Case Report

Ocular myasthenia gravis in toddler: A rare case report

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Abstract

Myasthenia Gravis is a rare autoimmune disorder affecting Nuero Muscular Junction, owing to presence of acetylcholine receptor antibodies. Ocular myasthenia gravis is a form of Myasthenia Gravis and accounts for 15% of all cases. prevalences estimates of 0.5 - 12.5/100,000/yr. Patient generally presents with Ptosis and have ocular involvement either at presentation or in the later course of disease. Ptosis and Diplopia are initial signs of Myasthenia Gravis in 50 % of the patients. We ophthalmologists from Sassoon Hospital are reporting a childhood case of ocular myasthenia. This case is being reported owing to its presentation in 17 the month of age.
Key Word: Ocular myasthenia gravis.

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INTRODUCTION

Myasthenia gravis is defined as an acquired autoimmune disorder where there is abnormal fatigability of muscles due to deficiency of acetylcholine receptors caused by circulating antibodies directed against them.[3] Ocular myasthenia is a form of myasthenia gravis clinically involving only the levator palpebrae superioris, the orbicularis oculi, and the extra ocular muscles without dysfunction of other muscles.[4] Ptosis and ophthalmoplegia, both unilateral and bilateral, constitute the only signs in about 20% cases while in about 70% cases, ocular symptoms mark the onset of generalized myasthenia gravis.[3] Two thirds of those with initial ocular involvement develop systemic symptoms within 2 years of onset.[4]The onset of Myasthenia Gravis is influenced by gender and age in a bimodal fashion. In patients younger than 40, women predominate.[5] In India, Myasthenia Gravis is reportedly more common in males than in females; the age of onset in males is in the sixth to seventh decade, and that in females is seen to be in the third decade.[4] Juvenile Myasthenia Gravis (JMG) is a rare disorder of childhood, but its incidence and prevalence vary geographically. Given the evidence that prepubertal JMG may behave quite differently in terms of disease severity and progression, this may impact on necessity for treatment and treatment response.

CASE REPORT

17 month female child presented to the outpatient department of ophthalmology with history of bilateral drooping of upper lid since 5 days. Mother gave the history of ptosis in left eye followed by right eye with restricted movements of left eye. History of variable ptosis was present. The child was born normally at full term with an uneventful perinatal and postnatal period. The milestones of the child were normal for that age group. No history of similar complaints in sibling. There was no history of sensorimotor symptom in her limbs or torso or dysphagia and dysarthria or no history of excessive lassitude. In the primary gaze position, the

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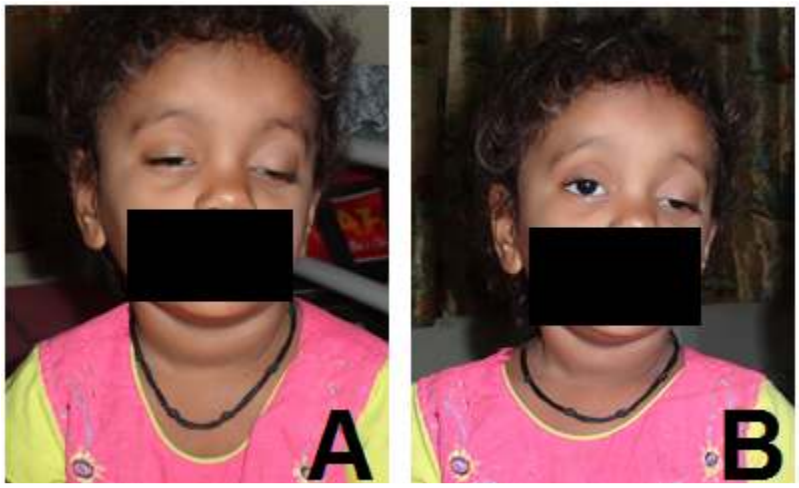
visual axes of both eyes were misaligned. The child was examined twice after a period of sleep and similar findings were recorded again. Neurological examination revealed no motor weakness, in coordination, ataxia, or a reflexia. Examination of the anterior and posterior segment of both eyes under general anesthesia was unremarkable. The forced duction test was negative. Magnetic Resonance Imaging (MRI) of brain plus orbit done to rule out intracranial Space Occupying Lesion pathology.



