

Myasthenia gravis as a presenting feature in a patient with SCLC: A case report

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Abstract:

Small cell lung cancer (SCLC) is the most frequent cancer histology associated with paraneoplastic syndromes. These syndromes are typically caused by ectopic hormone production or immune-mediated tissue destruction caused by neural antigen expression from cancer cells. Lambert-Eaton myasthenic syndrome is well known to be a classical paraneoplastic syndrome of small cell lung carcinoma (SCLC). Only a few cases of myasthenia gravis (MG) and SCLC were previously reported. The causal association between lung cancer and non-thymomatous myasthenia gravis has not been clarified yet. To date, there has been no evidence supporting the speculation that association of myasthenia gravis with lung cancer might be one of the phenotypes of paraneoplastic syndrome. We present a case of a 47-year-old male ex-smoker with SCLC associated with myasthenia gravis evidenced by the clinical findings of ptosis, dysphagia, proximal weakness, and positive repetitive nerve stimulation (RNS) test.

Abbreviation: MG(myasthenia gravis), SCLC(Small cell lung cancer), RNS (repetitive nerve stimulation), NMJ (neuromuscular junction), LEMS(Lambert-Eaton myasthenic syndrome). (LEMS),

Introduction:

Myasthenia gravis is an autoimmune neuromuscular disease caused by autoantibodies to postsynaptic acetylcholine receptors, blocking their attachment at the postsynaptic junction. This results in a lack of the excitatory effects of acetylcholine at the postsynaptic nicotinic receptors. MG is considered as a paraneoplastic syndrome associated with thymoma in 15% of MG patients. Extrathymic malignancies have been also reported to happen simultaneously with MG¹⁻⁵. Here we reported this case of lung cancer presenting with postsynaptic NMJ disorder (MG).

Case Report:

A 47 years old diabetic, hypertensive, ex-smoker gentleman got admitted under Neurology Unit II with the complains of progressive weakness of both upper and lower limbs for one month and difficulty in swallowing of liquid food for ten days. He also

gave history of weight loss in past six months but had no change in bowel and bladder functions, muscle twitching and gave no preceding history of anorexia, fever, cough or hemoptysis.

On examination, the patient was ill looking with below average body built. His vitals signs were normal. A hard, non tender, immobile swelling was noted over the sternum. On neurological examination, he had dysarthria, nasal intonation, ptosis on right side, left facial weakness, absent gag reflex and palatal palsy. Muscle power was 4/5, reflexes were normal and planters were bilaterally flexor. He had diminished ability and difficulty to sustain upward gaze for greater than 20 seconds. The patient was unable to maintain a sustained hold against gravity of the upper extremities while holding the arm in an outstretched position (Fig-1).

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Fig-1: Pictorial profile of patient

Respiratory system examination revealed diminished breath sound and dull percussion note over left lower lung field. All other systemic examination were normal.

His Hb% was 12.9 gm/dl, Total and differential white cell count was normal, Platelet count 2,34,000/cumm, ESR- 40 mm in 1st hr. His fasting Blood Sugar was 6.1 mmol/l and after breakfast was 9.7 mmol/l, HbA1C- 6.1%. Routine biochemical tests including renal function, liver function, electrolytes were normal. ECG was normal. Chest XR revealed opacities occupying left lung field with collapse of left lower lobe as evidenced by elevation of left hemi diaphragm (Fig-2).



Fig-2: CXR PA showing opacities occupying left lung field with collapse of left lower lobe

No abnormality was detected in MRI of brain as well as MRI of cervical spine.

We performed standard repetitive nerve stimulation (RNS) test, which is one of the most sensitive diagnostic tests in patients with NMJ disorders, to evaluate patient's muscle weakness. We first performed nerve conduction study (NCS) in upper and lower limbs that were normal in distal latency, velocity and amplitude. Repetitive nerve stimulation (RNS) study of facial and ulnar nerve showed significant decremental response from 6th onward; thus suggesting neuromuscular junction disorder (Fig-3). After these procedures, needle electromyography was done in upper and lower limb muscles; that was normal in every parameter.

AChR-ab or Voltage gated calcium channel antibody was not tested. To evaluate the findings in the chest x-ray and to search for the presence of thymoma, chest CT scan with contrast was done. No evidence of thymoma was noticed.

CT scan of chest revealed a broad non-enhancing based soft tissue mass suggestive of consolidation (?Primary) with pleural base in left para vertebral, left anterior chest wall, anterior mediastinum, extending up to chest wall in left para sternal region and right para tracheal lymphadenopathy (Fig-4).

FNAC from subcutaneous nodule over sternum was done by orthopedic surgeons. Smear shows

anaplastic cells with scanty cytoplasm round to oval hyperchromatic nuclei with coarse chromatin and inconspicuous nucleoli. These cells are arranged in clusters, rosettes and singly; compatible with metastatic small cell carcinoma of lung and histopathology report was positive for malignant cells; compatible with metastatic small cell carcinoma of lung (Fig-5).

