



The Hidden Culprit behind the Scene- Revealed

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Abstract

Myasthenia Gravis, a neuromuscular junction disorder most commonly occur in elderly males & younger women, most of whom have a hyperplastic thymus. It commonly present as bilateral ptosis, diplopia along with bulbar & proximal limb muscle weakness. Here we present a case report of very unusual presentation of myasthenia found to be associated with underlying thymic carcinoma with metastasis, which is a very rare association.

Case Report

A 52 year old female presented to medicine outpatient department with 3 days history of drooping of left eyelid especially while watching TV during evening with spontaneous recovery during morning hours. Patient was hospitalized and further evaluated. Her symptoms not associated with any local eye symptoms and her other eye was apparently normal. No history suggestive of bulbar and appendicular symptoms. No history of difficulty in breathing. No history suggestive of systemic symptoms. No previous history of similar illness.

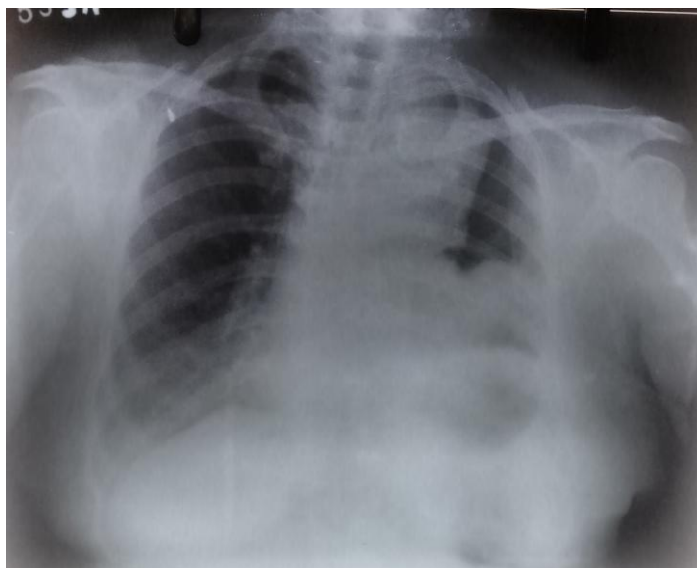
On examination, patient had no neurocutaneous markers. Vitals were stable. Neurological examination of higher functions were normal. Cranial nerves were normal except oculomotor nerve of left eye showing easy fatigability of left eyelid suggestive of ptosis. No definite weakness/fatigability of limb muscles and diaphragm. Motor, sensory and autonomic

systems were within normal limits. Gait and co-ordination was normal. Other systems within normal limits. Ice pack test showed positive results. Single breath count was 30.

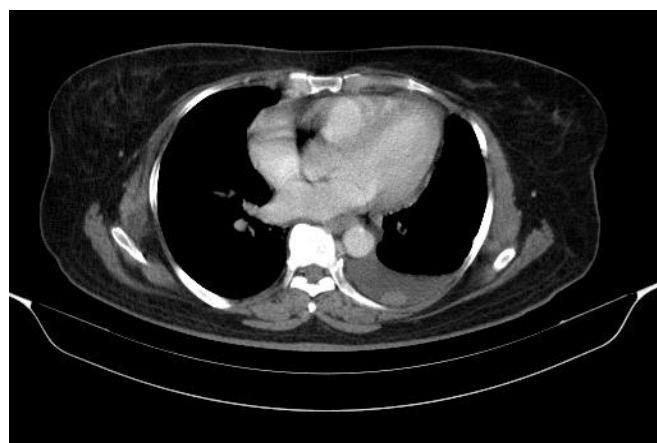
Provisional diagnosis of Ocular myasthenia with atypical features is made and the patient was further investigated.

Investigations

Complete blood count, RBS, RFT, LFT, Serum Electrolytes were within normal limits. ECG and Echo was normal. Chest X-Ray showed mediastinal widening with left lower zone opacity Serum Uric acid, calcium, cortisol, TSH, Free T3, T4 & Parathyroid hormone were within normal limits. Viral markers negative. RA factor, C-reactive protein, ANA profile, mantoux test, CEA, CA125, AFP were all negative. Serum ACE & serum protein electrophoresis were normal. USG abdomen showed no significant abnormality.



