

## Seronegative Myasthenia Gravis Presenting with Pneumonia, a Case Report and Literature Review

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### Abstract

**Introduction:** Myasthenia gravis (MG) is an autoimmune disorder in which signal transmission in the neuromuscular junction is impaired by antibodies to acetylcholine receptors in the post-synaptic membrane.

**Case Presentation:** An 84-year-old male was seen in the Emergency room complaining of fever, productive cough and shortness of breath. Community-acquired pneumonia (CAP) was diagnosed and treated with fluids and antibiotics; however, the patient's shortness of breath did not improve, and a few hours later he developed an acute desaturation. A CT scan of the chest excluded pulmonary embolism but was positive for the presence of a thymoma. Myasthenia gravis was confirmed after detailed history taking, and the patient was started on plasmapheresis along with oral steroids and azathioprine.

**Conclusion:** Respiratory failure secondary to pneumonia is an atypical manifestation that could be detected in patients affected by myasthenia gravis. Diagnosis of myasthenia gravis can be confirmed with history and physical exam, even with negative panels of acetylcholine receptor antibodies.

**Keywords:** Myasthenia Gravis; Community Acquired Pneumonia; Respiratory Failure; Thymic Hyperplasia; Thymectomy

### Introduction

Myasthenia gravis (MG) is an autoimmune disease with characteristic muscle weakness caused by antibodies that impair neuromuscular transmission. Impairment of neuromuscular transmission occurs by blocking acetylcholine receptors in the postsynaptic junction, which in turn causes respiratory, ocular, and bulbar muscle weakness in most patients. However, in up to 50% of patients with ocular MG and 20% of patients with generalized MG, radioimmunoprecipitation assay (RIPA) does not detect the presence of acetylcholine receptor antibodies [1].

### Case Summary

An 84-year-old white male came to the emergency room complaining of fever, productive cough, and shortness of breath. His physical examination revealed moderate general condition; body temperature: 39.3 °C, respiratory rate: 38/min, pulse rate: 122/min, oxygen saturation: 95%, and arterial blood pressure: 90/60 mm/Hg.

### Laboratory test results showed

Hemoglobin: 13.2g/dL

White blood cells: 9.810/mm<sup>3</sup>

Platelets: 229.000 mm<sup>3</sup>

Sodium (Na): 128 meq/L

Corrected Na: 137.5 meq/L

Potassium: 3.6 meq/L

Chlor: 104 mEq/L

Calcium: 8.4 mg/dL

Phosphate: 2.5 mg/dL

Blood urea nitrogen: 8 mg/dL

Creatinine: 0.58 mg/dL

Uric acid: 4 mg/dL

SGOT: 15 U/L, SGPT: 16 U/L

Total bilirubin: 0.3mg/dL

Total protein: 6.8 g/dL

Albumin: 4.2 g/dL

Hemoglobin A1c: 14.8% (4.6-6.2)

C- peptide: 0.12 ng/mL (0.9-4)

Blood gas pH: 7.11, pCO<sub>2</sub>: 15.6 mmHg, HCO<sub>3</sub>: 8.7 mmol/L, base deficit: -22.4.

A chest x-ray showed lobar pneumonia. On the basis of these findings, the patient was diagnosed with community acquired pneumonia (CAP). He was then admitted to the intensive care unit, where he was started on an infusion of intravenous fluids and antibiotics. The patient's temperature improved, but the shortness of breath that was found at presentation continued and became more evident at follow-up. History taking revealed that the patient's shortness of breath had increased over a short period of time. Spiral CT of the chest was performed to evaluate for possible pulmonary embolism. No evidence of pulmonary embolism was found, but a right anterior mediastinal mass was present, suspected to be a thymoma.

The thymus is an organ involved in generating T lymphocytes, which perform vital functions in the immune system. Abnormalities of the thymus include thymoma and thymic hyperplasia, and are found in 80% of cases of MG [2].

After 3 hours, the patient had a sudden episode of desaturation, and he began complaining of a sensation that "something is stuck in my throat." He was immediately intubated and mechanically ventilated.

No A/a gradient was seen on arterial blood gas, but in spite of this finding, multiple attempts at extubation were unsuccessful. Other causes of respiratory failure were therefore considered, including neuromuscular and cardiac. Upon gathering a more detailed history from the patient and his family, it was revealed that prior to hospitalization, the patient had been experiencing symptoms of upper and lower extremity weakness for the past month. He also complained of blurred vision (i.e., diplopia), mild dysphagia, a sensation of choking on lying down, and of being excessively tired by the end of the day for the past 6 weeks. The patient's presentation of neuromuscular

weakness warranted a neurological consult, which was arranged by the attending neurologist. Neurological examination demonstrated weakness of the bilateral deltoids, orbicularis oculi, biceps, interossei, triceps, plantar flexors, and ankle dorsiflexors. Sensory examination and other neurological tests were normal. Based on the patient's history and physical exam, a clinical diagnosis of myasthenia gravis was made, despite a negative acetylcholine receptor antibody panel.

