

A Typical Case of Myasthenia Gravis

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Mr. BC, 25 year old farmer from Sarlahi district, Hindu by religion, was admitted in medical ward of Kathmandu Medical College & Teaching Hospital on 2060/05/31 with the chief complaints of generalised weakness of whole body, easy fatigability, difficulty in speaking, drooping of both the eyelids for the past 9 months. All his symptoms used to be worse on exertion especially in the evening hours. These complaints were associated with diplopia on prolonged reading, fatigue on chewing, difficulty in swallowing solid foods and pain in the neck. On examination his vitals were within normal limits, ptosis 5 mm, ptosis time- 22sec, single breath counting up to 16, arm abduction time- 20sec. On systemic examination the only abnormality detected was grossly reduced power in all the muscles of the four limbs with normal reflexes, bilateral flexor planters and intact sensory system. His investigations

including Complete Blood Count, ESR, Random Blood Sugar, electrolytes, Chest X-Ray & Thyroid Function Test - were within normal limits, test for rheumatoid factor and antinuclear antibody were negative, which ruled out obvious autoimmune disorders. Tensilon test and Anti-acetylcholine receptor antibody were not done. CT scan of the chest showed enlarged thymus reported as thymoma. The Electromyogram revealed decrease in amplitude on repetitive stimulus consistent Myasthenia Gravis. He was treated with oral Pyridostigmine 60 mg 4 hourly which showed dramatic improvements. On missing a single dose the symptoms became worse which further confirmed the diagnosis. This patient was shifted to other centre to undergo thymectomy, where he underwent the surgery and the histopathology revealed thymic hyperplasia. The patient was remarkably improved after surgery.

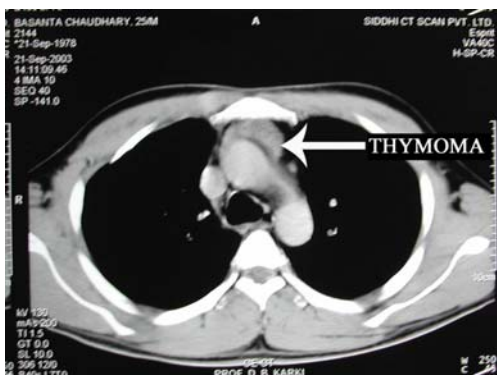
Discussion



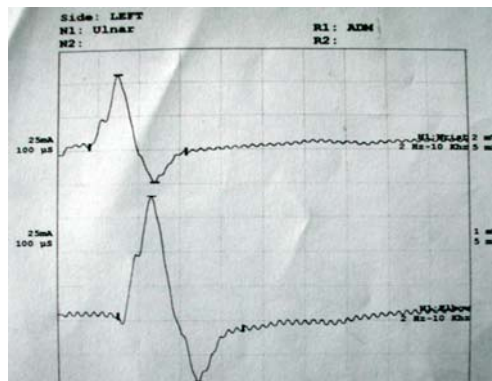
Before treatment



After treatment



CT showing Thymoma



EMG

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Historical Background

Thomas Willis (1621-1675), English physician, published a book *De anima brutorum* in 1672¹ in which he wrote about “a woman who temporarily lost her power of speech and became ‘mute as a fish’”. This has been interpreted as being the first written description of myasthenia gravis.



Thomas Willis

Mary Broadfoot Walker (1896-1974) introduced the use of physostigmine in myasthenia gravis. Recorded in 1934, as myasthenia gravis had symptoms like curare poisoning, the curare antidote physostigmine might help it so she injected some into her very droopy patients. Then, with utter surprise, like Lazarus rising from the grave, they rose and walked across the room. Dr. Mary Walker had made one of those great medical discoveries of a “specific” medicine for a specific disease, like a key turning on the lock.



Mary Broadfoot Walker

Myasthenia gravis is the most thoroughly understood of all human autoimmune diseases and has served as a model for the elucidation of mechanisms underlying other autoimmune disorders. It is a disorder of neuromuscular junction characterized by progressive inability to sustain a maintained or repeated contraction of striated muscle. The main pathology is blockage or lysis of the acetylcholine receptors of the post junctional membrane by antibodies directed against them. About 75% of patients have thymic abnormalities out of which 15% have thymoma. The remainders have other thymic abnormalities, like thymic hyperplasia. There is increased incidence of other autoimmune disease like hyperthyroidism, rheumatoid arthritis, Systemic Lupus Erythematosus which were ruled out in this case.

