

Thymoma Presenting with Myasthenia Gravis: A Case Report.

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A 20 year old man was referred to Mulago hospital with a diagnosis of Myasthenia Gravis (MG) which was suspected to be due to a thymoma. The patient came with complaints of blurring of vision for one year and body weakness for six months. He was investigated using conventional X-rays and C.T. The chest CT scan showed an anterior mediastinal mass. The diagnosis was confirmed on histology report which was consistent with thymoma. The patient was managed surgically, did well post operatively, and was discharged when his vision and muscle power had dramatically improved. On follow up for two years, patient was symptom free.

Introduction

Myasthenia Gravis (MG) is the most common disorder of the neuromuscular transmission¹. The hall mark of the disorder is a fluctuating degree and variable combination of weaknesses in the ocular, bulbar, limbs and respiratory muscles. Weakness is the result of an antibody-mediated T-cell dependant immunological attack directed at proteins in the post synaptic membranes of the neuromuscular junction. The diagnosis of MG can be established by clinical and serological testing. An important consideration is that about 15%-40% of Thymoma is malignant, 35%-40% of patients with thymoma have MG and about 10%-15% of those with MG have underlying thymoma.^{1,2}

Case Report

A 20- years old man was referred to Mulago hospital from a private clinic with a diagnosis of MG due to thymoma. His presenting complaints were; blurring of vision for two years, diplopia for two years and body weakness for six months. He was well until two years prior to admission when he developed these symptoms. The blurring of vision was initially mild but eventually worsened. He sought the help of an ophthalmologist who made a diagnosis of Ocular M.G. He was started on pyridostigmine and improved initially but the symptoms worsened later.

He soon developed an unusual fatigue in the evening. He had difficulty in holding small objects like pens and cups although, he felt strong. A chest CT scan which was done revealed an anterior mediastinal mass most likely a thymoma (Figure 10.1 A and B).

There was no history of difficulty in speech, nasal regurgitation, or chewing. He had no difficulty in breathing or chest pain. There was no history suggestive of superior vena cava syndrome or Horner's syndrome. There was no hoarseness of voiced or retrosternal pain. He gave no history of weight loss, fever, diarrhea or vomiting. There was no history of palpitation, backache or muscle wasting. This was his index admission. There was no history suggestive of metabolic diseases, Diabetes mellitus, hypertension or thyrotoxicosis. He had never had any operation however, had mild allergy to dust but was not allergic to any drug. There was no history of MG in the family. He was a banker who lived alone, did not smoke cigarette or drink alcohol.

On examination he was in good general condition with no anemia, jaundice, edema and or enlarged lymph nodes. His blood pressure was 120/70 mm Hg, pulse 66/minute, temperature 36.8. All systems were essentially normal. His hemoglobin, WBC, ESR, Renal and liver function test were within normal limits. Chest X-ray did not reveal any mediastinal mass or mediastinal widening. A diagnosis of a thymoma complicated by myasthenia gravis was made.

The patient underwent surgery. Using a midline incision, a Sternotomy was done. A thymus tumor was identified in both lobes. The gland was still encapsulated. The thoracic viscera were normal. Excision of both right and left lobes was done successfully. Postoperatively, the patient was admitted in intensive care unit for close monitoring. The specimen removed was sent for histology.

A post operative chest X-ray showed the tubes in situ and widening of the mediastinum possibly due to hemorrhage (Figure 10.2A). A repeat post operative chest X-ray showed right basal infiltrates with lingula opacity possibly collapse, elevated left hemi diaphragm and mild pleural effusion. (Figure 10.-2B)

Histology report was consistent with thymoma (Figure 10-3 A&B) and (Figure 4). The patient did well in the intensive care unit and was later transferred back to the parent ward where he was managed on analgesics, antibiotics, pyridostigmine and physiotherapy. The rest of the post operative days were uneventful. The patient was discharged on treatment and referred to the Surgical Out patient for follow up.

Discussion

Myasthenia gravis (MG) is a relatively uncommon disorder. However, it is the most common disorder of neuromuscular transmission¹. This is the first case seen in Mulago Hospital in twenty years. Age of onset is characterized by an early peak in the second and third decades (female predominance) and late peak in the sixth to eighth decade (male predominance). The patient presented here was in his twenties⁴.

