ORIGINAL RESEARCH PAPER

Ophthalomology

JUVENILE OCULAR MYASTHENIA GRAVIS – A CASE REPORT

KEY WORDS:

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ABSTRACT

Myasthenia Gravis is an Autoimmune disease in which antibody mediates damage and destruction of post synaptic Acetylcholine Receptors that occurs in striated muscles. When the symptoms of Myasthenia Gravis are isolated to the levator palpebrae superioris, orbicularis oculi and the ocular muscles, it is referred to as Ocular Myasthenia Gravis. Ocular involvement occurs in 90% of the cases and is the presenting feature in 60%. Here, we report a case of 14year old male child who presented with Drooping of Bilateral Eyes Upper lid, Right Eye(R/E) is more than the Left Eye (L/E) and double vision for two months which worsens towards evening. Icepack test, Cogan twitch sign, Fatiguability test and Neostigmine test were positive. Acetylcholine Receptor Binding Antibody came out in equivocal range (0.50nmol/L). After meticulous history taking, physical examination and serum antibody evaluation the case was finally diagnosed as a case of Juvenile Ocular Myasthenia Gravis involving both eyes. The case was then managed conservatively with Anticholinesterase agent (Pyridostigmine) following which the patient showed marked improvement in symptoms. However, since there is 90% chance of ocular myasthenia to get converted to generalized myasthenia, the patient is advised for frequent follow up. In patients with Ocular Myasthenia if they continue to have only ocular symptoms for three years it is very likely that their symptoms will not increase.

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease which results from antibodies that block or destroy the post synaptic Nicotinic Acetylcholine Receptors (AChR) at the neuromuscular junction. This prevents nerve impulses from triggering muscle contractions leading to easy fatiguability. Myasthenia Gravis can occur at any age.[1] Estimates of incidence vary in the literature, between 1.7-30.0 cases per million person years, with a prevalence of 77.7 cases per million persons.[2,3] A population based study found an incidence rate of 22 per million person years for myasthenia gravis, with ocular myasthenia gravis occurring at a rate of 11.3 per million person years.[4] Incidence of myasthenia gravis appears to be rising over time in patients over the age of 65.[5] In the paediatric population the incidence is estimated to be between 1.0 and 5.0 cases per million person years.[2]

A recent population based study found the incidence of juvenile myasthenia gravis to be 1.2 per million person years.[6] It is estimated that between 10% and 15% of all cases of myasthenia occur in the paediatric population.[7] This proportion may be higher in Asian populations.[8,9] In about two-thirds of individuals, the initial symptom of MG is related to the muscles around the eye.[10] The term "ocular myasthenia gravis" (OMG) describes a subtype of MG where muscle weakness is confined to the eyes, i.e. extraocular muscles, levator palpebrae superioris, and orbicularis oculi.[11] Two-thirds of the patients of OMG have both ptosis and diplopia and <10% of the cases have diplopia alone.

The case of a 14-year-old patient with ptosis and diplopia involving both the eyes has been presented and discussed.

Case Scenario

A 14year old male presented to our hospital with drooping of upper lids of both the eyes (R/E > L/E) for two months and complaint of double vision for two months with history of progressive worsening of symptoms towards the latter half of the day. There was no history of generalized easy fatiguablity. However the patient gives history if tiredness of the eyes and inability to study specially during evening and night. His previous ophthalmic history was unremarkable, also there is no significant history of any systemic diseases, any recent history of fever or any Gastrointestinal symptoms. All other members in the family are enjoying good health.

Fig 1: Patient at the time of presentation

On examination VA in R/E was 6/6 and L/E 6/9. Clinical test like the Ice pack test, Cogan Twitch sign and Fatiguability test were positive. Pharmacological tets viz Neostigmine test turned out to be strongly positive. Result if Acetylcholine Receptor antibody titre was 0.50nmol/L which lies in equivocal range. Chest radiography was done to exclude Thymoma .

On Local Examination

His head posture was Normal. There was no facial asymmetry.