Electromyography was performed, with repeated nerve stimulation resulting in significant decrement, consistent with a diagnosis of myasthenia gravis.

The patient was treated with pyridostigmine 150 mg/day and prednisolone 5 mg/day (dosing gradually increased to 45 mg/day). The patient's status greatly improved after a few days of treatment, with resolution of the patient's hypercapnia and dyspnea. His arterial blood gas (ABG) measurements came within normal levels, and he was extubated successfully thereafter. He was discharged after two weeks on steroids, azathioprine, and pyridostigmine. As the patient began to stabilize, a thymectomy was scheduled, and there were no complications after the surgery.

### Discussion

Myasthenia gravis is an autoimmune disorder in which impairment of neuromuscular transmission occurs by blocking of acetylcholine receptors (AChR) in the postsynaptic junction [6]. The blocking is caused by autoantibodies against AChR, and (to a lesser degree) MuSK receptors. However, in some cases there are no antibodies against either AChR or MuSK. In such a situation, the patient is referred to as having seronegative myasthenia gravis [3].

Respiratory failure is an atypical initial presentation of MG. More commonly, respiratory failure only occurs after the disease has progressed or compensatory mechanisms have been overwhelmed by a superimposed respiratory illness [4]. Myasthenic crisis can be caused by acute upper or lower respiratory tract infection, urinary tract infections, and can be associated with diabetic ketoacidosis.

Although clinical presentations of ocular, bulbar, and/or respiratory muscle weakness are obviously present, reflexes are usually preserved [4]. Rest and sleep are important measures to help reduce muscle weakness that is due to repeated use. Ptosis and diplopia are common initial symptoms due to early involvement of the cranial muscles. Difficulty swallowing is another known presentation of MG, and was demonstrated in our patient, who described a sensation of tightness in his throat prior to being intubated.

Muscle strength improves with rest in patients with MG. Therefore, physical exam results will vary, with some patients demonstrating normal neurologic exams. Preservation of reflexes and sensation is a key in differentiating MG from other neuropathies [5]. Other objective tests used for assessment and diagnosis of disease progression and activity include timed forward abduction, vital capacity, and muscle dynamometry.

There are some associated conditions that could exacerbate MG and they should be considered in the diagnosis. These conditions include thymic tumors and thyroid dysfunction (i.e., hypothyroidism and hyperthyroidism). As in our patient, CAP can exacerbate myasthenia and precipitate a myasthenic crisis. Differentials that should also be considered include spinal cord injuries, intracranial lesions, and opioid-induced respiratory depression.

MG can be treated both pharmacologically and nonpharmacologically. Treatments commonly employed include thymectomy, cholinesterase inhibitors, and immunosuppressants. Intravenous immunoglobulin and plasma exchange are also used as treatment options, but only as short-term and fast-acting therapies. Cholinesterase inhibitors are generally considered first-line treatment, and are often used in combination with immunosuppressants or thymectomy. Current opinion supports thymectomy being done in all patients who are under

the age of 60 and have undergone puberty, with or without the presence of thymoma. Clinicians should also focus on appropriate treatment of any underlying infection, taking care to avoid antibiotics that could precipitate a myasthenic crisis [6].

In our patient's case, antibodies against AChR and MUSK tested negative. This set of findings suggests a condition referred to as double-seronegative MG. Double-seronegative MG occurs in about 15% of generalized MG, and may be caused by infrequent autoantibodies such as anti-low-density lipoprotein receptor-related protein 4 (LRP4), and anti-cortactin [7]. Our patient's case demonstrated the importance of excluding chronic neurologic diseases that could be masked by acute infection. Detecting MG in the case of acute respiratory dysfunction is critical, and clinicians should always consider MG as one of the possible differential diagnoses. Detailed patient history and proper physical examination of the patient should narrow the differential diagnosis. Special attention should be paid to mild symptoms of neuromuscular weakness, such as fluctuant diplopia and ocular ptosis. Such symptoms could be an important factor in determining and diagnosing generalized MG accurately [8].

### Conclusion

While not typically associated with the disease, respiratory failure is a possible presentation of Myasthenia Gravis, and should be investigated in instances of unexplained respiratory failure. Respiratory failure was the initial manifestation of MG in multiple reports, with an occurrence of 14% to 18% of patients studied [9,10].

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