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Antibody positive Myasthenia Gravis associated with Chiari type I malformation and Thymoma

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Abstract
Myasthenia Gravis is an autoimmune disease that affects neuromuscular junction. It usually presents with weakness of proximal muscles and has predilection for extraocular and bulbar muscles. Chiari I malformation can sometimes mimicsero negative myasthenia gravis. But here we present a case with an unusual association with both Chiari malformation and antibody positive myasthenia gravis occurring in the same patient. The patient also had cervical spondylosis and thymoma. Myasthenia gravis was serologically proven and Magnetic resonance imaging confirmed syringomyelia and ectopic cerebellar tonsils. Such an association has not so far been reported in literature.
Keywords: *Myasthenia gravis, Chiari malformation, Syringomyelia.*

Case Report

This is the case of a 51 years old gentleman working as a carpenter hailing from Gudalloor, Tamil Nadu, India. He presented with a history of drooping of both eyelids, right more than left for one week associated with diplopia. He also noticed difficulty in lifting his arms above his head for 5 days associated with generalized tiredness. Two days later patient noticed slurring of speech and by the next day patient also developed nasal regurgitation of food. This is when he consulted in the nearby hospital for medical help. The patient attended the casualty of Government Medical College after referral from the local hospital. There was fluctuation of the symptoms during the day and there was slight improvement after rest. There were no new sensory deficits and there were no bowel or bladder symptoms. There was no fever, headache or vomiting and there were no complaints of any loss of weight or appetite. The patient had been on regular follow up from the Department of Neurosurgery of Medical College Calicut for complaints of neck pain radiating to right arm that started about one year prior. This was also associated with loss of pain and temperature

sensations over a localized area over the dorsum of right hand. He was diagnosed to have syringomyelia and cerebellar tonsillarectopia from neurosurgery department after imaging studies. Since then he is on symptomatic treatment and follow up from neurosurgery. He was on Pregabalin and vitamin supplements. He had no history of hypertension, tuberculosis, diabetes, malignancy or coronary artery disease in the past.

Examination

On examination in the casualty, he was moderately built and nourished. There was no pallor, clubbing, lymph node enlargement or pedal edema. Blood pressure was 110/70 mm of Hg and pulse rate was 78/minute. On nervous system examination, his higher functions were normal. He had prominent asymmetric ptosis involving the right eye more than the left. The pupils were bilaterally symmetrical, mid dilated and reacting equally to light and accommodation. There was restriction in left eye abduction. There was no sensory loss over the face but muscles of mastication were weak. The corneal and conjunctival reflexes were normal. Jaw jerk was absent. Nasolabial folds were symmetric on both sides but blowing out cheeks against resistance was weak bilaterally. There was palatal weakness of lower motor neuron type on both sides and gag reflex was absent. Shrugging of shoulders against resistance was weak. There was no obvious weakness of tongue muscles and there was no deviation of tongue on protrusion. On motor system examination, there was wasting of small muscles of hand on both sides and slight hypotonia in the upper limbs. Lower limb tone was normal. Movements at the shoulder joint had Grade 3 power while elbow and wrist power was grade 5. Hand grip was normal on both sides. Lower limb power was reduced at the hip joint (grade 4) while rest of the limb had grade 5 power. Deep tendon reflexes were brisk in the lower limb while sluggish in the upper limb. Plantar reflex was bilateral flexor. Sensory system examination showed dissociated sensory loss over the dorsum of right hand along C7 C8 dermatome levels with preserved touch and vibration sense wand absent pain and temperature. Cerebellar signs were absent and gait was normal. Skull and spine was normal. Considering the possibility of myasthenia we also performed ice pack test(ice on eyes test) and forward arm abduction test, and sustained up gaze test all of which were positive.