About (10 to 15) % percent of those with MG have underlying thymoma. The case presented here had Ocular MG. A chest CT scan revealed an anterior mediastinal mass which was removed at Surgery and confirmed a thymoma by histology^{1,5}.

The cardinal feature of MG is fluctuating skeletal weakness, often with true muscle fatigue. The fatigue is manifested by worsening contractile force of the muscle^{5, 6,10}. The patient presented here had unusual fatigue in the evenings and muscle weakness exhibited by difficulty in holding small objects like pens and cups

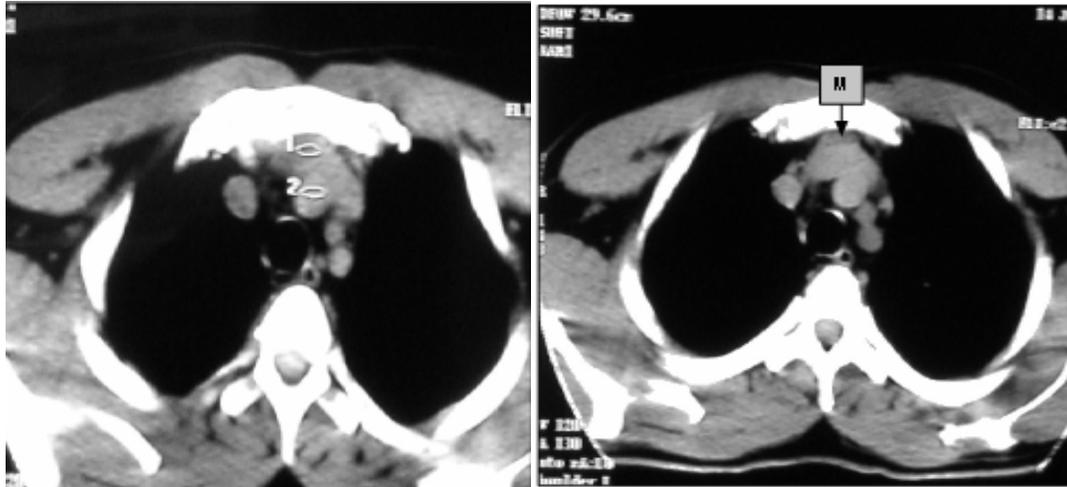
There are two clinical forms of MG: ocular and generalized. In ocular MG, the weakness is limited to the eyelids and extra-ocular muscles. In generalized disease, the weakness may also commonly affect ocular muscles, but it also involves a variable combination of bulbar, limb, and respiratory muscles^{7,8,9}. Ocular MG was more marked in the patient presented here than the generalized MG.

More than 50 % of patients present with ocular symptoms of ptosis and diplopia. Of those who present with ocular manifestations, about half will remain purely ocular, about 15% of the patients will present with bulbar symptoms. These include fatigable chewing, dysphagia and dysarthria⁸. Less than 5% present with proximal limb weakness alone. There were no bulbar symptoms in the patient presented here although he had proximal limb weakness^{8,9}. Eyelid muscle weakness can lead to ptosis that can vary through out the day. Extra ocular muscle weakness produces binocular diplopia that disappears when the patient closes or occludes one eye⁷. The patient above had complaints of blurring of vision and diplopia.

Muscles of jaw closure are often involved and produce weakness with prolonged chewing; oropharyngeal muscle weakness produces dysarthria and dysphagia. Facial muscles are frequently involved and make the patient appear expressionless⁶. These symptoms were not exhibited in this patient.