Specialist consultation was taken from oncologist, and a CT guided FNAC from lung lesion was done, which was positive for malignancy suggestive of SCLC.

So, the patient was finally diagnosed as a case of Metastatic small cell carcinoma of lung with concurrent Myasthenia Gravis and DM, HTN, CAD (S/P PCI to LCX)

For his treatment he received Pyridostigmine 30mg 8 hourly, dietary adjustment to control diabetes, Aspirin (75 mg) OD, Bisoprolol (5mg) OD, Losartan potassium (25 mg) OD. Chemotherapy combined with thoracic radiation therapy (TRT) was his next treatment plan. Unfortunately the patient died 10 days later before therapy could be started.

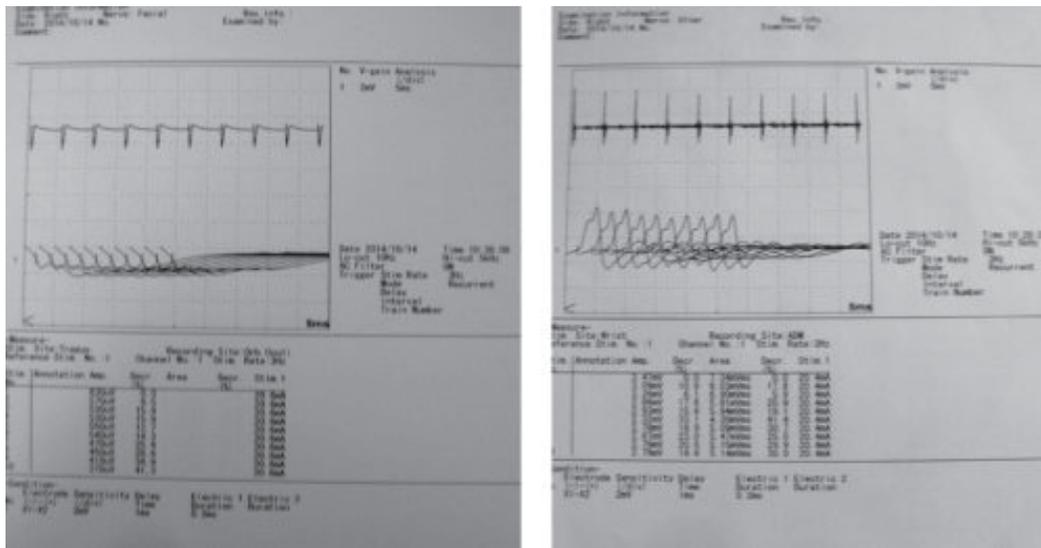


Fig-3: Repetitive nerve stimulation (RNS) study data of facial and ulnar in reported patient.

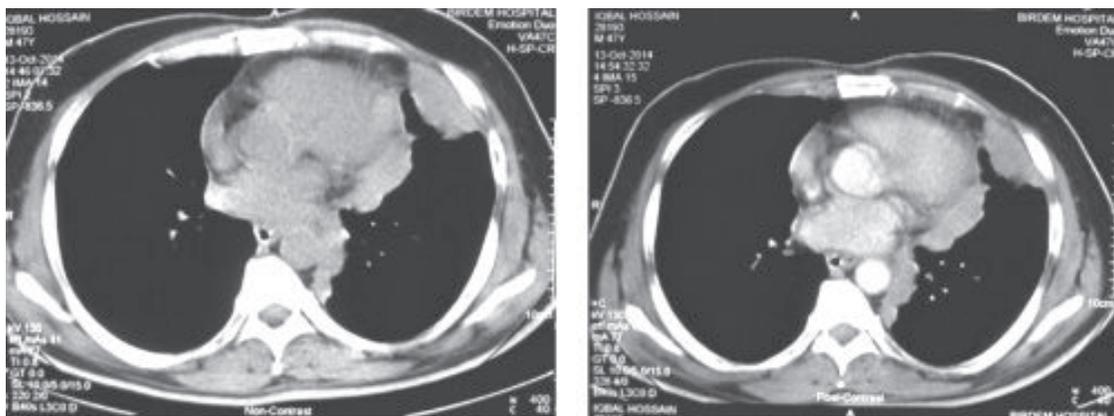


Fig-4: CT scan of chest revealed a broad non-enhancing based soft tissue mass and right para tracheal lymphadenopathy