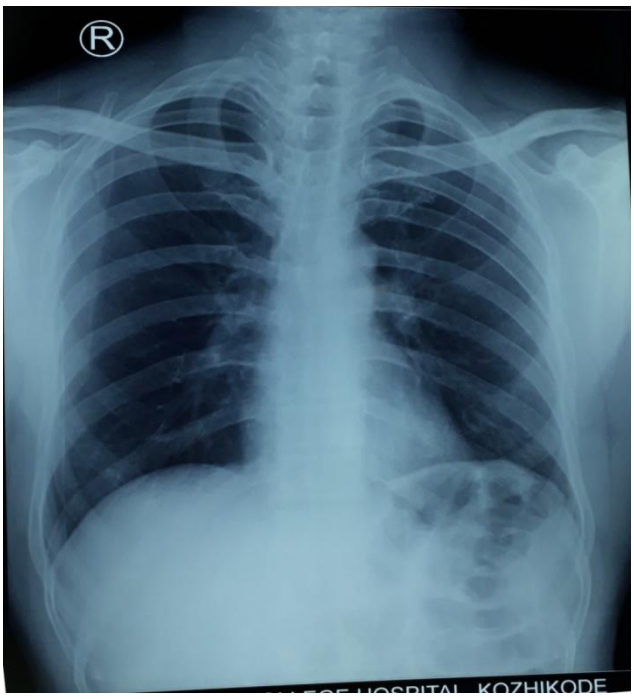
Working Diagnosis

With the fluctuating nature of ptosis and bilateral multiple cranial nerve involvement, Myasthenia gravis was considered as the first possibility. But the background history of syringomyelia posed a diagnostic confusion as to whether the current episode was an expansion of syrinx involving brainstem structures.

Initial Investigations

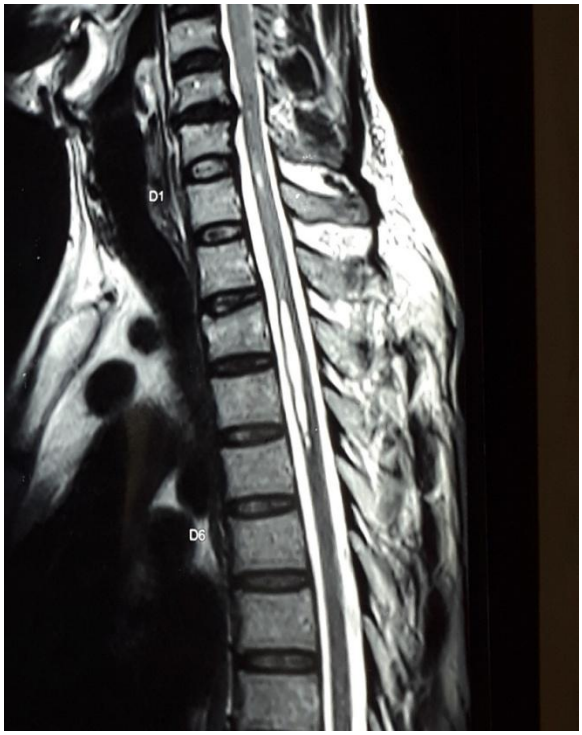
Total Count	12,700/mm3
Hemoglobin	16.2 gm%
Platelet Count	3.46 Lakhs /mm3
Random Blood Sugar	112 mg%
Blood Urea/Creatinine	32/1.1
Serum Sodium/Potassium	137/4.4
Liver function test	
Bilirubin direct/Indirect	1.2/0.3
Total Protein/Albumin	7/4.3
SGOT/SGPT	40/33
ALP	204
ESR	11 at 1 hour

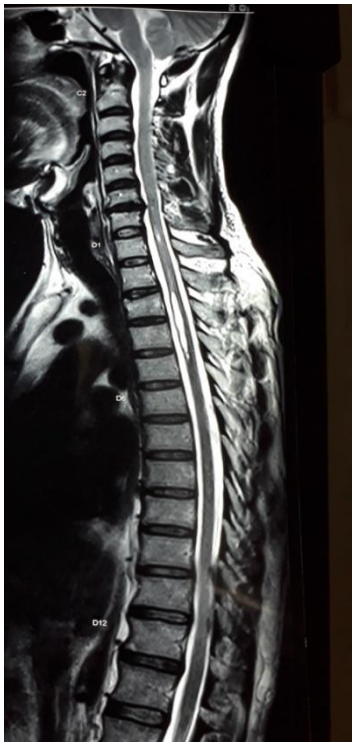
Chest Xray PA view



Magnetic resonance imaging 2017

- Low lying tonsils of cerebellum with syrinx involving dorsal cord-T1-T4 levels -3.9cm
- Disc desiccation, right posterolateral disc bulge causing indentation of exiting nerve roots on right side, thecal sac indentation at C6/C7





