Case report

Amyotrophic lateral sclerosis presenting with orthopnea in a patient with COPD and obstructive sleep apnea

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Abstract
Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease (MND) is a relentlessly progressive neurological disorder causing peripheral muscular weakness and resultant respiratory failure. In this article, we report a case of ALS with chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) with orthopnea as initial symptoms.

Key words: Amyotrophic lateral sclerosis, motor neuron disease, orthopnea, respiratory failure, obstructive sleep apnea, hamartoma

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative condition first described in the nineteenth century. It is also known as motor neuron disease (MND) in view of its propensity to cause upper and lower motor neuron involvement, and acquired the appellation "Lou Gehrig's disease" after a famous baseball player who was diagnosed with the disease¹. The disease has a unique clinical picture where signs of lower motor neuron involvement (such as muscle weakness, atrophy and fasciculations) coexist with signs of upper motor neuron involvement (such as hypertonia and hyperreflexia). Usually, respiratory muscle weakness develops after limb muscles and bulbar involvement has progressed for several months or years in a predictable pattern²; rarely though, respiratory failure can be the presenting problem. Respiratory muscle weakness with its attendant complications is usually a late occurrence, but can rarely manifest at presentation³.

Case report

A 54 year old male school teacher presented with a history of progressive orthopnea, chronic cough and exertional dyspnea since twelve months. He reported daytime somnolence and also had a history of snoring confirmed by his spouse. He was an ex-smoker, with a history of 10 cigarettes per day. He had visited several health facilities, principally for his orthopnea (he had taken to sleeping in a reclined position), and was on bronchodilator drugs with only partial relief. No history of allergy to dust, chalk-powder, etc.

On examination, the patient was ectomesomorphic. His jugular venous pressure was elevated, but there was no pedal edema. Cardio-respiratory examination was normal. The patient scored high on the Epworth score, raising a possibility of an associated obstructive sleep apnea.
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The ECG was normal and an echocardiogram showed normal left ventricular function. Chest radiography was unremarkable except for a calcific nodule in the mid zone of the right lung (Fig 1). Spirometry showed a moderate restrictive pattern, but no significant associated obstructive defect. Arterial blood gases revealed chronic type 2 respiratory failure with bicarbonate retention. Though a computed tomographic pulmonary angiography (CTPA) on a dual-source 64-slice scanner was found to be of low probability for pulmonary thromboembolism, it revealed evidence of pulmonary artery hypertension (cor pulmonale) (Fig 2). A lesion compatible with a hamartoma was observed in the right middle lobe (Fig 3) with a characteristic appearance of ‘popcorn’ calcification.

By the time the patient was reviewed in our out-patient department with the reports of the above investigations, his breathlessness and wheezing had worsened and cough became productive with colored sputum. At this stage he was admitted for treatment of acute exacerbation of chronic bronchitis (AECB) and for further investigation.

When he was made to lie in supine position (a position that he had consciously avoided during the last several months) and he became perceptibly breathless, with diminished abdominal-diaphragmatic movements. There was no history of diplopia or weakness in his upper arms but mild difficulty in rising from a low chair. A neurologist was consulted to rule out a neuromuscular process.

A detailed neurological history revealed that the patient was having fasciculations in bilateral upper and lower limbs muscles for several months. There was wasting of small muscles of both his hands and profound fasciculations were evident in both his lower and upper limbs. Muscle tone in the lower limbs was increased, motor weakness (grade 4-4+ power in both the limbs, both proximal as well as distal) and an extensor plantar reflex bilaterally were also evident. He was also noted to have mild bifacial weakness along with sluggish gag reflex. However tongue movements were normal and there were no abnormal skin changes to suggest heavy metal toxicity. On the next day, the patient became febrile and was placed on non-invasive ventilatory support for his increased work of breathing and respiratory acidosis. Investigations for serum anti acetylcholine receptor antibodies and anti-nuclear antibodies (ANA) were found to
be negative. Creatine kinase level was slightly elevated (194 U/L) but serum electrolytes, serum ionized calcium and magnesium were normal. A heavy-metal screen was performed which was normal.

The patient’s condition gradually improved and was subsequently discharged on non-invasive mask ventilation.

At out-patient follow up, an electro-neuro-myography (ENMG) and an attended home polysomnography (PSG) with EEG monitoring was performed. PSG revealed significant episodes of hypopnea, obstructive apnea and a few central apneas as well. The nerve conduction study revealed reduction of compound motor action potential amplitudes but no conduction block, while sensory nerve conduction studies were within normal limits.

The needle electromyography of the biceps, the first dorsal interossei, abductor pollicis brevis, quadriceps, tibialis anterior and the extensor digitorum brevis muscles showed spontaneous activity in the form of fibrillations and fasciculations with large amplitude and wide duration motor unit action potentials and reduced recruitment. The repetitive nerve stimulation test of the nasalis, trapezius and abductor digiti minimi muscles was within normal limits. The ENMG findings were suggestive of an acute and chronic denervating neurogenic disorder with re-innervation. A diagnosis of MND-ALS was made, presenting as chronic type 2 respiratory failure.

**Discussion**

ALS most commonly presents with asymmetric limb weakness in about 80% of the cases. ‘Dyspnea-onset ALS’ is a rare entity, occurring in about 1-3% of ALS patients.\(^3\) Late in the course of MND, respiratory failure often develops due to respiratory muscle weakness. Orthopnea is reflective of significant weakness of diaphragmatic muscles. Sleep disturbances are well recognized in ALS\(^6,7\) due to decrease in upper airway tone bilateral weakness of the diaphragmatic and intercostal muscles consequent upon the involvement of the motor neurons subserving the bulbar, phrenic and intercostal muscles. The degeneration of central respiratory neurons can lead to apneas which can be either central or obstructive causing sleep disruption.

In this case, chronic type 2 respiratory failure was confirmed by arterial blood gases drawn prior to his AECB. In view of his significant daytime somnolence, a sleep study was performed and OSA was confirmed. Unlike the usual profile of OSA, this patient was not obese suggesting a causal role of ALS in the genesis of his sleep apnea. It is probable that sleep apnea was exacerbated in the supine position and contributed to some extent to the orthopnea. Also the patient had COPD and his main symptom, orthopnea, was very likely exacerbated by the disordered diaphragmatic mechanics due to COPD superimposed on his neuromuscular process. A remarkable finding of this case was the complete lack of perception of any neurological symptoms in spite of the presence of well-established ALS.

Another intriguing finding in this case was ‘hamartoma’. Due consideration was given to the fact that this lesion could in fact be malignant, with the neurologic features representing non-metastatic manifestations of lung cancer. The appearance of the ‘hamartoma’ on CT when classical is considered specific enough to obviate the need for further diagnostic investigation. The pattern of neurological manifestation in this patient, i.e., features of motor neuron involvement is also not the usual one seen in the non-metastatic neurological manifestation of lung malignancy\(^8\). Therefore, a trans-thoracic cutting needle biopsy was withheld for the time taking into account the fact that a fair distance of lung parenchyma would need to be traversed by the needle while accessing the lesion in a breathless patient with COPD and borderline respiratory reserve. Yet, we do believe that this lesion merits follow up over a period of at least a year or two.

**Conclusion**

Orthopnea as the leading symptom is a rare presenting complaint in ALS, as is the failure by the patient to perceive peripheral muscle weakness in well-established ALS. Associated COPD and sleep apnea can confound the presentation of ALS and may be important in exacerbating orthopnea in such condition.

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**Acknowledgment:** None

**References**