

CASE REPORT

JUVENILE MYASTHENIA GRAVIS: A CASE REPORT AND REVIEW

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Abstract

Juvenile myasthenia gravis is an autoimmune neuromuscular disorder associated with muscle weakness. It is the most common variant of pediatric myasthenia gravis and accounts for at least 10% of all myasthenia gravis cases. Juvenile myasthenia gravis poses as a diagnostic challenge for the medical community due to its many clinical presentations. We report the case of an 11 years who presented with wheezing and dysphagia presumptively treated for asthma and anaphylaxis. Only after she developed a myasthenic crisis with progressive muscle weakness with respiratory failure that improved after a tensilon test was the diagnosis of myasthenia gravis considered. The clinical presentation of juvenile myasthenia gravis and the diagnostic tests and treatments are reviewed.

Key words: Neuromuscular disorders, Children, Autoimmunity, Asthma

Introduction

Myasthenia gravis (MG) is a potentially catastrophic disorder of neuromuscular transmission that causes abnormal muscular weakness. The majority of patients with MG are adults. (1) However, myasthenia gravis also occurs in the pediatric population as one of three subtypes; congenital, transient neonatal, or juvenile MG. In fact, recent studies report that children account for up to 29% of all patients with MG. (2,3) One half to 2/3 of these children are not diagnosed within the first year of disease onset. (4) This is concerning since late diagnosis and treatment of myasthenia gravis is associated with a decrease in remission rates and a poorer prognosis. Early detection is important but challenging since children may present to a variety of pediatric specialists with complaints varying from ptosis and diplopia to dysphagia and dyspnea. Health care providers need to recognize the clinical manifestations associated with MG that may be non-specific. We review the literature and report a case of a patient treated for an asthma exacerbation and anaphylaxis who was eventually diagnosed with myasthenia gravis.

Case Report

An 11-year old African American female presented to the emergency room with a chief complaint of difficulty swallowing. Her medical history was significant for persistent asthma and recurrent pneumonia requiring two recent hospitalizations and one admission to the ICU where she was intubated. Three days prior to this admission she was started on cefprozil for an ear infection and advised to use her albuterol for a presumed asthma exacerbation. On the day of admission, she developed dysphagia after eating a snickers bar. In the emergency room, she was afebrile and her physical examination was significant for the presence of drooling with mild exophthalmos

and diffuse expiratory wheezing on lung examination. A complete blood count and basic metabolic panel were normal and her chest X-ray showed a left lower lobe pneumonia. The patient was hospitalized with a diagnosis of anaphylaxis after eating peanuts in the snickers bar, pneumonia and an asthma exacerbation. She was started on IV fluids, cefuroxime, solumedrol, and benadryl. She was given nebulized albuterol every 3 hrs. Over the following twelve hours the patient developed hypoxia with respiratory distress and bilateral ptosis with facial muscle weakness. She was transferred to the intensive care unit on 50% oxygen where she deteriorated and required continuous positive airway pressure. Neurology was consulted and a tensilon test was ordered. After the patient had no response to a 0.5 mg test dose of edrophonium, she received 9mg IV and had an immediate resolution of her ptosis. To estimate the strength of her diaphragm and accessory inspiratory muscles before and after edrophonium, her negative inspiratory flow (NIF) was measured. There was an improvement of -18cm H₂O to -80cm H₂O with a normal value less than -40cm H₂O. She was diagnosed with juvenile MG and started on pyridostigmine, an acetylcholinesterase inhibitor, IV every 3 hours. The patient remained asymptomatic. Because of her exophthalmos on exam, and a family history of systemic lupus erythematosus (SLE) multiple blood tests were performed. A thyroid stimulating hormone was low at 0.14 mIU/L but her free T₃ of 3.5 pg/ml, free T₄ 0.98 ng/L, and thyroid peroxidase antibody titer less than 2 IU/ml were all normal. An ANA titer was 1:40. Acetylcholine receptor antibodies (AChRAB) were not detected. A CT Scan of her neck was negative for a thymoma or thymic hyperplasia. She was discharged home one week later on oral pyridostigmine.

