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CASE REPORT

Myasthenia gravis juvenile: diagnostic difficulty in pediatrics

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Abstract

Introduction: Myasthenia gravis (MG) is an autoimmune disease of the postsynaptic portion of the neuromuscular junction. It is the production of autoantibodies directed against receptors of the individual, destroying them. In most patients, MG is caused by anti-acetylcholine (Ach) antibodies. It is the most common disease among those that affect the neuromuscular junction. It is characterized by muscle weakness, which improves with rest and worsens with physical or emotional effort. Before age 18, it is called myasthenia gravis juvenile (MGJ). **Case report:** A 13-year-old patient developed progressive palpebral ptosis, weakness of the cervical, facial and limb musculature. It also evolved with intense gastroesophageal reflux and bronchospastic pneumonia. The picture evolved so that the child was taken to various public and private pediatrics services without having a prompt diagnosis or clinical suspicion. Only after several months and successive hospitalizations, including in the ICU, the diagnosis was made and the patient returned to normal life. **Discussion:** The presented case constitutes an entity of low incidence and of difficult diagnosis when already advanced and with associated complications overlapping the typical manifestations. There are other descriptions in the literature corroborating this statement. After 9 months of exacerbations and remissions, the patient was properly diagnosed and treated, evolving well. **Conclusion:** It is understood that this work is of great importance, drawing attention to the importance of myasthenia and for rare diseases as a whole. Shortage of data is a challenge.

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INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease that affects the postsynaptic membrane of the neuromuscular junction. Individuals with MG produce antibodies that block and destroy their own receptors, thus impairing the transmission of nerve impulses and muscle contraction. In most patients, MG is caused by antibodies blocking acetylcholine (ACh) receptors. It is the most common disease of the neuromuscular junction. Patients with MG experience fluctuating muscle weakness that improves with rest and worsens with physical exercise and stress.[1] When it affects individuals aged less than 18 years, the disease is called juvenile myasthenia gravis (JMG).[2]

MG is more commonly seen in females aged 20-34 years and males aged 70-75 years, and predominantly affects females.[1,3] JMG accounts for about 10% of all cases of myasthenia gravis, and is known as a rare disorder in pediatric populations.[3]

Manifestations of the disease may be generalized or affect only specific muscle groups. Since it is an autoimmune condition, MG may coexist with other diseases of its kind, such as autoimmune thyroiditis and thymus-related autoimmune disorders.[1,4] Therefore, patients with the condition must be thoroughly examined. This paper reports the challenges faced with diagnosing a patient with JMG, a condition rarely seen in pediatric populations with clinical manifestations also observed in other diseases.

CASE REPORT

A previously healthy 13-year-old female born and living in the Brazilian northern city of São Luís in the State of Maranhão reported that nine months prior to her arrival at our center she saw that her voice was becoming more nasal, her facial expressions began to fade, her eyelids drooped, and the muscles in her neck, arms, legs, and jaw felt weaker. As her condition worsened, she lost her appetite and developed dysphasia, dysphagia, and intense gastroesophageal reflux. She first sought care at a pediatric emergency unit, where she spent a day at the ward. She was placed on non-invasive ventilation on account of respiratory symptoms. Her condition deteriorated, and on the next day she was referred to a pediatric intensive care unit (PICU). She was treated for anaphylactic reaction and aspiration pneumonia. She was prescribed antibiotics and placed on a mechanical ventilator. The patient was hospitalized for nine days this time. After that, she was sent back to the ward and stayed there for another ten days. She was discharged as soon as her condition improved.

A long period of time transpired as the patient tried to go back to life as usual. Her attempts were however frustrated by periods of symptom exacerbation and remission. She had trouble doing things such as walking, going to school, eating, and even sleeping. Her caretakers took her to a number of pediatrics and otolaryngology services, but she remained undiagnosed. The disease worsened six months later and she was admitted at a pediatric emergency unit. She was again diagnosed with aspiration pneumonia and progressed to acute respiratory failure, for which she was prescribed invasive mechanical ventilation. Two days later the patient was transferred to a PICU, where she was tested for MG for the first time. Electroneuromyography findings supported the diagnosis of MG, with decreases greater than 40% in evoked potentials after repeated stimulation of peripheral nerves at 3.5 and 7 Hz. Her acetylcholine receptor (AChR) antibody test was positive (4.6nmol/L) and she was negative for muscle-specific kinase (MuSK) antibodies. Other tests were run to rule out possible associated conditions. Magnetic resonance imaging (MRI) scans of the mediastinum did not show alterations. Pelvic and thyroid ultrasound examination was normal. Her complete blood count, kidney and liver function, electrolytes, erythrocyte sedimentation rate, and rheumatic activity were normal. The patient was prescribed pyridostigmine and prednisone. Her symptoms resolved gradually and her quality of life was restored. The patient was discharged and enrolled in outpatient follow-up.