Examination Of Right Eye

On Proper examination of the Right eye, eyebrow was found to be raised, frontal crease appears normal and there was no brow laxity. Drooping of the Right Upper Lid was present. MRD 1 was 2 mm, MRD 2 was 5 mm and MCD was 10mm. LPS Function as assessed by Berke's method was estimated to be 14mm and by Putterman's method (MLD) was 8mm. Lower lid margin just touches the limbus**. Bell's phenomenon was normal**. Palpabral aperature was narrow, vertically 7mm and horizontally 30mm.

Fig 2: Measuring MRD 1

Extraocular movements was Normal. Conjunctiva was clear, clear cornea with intact sensations. Anterior chamber, iris, pupil and lens all appered to be normal under slit lamp examination.

Examination Of Left Eye

Left eye examination appears to be normal except that the vertical palpebral aperture was narrow about 8mm.

Clinical Tests

The clinical tests done to aid in the diagnosis are Fatigability Test, Sleep Test, Cogan Twitch Sign, Ice Pack Test came out to be positive. The patient responded strongly to Pharmacological test like Phenylephrine test, Neostigmine test .

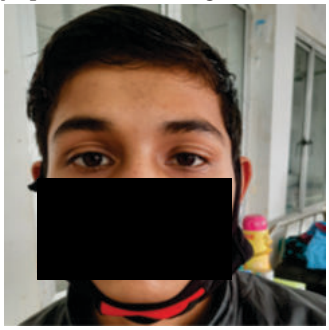

Fig 3: Patient during morning hours

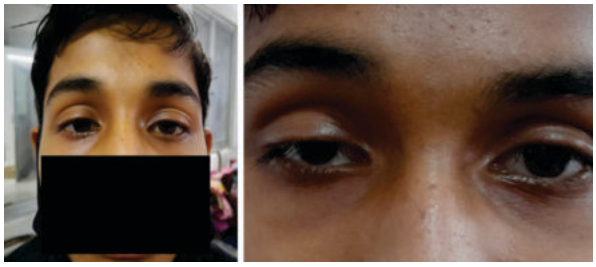

Fig 4: Patient during evening hours

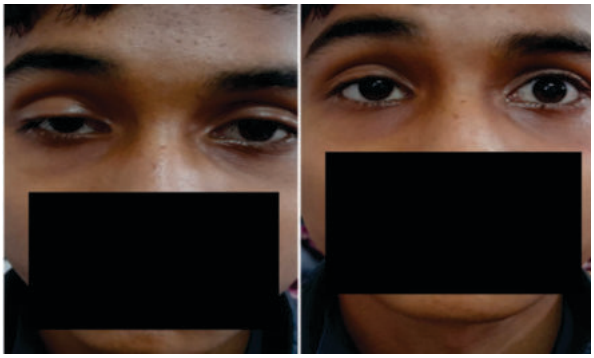

Figure 5: Before and after Icepack test

Based on the above findings and in co ordination with the neurology team the case was finally diagnosed as a case of Juvenile Ocular Myasthenia Gravis. Treatment was then started with Anticholinesterase Agent namely Pyridostigmine 60 mg TDS at which the patient responded and showed marked improvement in symptoms. The patient is still on treatment and is adviced for frequent follow ups.

Fig 6: Patient at 2 weeks follow up

DISCUSSION

Our patient had signs and symptoms that were confined to extraocular muscles worsening towards the evening which is typical of Ocular Myasthenia Gravis.Considering the age factor it can be concluded that it is a case of **Juvenile Ocular Myasthenia Gravis**. Involvement of eye muscles in Myasthenia Gravis is due to the fact that repeated use of the extra ocular muscles leads to their fatiguability because of decrease availability of Acetylcholine Receptors. Extraocular muscles are more commonly affected as they have a faster and higher synaptic frequency than limb muscles, which makes them more susceptible to fatigue. Also, they are affected more frequently because the tonic muscle fibers are necessary to maintain a position of the gaze, and these fibers have a smaller amount of ACh receptors, which makes them more susceptible to the loss or damage of receptors.[12]