Neck extensor and flexor muscles are commonly affected. The weight of the head may overcome the extensors producing a "dropped head syndrome". Involvement of the limbs produces predominantly

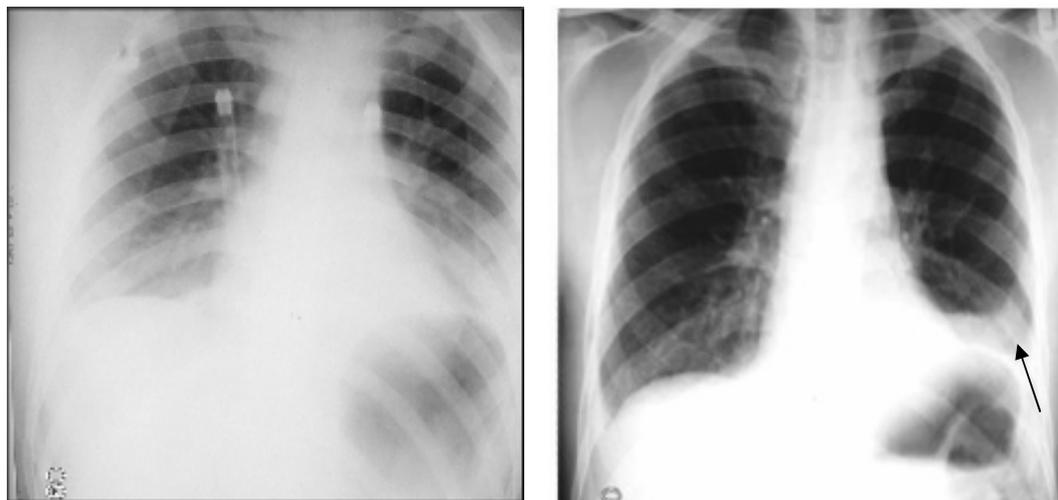
proximal weakness similar to other muscle diseases¹⁰ Predominantly distal presentations of otherwise typical myasthenia can occur. As already mentioned above the case presented here had weakness of the upper limb but not of the lower limbs. Involvement of the muscles of respiration produces the most serious symptoms in MG, such as respiratory insufficiency and pending respiratory failure, called “myasthenic crisis.”^{5,6}. This was not seen in this patient



A

B

Figure 10-1 Thymoma **A**, A scan at the level of T3; a soft tissue mass of 43HU and Brachiocephalic artery of 53.6 HU are seen. **B**, A chest CT scan at a level below T3; a retrosternal mass (M) is seen.



A

B

Figure 10.2 Chest X-rays. **A**, A supine post operative X-ray showing the chest tube in situ, and widening of the mediastinum. **B**, An erect postoperative X-ray a right basal infiltrates and opacification of the lingual lobe (arrow).

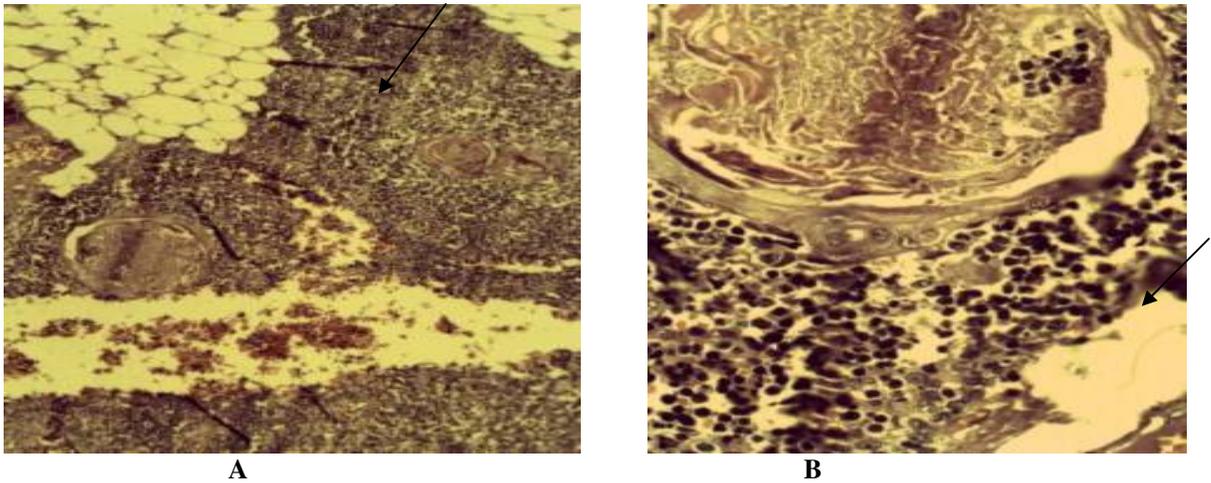


Figure 10-3 Thymoma Histology report. A, A section of the tumor consisting of matured lymphoid cells with Hassall's corpuscles and fat. B, Abortive Hassall's corpuscle lined by epitheloid cells and lymphocytes.

