Autoimmune Myasthenia Gravis in Two Brothers

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Abstract

Two brothers with immune-mediated myasthenia gravis are presented for the rarity. The clinical presentation was dissimilar. Both had acetylcholine receptor antibody positivity and one had thymoma. Both responded to immunomodulation and thymectomy. Relevant literature is reviewed. ©

Introduction

Myasthenia gravis is an immunological disorder of the myoneural junction resulting from antibodies to acetycholine receptors. The antibodies are believed to originate in thymus and reach the skeletal neuromuscular junctions via the blood stream. Generally, immunological myasthenia gravis is sporadic. Familial cases are uncommon and constitute less than 5% of all the myasthenia gravis patients.[1] There are probably some hereditary factors in the development of myasthenia gravis as up to 30% of patents with myasthenia gravis have family history of other immunological disorders and MHC genes are under discussion.[1]

HLA A1, B8 and DRW3 antigens have been found with higher frequency in females with thymic hyperplasia and HLA A3, B7 and DR 2 are found more often seen in male patients with thymoma.[2] Concordance has also been shown in monozygotic twins, further supporting the genetic predisposition to this immunological disorder.

In clinical practice, it is very uncommon to see familial immunological myasthenia gravis and hence we report two brothers with this condition.

Case Report

YT, 30 years old male, presented with weakness of all four limbs of three months duration. He had difficulty in rising from ground, climbing stairs and combing his hair. He could use his fingers normally for the daily chores. He developed swallowing difficulty two weeks before presentation. He felt stronger in the mornings. There was no diplopia or ptosis. He had suffered poliomyelitis at age of two years, which had left both his thighs and legs weak. The patient also suffered generalised seizures in 1996, was investigated and no cause was detected. He was treated with phenytoin and was seizure-free. Medication was stopped successfully in 1999. The neurological examination showed nasal twang to speech, palatal weakness and mild neck flexor weakness. He had proximal weakness of shoulder girdle muscles with fatigability of outstretched hands. The lower limbs were wasted asymetrically and were weak at the hip, knee and the distal musculature, being asymmetric and more on the left side. The sensory system was normal. Deep tendon reflexes were normal in upper limbs, both knee and ankle jerks were not elicited.

Haemogram, blood sugar, serum CPK, liver and kidney function function tests were normal. AchR antibodies were strongly positive at 11.9 mmol/l and the repetitive stimulation test at slow rates confirmed decremental response (32-41%) in abductor pollicis brevis, orbicularis oculi and extensor indices muscles. The lower limb examination showed giant motor units and incomplete interference pattern confirming the old anterior horn cell disease. Prostigmine test was strongly positive. CT scan of the thorax was normal.

The diagnosis of mysthenia gravis was thus established and he was treated with acetylcholine esetrase inhibitors. He received plasmapheresis and then underwent thymectomy. Histopathology of the thymic tissue showed reactive follicular hyperplasia. He has remained well on maintenance dose of prednisolone 10 mg/day, azathioprine 50 mg twice daily and pyridostigmine 60 mg twice daily. His 23 years old brother, MT presented in October 2000 with drooping of eyelids, swallowing difficulty, changes in speech and limb weakness. His symptoms remarkably worsened with exertion and in the evenings. On examination, he had eyelid fatigability, bilateral ptosis and palatal weakness. His neck and trunk muscles were also weak. He had mild weakness of the shoulder firdle muscles. His AchR antibody levels were 20.6 mmol/L and CT thorax showed a lobulated isodense mildly enhancing mass in the anterior mediastinum suggesting a thymoma with mixed epithelial and lymphocytic morphology. He has also remained symptom-free on maintenance immunomodulation, similar to

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his elder brother.

Discussion

The index case presented with a subacute limb girdle syndrome and dysphagia. There was no involvement of ocular or facial musculature. This would raise a differential diagnosis of inflammatory myopathy. However, the normal CK and normal electromyography made it very unlikely. The presence of fatigability and demonstration of the decremental response combined with the AchR antibody positivity confirmed the diagnosis of myasthenia gravis of immunological origin. The poliomyelitis and seizure disorder was not likely unrelated to the myasthenia. His brother, on the other hand, presented with more conventional pattern of ptosis and diplopia. He also had mild limb weakness. His investigations confirmed immune mediated myasthenia gravis. Thus, these two brothers had immunologically mediated myasthenia with some difference in the clinical presentation.

The occurrence of other immunological conditions in family members of patients with myasthenia is well known. However, reports of familial autoimmune myasthenia gravis (FAMG) are few. FAMG with similar and varying clinical presentations in family members have been noted.[1,2] Such families and the studies on monozygotic twins suggested a genetic predisposition. Most such familial cases have been reported in siblings and autosomal recessive transmission has been considered. Rarely, vertical transmission to suggest dominant trait has been seen. MHC genes have been studied in these families but have been found to be less important in cases of FAMG.[1] Our patients did not have consanguinity and no other generations were affected, making it difficult to speculate on the type of genetic transmission.

Most families with FAMG report positivity of AchR antibodies but all affected members may not have them.[3] Whether such patients have other immunological markers like the MUSK antibodies is unclear. Non-conventional antibodies have been described in a family with FAMG but their causative role is uncertain.[4]

Information on familial myasthenia with thymoma is further rare and only few such reports are available. In one family both brothers had thymomas[5] and in the other, one of the brother had mysthenia without thymoma and the other had thymoma without myasthenia.[1] In our patients, both had myasthenia but one had thymoma. Both our patients have stabilized with thymectomy and immunomodulation, in keeping with the immune theory. Long term follow up on these patients will be of much value to know the behaviour of the familial myasthenia and also emergence of other immunological abnormalities.

In conclusion, we present a rare clinical situation of familial autoimmune myasthenia with thymoma, for its rarity.

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Announcement

35th (XXXV) Annual Conference of Indian Society of Nephrology (ISNCON 2004) will be held at **Department of Nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi between November 18-20, 2004.**

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