MG in childhood can be classified as congenital MG (CMG), congenital transient MG (CTMG), and juvenile MG (JMG). CTMG is given by the passage of anti-ACh antibodies from the mother through the placenta. As reported by Mullaney *et al*., 15% of these patients have systemic and ocular symptoms which resolve at approximately 2 months of life. Babies have generalized hypotonia, weak crying, respiratory distress, poor suction, and extraocular muscle weakness.[13] Symptoms are usually self-limited. This pathology does not require long-term treatment once autoantibodies are no longer present.[14]

CMG is caused by pre- or postsynaptic structural or functional abnormalities in the neuromuscular junction, which will lead to abnormal ACh release or ACh receptor dysfunction. Symptoms usually begin around 2 years. Diagnosis is made with early symptoms of MG, a relative affected by the disease, and the absence of fluctuations in the course of the disease. CMG is not an autoimmune form of the disease; it requires supportive therapy. Treatment with anticholinesterase agents is usually useful.[12]

Finally, juvenile OMG is the most frequent (75% of cases). It is due to a blockade of ACh receptors. It has a later onset and affects children between 0 and 19 years old. Before the onset of symptoms, children have a healthy psychomotor development, and sometimes, it is preceded by an infection. This type of myasthenia is subdivided into OMG and systemic or generalized MG.[13]

OMG in children is a rare disease with an approximate

incidence of 3–9.1 cases per million per year and occurs mostly in Asian children. In 90% of these cases, there are ocular alterations such as ptosis and ophthalmoplegia associated with systemic symptoms.[15,16]It is essential for ophthalmologists to know this pathology as 90% of children with MG will have ophthalmological symptoms, and 50% go first to ophthalmologist.

The diagnosis of OMG is usually clinical. Clinical test like Ice-pack test, Fatiguability test, Cogan Twitch Sign and Pharmacological test like Neostigmine test aids in confirmation of the diagnosis. Also, this can be supported by a combination of Laboratory, Radiological imaging and electrophysiological test.[18,19]Chest Radiography is important to rule out thymoma.

Treatment includes symptomatic, supportive and immunological approaches. Acetylcholine esterase inhibitors increase the duration of the neurotransmitter at the neuromuscular junction. Pyridostigmine is considered the first-line treatment. Immunosuppressives are given who does not responds to monotherapy of Acetylcholinesterase. It aids to achieve pharmacological remission and maintenance of good quality of life. Corticosteroid namely Prednisolone, treatment is the first immunosuppressive therapy used. T. Low-dose corticosteroid therapy has been shown to reduce the risk of the conversion of OMG to GMG.[18,20,21]Steroid sparing agent like Azathioprine, Methotrexate and Mycophenolate are used in place of steroids if the adverse effects of the later is to be avoided or when pharmacological remission is not achieved by the steroids alone. Cyclosporine, Cyclophosphamide, Intravenous immunoglobulin and Plasmapheresis are the other treatment modalities available for patients with Myasthenia Gravis. Thymectomy is recommended for patients with Thymoma.

The good news for the patient with OMG is that if they continue to have only ocular symptoms for three years, there is a very good chance that their symptoms will not increase.[19]

CONCLUSION

After meticulous history taking, physical examination, clinical tests, Antibody titre assessment and a series of radiological investigations our patient was finally diagnosed as a case of Juvenile Ocular Myasthenia Gravis, considering the age of presentation. The patient responded to monotherapy of Anticholinesterase Agent Pyridostigmine 60mg TDS. He is still on medications and is on regular follow up.

