Myasthenia Gravis

Alternative Names
MG

Record Category
Disease phenotype

WHO-ICD
Diseases of the nervous system > Diseases of myoneural junction and muscle

Incidence per 100,000 Live Births
6-10

OMIM Number
254200

Mode of Inheritance
Usually sporadic

Gene Map Locus
N/A

Description
Myasthenia Gravis (MG) is a chronic, progressive, autoimmune disorder involving neuromuscular junctions. The disease is characterized by muscle weakness and abnormal fatigability on exertion. Most commonly affected muscles are those of the eye and eyelid, face, and the muscles controlling chewing, talking, and swallowing. Noticeable symptoms of the disease, therefore, are ptosis, diplopia, unstable gait, weakness in arms, legs, and neck, and difficulty in controlling facial expression and swallowing. At times, myasthenic crises may occur when the muscles involved in breathing weaken enough to endanger ventilation. The underlying defect in MG is an autoimmune response of the body towards acetylcholine receptors at the neuromuscular junctions. Damage to the acetylcholine receptors affects muscle contraction. It has also been noticed that the thymus is abnormally enlarged in patients with MG.

Diagnosis of MG is confirmed by running a blood check to test for the presence of antibodies against acetylcholine receptors. The disease is managed by administration of anticholinesterases, immunosuppressants, thymectomy, plasmapheresis (a technique in which the abnormal antibodies are removed), and/or transfusion of normal antibodies from donated blood. Prognosis for patients undergoing treatment is very good and muscle weakness is reduced. In fact, some patients may actually go into remission following treatment, and become totally asymptomatic.

Molecular Genetics
Nothing much is known about the genetics of MG, although, it has been seen to be inherited as a genetic disease. Familiar predisposition may be due to autoimmunity in general and 1 to 4 % of cases are familial without a simple Mendelian pattern. Interestingly, a neonatal transient form of the disease may also be acquired by babies born to mothers with the disease. It has been postulated that at least some forms of MG are due to genetic defects in the formation or release of acetylcholine, opening of acetylcholine receptor channels, and/or structure of the receptors.

Epidemiology in the Arab World
Libya
Radhakrishnan et al. (1988) conducted a retrospective study (January 1983 to December 1986) which included 24 patients (18 index cases) with spinal muscular atrophy (hereditary motor neuropathy, HMN), 9 with myasthenia gravis (MG), 6 with progressive supranuclear palsy (PSP), and 5 with subacute sclerosing panencephalitis (SSPE). The adjusted average incidence of MG was 4.4/million/year, 2.1 for males and 6.8 for females. The female:male incidence ratio was 3.2:1.
In 1996, El-Zunni et al. retrospectively studied 18 cases of MG (October 1991 to December 1994). The female to male ratio was 2.6:1 (13 females and five males). The mean age of presentation was 13.3 years later for male patients compared to females (mean age of presentation in females was 26.5 years and in males 39.8 years). The average time interval between the onset of symptoms and diagnosis was 2.5 years. At the time of diagnosis 94.5% (17 cases) of the cases had generalized MG and 5.5% (one case) had ocular symptoms only. In 11.1% (two cases) of patients an association with thyroid disorder was observed. Repetitive nerve stimulation (RNS) test was abnormal in 83% (15 cases) of the cases. All cases were initially treated with anticholinesterase and 22.2% (four cases) also additionally required steroid therapy. Thymectomy was performed on eight cases, four of which had thymus hyperplasia. None of the cases had any thymoma. Of these eight cases, one case (12.5%) had complete remission, five cases (62.5%) were doing well with a reduced dose of anticholinesterase and +/- steroids. However, two cases (25%) required intermittent plasmapharesis and immunosuppressants in addition to anticholinesterase and steroids.

Oman
Al-Four et al. (1995) reported a case of myasthenia gravis crisis in a 15-year-old boy admitted with acute respiratory distress. His symptoms were fever, cough, nasal regurgitation, and dysphagia, with a past history of easy fatigability and of a mild similar condition one year ago, for which no diagnosis was made. Clinically, he was conscious, distressed, restless, breathless, and febrile, with conjunctival congestion. His speech was with usual timbre and dysarthric mushy quality, pupils were equal and reactive to light, and all cranial nerves were intact. As his condition was deteriorating, intubation and intermittent positive pressure ventilation as well as chest physiotherapy were done. Investigations revealed normal chest X-ray (except for hilar haziness) and positive neostigmine test (edrophonium was unavailable). Electromyography was not done. The patient’s muscle power improved and he was extubated as he was started on gradually increased doses of corticosteroid, immunosuppressants, and a cholinesterase inhibitor, as well as broad spectrum antibiotics. Thymectomy was planned to achieve long remission. The authors advised early and effective antibiotic therapy, respiratory assistance and physiotherapy as well as plasmaphoresis for patients in crisis.

Koul et al. (1996) described eight patients (two males and six females) with myasthenia gravis seen over a period of five years. Their mean age of presentation was three years and 11 months. In five of the children, symptoms started when they were below the age of two years. Of these, four were diagnosed with congenital MG, based on their testing negative for acetylcholine receptor antibodies. These patients with CMG responded poorly to Pyridostigmine, and no progression in the disease course was noticed in two patients when followed up for two years. Corticosteroids and immunoglobulins did not improve the clinical condition of one child. Of the patients with CMG, two were siblings, and the father of one female patient, (who was found to have clinical and biochemical hyperthyroidism as well) had hyperthyroidism but no myasthenia gravis. Investigations conducted on all the patients included collagen workup (negative), electromyogram (decremental response in six), tensilon test (positive in all), and CT mediastinum (showed enlarged thymus in three out of six patients, two of which underwent thymectomy). As regards the treatment, three patients received immunoglobulins and four patients received corticosteroids, and only one from each group showed good response. On the other hand, only one child who developed myasthenic crisis received plasmapheresis (which was not useful), and Azathioprine.

