the patient was started on plasma exchange for a total of 5 sessions. The delay in starting his plasma exchange was likely related to a combination of factors –

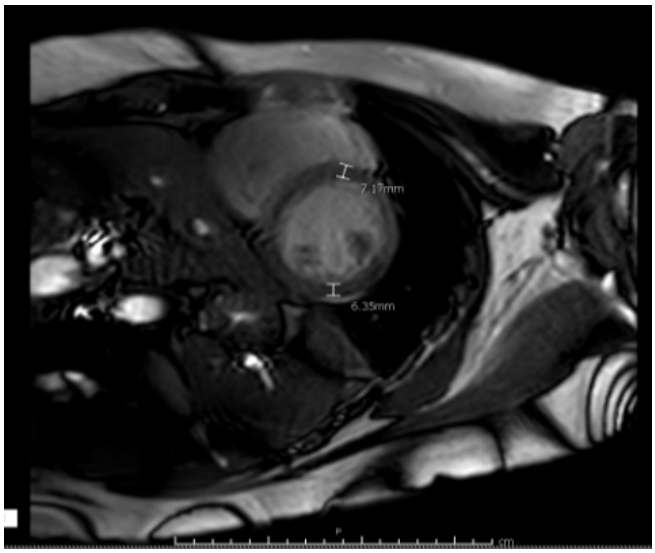

Figure 1. Cardiac MRI showing constrictive pericarditis with pericardial effusion.

his recent treatment with IVIG (Plasma exchange would remove the infused immunoglobulins) as well as his fever on day 3 with suspected infection related exacerbation. We did not start him on IVIG initially because we believed that though it helped him transiently, he would likely not benefit with a repeat dose in 2 weeks.

He began to experience improvement midway through his plasma exchanges and was extubated; however, he was re-intubated on hospital day 6 due to increasing respiratory fatigue. Upon completion of plasma exchange, the patient had improved significantly and was extubated successfully on hospital day 10. A repeat echocardiogram showed improved ejection fraction of >55%. He was eventually discharged on a steroid taper, lisinopril, and metoprolol. Close outpatient follow-up has been kept with the patient. He has experienced some weight gain while on 15 mg of prednisone and such dose was reduced in subsequent visits. He is taking prednisone 10 g daily as well as Mestinon 60 mg every 8 hours. His steroids are being slowly tapered to a stop. He is adhering to a strict exercise routine and his overall health is under control.

Follow-Up

At the time of his diagnosis of MG, the patient received a CT thorax with contrast, which showed a 41 x 32 x 45 mm anterior mediastinal mass with no thoracic adenopathy or pericardial involvement. The patient was referred to cardiothoracic surgery for video-assisted thoracoscopic thymectomy, which proceeded about 3 months after initial diagnosis without complication (Figure 2).

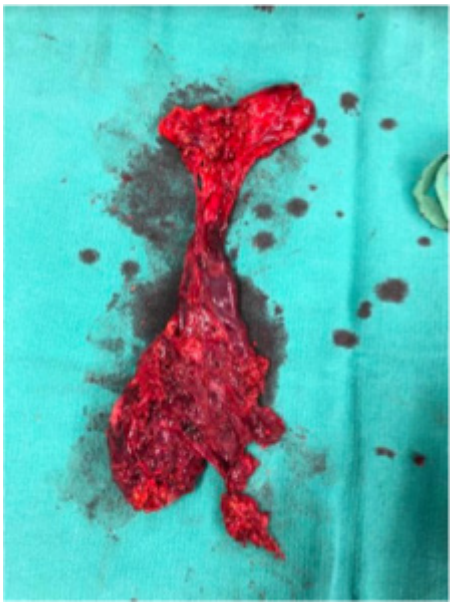

Figure 2. Image of patient's thymoma post-surgical resection.

Surgical pathology confirmed thymoma. He received postoperative proton therapy for eradication of additional thymoma tissue. The patient continues to follow-up with neurology and cardiology as well as CT surgery. He complains of continued hoarseness, however his weakness and ptosis have resolved. He has had no further episodes of myasthenic crisis for 15 months following thymectomy. The patient has stayed on metoprolol and lisinopril, Repeat echocardiogram four months after hospitalization did not show any lasting abnormalities.

Discussion

Pericarditis in association with MG is extremely rare but has been previously reported.[2] More commonly, MG is associated with myocarditis, with or without concurrent myositis, especially in patients taking immune checkpoint inhibitors.[10-12] Myocarditis in MG has been associated with the production of antibodies against striated muscle (anti-striational), however there is not an association in the literature with pericarditis in MG and anti-striational antibodies. Anti-striational antibodies are positive in many patients with thymoma,[13] which is likely the reason for the positive test in our patient.

Several mechanisms of pericarditis in MG have been described in the literature. These include constrictive pericarditis with invasion of thymoma into the pericardium,[14] as well as post-radiation pericarditis.[15] We propose antibodies from the patient's thymoma created immune complexes, which deposited in the pericardium, leading

to inflammation and a concomitant decreased ejection fraction. We also hypothesize that this immune-complex mediated mechanism is why this patient responded well to plasma exchange, and why the patient's cardiac function returned to normal after treatment. Though rare, cardiac involvement should always be on the radar of the physician treating a patient with MG, and unrecognized pericarditis in particular can progress to constriction and tamponade, further complicating tenuous respiratory and cardiac status of patients with myasthenic crisis.

Other cardiac manifestations of myasthenia gravis include a wide spectrum that ranges from asymptomatic patients to severe cases of arrhythmias and cardiac arrest.[16] Some patients, especially those with MG associated with thymoma are known to have a propensity for heart related disease. The electrocardiographic manifestation of cardiac involvement of myasthenia gravis are nonspecific.[17] A rare manifestation of myasthenia gravis mostly seen on thymoma-associated MG is myasthenia-related myocarditis which can be lymphocytic and involve giant cells. Few cases have been reported describing this condition and the pathogenesis is unknown. Stress-induced cardiomyopathy is also being described and is mostly related with myasthenia gravis exacerbation.[18]

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