DISCUSSION

Since it shares signs and symptoms with other conditions, the diagnosis and treatment of MG may be delayed.[3] The patient described in this report spent nine months being hospitalized and treated for complications of the disease, without knowing the underlying condition affecting her.

The most common symptoms include weakness in the neck, double vision, drooping of eyelid, arm and leg proximal weakness, difficulty chewing, dysphagia, and dysphasia.[1,5] The most important clinical complications in MG are quadriparesis and respiratory failure, which in the presented case characterized an episode of myasthenic crisis.[6]

Advances in intensive care medicine have set the death rate of patients with MG at an extremely low level (1.7 per million population). Diagnosis of the condition involves the assessment of patient history, AChR antibody tests, MuSK antibody tests, and electroneuromyography.[1,7]

According to the classification proposed by Osserman and Genkins based on patterns of muscle involvement, patients with MG fit into four groups table 1. The first group comprises individuals with ocular MG, with a prevalence of about 25%. The second group is subdivided into mild generalized MG, with a prevalence of 35%, and moderately generalized MG, with a prevalence of 20%. The third group includes patients with acute fulminating MG, with a prevalence of 11%. The fourth and last group comprises patients with late severe MG, with a prevalence of 9%.[1]

The treatment of MG aims to control characteristic motor symptoms, decrease exacerbation, extend the length of remission periods, and address myasthenic crisis episodes.[8]

Drug therapy may be designed to provide symptom relief and decrease autoantibody production. Symptom relief medication increases the action of acetylcholine in

Table 1. Osserman and Genkins classification system of myasthenia gravis[8].

Group	Prevalence	Signs
Group 1: Ocular MG	25%	Ptosis, double vision.
Group 2a: Mild generalized MG	35%	Ocular and extremity involvement; no prominent bulbar symptoms
Group 2b: Moderately generalized MG	20%	Ocular and bulbar symptoms; variable involvement of appendicular muscles; no myasthenic crisis
Group 3: Acute fulminating MG	11%	Generalized signs of prominent bulbar involvement; myasthenic crisis.
Group 4: Late severe MG	9%	Generalized involvement with prominent signs of bulbar involvement; myasthenic crisis.

the synaptic cleft to enable the recovery of muscle strength. Immunomodulators have been used to decrease the production of autoantibodies. The most commonly used drugs are prednisone, cyclosporine, azathioprine, cyclophosphamide, and human immunoglobulin.[1,9]

Thymectomy is usually reserved for more severe cases or individuals with thymomas. Since the thymus is largely connected to the production of antibodies connected with the disease, its surgical removal improves patient quality of life by as much as 70%.[1,8]

Although it is an expensive time-consuming therapy, plasma exchange has its use in patients at risk of dying.[9]

Supplementary therapies are important at helping patients readjust to activities of daily living, and may include hydrotherapy, physical therapy, occupational therapy, and physical activity.[5]

Differential diagnosis must include conditions such as drug-induced myasthenic syndromes, Lambert-Eaton myasthenic syndrome, botulism, and intracranial lesions. Our patient did not have a history of trauma or of taking medication before the onset of clinical manifestations from MG. Individuals with *Clostridium botulinum* infection usually present with acute flaccid paralysis and gastrointestinal symptoms. Most of the described cases of botulism in Brazil have been associated with the intake of botulinum neurotoxin subtype B2, a variety linked to fast progression.[10] Chest MRI scans did not show lung tumors, thus ruling out Lambert-Eaton myasthenic syndrome.

While reporting a similar case of MG and making comments about the relevance of the disease, Castro (2015) characterized it as a rare, challenging-to-diagnose disease in childhood known to cause secondary complications that increase morbidity, mortality, length of hospitalization, and the cost of treatment for patients and public healthcare services.[7]

This study aimed to draw attention to the importance of MG and rare diseases in general. Collecting more data is an important challenge to improve our comprehension of diseases and their healthcare and epidemiological implications.[9]

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