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OCULAR MYASTHENIA GRAVIS IN A PRE-SCHOOL CHILD: A RARE CASE REPORT

Ophthalomology

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ABSTRACT

We report a case of pediatric ocular myasthenia gravis. The child was a 4 -year- old boy who presented with bilateral ptosis and ophthalmoplegia in the right eye following the history of fever and cough for 10 days.The pathogenesis of myasthenia gravis is autoimmune, the real etiology, however, remains unknown. Virus has been suggested as an etiological agent of the disease. In this case symptoms begin after 10 days of proven viral infection . Ice test was positive , Neuroimaging and acetylcholine receptor antibody testing were unremarkable. Symptoms improved with pyridostigmine, with full resolution of ophthalmoplegia by 6 -month follow-up.

KEYWORDS

INTRODUCTION:

Myasthenia gravis (MG) is an autoimmune disorder in which acetylcholine receptor antibodies attack the post-synaptic membrane of the neuromuscular junction, resulting in muscle fatigue. The incidence rate is 1.2 per 1 million children per year. The average age of onset in children is 7 years. Ocular types of MG are more frequent than generalized and the age of onset is earlier than generalized type. (1-3) It is also a rare disorder, especially in children(4) and in our institution hence this case report.

Weakness varies daily and from hour to hour, typically rising toward the end of the day. MG should be contemplated in every child with ptosis and diplopia. Diagnostic tests include serum acetylcholine receptor antibody levels, repetitive nerve stimulation test (RNST), Neostigmin test, and the ice test. None of these tests, however, are 100 % sensitive or specific. (5-7) The aim of reporting this case is to assess various tests for the diagnostic enforcement of ocular MG based on our clinical experience at our institution and to prevent its recurrence.

Case Report:

A boy aged 4 years presented in April 2024 with chief complaints of upper eyelid drooping of both eyes with more in the left upper lid and double vision with both eyes open. 0cular symptoms were started after 10 days of fever and cough and have progressed over the past 3 months, inconsistent, and this is marked towards the end of the day, whereas it vanishes off the next morning after resting at night. Neither other complaints of generalized body weakness, difficulty with speech, or swallowing nor family history with an illness like this, thyroid disease, grave disease, and diabetes mellitus have been reported. Physical examination significant findings were the left eyelid had more ptosis compared to the right lid with a right interpalpebral height of 8 mm, left eye 5 mm (normal 12 mm), and restriction of movement superior and medial in the right eye, left eye ocular motility was normal. At first, the child came into the pediatric department then because of his eye complaints, the child was referred to our department and suspected with a neuromuscular disorder and then he was undergone with the procedure of ice test. The result was positive and thus referred to the pediatric neurology department. Their electromyography (EMG) examination of muscle levator palpebrae superioris, has been checked and that gave a decreased response which is greater than 10%, which means positive for myasthenia gravis.

The neostigmine was given 0.04 mg/kg intramuscularly and was also given atropine sulfate 0.01 mg/kg intramuscularly ± 30 minutes before neostigmine. The clinical improvement response of weakened muscle strengthening had been observed for 15–30 minutes. The following picture shows images from the child before(Figure 1a) and after neostigmine injection (Figure 1b).

From the laboratory finding, the acetylcholine receptor antibody came out to be 0.25 nmol/L which was normal, in general juvenile stage MG patients have not reported autoantibodies found with the classical diagnostics for AchR and MuSk antibodies in approximately 30% of patients. Free T4 and TSH levels were normal. We also did not find any thymic mass from the chest x-ray. He was diagnosed as MG Class 1 (Ocular type) based on classification from the Medical Scientific Advisory Board (MSAB) of the Myasthenia Gravis Foundation of America (MGFA).

He was initiated on pyridostigmine 7 mg/kg per day, divided into 3 doses for therapy. He did not experience an exacerbation of eyelid ptosis, or other weakness and deterioration, and has been recovering from 3 months as shown in (Figure 2a) and full resolution of symtoms by 6 months (Figure 2b)

DISCUSSION:

MG is a neuromuscular transmission disorder that causes skeletal muscle fatigue and fluctuating weakness. Juvenile MG is a rare disorder of childhood, but its incidence and prevalence vary geographically. Ocular types are more common than generalized types. The juvenile type is the most common form in pre–pubertal age (< 12 years old). It did not have a familial pattern and had the characteristics of an autoimmune mechanism. (4)

Pathophysiology of MG through an autoimmune mechanism. The real etiology, however, remains unknown. Virus has been suggested as an etiological agent of the disease. The presence of antibodies to the acetylcholine receptor in the nerve-muscle link reduces the transmission of nerve impulses to the muscles. HLA antigen (Human Lymphocyte Antigen) plays an important role in autoimmune diseases and is often linked with myasthenia gravis. The presence of this antigen increases the incidence of MG especially in children who are seropositive to the acetylcholine receptor. (8)

Myasthenia gravis is considered a disease caused by B cells because B cell is the one that produces anti-AChR bodies. However, the new findings show that T cells produced by Thymus have an important role in the pathophysiology of myasthenia gravis. This is indicated by the large number of children with myasthenia experiencing thymic and thymoma hyperplasia and thymectomy can reduce the clinical sign of myasthenia gravis. However, the study showed a sensitivity of 89.5%, specificity of 87.5%, and accuracy of 88.6% for CT compared to plain radiography. (9) CT is superior to plain radiography in the diagnosis of thymoma. (10) However in our, case we did a chest x-ray and there was no sign of thymoma.

