Clinical profile of myasthenia gravis in the Sultanate of Oman

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ABSTRACT

Objective: Clinical study and follow up of myasthenia gravis patients in Oman.

Methods: Follow up of 50 consecutive myasthenia gravis patients referred to the Sultan Qaboos University Hospital, Oman for a median period of 3 years from 1997 to 2000. We based the diagnosis on the clinical picture, repetitive nerve stimulation tests and edrophonium test. We performed a computerized tomography scan of the chest and anti-acetylcholine receptor antibodies. We reviewed the results of immuno modulatory treatment including thymectomy and compared these with other studies.

Results: Of 50 patients, 6 had purely ocular myasthenia. Of the 44 with generalized myasthenia, 28 had bulbar involvement and 12 required ventilatory support. Eight out of 29 thymectomized patients had drug free remission after 2 years. There was worsening of myasthenic symptoms in only one out of 8 pregnancies and deliveries.

Conclusions: Bulbar and ventilatory involvement are more common in our series as compared with western data. Pregnancy and delivery were well tolerated.

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Myasthenia gravis is a common disease, usually autoimmune due to production of anti-acetylcholine receptor antibodies. The disease presentation is varied, ranging from mild to life-threatening.[1] As autoimmune diseases are common in the Arabian Peninsula we conducted a retrospective study of the clinical manifestations and course of patients with myasthenia gravis and compared these with other studies.

Methods. We followed up 50 consecutive myasthenia gravis patients referred to the Sultan Qaboos University Hospital, Oman for a median period of 3 years from 1997 to 2000. We based the diagnosis on the clinical picture, repetitive nerve stimulation tests and edrophonium test. A decrement of more than 10% was considered abnormal. We also performed computerized tomography (CT) scan of chest, thyroid function tests, autoimmune profile and acetylcholine receptor antibodies. We reviewed the results of immuno modulatory treatment including thymectomy and the effects of pregnancy on the condition and compared our results with other studies.

Results. The mean age was 27 years, ranging from 5 to 63 years. Male to female ratio was 2:3. Six had the ocular form of the illness with double vision, ptosis and ocular weakness. Forty-four had generalized symptoms. Ocular symptoms, signs and facial weakness were present in 40 of these patients; 28 had additional bulbar involvement with difficulty in chewing, swallowing, choking, sensation of food being stuck and low volume speech. Twelve had ventilatory impairment and this was the initial manifestation in 8 patients. Among the

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patients with generalized disease, one patient had maximum weakness involving the forearm muscles, all the others had more marked proximal weakness involving both upper and lower limbs. Results of tensilon test were positive in all patients and the repetitive stimulation test in all patients with the generalized disease was positive. The CT scan showed thymic hyperplasia in 10 patients and was normal in the others. There was no thymic tumor in this series. Four patients had coexisting thyroid diseases. One had thyrotoxicosis and 3 had hypothyroidism. One patient with ocular myasthenia had diabetes mellitus. Antinuclear antibodies were present in one patient. Anti-acetylcholine receptor antibodies were present in 80% of generalized patients and in 50% with the ocular form. One patient had epilepsy on treatment. All patients were initially treated with anticholinesterases. Three patients with the ocular form of the disease and 7 with the generalized form needed only these drugs. Steroids and azathioprine were used in 40 patients and cyclosporine in 2. In patients with moderately severe myasthenia, prednisolone was started in a dose of 1 mg per kilogram body weight and continued for a mean period of one year, before gradually tapering. Prednisolone was well tolerated with only 2 developing diabetes mellitus. Where child bearing was not a concern, azathioprine was started in a dose of 2 to 3 mg per kilogram body weight in 30 patients. Twelve patients developed myasthenic crisis and they were successfully treated by intravenous immunoglobulins in 11 and plasmapheresis in 2. Trans sternal thymectomy was performed on 29 patients (28 generalized and one ocular). In others it was not carried out because myasthenia responded well to treatment or because the patients refused. Thymectomized patients did better with 9 attaining drug free remission, compared to none in the non thymectomized group after 2 years. The mean time between onset of symptoms and thymectomy was 6 months. Ten of the thymectomized patients needed further immune suppression. The remaining patients needed only pyridostigmine. Twenty patients had thymic hyperplasia, 5 had normal thymus and 4 had thymic atrophy. None of the patients had thymic tumor and there was no postoperative complication. We supervised 8 pregnancies and deliveries in this group. Only one deteriorated transiently, needing intravenous immunoglobulins. She was a multigravida and worsening occurred during the last trimester. The neonates were healthy and needed no support.

Discussion. Oculomotor symptoms of ptosis and diplopia are the initial symptoms in two thirds of patients.[1] Almost all have these symptoms after 2 years. Ten percent of patients have the ocular form of the disease as in our series. Thirty percent of patients in a series had oral, pharyngeal or laryngeal symptoms and half had dysphagia.[2] The common symptoms were cough during swallowing, feeling of food being stuck behind the sternum, nasal regurgitation, feeling the need to clean the mouth, difficulties in bolus formation and movement and abnormal posture during swallowing. Bulbar symptoms in our patients were similar, but were more frequent as more than 50% patients experienced them, compared to 30% in Carpenter's series.[2] Proximal muscular weakness is common in generalized myasthenia and is sometimes symmetrical. In 10% of patients this can be the initial manifestation and rarely may be limited to single muscle groups such as neck or finger extensors or hip flexors. Limb muscle weakness was the initial symptom in 4 out of our 44 patients with generalized myasthenia. Ventilatory failure was the initial manifestation in 8 of our patients, as the symptoms of weakness were ignored by the patients. Myasthenia gravis is often associated with other immune mediated disease especially rheumatoid arthritis and hyperthyroidism. In children, an association with epilepsy has been noted. In a large series, 7% had diabetes mellitus before treatment with steroids, 6% had thyroid disease, 3% had nonthymic neoplasm and more than 2% had rheumatoid arthritis.[1] Transient myasthenia gravis has been observed in human immunodeficiency virus infection and after bone marrow transplantation. In our series, the association has been with thyroid diseases and diabetes mellitus. Pregnancy may improve, worsen or have no effect on myasthenic symptoms. Primigravids may worsen during first trimester, while in subsequent pregnancies, worsening occurs during the last trimester, delivery or the post partum period.[1] In general, pregnancy was well tolerated by our patients.

Early thymectomy is now a standard treatment in generalized myasthenia and ocular myasthenia, refractory to anticholinesterase and immunosuppressive drugs. Nine out of our 29 thymectomized patients reached stable drug free remissions. The remission rate after thymectomy in non tumor patients is approximately 35%, provided it is carried out in the first or second year after disease onset, 5% benefit significantly. Maximum response is attained by 3 years, but any weakness persisting one year after thymectomy is unlikely to remit without immunosuppressive treatment.[3]

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References

1. Sanders DB, Howard JF Jr. Diseases of neuromuscular transmission. In: Bradley WG, Daroff RB, Fenichel GM, Marsden CD, editors. Neurology in Clinical Practice. Boston (MA): Butterworth-Heinemann; 2000. p. 2167-2185.
2. Carpenter RC, McDonald TJ, Howard EM. The otolaryngologic presentation of myasthenia gravis. ***Laryngoscope*** 1979; 89: 922-928.
3. Scadding GK, Hovard CW, Ange MG, Domb I. The long term experience of thymectomy for myasthenia gravis. ***J Neurol Neurosurg Psychiatry*** 1985; 45: 401-406.