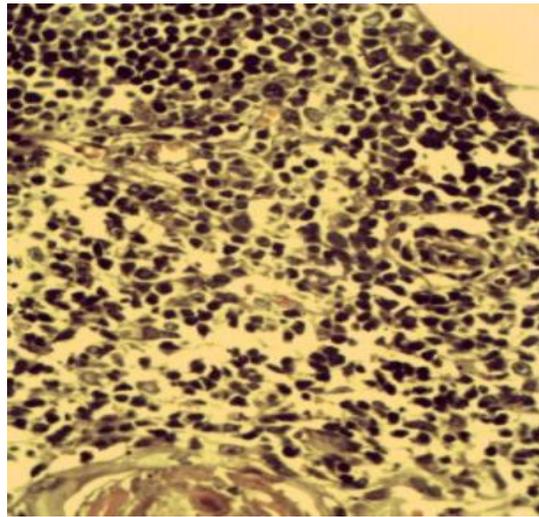


Figure 10-4 Thymoma Histology report. Outer cortex with mature lymphocytes, medulla composed of plump ovoid epitheloid cells with vesicular nuclei and Hassall's corpuscles at varying stages of maturity.

Early in the disorder, the symptoms of MG are often transient in many patients, with hours, days, or even weeks free of symptoms. New symptoms often develop weeks or months later. The maximal extent of the disease is seen in 77% of patients by three years of onset.

The diagnostic approach to myasthenia is focused on confirming the clinical diagnosis established by the history and typical examination findings described above. Bedside tests (the tensilon test and the ice pack test) are easy to perform and are sensitive, but they have major limitations due to concerns about excess false-positive results with these techniques. Confirmation by these tests alone is unwise.

More reliable laboratory methods that aid in the confirmation are serologic test for autoantibodies and electrophysiological studies (repetitive nerve stimulation studies and single-fiber EMG). It should be kept in mind that the diagnostic sensitivity of these studies also vary considerably depending on whether the patient has ocular or generalized disease.

Differential diagnosis

Many of the disorders that are likely to be confused with myasthenia gravis (MG) involve weakness of the extra ocular muscles. The diagnosis of ocular myasthenia is often difficult to establish with certainty, since the confirmatory tests are often negative.

The differential diagnosis of ocular myasthenia gravis includes Grave's disease, chronic progressive external ophthalmoplegia (CPEO), as well as multiple cranial neuropathies from structural or inflammatory disease of the brainstem and basilar meninges.

Generalized fatigue and number of neuromuscular disorder can also be confused with myasthenia. Electrodiagnostic studies are particularly crucial in the differential diagnosis of these other neuromuscular disorders. Fatigable weakness, an important aspect of MG, must be distinguished from complaints of generalized fatigue or tiredness.

Amyotrophic lateral sclerosis (ALS) is a progressive disease that, like myasthenia, can involve the bulbar muscles and can produce a false-positive tensilon test even rarely a false-positive test for AChR-Ab. The Lambert- Eaton myasthenic syndrome (LEMS) shares the same pathologic site with MG and has a similar pathophysiology. However, the clinical presentation in LEMS is markedly different than in MG. Proximal leg weakness is typically the earliest and most prominent symptom. Involvement of the bulbar muscles or diplopia is rare, but ptosis is frequently seen. Symptoms in LEMS are more likely to be present in the morning and to improve with exercise. Autonomic dysfunction is frequent in LEMS.

Botulism can be confused with myasthenia because it also prominently affects the bulbar and eye muscles. An autoimmune form of MG occurs in approximately 1% of the patients treated with penicillamine. There are several rare forms of congenital myasthenic syndrome. They should be considered when there is positive family history, a lack of response to anticholinesterase drugs, and the absence of AChR-Ab.

Conclusion

Patients with MG should be investigated for Thymoma. Thymectomy can be curative as seen in this patient.

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