Case Reports in Neurology

Case Rep Neurol 2014;6:213–216

DOI: 10.1159/000366191
Published online: August 14, 2014

1662–680X/14/0062–0213$39.50/0
www.karger.com/crn

Amyotrophic Lateral Sclerosis Presenting Respiratory Failure as the Sole Initial Manifestation

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Key Words
Amyotrophic lateral sclerosis · Respiratory failure · Chronic obstructive pulmonary disease

Abstract
It is rare that amyotrophic lateral sclerosis (ALS) presents with respiratory failure as the sole initial manifestation. A 72-year-old man with mild chronic obstructive pulmonary disease developed exertional dyspnea for 13 months. He then progressed to limb weakness that led to the diagnosis of ALS. Although rare, ALS can present with respiratory failure as the sole initial manifestation more than 1 year prior to limb weakness. © 2014 S. Karger AG, Basel

Introduction

Respiratory failure is common in the advanced stages of amyotrophic lateral sclerosis (ALS) and is the major cause of morbidity. In contrast, it is rare that ALS presents with respiratory failure as the sole initial manifestation [1–8]. The majority of patients in previous reports are men, and the interval between respiratory failure and limb weakness is between 0 and 3 months. We here present the case of a male patient with ALS who had respiratory failure 13 months prior to the appearance of limb weakness.

Case Report

A 72-year-old male gradually developed exertional dyspnea 13 months before his admission to our hospital. He had a history of a lacunar stroke (at the thalamus with mild right

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leg weakness and numbness without difficulty, which remained unchanged before his admission). He had an occasional cough because of his mild chronic obstructive pulmonary disease (COPD), but he never had dyspnea before. He was first suspected of suffering from heart failure, but his chest X-ray and serum brain natriuretic peptide level were normal. The patient was then suspected to have a worsening of his COPD, and medication for COPD was started in the respiratory disease department, without any benefits. When he was admitted to the neurology department 13 months after symptom onset, he had lost 10 kg. He had no atrophy or fasciculation of the tongue and had no dysarthria or dysphagia but a pre-existing mild right leg weakness. His pinprick sensation had mildly decreased in the right leg. However, on examination, he had a mild fasciculation in his shoulder, the pectoralis major, his arm and his platysma muscles bilaterally. The patient's deep tendon reflexes were exaggerated bilaterally, and his plantar reflexes were extensor. A spirometer showed a normal forced expiratory volume in 1 second of 81.3% (normal >71%), while he had a markedly low percent vital capacity of 41.3% (normal >90%). The blood gas analysis (in room air) showed hypercapnia (pO_2 75.8 mm Hg, pCO_2 54.4 mm Hg), and his chest X-ray indicated bilateral phrenic nerve palsy (fig. 1). Electromyography revealed an acute denervation and fibrillation potentials in the diaphragm, tongue, limbs and paraspinal muscles with almost the same severity. A nerve conduction study showed normal results. All laboratory tests were normal. Brain and cervical MRI revealed an old thalamus stroke on his left side. These findings confirmed the diagnosis of ALS. Three days after his admission, he suddenly felt drowsy, and a second blood gas analysis revealed anoxia and CO_2 narcosis. He was placed on artificial ventilation, which improved his consciousness. The patient was started on non-invasive ventilatory support and was discharged from the hospital.

Discussion

It is rare that ALS presents with respiratory failure as the sole initial manifestation [1–8]. In such cases, patients often visit pulmonary disease departments first and diagnosing ALS is extremely difficult. In the previous reports, the interval between respiratory failure and limb weakness is between 0 and 3 months (table 1). The only exception is case No. 5 by Chen et al. [8] who presented with limb weakness 12 months after respiratory failure. Our patient's clinical manifestation is similar to that of case No. 5 – he also presented with limb weakness 13 months after respiratory failure.

Clinical features of ALS cases who present with respiratory failure as the sole initial manifestation [1–8], including ours, are unique because (1) all patients, except for one case (by Parhad et al. [3]), are men, with the rate being higher than in the total ALS cohort, (2) motor weakness and atrophy following respiratory failure are present in the limbs, which is in contrast to the observation of bulbar palsy often preceding or occurring together with respiratory failure [9], and (3) preceding pulmonary diseases (COPD, pneumothorax, atelectasis, etc.) occurred in half of the patients – a rate which is higher than that in the total ALS population.

