Congenital Myasthenia Gravis

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ABSTRACT

Congenital Myasthenia Syndromes (CMS) are a rare group of inherited disorders of the neuromuscular junction which presents in the infancy. There are considerable overlaps between CMS and autoimmune forms of Myasthenia Gravis. Here we report a case of CMS which presented to us where the father is also affected and on treatment.

KEY WORDS: CMS, Auto immune Myasthenia Gravis, CHRNE, Pyridostigmine, Tensilon test

Introduction

Congenital myasthenia syndrome (CMS) are rare and forms a group of inherited disorders characterised by a dysfunction of neuromuscular transmission. The diagnosis of CMS is based on clinical symptomatology and response to pyridostigmine. Onset of symptoms occurs in first few months of life with ptosis, restricted ocular movements, mild proximal weakness and difficulty in swallowing. It can also be diagnosed based upon absence of antiacetylcholine receptor antibodies, EMG evidence of neuromuscular transmission defect. In most of the centres such advanced investigations are not possible and the broad heading of CMS applied.

Case Report

Here we report a 2 year old male child (Fig. No.1) who presented with complaints of decreased activities in the evening times, decreased speech output and difficulty in seeing objects more towards the evening times of 6 months duration accompanied by his father. He was born of full term normal vaginal delivery and his motor and language milestones are high normal. On examination he was an average sized calm child with bilateral ptosis and shrill speech. DTR’s were normal and other neurological examination were normal. His father (Fig. No.2) diagnosed as myasthenia gravis and he was on treatment with pyridostigmine at appropriate dose.

A diagnosis of myasthenia was done based on clinical grounds, tensilon test was done to him which showed good response in the form of improvement in ptosis and motor activity.
He was further subjected to nerve conduction tests which showed decremented response on repetitive stimulation and this child was put on pyridostigmine at appropriate dose.

**Discussion**

CMS includes a heterogeneous group of disorders, characterized by dysfunction of NMJ transmission, which are present since birth and are genetically inherited[1]. Although many cases of myasthenia have been described, the distinction between acquired autoimmune form and congenital forms has been increasingly recognized and emphasized[2-5]. Two major features that distinguish CMS from acquired autoimmune myasthenia gravis (MG) are a positive family history and absence of AChR antibodies[6-11].

While a positive AChR antibody test excludes the diagnosis of CMS, a negative test in a sporadic case does not necessarily imply a diagnosis of CMS because a high proportion of juvenile patients with autoimmune MG are also seronegative[2]. On other side Muscle-specific receptor tyrosine kinase (MuSK) antibodies have been detected in more than half of the patients presenting with seronegative (no acetylcholine receptor antibodies) autoimmune myasthenia[12-13].

The current thrust of research is naturally directed towards elucidation of molecular basis of such disorders[14]. There are 91 different CHRNE mutation entries reported in the human gene mutation database (http://www.hgmd.cf.ac.uk), including 35 missense/ nonsense mutations, 14 splicing mutations, 17 small deletions, 18 small insertions, 3 regulatory mutations, 3 large deletions, and 1 large insertion.

Our patient clinical course is similar to other patients with mutations of the CHRNE gene [15-19], including a family history of consanguinity, a brief asymptomatic interval between birth and onset of ptosis, prominent early bulbar involvement, and profound ophthalmoplegia[17]. They differ from previous published cases that reported nonconsanguinity, and worsening during adult life [19], decreased movements in utero[20]. Patients with symptoms and signs similar to our patients could be mistaken for chronic progressive external ophthalmoplegia or autoimmune myasthenia gravis if evaluated later in life without careful attention to the clinical history. The ice pack test, which is commonly used in the diagnosis of autoimmune myasthenia gravis, led to dramatic improvement in ptosis of our patients and may prove to be a valuable diagnostic test in patients with CHRNE mutations. A genetic diagnosis is the most accurate method to confirm the CMS subtype and select the most appropriate treatment [21]. For example, pyridostigmine is effective in CHRNE mutations and certain other CMS variants. Pyridostigmine is contraindicated in patients with CMS with COLQ or DOK7 mutations or with slow channel defects [14,21], while ephedrine has good long-term effectiveness in patients with COLQ or DOK7 mutations [14,22,23]. A molecular approach to diagnosis will likely become more frequent as more genes responsible for CMS are identified and as the ease and availability of genetic testing improves [17].
Conclusion
To conclude, though there are considerable overlaps between CMS and Auto Immune MG, a thorough clinical history and gene mutation analysis will differentiate the same. Collaboration between clinicians, geneticists and neurobiologist is essential for complete characterization of the CMS and for the understanding of the fundamental mechanisms of neuromuscular transmissions.

References