The prevalence of Myasthenia is 4 in 10000. Females are affected more than the males in the ratio of 3:2 with mean age of onset 15-50 yrs. The cardinal features are weakness and fatigability of skeletal muscles, usually occurring in a characteristic distribution. The weakness tends to increase with repeated activity and improve with rest. Ptosis and diplopia occur early in the majority of patients. Weakness remains localized to the extraocular and eyelid muscles in about 15 percent of patients. When the facial and bulbar muscles are affected, there may be a characteristic flattened smile, “mushy” or nasal speech, and difficulty in chewing and swallowing. Generalized weakness develops in approximately 85 percent of patients and it may affect the limb muscles, often in a proximal distribution, as well as the diaphragm and the neck extensors. If weakness of respiration becomes severe enough to require mechanical ventilation, the patient is said to be in crisis.

On physical examination, the findings are limited to the motor system, without loss of reflexes or alteration of sensation or coordination. The clinical severity of myasthenia gravis is usually graded functionally and regionally, according to an adaptation of a scale devised by Osserman: Grade -I involves focal disease (e.g., restricted to ocular muscles); grade II, generalized disease that is either mild (IIa) or moderate (IIb); grade III, severe generalized disease; and grade IV, a crisis, with life-threatening impairment of respiration.

The diagnosis of myasthenia gravis is done by Tensilon test, Electromyography and demonstration of anti-acetylcholine antibody level of more than 5×10^{-10} mmol/L. Electromyogram shows the characteristic decremental response on repetitive

stimulation. The anti-acetylcholine antibody test is specific, and is positive in 90% of cases with generalized myasthenia gravis and in 60% of those with the ocular type. Anti-skeletal muscle antibody suggests the presence of thymoma but all patients must undergo CT scan of the chest to exclude thymic abnormalities.

Pyridostigmine is the most widely used anticholinesterase in myasthenia gravis. The dosage and schedule of administration must be tailored to the patient's needs. The maximal useful dosage of pyridostigmine rarely exceeds 120 mg every three hours.

Surgical thymectomy is indicated for its therapeutic effect in myasthenia gravis or to prevent the spread of a thymoma. The goal of thymectomy as a treatment for myasthenia gravis is to induce remission, or at least improvement, permitting a reduction in immunosuppressive medication. There is now a broad consensus that patients with generalized myasthenia gravis who are between the ages of puberty and about 40 years should have surgical thymectomy.

After thymectomy, clinical remission occurred in approximately 35 percent of patients and improvement was seen in another 50 percent. The mechanism by which thymectomy produces benefit in myasthenia gravis is still uncertain. It may be because of removal of immuneactive cells.

Immunosuppressive therapy is indicated when weakness is not adequately controlled by anticholinesterase drugs. Prednisone, azathioprine, and cyclosporine are the agents now used for long-term immunosuppression. Corticosteroids improve 70% of the disease but the improvement is preceded by exacerbation thus its use should be initiated in hospital. The dose gradually, beginning with a daily dose of 15 to 20 mg of prednisone and increasing it by about 5 mg every two or three days. The rate of increase must be guided by the patient's clinical response, and the end point is either a satisfactory clinical response or a dose of 50 to 60 mg per day. Improvement usually begins in 2 to 4 weeks, with maximal benefit realized after 6 to 12 months or more.

Plasmapheresis removes antibodies from the circulation and produces short-term clinical improvement in patients with myasthenia gravis. It is used primarily to stabilize the condition of patients in myasthenic crisis or for the short-term treatment of patients undergoing thymectomy. Typically, five exchange transfusion of 3 to 4 litres each are carried

out over a two-week period. The effect of plasmapheresis is rapid, with improvement occurring within days of treatment.

Conclusion

Myasthenia gravis is associated with thymic abnormalities in about 85% of cases. This may be thymoma or thymic hyperplasia. Thymoma is more common in people who are above 60 yrs of age. CT chest is a must in suspected myasthenia. Thymectomy must be undertaken for its therapeutic effect in myasthenia or to prevent the spread of thymoma.

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