Journal of Neuroinfectious Diseases
ISSN: 2314-7326

Case Report Open Access

Unmasking of Myasthenia Gravis by Rickettsia Meningitis

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Abstract

Myasthenia gravis is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body, including the arms and legs. There is no cure for myasthenia gravis, but it is treated with medications and sometimes surgery. Here, we describe the case of a 64-year-old man who presented with a 3 day history of fever, chills, diarrhea and generalized fatigue after returning from a recent trip to India. He was initially diagnosed with traveler's diarrhea and began receiving IV hydration and was started on oral Azithromycin. The present case was special and extremely rare, as unmasking of MG occurring only few hours after a single oral dose of azithromycin with an initial manifestation of isolated respiratory compromise in a patient with Rickettsia meningitis is the first in literature.

Keywords: Myasthenia Gravis; Antibiotic; Infection; Rickettsia

Introduction

Myasthenia Gravis (MG) is an auto-immune disease that is diagnosed by the combination of relevant symptoms and signs and a positive test for specific autoantibodies [1]. It is the most common disorder of the neuromuscular junction, leading to generalized or localized weakness characterized by fatigability [2]. Myasthenic crisis is a complication of MG characterized by worsening muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation [2]. Factors precipitating myasthenic crisis should be quickly identified and promptly mitigated; however, half of these patients have no identifiable precipitant [2].

Case Presentation

We describe the case of à 64 year old man who presented with a 3 day history of fever, chills, diarrhea and generalized fatigue after returning from a recent trip to India. He was initially diagnosed with traveler's diarrhea and began receiving IV hydration and was started on oral Azithromycin. A few hours after the first dose, the patient developed sudden onset dyspnea. Arterial blood gases (ABGs) showed a normal pH with low pCO_2 of 23 mmHg and a low pO_2 of 73 mmHg, and his Negative inspiratory force (NIF) test was at -169 cm H_2O. The patient was kept on worsening with excessive use of accessory muscles for breathing and required Intensive Care Unit and Bilevel Positive Airway Pressure (Bipap) use. Simultaneously, his neurological exam, including motor power and cranial nerves, was completely normal. Computed Tomography (CT) Angiography of the chest, echocardiography of the heart, Magnetic resonance imaging (MRI) of the brain, Electromyography (EMG), which included the diaphragm, and Nerve conduction study (NCS), including repetitive stimulation of the median and accessory spinal nerves, did not reveal any abnormality. Blood studies, including Epstein–Barr virus IgM, Cytomegalovirus IgM, antinuclear antibody (ANA), Brucella titers, and Tuberculosis Polymerase chain reaction (PCR), were all within normal limits. With no source of infection identified, lumbar puncture was performed, and Cerebrospinal fluid studies revealed an elevated protein (1.17 g/L) and White Blood Cell Count (270) with neutrophilic predominance (87%).

The patient was empirically started on ceftriaxone, vancomycin, and doxycycline for meningitis of unclear etiology pending further studies. Few days later, a borderline Rickettsia IgG (1/64) was noted with negative IgM and Weil Felix tests, indicating recent rickettsia infection. The patient was later on discharged on doxycycline after gradual recovery with a diagnosis of Rickettsia meningitis. At the same time, antibodies to acetylcholine (Ach) receptors turned out to be positive (21 nmol/L), but were thought to be falsely elevated in light of the infection and the absence of clear symptoms related to myasthenia gravis. Four months later, the patient started experiencing severe dysarthria and dysphagia following an upper respiratory tract infection. NIF test was -60 cm H_2O. Electrophysiological testing, with repetitive stimulation of the left facial nerve at baseline and up to 5 minutes after a 1 minute tonic contraction of the orbicularis oculi, showed a decremented response indicating a disorder in the neuromuscular junction at the post- synaptic cleft, consistent with Myasthenia Gravis. A repeat Ach receptor antibodies was 75 nmol/L. He was started on Pyridostigmine (Mestinon) 60 mg orally three times daily along with gradual titration of prednisone reaching 50 mg orally daily, with minimal control of symptoms, until initiating intravenous immunoglobulin (IVIG) 2g/kg intravenously (IV) over 5 days, with marked improvement thereafter. Myasthenia Gravis (MG) is a rare autoimmune disease in which antibodies usually bind Acetylcholine (Ach) receptors in the postsynaptic membrane at the neuromuscular junction, leading to skeletal muscle weakness [1]. Around 20% of newly diagnosed MG can present with a crisis as the initial manifestation of the disease, defined as the need for mechanical ventilation regardless of respiratory indices [2].

Discussion

It has been hypothesized that microorganisms may trigger MG exacerbation and crisis with the induction of an autoimmune response mounted against self-antigens through cross reactivity and molecular mimicry. Another mechanism could also be the polyclonal activation of B- and T- lymphocytes, including the autoreactive cells. These mechanisms remain hypothesis yet to be proven [3]. In general, MG symptoms develop one to few days after initiation of antibiotics [4]. Azithromycin, which was considered a well-tolerated antibiotic in MG, has been reported to exacerbate MG in two cases. In the first, a boy previously known to have MG, developed generalized weakness, respi-

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Received December 13, 2018; **Accepted** April 03, 2019; **Published** April 10, 2019

Citation: Nawfal O, El-Halabi T, Agha M, Makki A (2019) Unmasking of Myasthenia Gravis by Rickettsia Meningitis. J Neuroinfect Dis 10: 287. doi:10.4172/2314-7326.1000287

ratory distress and unresponsiveness requiring intubation within 10 minutes of administration of IV azithromycin [5]. In the second case, a 71 year old man complained of progressive diplopia 4 days after being prescribed oral azythromycin [6]. He progressed to have bulbar symptoms and underwent thymectomy. Post-op, he developed respiratory distress, was intubated and started on IVIG. In both cases, there was no concomitant rickettsia infection reported or that the authors tested for its presence. What distinguished our case from the above reported ones was the isolated respiratory distress developing few hours after a single dose of oral azithromycin. That brought up the challenge of whether rickettsia meningitis was the main factor in unmasking his MG.

Although MG is an autoimmune disease, infections caused by viruses, bacteria, and other microbes have been implicated in the disease manifestations. Leis et. al reported 6 cases of neuro-invasive West Nile Virus manifesting as poliomyelitis with MG symptoms developing 3 to 7 months after the acute infection [7]. Post-infectious MG has also been described in a child 2 weeks after an acute episode of varicella (chicken pox) infection [8]. However, Rickettsia meningitis was never reported before to be associated with unmasking of MG.

Conclusion

The present case was special and extremely rare, as unmasking of MG occurring only few hours after a single oral dose of azithromycin with an initial manifestation of isolated respiratory compromise in a patient with Rickettsia meningitis is the first in literature. This again proves that physicians should have a low threshold to suspect MG in atypical tough cases manifesting initially with unexplained respiratory symptoms after an infection, so that safe anti-infectious treatment can be administered.

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