REFERENCES

1. *"Myasthenia Gravis Fact Sheet". NINDS. 10 May 2016. Archived from the original on 27 July 2016. Retrieved 8 August 2016*
2. McGrogan A, Sneddon S, de Vries CS. The incidence of myasthenia gravis: A systematic literature review. 2010;34:171-183.
3. Carr AS, Cardwell CR, McCarron PO, McConville J. A systematic review of population based epidemiological studies in myasthenia gravis. *BMC Neurology*. 2010;10:46.
4. Hendricks TM, Bhatti T, Hodge DO, Chen JJ. Incidence, epidemiology, and transformation of ocular myasthenia gravis: A population-based study. *Am J Ophthalmol*. 2019;205:99-105.
5. Maddison P, Ambrose PA, Sadalage G, Vincent A. A prospective study of the incidence of myasthenia gravis in the East Midlands of England. *Neuroepidemiology*. 2019;53:93-99.
6. Mansukhani SA, Bothun ED, Diehl NN, Mohney BG. Incidence of ocular features of pediatric myasthenias. *Am J Ophthalmol*. 2019;200:242-249.
7. Phillips LH, Torner JC, Anderson MS, Cox GM. The epidemiology of myasthenia gravis in central and western Virginia. *Neurology*. 1992;42:1888-1893.
8. Zhang X, Yang M, Xu J, Zhang M, et al. Clinical and serological study of myasthenia gravis in HuBei Province, China. *J Neurol Neurosurg Psychiatry*. 2007;78:386-390.
9. Chiu HC, Vincent A, Newsome-Davis J, Hsieh KH, Hung T. Myasthenia gravis: Population differences in disease expression and acetylcholine receptor antibody titers between Chinese and Caucasians. *Neurology*. 1987;37:1854-1857.
10. Engel AG (2012). *Myasthenia Gravis and Myasthenic Disorders* (2nd ed.). Oxford University Press, US. pp. 109–110. ISBN 978-0-19-973867-0. Archived from the original on 8 September 2017
11. Nair AG, Patil-Chhablani P, Venkatramani DV, Gandhi RA (October 2014). "Ocular myasthenia gravis: a review". *Indian Journal of Ophthalmology*. **62** (10):985–991. doi:10.4103/0301-4738.145987. PMC 4278125
12. Gilhus NE, Skeie GO, Romi F, Lazaridis K, Zisimopoulou P, Tzartos S. Myasthenia gravis-autoantibody characteristics and their implications for therapy. Nat Rev Neurol 2016;12:259-68.
13. Mullaney P, Vajsar J, Smith R, Buncic JR. The natural history and ophthalmic involvement in childhood myasthenia gravis at the hospital for sick children. Ophthalmology 2000;107:504-10.
14. Mittal MK, Barohn RJ, Pasnoor M, McVey A, Herbelin L, Whittaker T, *et al.* Ocular myasthenia gravis in an academic neuro-ophthalmology clinic: Clinical features and therapeutic response. J Clin Neuromuscul Dis 2011;13:46-52.
15. Smith SV, Lee AG. Update on ocular myasthenia gravis. Neurol Clin 2017;35:115-23.
16. Motobayashi M, Inaba Y, Nishimura T, Kobayashi N, Nakazawa Y, Koike K. An increase in circulating B cell-activating factor in childhood-onset ocular myasthenia gravis. Pediatr Neurol 2015;52:404-9.
17. Pineles SL, Avery RA, Moss HE, Finkel R, Blinman T, Kaiser L, *et al.* Visual and systemic outcomes in pediatric ocular myasthenia gravis. Am J Ophthalmol 2010;150:453-9000
18. Smith SV, Lee AG. Update on Ocular Myasthenia Gravis. Neurol Clin. 2017 Feb;35(1):115–23
19. Nair AG, Patil-Chhablani P, Venkatramani DV, Gandhi RA. Ocular myasthenia gravis: a review. Indian J Ophthalmol. 2014 Oct;62(10):985–91.Update on Ocular Myasthenia Gravis. Neurol Clin. 2017 Feb;35(1):115–23.
20. Gilhus NE. Myasthenia gravis. N Engl J Med. 2016 Dec;375(26):2570–81.
21. Benatar M, Mcdermott MP, Sanders DB, Wolfe GI, Barohn RJ, Nowak RJ, et al.; Muscle Study Group (MSG). Efficacy of prednisone for the treatment of ocular myasthenia (EPITOME): A randomized, controlled trial. Muscle Nerve. 2016 Mar;53(3):363–9.