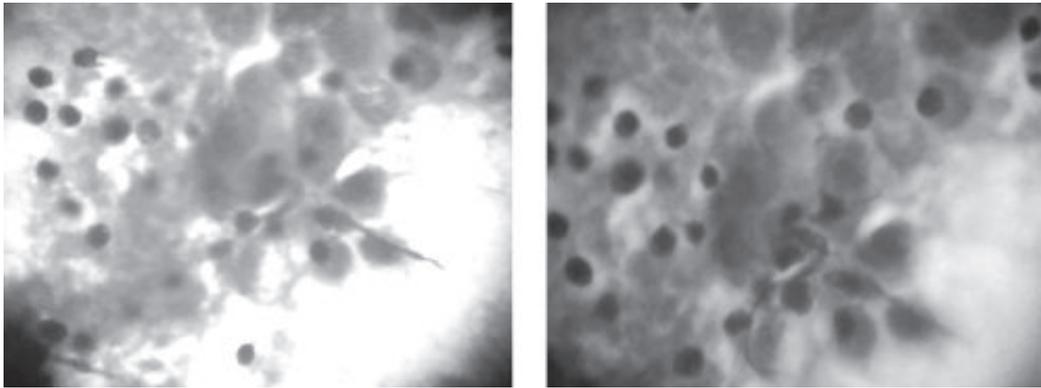


Fig.-5: Smear showed anaplastic cells compatible with metastatic small cell carcinoma of lung

Discussion:

Paraneoplastic syndromes are common findings in lung cancer. They often are incidental

findings serving as a harbinger to the underlying disease. They comprise syndromes involving the neuromuscular junction, vascular, hematologic, and metabolic syndromes as well as connective tissue and skeletal tissue disorders⁶. Paraneoplastic disorders are diagnosed in up to 15% of patients with the highest incidence occurring in NSCLC. Neurological paraneoplastic syndromes have an incidence of 0.01% of cancer patients, often imposing a burden on the patient's ability to carry out their activities of daily living⁷. These neurological syndromes comprise syndromes such as Lambert-Eaton myasthenic syndrome (LEMS), limbic encephalopathy, polyneuropathy, cerebellar degeneration, opsoclonus-myoclonus, and autonomic neuropathy^{6,7}.

Traditionally myasthenia gravis has been associated with several autoimmune diseases including lupus erythematosus, rheumatoid arthritis, diabetes mellitus type 1, Hashimoto's thyroiditis, grave's disease, and part of the paraneoplastic spectrum in thymic diseases such as thymoma⁸.

The correlation between myasthenia gravis and primary lung carcinomas has not been established, as has clearly been defined for Lambert-Eaton syndrome and small cell carcinoma of the lung. There are few reports on primary lung carcinomas which complicate MG, in the medical literature⁹⁻¹⁴.

According to literature review, there are two types of association between lung cancer and MG. The more common is the occurrence of lung cancer in MG patients after many years of treatment that can be a coincidental finding⁹⁻¹⁷. Another type is presentation of cancer simultaneously with MG, which is a rarer report¹⁷⁻¹⁹.

Only a few cases showing combined MG and SCLC features have been reported^{20,21}. They were male and aged 49 to 56. Three cases were seronegative. In two cases, SCLC was found at the time when the diagnosis of MG was made. In Myoshi's case, SCLC was found 18 months after the diagnosis of MG. Three cases had classical oculo-proximal muscle weakness of MG.²¹ One case had bulbar weakness. One case presented with MG crisis²².

Anti-acetylcholine receptor antibodies (Anti-AChR abs) are the causative agents in myasthenia gravis²³. These antibodies affect neuromuscular transmission by functional impairment of the AChR and accelerated degradation and complement activation at the AChR, ultimately leading to the loss of neurotransmission. 20% of these individuals, however, are referred to as seronegative patients. These individuals do not possess the classic anti-AChR abs rather they possess Anti-MuSK abs, an antibody towards argin/MuSK signaling pathway responsible for the functional maintenance of the postsynaptic neuromuscular junction²⁴.

The standard diagnosis of myasthenia gravis relies on the reliable demonstration of anti-AChR abs or anti-MuSK abs; however, these may not always be

available. Electrophysiologic testing through repetitive nerve stimulation may be used alternatively to detect a neuromuscular transmission defect (sensitivity 95–99%). In 1992, Chini et al. demonstrated the potential for small cell lung carcinoma, non-small lung carcinoma, and neuroblastomas to express the $\alpha 3$ subunit nAChR²⁵. They further established the cross reactivity of autoantibodies against $\alpha 3$ -nAChR against the $\alpha 1$ nAChR²⁵⁻²⁷. In our case, considering the diagnosis of SCLC and cost of testing for anti-ACR abs or anti-MuSK abs, these tests were not done.

In conclusion, this case was a typical MG but his symptoms were the only clinical presentation of his underlying lung cancer; it means that MG can be a paraneoplastic syndrome, such as Lambert-Eaton myasthenic syndrome.

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