Why respiratory failure becomes the sole initial manifestation in these patients remains uncertain. However, it is reported that denervation by electromyography was more severe in the diaphragm than in any other skeletal muscles [7, 8], and, in these patients, a cell loss of the anterior horn was most severe in the cervical spinal cord along the neuraxis [8]. Therefore, in these patients, phrenic anterior horn cells might have been involved early. The Mechanisms accounting for male preponderance remain unsolved. As for the comorbidity of preceding pulmonary diseases and ALS, experimental studies suggest that comorbid muscle

weakness [by orthopedic (limbs), pulmonary (diaphragm) etiologies, etc.] might hasten anterior horn neurodegeneration since fast fatigable motor units are more vulnerable to degenerative disease processes in ALS mice [10].

In conclusion, although rare, ALS can present with respiratory failure as the sole initial manifestation more than 1 year prior to limb weakness.

Acknowledgement

None of the authors received any financial support relevant to this study.

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Table 1. ALS presenting respiratory failure as the sole initial feature

Year	Author	Patient	Age at onset, years	Sex	Comorbid disease	Respiratory failure	Internal between respiratory failure and limb weakness, months	Type of limb weakness	Diagnosis	Management
1957	Miller [1]	case 2	71	M		exertional dyspnea	9? with weight loss	distal limb weakness	ALS, bedside	
1977	Fromm [2]	case 1	68	M		acute respiratory failure	2	distal limb weakness	ALS, pathology	mechanical ventilation
		case 2	69	M	COPD	acute respiratory failure	0	distal limb weakness	ALS, pathology	mechanical ventilation
1978	Parhad [3]	case 2	46	F	COPD	acute respiratory failure	1–2?	distal limb weakness	ALS, bedside	mechanical ventilation
1985	Meyrignac [4]	1	59	M		Exertional, then acute respiratory failure	3?	distal limb weakness	ALS, pathology	mechanical ventilation
1986	Al-Shaikh [5]	1	65	M	pneumo-thorax	sleep apnea, then acute respiratory failure	2	tongue and distal limb weakness	ALS, EMG	mechanical ventilation
1988	Carre [6]	1	67	M	obesity	sleep apnea	3	distal limb weakness	ALS, EMG	tracheostomy, nocturnal ventilatory support
1996	de Carvalho [7]	case 1	51	M		exertional dyspnea	1	distal limb weakness	ALS, EMG	mechanical ventilation
1996	Chen [8]	case 1	69	M	atelec-tasis	exertional dyspnea	0	distal limb weakness	ALS, pathology	mechanical ventilation
		case 5	68	M		exertional dyspnea	12	distal limb weakness	ALS, EMG	mechanical ventilation
		case 7	72	M		exertional dyspnea	2	distal limb weakness	ALS, pathology	mechanical ventilation
2014	present case	1	72	M	COPD	exertional dyspnea	13	distal limb weakness	ALS, EMG	mechanical ventilation

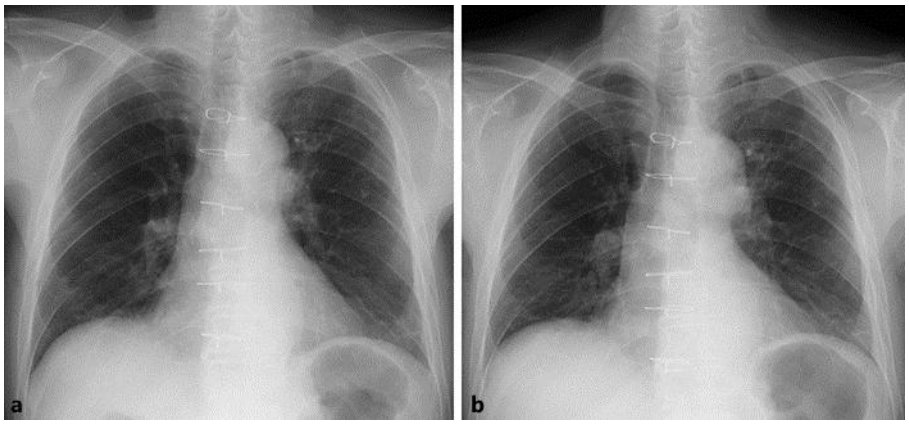

Fig. 1. Plain chest X-rays of the patient. **a** Deep inspiration. **b** Expiration. His chest X-ray showed almost no movement of the diaphragm at deep inspiration and expiration, indicating bilateral phrenic nerve palsy.