Dashora et al. (1999) reported an unusual presentation of myasthenia gravis as acute fulminant respiratory failure in a 14-year old Omani girl who presented with a three days history of fever and throat pain along with difficulty in swallowing and breathlessness at the day of presentation. She was febrile, in severe respiratory distress, normotensive, her throat was filled with secretions, and her chest had bilateral crepitations and ronchi. Neurologically, she was drowsy with bilateral drooping of eyelids with normal ocular movements, and there was no local neurological deficit. An initial diagnosis of respiratory infection was made, but then she developed respiratory arrest, for which she was intubated and mechanically ventilated. A diagnosis of myasthenia gravis was suspected in view of the bilateral ptosis and sudden respiratory distress, and she dramatically improved as she received a parasympathomimetic drug intramuscularly and was extubated on the same day. She was then referred to a tertiary hospital where she was found to have in addition to the bilateral ptosis, palatal weakness and easy fatigability of limbs. The diagnosis of myasthenia gravis was confirmed by a positive
Tensilon test and strongly positive acetylcholine receptor antibodies in her serum. Chest x-ray and CT scan of the chest excluded the presence of thymic mass. Other investigations which included serum biochemistry, CK, and thyroid function test were normal. She was managed by intravenous immunoglobulin 400 mg/kg/day for five days along with parasympathomimetics and immunosuppressants, and upon discharge she was asymptomatic.

Jacob et al. (2003) conducted a retrospective study over a period of 3 years on 50 patients (male: female ratio of 2:3) diagnosed with myasthenia gravis. Only six patients had purely ocular, while 44 had the generalized form. Bulbar involvement was seen in 28 patients. Four patients had coexisting diseases as well (one with thyrotoxicosis and three with hypothyroidism, while one with the ocular form had diabetes mellitus, and one had epilepsy). Ventilatory support was needed in 12 patients. Investigations done included Tensilon test (positive in all), and repetitive stimulation test (positive in all patients with the generalized disease). CT scan showed thymus hyperplasia in 10 patients. Anti-acetylcholine receptor antibodies were found in 80% of generalized patients and in 50% of the ocular form. Immunoglobulins and plasmaphoresis were successfully used to treat myasthenic crises. Trans sternal thymectomy was done in 29 patients with good outcome, as only 10 patients required further immune suppression while the rest needed only pyridostigmine and nine had a drug free remission period of two years. Only one pregnancy (multigravida) out of eight deteriorated during the last trimester and was managed by immunoglobulins. All babies were born healthy and needed no support. Jacob et al. (2003) realized that both bulbar and ventilatory involvement were more in their series when compared to data from western societies.

Zachariaiah et al. (2004) reported a ten-year old girl with juvenile myasthenia gravis, who presented with a one-year history of drooping of her eyelids which started gradually and varied in severity, being more at the end of the day or when tired. There was no history of fever, seizure, difficulty in swallowing, chewing or talking, and she was not on any medications. All her family members were normal. Examination revealed no abnormality, but neurologically, there was severe ptosis of the right upper lid with restricted ocular movements except for adduction, while the left eye showed mild ptosis with limited upward eye movement, which increased upon sustaining an upward gaze. Both papillary reflexes were normal, and so were the anterior and posterior segments of both eyes. According to the above findings, myasthenia gravis was suspected, and was diagnosed by complete resolution of ptosis and ophthalmoplegia upon intramuscular injection of neostigmine (0.04 mg/kg). The diagnosis was confirmed upon detection of an abnormally elevated level of acetylcholine receptor antibody (5272.30 nmol/l). Chest X-ray showed no mediastinal widening while other serological investigations (ANA, TFT, and ESR) were normal. This patient was managed by a cholinesterase inhibitor (30mg six hourly) and she showed marked improvement in ptosis and ophthalmoplegia on follow up.

**United Arab Emirates**

In 1995, Al-Attia and George studied 28 patients (Arabs and Asians) in the UAE with systemic lupus erythematosus. Anti-cardiolipin syndrome, Sneddon's syndrome, shrunken lung syndrome, sicca complex, thyrotoxicosis and myasthenia gravis were also present in this small group of patients.

**References**


Radhakrishnan K, Thacker AK, Maloo JC, Gerryo SE, Mousa ME. Descriptive epidemiology of some rare neurological diseases in Benghazi, Libya. Neuroepidemiology. 1988; 7(3):159-64. PMID: 3405368

Related CTGA Records
Spinal Muscular Atrophy, Type I
Systemic Lupus Erythematosus

External Links
http://www.bbc.co.uk/health/conditions/myasthenia1.shtml
http://www.emedicine.com/emerg/topic325.htm
http://www.mayoclinic.com/health/myasthenia-gravis/DS00375
http://www.myasthenia.org/

Contributors
Eiman Ibrahim: 4.10.2007
Eiman Ibrahim: 17.9.2007
Ghazi O. Tadmouri: 2.5.2007
Eiman Ibrahim: 26.4.2007
Pratibha Nair: 26.4.2007
Eiman Ibrahim: 17.4.2007
Eiman Ibrahim: 18.4.2007

http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=589