*10.5*7.9*6.2cm with mediastinal invasion, pleural and diaphragmatic deposits and pleural based nodules-possibility of invasive thymoma/thymic carcinoma may be considered. suggested biopsy correlation".*



Neostigmine test was positive
Before Giving Neostigmine- Left Eye Ptosis



After Neostigmine Test- Ptosis Improved



Anti Acetyl-choline Receptor Antibody - 7.18nmol/liter (Normal <0.25)

Anti MUSK Ab was negative

Repetitive nerve stimulation study showed no decremental response.

MRI Brain & Orbit was normal. CT Thorax (Plain & contrast) was done. It showed "A homogeneously and moderately enhancing soft tissue density lesion involving the left prevascular & paravertebral space on left side measuring

Patient was started on Tablet Pyridostigmine 60mg thrice daily and her ptosis improved. On 10th day of admission, CT guided biopsy was done. Report came as Thymic carcinoma, Masaoka's stage 4A. On day 14, patient developed myasthenic crisis in the form of

generalised muscle weakness and diaphragmatic palsy even after classic antimyasthenic treatment without steroids. Emergency Intubation was done & plasmapheresis was given. Now the patient is clinically improving.

Discussion

Myasthenia Gravis (MG), peaks of incidence occur in women in their 20's and 30's and in men in their 50's and 60's. Age and sex of presentation in our case is unusual. Theoretically, thymus is abnormal in approximately 75% of patients, in 65% patients thymus is "hyperplastic", rest 10% have thymomas. Thymic carcinomas are rarely associated with MG. Muscle like- myoid cells within thymus serve as a source of autoantigen and trigger the autoimmune reaction within the thymus gland.

Thymomas are neoplasms arising from or exhibiting differentiation toward thymic epithelial cells, into which immature T cells are mixed in various ratios. Because of the existence of immature T cells, thymomas can be thought as of as functional tumors. Thymic carcinomas are malignant epithelial tumors with overt cytological atypia, and a lack of thymus-like features. This is one of the reasons why MG can accompany thymoma, but theoretically not thymic carcinoma. Thymomas have varied presentation ranging from asymptomatic incidental mediastinal masses to locally extensive tumor with compressive symptoms and distant metastasis. Our patient with ocular myasthenia, otherwise asymptomatic incidentally detected to have thymic carcinoma with metastasis, is extremely a rare presentation. Osserman classification is used to assess severity of MG

Grade 1- Focal disease restricted to ocular muscle

Grade 2-

- (a) Mild generalized disease, prominent limb involvement
- (b) Moderate generalized disease, prominent bulbar involvement

Grade 3- Acute severe generalized disease with respiratory symptoms

Grade 4- Severe generalized disease with respiratory symptoms within 2 years

Our patient with ocular myasthenia developed to secondary disease with severe respiratory symptoms within a span of few days, even after treatment is extremely a rare presentation.

Treatment involves early radical resection of the tumour along with pharmacological treatment of MG and continuous follow up. In locally advanced cases when the tumor invading pleura or pericardium as in our case, complete radical surgery is not possible and adjuvant treatment in form of radiotherapy and chemotherapy is required which is being planned for our patient. Pre surgical plasmapheresis or immunoglobulin infusion helps in removal of circulating pathogenic antibodies to a significant level.

Conclusion

Thymic carcinomas can accompany MG, although rare. The 5-year survival rates for all stages of thymoma and thymic carcinomas are 78% and 40%, respectively. When there is an unusual presentation of MG, a thorough search for underlying thymic malignancy is much needed, as it may lead to rapid progression of the disease. Timely surgery for the tumor along with pharmacotherapy for MG may lead to recovery of the patient. Thus, this case is an extremely rare presentation of myasthenia found to have underlying thymic malignancy which is again very unusual. This case highlights the importance of high degree of clinical suspicion of the disease when there is an atypical presentation and search for even the rarest association of that disease. Sometimes, the association might be the hidden culprit behind the entire scene which if not revealed and addressed properly, will lead to poor survival of the patient.