Before **[A]** and after **[B]** Tensilon test

Ocular examination revealed chin lift with compensatory bilateral frontalis over action. Margin Reflex Distance (MRD) was 2mm in RE and -1mm in left eye. Levator Palpebrae Superioris function was fair in both eyes. Extra ocular muscles (EOM) were restricted in medial gaze in left eye and normal in right eye. The child was attentive to both visual and auditory stimuli and frequently changed his head posture to look in the direction of origin of the visual or auditory stimuli. Bells phenomenon was normal and no jaw winking was observed. Pupils were equally reacting to light. Direct, consensual and accommodation reflexes were normal. History and ocular examination was suggestive of ocular myasthenia gravis. Repetitive nerve stimulation studies and Single fiber electromyography (SFEMG) were done which showed decremental response suggestive of Myasthenia Gravis. Then child was subjected to Tensilon test (edrophonium test (0.15 mg /kg body weight intravenously), which was unequivocally positive with improvement of the ptosis and ophthalmoplegia. Ice pack test was done by applying ice to eyes for 2 minutes which showed improvement of ptosis in both eye by 2 mm following removal of ice pack. Subsequently, a serum analysis of antiacetylcholine receptor binding antibodies was performed. Abnormal titers of anti-acetylcholine receptor binding antibodies (5.8 nmol/l; normal is less than 0.8 nmol/l) were present which confirmed the diagnosis of autoimmune juvenile myasthenia gravis (JMG). The child was started on tablet pyridostigmine 3mg once daily along with oral prednisolone (0.5 mg/kg body weight) and followed up regularly. Counseling of parents regarding side effects of corticosteroids is done and dietary advice is also given. Marked improvement of the ptosis and ophthalmoplegia was observed which persisted at 11 months of follow up. Systemic steroids were gradually tapered off after 6 months.

DISCUSSION

Myasthenia Gravis results from antibody-mediated, T cell-dependent immunologic attack on the postsynaptic membrane of skeletal muscle end plates.[5] Patients with Acetylcholine Receptor antibodies are often referred to as seropositive. Acetylcholine Receptor binding antibodies are present in approximately 80% of patients with generalized Myasthenia Gravis, but in only 55% of patients with ocular Myasthenia Gravis. About one-half of prepubertal children with Myasthenia Gravis are Seronegative. Antibodies to muscle-specific kinase (MuSK) and to Leucine rich protein 4 (LRP4) have been reported in some seronegative patients. Ocular Myasthenia Gravis is a subtype of Myasthenia Gravis where the weakness is clinically isolated to the EOMs, levator palpebrae, and orbicularis oculi.[1] EOMs are more commonly affected as twitch fibers in EOMs develop tension faster and have a higher frequency of synaptic firing than limb muscles. This makes them more susceptible to fatigue. Furthermore, tonic muscle fibers are necessary to sustain the gaze in any direction. This type of fiber has fewer ACh receptors, which makes them more susceptible to receptor loss or damage.[6] Expectedly,