Discussion

Myasthenia Gravis (MG) is associated with impaired neuromuscular synaptic transmission leading to abnormal muscle weakness. Most cases are due to circulating receptor-binding antibodies which cause a decreased number of available acetylcholine receptors in the neuromuscular synapse. (1,4,5) In the pediatric population there are three variants of MG: transient neonatal, congenital, and juvenile. (1,5) Transient neonatal MG usually occurs in newborns born to mothers with MG due to passive transmission of abnormal antibodies through the placenta. (5) This disorder differs from the rare cases of congenital MG, in which children have episodic apnea and weakness of extraocular, pharyngeal, and respiratory muscles. (1) They inherit defects to the neuromuscular synapse, so they rarely have elevated levels of AChRA. (5)

Juvenile myasthenia gravis (JMG) is the most common type of pediatric MG and the subtype of MG that our patient exhibited. It is similar to the adult autoimmune disorder, but children often exhibit

more severe symptoms. JMG presents as one of two variants, ocular or general. Ocular MG is due to neurologic involvement limited to the ocular muscles. Studies report 26-31% of prepubescent patients will present with ocular symptoms compared to 9-16% of pubescent patients. (3,6) As many as 80% of ocular MG cases progress within the first 2 years to systemic involvement presenting as limb-girdle and distal muscle weakness. (4,5) The most common sign seen in children approximately 65% of the time is ptosis, but older children may also complain of diplopia. (4) Dysphagia and facial weakness are seen in 25% of patients. (4,5) Fatigue and weakness of the limbs are also common. Unfortunately, many children present in a myasthenic crisis made up of bulbar symptoms and respiratory weakness that can lead to respiratory depression as seen in our patient. Unlike adults who present with respiratory symptoms 10% of the time, children, especially those that are prepubescent, present 50% of the time with respiratory complaints. (3,7,8) This is partly due to a delay in diagnosis because of the unfamiliarity of practitioners with the disease and the wide range of presentations. There are many case reports of children presenting with complication of MG prior to their diagnosis including aspiration pneumonia, recurrent atelectasis, and stridor to name a few. Our patient had a history of recurrent pneumonia and dysphagia on two separate occasions requiring intubation at her previous hospital admission. It was not until she developed ptosis that MG was considered in the differential. Establishing this diagnosis is complicated by the fact that the signs and symptoms can involve almost any muscle group, fluctuate daily, and worsen with infection, antibiotics, surgery, heat and stress. (9) A high index of suspicion is most important to make the diagnosis.

If MG is suspected there are many simple tests that can be performed in a clinically stable patient including a prolonged upgaze, holding the head up from the exam table, and repetitive opening and closing of the hands. (1,4,5) Patients with MG are unable to continue these tasks due to fatigability. In a hospital setting, the gold standard for diagnosing MG is the tensilon test. After the rapid-acting cholinesterase inhibitor is administered intravenously, the patient with MG should have improvement of symptoms within seconds. Our patient had immediate resolution of her ptosis and improvement in her respiratory muscle strength. Additional tests to support the diagnosis may include electromyography (EMG) and testing for autoantibodies. Results of EMG testing is similar to repeated fatigability, with repetitive nerve testing there is a decrease in amplitude of muscle potential and reversible with a cholinesterase inhibitor. (5) Testing for acetylcholinesterase inhibitors should be performed but is less helpful in making a diagnosis of JMG. About one-third to one-half of affected adolescents show elevations in AchRab. (3,6,8,9) A few studies have also reported anti-muscle specific kinase antibodies (MuSK) in patients with JMG which were not evaluated in our patient. (10)

Autoimmune disorders have a higher prevalence in JMG and their relatives. Rheumatoid arthritis, juvenile-onset diabetes mellitus, asthma and thyroid disease have been seen in as many as 9.4% of children with JMG compared to age-matched controls. (10) Our patient will be followed closely for thyroid disease due to her elevated thyroid stimulating hormone and exophthalmus. She also had a family history of SLE. Testing including an antinuclear antibody, thyroid panel, and antibodies for lupus are recommended in the workup for JMG. The thymus also plays a role in this autoimmune disease process which is thought to be the site where AchRab are produced and therefore imaging of the thymus is recommended to look for a thymoma or thymic dysplasia. (9) Thymomas and thymic dysplasia are rarely documented in JMG, and more likely to be found in peri- and post- pubertal MG that are seropositive for AchRab. (10) It is therefore not surprising that our patient who was negative for these antibodies had a negative CT scan for thymic abnormalities.

The mainstay of treatment for maintenance of juvenile myasthenia gravis usually starts with acetylcholinesterase inhibitors such as pyridostigmine or neostigmine bromide. (1,4,5) There are other treatments options that are used based on the patients symptoms and response to acetylcholinesterase inhibitors. Immunosuppressive agents and immune modulators have been used in combination to aid in therapy as well as plasmapheresis and IVIG for short term therapy. (1,4,5) A current controversial treatment includes thymectomy, but it is still unclear who will benefit and therefore not currently considered first line.

In summary, we describe a case of a patient with a previous history of asthma that presented in what was thought to be another asthma attack and anaphylaxis with a final diagnosis of myasthenia gravis. Not until she presented in crisis with ptosis was MG considered as a possible diagnosis. This case will hopefully advise physicians that myasthenia gravis can present as any degree of muscle weakness of the ocular, bulbar, limb or respiratory muscles. A high index of suspicion is needed to make an early diagnosis which is associated with a better prognosis.

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Conflict of Interests: None

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