Further Investigations and Management

With a clinical diagnosis of Myasthenia Gravis and with impending respiratory failure in view of rapidly evolving bulbar symptoms, we started the patient on pyridostigmine 30 mg from the casualty. Meanwhile we got a repeat MRI to look for syrinx expansion. The repeat MRI showed syrinx at C7/T1 and T3/T5 levels along with widespread degenerative changes involving cervical and thoracic vertebrae.

After the initial dose of pyridostigmine, the patient had significant clinical improvement and the nasal regurgitation while feeding disappeared completely. This further strengthened our clinical suspicion. We also sent for an Acetylcholine receptor (AchR) antibody and did repetitive nerve stimulation test. Only a limited repetitive nerve stimulation study(RNS) was possible as the patient's bulbar symptoms recurred while tapering pyridostigmine before conducting RNS. The RNS study showed no decremental response. The AchR antibody result came to be positive with a titre well above the cut off thus confirming the diagnosis. Chest X ray was apparently normal but because there is a strong association of myasthenia gravis with thymic abnormalities, a CECT thorax was done to look for the same. The CECT thorax showed anterior mediastinal mass measuring 2.6 x 2.8 x 3cm suggestive of thymoma.

Discussion

Chiari malformations are structural defects which involves herniation of brain matter through the foramen magnum. It is classified into four types depending on the extent of herniation and other associated defects. The type I Chiari malformation involves herniation of cerebellar tonsils through the foramen magnum and is commonly associated with syringomyelia. Syringomyelia is a structural deformity of the spinal cord which causes formation of a fluid filled cavity (syrinx) within the spinal cord. The syrinx may expand causing various manifestations. The syrinx usually involves the cervical spinal cord may cause dissociated sensory loss (absent pain and temperature with

preserved touch and vibration sense). Connective tissue disorders, Ehlers Danlos syndrome, tethered cord syndrome, hydrocephalus, Marfan's syndrome have been described in association with Chiari malformation.

Myasthenia gravis is an autoimmune neuromuscular junction disorder that presents with proximal muscle weakness and fatiguable cranial nerve palsies. Antibodies implicated in this disorder are anti AChR antibody, anti-Musk antibody and anti lpr4 and agrin in a few cases. The anti AchR antibody is about 85% sensitive and highly specific for myasthenia. Drugs like D penicillamine are known to cause myasthenia like syndrome but these are readily reversible after the discontinuation of the drug. Many other drugs like antibiotics anti malarials and many other classes of drugs are known to worsen symptoms in known myasthenia patients[(1)]. A number of conditions can mimic myasthenia gravis and pose diagnostic dilemma. Chiari I malformation has been described as one such mimic[(2)]. The study by Muthuswamy et al describes a case report in which Chiari I malformation was initially confused with myasthenia but later was proven with magnetic resonance imaging and antibody tests to be a case of pure Chiari I malformation alone[(2)]. Some other studies describe the diagnostic challenges in a cases of myasthenia superimposed patients with traumatic spinal cord injuries[(3,4)]. A study by Sumitha etal describes a case report of a patient traumatic tetraplegia and post traumatic syrinx who later developed ocular myasthenia[(5)]. But here the disease was antibody negative.

Loeys Dietz syndrome is a syndromic association in which Chiari malformation and thymoma can co exist along with other defects[(6)]. Other than this we could not find any case studies associating Chiari malformation with thymoma and antibody positive myasthenia gravis. Our case report describes a patient with symptomatic syringomyelia who later developed myasthenia gravis. Whether syrinx development or expansion exposes body to yet to be described auto antigens that may have triggered the auto antibody production remains elusive. Further such studies may validate this association.

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