CLINICAL VIGNETTE

Myasthenia Gravis Unmasked by Azithromycin: A Case Report

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Case Report

A 71-year-old male with a history of hypertension presented with ten days of sinus congestion, otalgia and cough. He was prescribed azithromycin for sinusitis. Four days later, he complained of progressive diplopia. He noted episodes of horizontal diplopia lasting seconds to minutes and occurring most often in the evening. These symptoms were not associated with headache, dyarthria, or unilateral skeletal weakness. Other than hypertension, his past medical history was remarkable only for multiple basal and squamous cell skin cancers. His only medications were a beta blocker for management of his hypertension and an aspirin, in addition to his antibiotic. He worked as a chaplin and had no history of illicit drug use or alcohol abuse. On physical examination, his vital signs were normal. His visual acuity was grossly intact, and his neurologic exam was unremarkable, except for bilateral ptosis.

The patient had laboratory analysis for acetylcholine receptor antibodies, which returned positive. His subsequent course was marked by progression of his diplopia and the development of bulbar symptoms with dysarthria and dysphagia. He was treated with steroids and pyridostygmine with initial improvement. However, he subsequently had progression of his dysarthria and underwent thymectomy. Post operatively, he developed progressive respiratory muscle weakness, was intubated and started on IVIG without significant improvement. He started plasmapheresis with improvement in his respiratory status, and ultimately was extubated.

Discussion

Myasthenia gravis is an autoimmune disease affecting the acetylcholine receptors of the neuromuscular junction. It manifests in one of two ways, ocular and generalized. The ocular form affects the ocular muscles alone, while generalized also involves bulbar, respiratory and limb muscles. The prevalence of all forms of myasthenia is 2 per 10,000 and has a peak occurrence in both the third and the seventh decades[1].

Clinically, myasthenia presents in the form of muscle weakness. Fifty percent of cases will present with ocular symptoms (diplopia, ptosis), as was the case here. Typically, the symptoms fluctuate over the course of the day, with mild or no symptoms in the morning and more severe symptoms in the afternoon and evening[2]. With the generalized form of the disease, bulbar muscle weakness results in dysarthria, dysphagia and fatigue with chewing. Often, slurring will become more pronounced with prolonged speaking. Ultimately, oral muscular weakness can deteriorate to the point of aspiration. However, the most serious consequence of the disease is respiratory muscle weakness. By affecting the negative inspiratory force, myasthenia can provoke respiratory collapse, known as myasthenic crisis[3]. The long-term clinical course of myasthenia gravis is one of relapsing and remitting symptoms during the initial few years of the disease with the peak severity of disease activity in the first two years. Thereafter, with immunomudulatory therapy, the frequency of exacerbations decreases and, in many cases, remission can be achieved[4].

The diagnosis of myasthenia is made based on the typical history of ocular, bulbar or limb muscle weakness. Physical findings indicative of the disease are ptosis, dysarthria, and diploplia. If the muscles of the neck are affected, a head droop may be obvious. Specific physical exam tests associated with myasthenia are the ice pack test and the Tensilon test. In the ice pack test, ice is applied to the closed eyelid for two minutes. The subsequent degree of ptosis will be exaggerated in a patient with myasthenia. With intravenous Tensilon, a acetylcholinesterase inhibitor, myasthenic patients will demonstrate improved strength in affected muscles. Once the clinical diagnosis is made, serologic testing for acetylcholine receptor antibodies (AChR-AB and MuSK-Ab) will confirm the diagnosis in upward of 90% of patients with generalized disease and 50% of those with ocular disease.

The treatment for Myasthenia is based on the severity of disease and response to previous therapy. Initial therapy is with pyridostigmine, a long acting

acetylcholinesterase inhibitor, which is titrated to optimal effect[5]. The majority of patients will also need some form of immunotherapy to manage their symptoms. Glucocorticoids, cylosporine, or azathioprine are often used in conjunction with pyridostigmine[6]. During myasthenic crisis, patients may require treatment with IVIG or plasmapheresis, which are rapidly effective, but not long-lived[7]. Since the acetylcholine receptor antibodies originate in B Cells of the thymus, thymectomy has long been an effective treatment for the disease. The surgery should be considered in patients with generalized disease, and patients should be advised that the benefit from thymectomy may take years to be realized. Additionally, myasthenia patients should receive the pneumococcal vaccine and have yearly influenza vaccination.

Lastly, it should be noted that certain medications do exacerbate the symptoms of myasthenia. As was the case in this patient, azithromycin (as well as other macrolide antibiotics) can worsen the muscle weakness. Other medications that should be avoided include beta blockers, fluoroquinolones, aminoglycosides, magnesium sulfate, muscle relaxants, opioids, and statins[8]. If absolutely needed, these medications can be used, with close monitoring of the patient's clinical response.

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