Thymoma in Myasthenia Gravis
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Introduction
Myasthenia Gravis is an auto-immune, neuromuscular junction disease caused by acetylcholine receptor antibodies in 85% of the cases. Fatigability and muscle weakness are the typical characteristics of myasthenia gravis.1 Thymoma is the anterior mediastinal neoplasm which originates within the thymal epithelial cells.2 Myasthenia Gravis (MG) and thymoma can occur in association with each other. When this happens, MG is considered a paraneoplastic disease resulting due to the presence of thymoma; such a condition accounts for 15% of all the MG cases.350% of thymoma patients develop MG.4, 5 In MG, thymomas are thymic epithelial cells derived neoplasms and are of cortical subtype usually.6 These thymomas have morphological similarities with the thymic cortex. They both have the capacity to illicit the maturation of naïve CD4 T cells and migrate mature naïve T cells to the periphery. Thymomas which are devoid of this ability like the thymoma resembling the medullary thymic tissue do not induce MG.7 This case report describes a young patient of myasthenia gravis with bulbar presentation.

Case Report
A 22 year old male University student, unmarried, resident of Islamabad, initially presented in the ENT Outdoor Patient Department (OPD) with the complaints of dysphagia and dysarthria for 6 months. On examination he had laryngeal edema. He received oral Coamoxiclav, Citrizin, and Serratiopeptidase as the treatment, but his symptoms gradually worsened. He was noticed to have some facial muscle weakness. He was referred to the neurology department. Neurological examination showed signs of bulbar weakness. There were no other signs and symptoms to direct a diagnosis. He was diagnosed with a rare descending form of Gullian Barre Syndrome. Nerve conduction studies reported negative for Gullian Barre syndrome. Receptor nerve stimulation test at low rate of stimulation showed >10% decremental response in the proximal muscles, pointing towards MG. Acetylcholine receptor antibody titer turned positive i.e. 60nmol/L (less than 0.25nmol/L = negative). He was diagnosed to be suffering from Myasthenia Gravis. Despite this significant elevation, no signs of generalized myasthenia were detectable. He was treated with AchE inhibitor, pyridostigmine, steroids, and prednisolone. His condition did not improve much in the next 4 weeks. Azathioprine 50mg along with B12, Folic Acid, and Calcium Supplements were added in the treatment. He was able to ingest liquids, a soft diet, and speak a few sentences after medication. At this time a contrast enhanced Chest CT Scan was ordered and it showed soft tissue mass 2x2 cm in the superior mediastinum consistent with prominent thymus gland, i.e. Thymoma (Figure1). His trans-sternal thymectomy was done on 15-03-2012. The chest and neck portion of the thymus was removed along with fibro fatty tissue between the in nominate vein superiorly and pericardium inferiorly and between the two phrenic nerves on either side (Figure 3). A 2.5x3.0 cm, well encapsulated, firm adenoma with no local infiltration of tissues in left lobe of thymus gland was found. Histopathological examination of the specimen was performed post operatively (Figure 3).

Fig 1:Thymoma visible in a CT scan
Fig 2:Mid sternal incision; thymoma can be seen.
The patient remained in surgical intensive care unit for two days and then was transferred to surgical floor. Chest therapy was done. He was given IV fluids, IV antibiotics, epidural analgesia and the oral medications already prescribed. Chest drain was removed on the second post-operative day. A complete follow up of the patient was done for 6 months in both the surgery as well as neurological clinics. There was marked improvement observed in his initial symptoms of dysphagia and dysarthria. After surgery he was off steroids and was well controlled on pyridostigmine bromide 60 mg thrice a day and Azathioprine 50 mg 12 hourly.

Discussion

Myasthenia Gravis (MG) is a relatively rare auto-immune neuromuscular disorder that is characterized by fluctuating weakness of the voluntary muscle groups. The pathophysiology of the disease is that antibodies are formed against Nicotinic Post synaptic receptors at neuro-muscular junction of skeletal muscles. MG has a bimodal peak, i.e. it occurs in females below 40 years and male above 60 years of age. The most common presentation (90%) of MG is that of ocular weakness (ptosis/accommodative insufficiency/oculomotor paresis) and it is referred as ocular MG. The second most common presentation is bulbar weakness, which usually progress to Generalized MG. Isolated bulbar weakness is common in late onset MG and may be confused with the disease of oropharynx and neurological conditions. According to Myasthenia Gravis Foundation of America Clinical Classification, eye muscle weakness is standard along with varying weakness of limb, axial, bulbar or respiratory muscle in all classes. Up to 75% of patients have an abnormality of the thymus, 70-85% has thymic hyperplasia, and 10-15% has a thymoma. Thymoma is a tumor originating from the epithelial cells of the thymus. It is an uncommon tumor, known for its association with the neuromuscular disorder myasthenia gravis, mostly the cortical subtype (WHO type B).

Cortical thymomas usually have some morphological similarities with thymic cortex, and they have the capacity to propagate the maturation of immature naive CD4 T cells and export mature naive T cells into the periphery. Thymomas lacking this ability do not induce MG. Thymomatous MG (T-MG) is considered to have a worse prognosis compared with non-thymomatous MG. Patients with T-MG have high-grade symptoms with low rate of remission even after therapy. The diagnosis of MG should be confirmed by the detection of AChR antibodies, present in most MG cases. It can be confirmed pharmacologically by edrophonium test which is positive in 90% of MG patients, giving an immediate but transitory improvement of MG signs. These antibodies are present in almost all patients with a Thymoma. In two thirds of MG patients, failure of neuromuscular transmission leads to decremental response to repetitive nerve stimulation by electromyographical (EMG) examination. The diagnosis of a thymoma in MG is finally established by histopathological examination of the specimen postsurgically. Titin and RyR antibodies and radiological examination of the anterior mediastinum have similar sensitivity for the presence of a thymoma in MG. However, the presence of Titin and RyR antibodies in a MG patient younger than 60 years strongly suggests a Thymoma, while the absence of such antibodies at any age strongly excludes thymoma. The treatment of thymoma is a radical excision of the neoplasm. Thymectomy can be performed trans-sternally, or through video assisted thoracoscopic approach with almost similar outcomes.

In present case, the unusual finding was the purely bulbar weakness that was not very responsive to standard medications for MG. Although the bulbar form of myasthenia is usually seen in case of late-onset myasthenia, we observed it in a case of early onset myasthenia. We performed trans-sternal thymectomy in our case to remove thymoma instead of using video assisted thoracoscopic approach.

Myasthenia gravis is a disease of old age especially in males and the most common presentation is ocular. The bulbar presentation in MG is a rare finding to be found in a young patient. The rarity of this form of disease made it an interesting case to be studied.

References