The most frequent clinical presentation of myasthenia gravis in children is with ptosis, which is often associated with other ocular symptoms namely unilateral or asymmetric ophthalmoplegia, strabismus, and lid twitch, which may only be elicited after continued upgaze. (11) These symptoms cause particular problems in children as, if severe, they may cause persistent amblyopia. (12) Most children also develop generalized muscle weakness, which presents as painless fatigability of limb musculature, with resultant dysphonia, dysphagia, and proximal limb weakness. Weakness is often fluctuating and usually becomes more pronounced throughout the day and improves with rest. Children are at risk of choking or aspiration and are at increased risk of chest infection. Occasionally, impairment of the respiratory muscles necessitates ventilatory support. This is known as "myasthenic crisis".

Prepubertal MG is more likely to manifest as ocular myasthenia. There

is an equal male-to-female ratio, in contrast to the female predominance that is seen in peri-/post-pubertal children, and a better prognosis, with a higher rate of spontaneous remission in prepubertal presenters. Peri- or post-pubertal patients presenting with MG share more similarities with adult-onset MG

Ptosis, however, may be caused by a variety of disorders, so the distinction between myasthenic and nonmyasthenic ptosis is critical. Diagnostic tests to establish the diagnosis of MG include the ice test, repetitive nerve stimulation test(RNST), neostigmine test, and serum acetylcholine receptor antibody levels. Bronstein and Desmedt later showed that the local cooling improved myasthenic neuromuscular block, whereas warming had the opposite effect. The Cooling process can improve neuromuscular transmission so the placement of ice for 5–10 minutes on the eyelid will improve ptosis. The result is positive if there is resolution of ptosis. This test has a sensitivity of 96% while the specificity is 88%. (13,14) Clinically, the use of the ice test is more advantageous than the Neostigmine test because this test is rapid, simple, and inexpensive with a high degree of specificity and sensitivity. The ice test is particularly useful in children whom the use of anticholinesterase agents is contraindicated by cardiac status.

Repetitive Nerve Stimulation has a sensitivity of 82% with a specificity of 100%. However, the sensitivity of RNS is different for some subgroups where ocular type sensitivity is only 67%. The recommendation for electrophysiological examination that is recommended to obtain high and better sensitivity is SFEMG (Single Fiber Electro Myography). (15)

The Neostigmine test may produce false–positive and false–negative results and also carries cardiac risk and other complications (including significant bradycardia, loss of consciousness, and death). (16)The sensitivity of the anti-acetylcholine receptor antibody test is 50% to 75% in subjects with ocular myasthenia. Although its specificity is high, the anti-AChR antibody concentration cannot be used to predict individual severity. In children with negative antibodies to the acetylcholine receptor, but symptoms appear at a younger age, there might be such a congenital myasthenia gravis and about 40–50% of them have antibodies to muscarinic receptors. (17)

In developing countries like us, antibody testing is still very difficult to do routinely, but somehow we managed to do this test but the results were negative. The ice test and SFEMG test are still the first choice because they are fast, easy, affordable, and not invasive and lead to our diagnosis. Neostigmine test also helps, but close monitoring of vital signs is needed, knowing the dangerous side effects of cholinergic that can occur. Management of juvenile ocular myasthenia gravis is intended to reduce the symptoms of the disease and reduce the severity of the disease to develop into a generalized type.

The administration of pyridostigmine as an acetylcholinesterase inhibitor is the main choice. Acetylcholinesterase inhibitors retard the degradation of Ach that occurs by enzymatic hydrolysis in the neuromuscular junction. As a result, the effect of Ach is prolonged, leading to a variable improvement in strength. Acetylcholinesterase inhibitors are the first line of treatment due to their safety and ease of use. It provides only symptomatic therapy and is usually not sufficient in generalized MG. Nonetheless, in some children, this is the only therapy ever needed for good control. For children and younger adolescents, the initial dose is 0.5 to 1 mg/kg every four to six hours, up to a daily dose of 7mg/kg. In this child pyridostigmine dose is 1 mg/kg every 4–6 hours. If the acetylcholinesterase inhibitor still does not provide a good response, it can be combined with an immunosuppressant agent such as prednisolone. Remission or improvement occurs in 65–75% of children. Other therapies include thymectomy, azathioprine, cyclosporine, and intravenous immunoglobulin.

The prognosis of children with MG is better than adults. Many cases had remission without treatment, therapy requires long–term follow-up in children over the age of 3 years. A cross-sectional study by Ahigeaki in Japan in 607 MG ocular children found that regular use of drugs for 2 years would reduce the complications of diplopia and improve the quality of life. (18)

CONCLUSION:

Ocular myasthenia gravis in a child is a very rare case, and it can be diagnosed through a few relevant tests for myasthenia gravis. The child was given the first line of anti-myasthenic treatment with pyridostigmine. Clinical improvement can be reached after 3 months of therapy. Monitoring and management are needed in the long term to reduce the risk of recurrence and progression of the disease to a general type. The other important thing in the successful management of myasthenia is looking for the etiology. Knowing the etiology, management therapy would be more precise and effective.

Figure 1a and 1b -

Figure 2a and 2b -

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