due to variable involvement of different EOMs, motility patterns are not characteristic of lesions of one or more nerves.[1] Ptosis and Diplopia are the initial signs of the disease in over 50% of Myasthenia Gravis patients.[6] 50-80% of these patients go on to develop generalized disease. In the majority of cases (90%), progression of Ocular Myasthenia Gravis to its generalized form will occur within the first 2 years after ocular symptoms begin.[8] In our case patient had presented with asymmetrical ptosis which is most frequent presentation. This is often associated with other ocular symptoms namely unilateral or asymmetric ophthalmoplegia, strabismus, and lid twitch, which may only be elicited after sustained upgaze.[10] These symptoms cause particular problems in children as, if severe; they may cause persistent amblyopia.[9] As per some reports, LPS is the most commonly affected muscle followed by orbicularis oculi. The most commonly affected EOM is the medial rectus followed by the superior rectus. Ocular Myasthenia Gravis can mimic any commitant or in-commitant strabismus ranging from nerve palsies, gaze palsies, unilateral or bilateral internuclear ophthalmoplegia to even complete ophthalmoplegia. Clinically, Ocular Myasthenia Gravis should be suspected in any variable incommitant strabismus, with or without ptosis.[4] In most patients with Ocular Myasthenia Gravis pupillary examination is, usually, normal, and this serves as a useful tool to distinguish Ocular Myasthenia Gravis from conditions such as pupil involving third nerve palsy, Horner's syndrome and botulism.[1] There are different serological tests to aid the diagnosis. Serum anti-ACh Receptor Antibody Titer is important serological test .Although this test is relatively sensitive and specific for MG, 10% to 15% of patients with systemic Myasthenia Gravis will test negative, as will 30% to 50% of patients with ocular Myasthenia Gravis.[7] In our case, detection of antibodies to the Acetylcholine Receptor supports the diagnosis of JMG. In young children where Acetylcholine Receptor anti- bodies are negative this can lead to difficulty in differentiating from CMS. MuSk assays are used when anti-ACh receptor antibody titers are negative. Muscle Specific Tyrosine Kinase positive Myasthenia Gravis is rare in children and associated with more severe disease. Thymus hyperplasia is the commonest abnormality of the thymus in JMG. Hence we imaged thymus in our case though Thymoma is particularly rare in prepubertal children.[6] Thymectomy has been widely performed in an effort to achieve medication-free remission in Myasthenia Gravis following Blalock's early observations of remissions following thymectomy in non-thymomatous Myasthenia Gravis. To date, there have been no prospective, randomized studies completed to assess the technique or effectiveness of thymectomy in non-thymomatous MG.[5] Treatment of JMG has largely been extrapolated from adult studies and experience with adult patients. There are very few studies looking specifically at interventions in children, particularly prepubertal children. Acetyl cholinesterase inhibitors are first-line treatment in JMG and provide symptomatic relief. In mild cases and in some cases of ocular myasthenia gravis, Acetyl cholinesterase therapy may be sufficient. Pyridostigmine is a long-acting cholinesterase inhibitor that is commonly used. Dosing is usually 4–6 times per day and is tailored to effects.[4] Frequently some form of immunosuppressant or immunomodulation is required to improve symptoms of JMG. Corticosteroids are often effective and are the mainstay of therapy .Because of the numerous adverse effects associated with long-term high-dose steroids, steroids are often used in combination with a steroid-sparing immunosuppressant, for example, azathioprine. Corticosteroids the most commonly used immunomodulator, which leads to remission or marked improvement in 70-80% patients with Ocular Myasthenia Gravis and Generalized Myasthenia Gravis.[4,10] It may also reduce the progression of Ocular Myasthenia Gravis to Generalized Myasthenia Gravis. Moderate dose (50–60 mg) daily prednisone, tapered over 6 weeks, followed by 10 mg or less daily, resolves Diplopia in primary and downward gaze more frequently than with pyridostigmine alone. Although azathioprine appears to be effective, it can take 6 months to improve the ocular motor dysfunction and is less practical for patients needing a rapid response. Children are at particular risk of steroid side effects, including growth failure, susceptibility to severe infection, and delay in receiving live vaccinations.[11] As this child presented with myasthenia at an age below two years, familial infantile myasthenia was considered; it was ruled out in absence of family history and involvement of extra ocular muscles. Congenital myasthenia gravis described by Bowman and Levin was another possible diagnosis as the extra ocular muscles were predominantly involved but congenital myasthenia usually has familial occurrence and does not respond to steroid therapy.[2] Our patient was diagnosed to have juvenile myasthenia, a variant of adult myasthenia with similar clinical presentation and autoimmune mechanism. The remarkable response of the child to systemic steroid therapy confirms the autoimmune mechanism. This case of childhood ocular myasthenia of the juvenile subtype in a female child is being reported for its rare occurrence at the early age of 17 months. To our knowledge, this is one of the youngest patients of childhood myasthenia of the juvenile subtype reported so far.[2]

CONCLUSION

Although myasthenia gravis is one of the common disorders of the neuromuscular junction, ocular myasthenia is often misdiagnosed in the initial stages due to its fluctuating nature. With a high index of clinical suspicion, simple clinical tests accompanied by pharmacological tests can be useful in diagnosing the condition. In developing countries like ours, where sophisticated investigations are not available and cost factor is one of the major drawbacks, utilizing clinical acumen becomes all the more important in such patients with acquired ptosis and ophthalmoplegia, irrespective of age.

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