Paraneoplastic Inverse Myasthenic Syndrome as a Presentation of Bronchogenic Carcinoma

GS Chowdhary¹, Malav Jhala²

Abstract
Tumours may produce growth factors and cytokines responsible for signs and symptoms distant to the primary or metastatic site. This may be the first sign of a malignancy and its recognition may be critical for early cancer detection. Moreover, proper diagnosis spares the patient of extensive and expensive search for an alternate cause of the neurological dysfunction. In neurological paraneoplastic syndromes like Lambert Eaton Myasthenic syndrome associated with small cell lung cancer, evidence of autoimmunity against presynaptic neuro-muscular junction by anti voltage gated calcium channel anti bodies is well documented. 60% of patients with LEMS are associated with an underlying cancer, usually SCLC. We report a 49 year old male, with over thirty pack years of smoking, who presented with dysautonomia, constitutional symptoms and weakness of all four limbs. Investigations confirmed axonal motor neuropathy with limited stage SCLC with fibro nodular lesions right upper lobe and mediastinal lymphadenopathy. He improved dramatically following chemotherapy and radiotherapy.

Introduction
The proportion of lung cancers presenting as small cell histology are between 10-20 % in men and 10-30 % in women, the predominant risk factor being tobacco exposure in over 90% of cases diagnosed.¹² Usually SCLC presents with respiratory symptoms, only a few patients are asymptomatic at diagnosis. The Paraneoplastic spectrum of SCLC differs from that of NSCLC. Neurological Paraneoplastic syndromes include sensory, sensorimotor and autoimmune neuropathies and encephalomyelitis.¹³ Symptoms may precede the diagnosis by many months and are often the presenting complaint. These neurological symptoms are unrelated to tumour bulk and may not improve despite anti-cancer therapies. LEMS is manifested by proximal muscle weakness which improves with continued use, hypo reflexia and dysautonomia.⁶⁻⁷ This article reports a case of a patient who presented with dysautonomia followed by proximal muscle weakness more than six months ago. He was subsequently diagnosed to have SCLC and improved following Cisplatin and Etopside based chemotherapy.

Case Report
A 49 year old male, heavy smoker, presented in Oct 2011 with 3 months history of dryness of mouth and eyes. Soon he developed weakness of all four limbs and anorexia. He had lost 10 kgs weight over the preceding 6 months. He also had scanty productive cough off and on. The patient’s height was 171 cm and he weighed 62 kg. General examination revealed body temperature of 98.4°F, Pulse 88/min and BP 130/90 mm Hg. He had xerostomia and xerophthalmia. There was no pallor, peripheral adenopathy, clubbing or xerostomia. There was no pallor, peripheral adenopathy, clubbing or edema, nor any features of SVC syndrome. Neurologically he had normal higher mental functions and no cranial nerve deficit. He had proximal weakness of both upper and lower limbs with G:IV/V power, hand grip of 70-80% and flexor plantar response bilaterally. He had hypeorelexia in all four limbs but there was no sensory loss. Other systemic examination was unremarkable.

Investigations
Baseline haemogram revealed normal CBC, ESR, RFT, LFT, Blood Sugars and ECG. Chest X-ray showed ill defined homogenous opacity in right mid zone with superior mediastinal widening suggestive of paratracheal adenopathy. USG Abdomen-Normal. Neostigmine test was negative. Electrodiagnostic studies confirmed low amplitude muscle action potential on single stimulus of a nerve (in contrast to myasthenia gravis where it is normal) and incremental response on fast rates of stimulation and with strong voluntary contraction. Single fibre EMG showed a jitter response which is classic of LEMS. Upper GI Endoscopy revealed antral gastritis and colonoscopy seen upto terminal ileum was normal. Biopsy revealed non specific inflammation.

CECT Thorax showed fibro nodular lesions in right upper lobe with fluid in the horizontal fissure with mediastinal nodes (pretracheal, para tracheal, precarinal, subcarinal, right hilar) and SVC thrombosis. CECT Abdomen was normal. Nerve conduction studies showed decreased amplitude in motor nerves with normal sensory conduction suggestive of axonal neuropathy. Electromyography was normal. Whole Body FDG PET Scan revealed FDG-avid Mediastinal lymph nodes in pretracheal, prevascular, left paratrachel, Right paratracheal (SUV 6.9) and multiple discrete non-FDG avid bilateral axillary nodes. MRI Brain was normal. Bone scan was normal.

Mediastinoscopy was done and biopsy of mediastinal nodes confirmed Metastatic small cell carcinoma. Immunohistochemistry was immunoreactive for keratin and epithelial membrane antigen.

The patient received 6 cycles of chemotherapy (IV Etoposide 100 mg/m² D1 to D3 + IV Cisplatin 80 mg/m² D1 only) along with 4500 cGy thoracic radiotherapy and later prophylactic cranial irradiation. The patient received oral prednisone 1 mg per kg along with oral pyridostigmine 60 mg, 3 times a day. He also received capsule Fluoxetine 20 mg per day for depression.

¹Head, Dept. of Oncology, ²Resident, Dept. of Medicine, INHS Asvini, Mumbai, Maharashtra
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depression. The patient responded well and is symptom free on follow up. He regained normal power in all limbs but had persistence of xerophthalmia and xerostomia. He is independent for activities of daily living.

Discussion

SCLC presenting with neurological paraneoplastic syndromes i.e. with remote effects of tumour products is a rare manifestation. 5-15% of lung cancer patients are identified when they are asymptomatic. Most however present with loco-regional obstructive respiratory symptoms or site specific metastatic symptoms or constitutional symptoms. A small percentage may present with Paraneoplastic manifestations. In many cases their pathophysiology is related to tumour protein or cytokine release with biological effects. Neurological paraneoplastic syndromes portend a poor prognosis to lung cancer patients. Anti-VGCC antibodies directed against pre-synaptic neuro muscular junction in LEMS is responsible for inverse Myasthenic syndrome manifesting with dysautonomia and proximal muscle weakness, as in our patient.

Definitive therapy for SCLC limited stage usually includes 6 cycles of etoposide with Cisplatin for every three weekly. 40 Gy of radiotherapy to the chest wall mass is added for symptomatic or progressive regions. If neuro imaging does not reveal brain metastasis, PCI may be added with the aim of lengthening survival, since brain metastasis are found in 65% of patients at post mortem. PCI is recommended 2 weeks after completion of all chemotherapy to complete and very good partial responders. The role of surgery in limited disease SCLC is reserved for select patients, e.g. with a solitary pulmonary nodule.

Conclusion

This case highlights the rare presentation as dysautonomia and proximal weakness in a case of paraneoplastic inverse myaesthenic syndrome.

References