

An Unusual Case of Respiratory Failure

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Respiratory failure due to respiratory muscle weakness is usually a feature of advanced motor neuron disease (MND), but it is much less common as a presenting feature and may be overlooked if the axial muscles are selectively affected. A high index of suspicion is required to ensure early intervention with potentially life-saving assisted ventilation. This article reports the case of a man with MND whose initial symptoms were of breathlessness. The evaluation of respiratory failure and its presentation in patients with MND is discussed.

CASE PRESENTATION

Initial Presentation and History

A 59-year-old male construction worker presented with a 6-month history of cough, wheezing, and exertional breathlessness. His exercise tolerance was 100 yards while walking on level ground. His symptoms were associated with mild orthopnea but no paroxysmal nocturnal dyspnea or ankle swelling. Cough was productive of mucoid sputum, but the patient had no history of hemoptysis. He reported daytime somnolence and also admitted to recurrent chest infections, particularly during the winter months.

The patient had a history of recent loss of appetite and weight loss (6 kg). His general practitioner diagnosed his chest symptoms to be from a minor exacerbation of chronic obstructive airway disease and prescribed antibiotics and steroids, which provided some symptomatic improvement. Despite treatment, his symptoms prevented him from working for 2 weeks before the current presentation. He was a current smoker, with a total smoking history of 45 pack-years. His only medication was an albuterol inhaler.

The patient had a history of asthma, which had resolved in childhood by the age of 7 years. His other medical history included a cerebral aneurysm clipped in 1972; pneumonia in 2001, for which he was treated at home for 3 weeks; and type 2 diabetes controlled on diet alone.

Physical Examination

On examination, the patient was plethoric, with central cyanosis but no obesity. Pyrexia and tachypnea

were both absent, and there was no clubbing or lymphadenopathy. Cardiovascular examination was normal and showed no clinical evidence of heart failure. Respiratory system examination was unremarkable except for widespread wheezes bilaterally. Abdominal examination revealed 1 cm of palpable liver. Neurologic examination was normal.

Diagnostic Evaluations

Electrocardiogram showed sinus rhythm with P pulmonale and deep S-waves in leads V₁ through V₄. Chest radiograph was normal. Arterial blood gases showed pH of 7.33, bicarbonate level of 29.3 mEq/L with a base excess of 5.9 mEq/L, PCO₂ of 72 mm Hg, and PO₂ of 46 mm Hg. Hematologic investigations showed polycythemia with a hemoglobin level of 18.8 g/dL and a hematocrit of 54%. Serum creatinine and electrolytes were normal except for an elevated venous bicarbonate level of 43 mEq/L.

At this stage, the provisional diagnosis was type 2 respiratory failure secondary to chronic obstructive pulmonary disease (COPD) with secondary polycythemia. However, pulmonary function tests (Table 1) showed a mild restrictive pattern with normal diffusion and evidence of air trapping. Echocardiogram showed mild left ventricular hypertrophy and right ventricular and right atrial dilatation, with moderate impairment of right ventricular function. The pulmonary arterial pressure was elevated at 37 mm Hg. A ventilation-perfusion scan showed a low probability of pulmonary embolism. A computed tomographic scan of the thorax to investigate the weight loss was normal.

These investigations clearly pointed to an extraparenchymal restrictive defect, and this conclusion led to a reappraisal of the clinical findings. A more detailed neurologic examination revealed normal cranial nerves except for weakness in the sternocleidomastoids bilaterally. The patient had no tongue fasciculations, and facial

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Table 1. Pulmonary Function Test Results in Case Patient

Test	Result
Spirometry	
FEV ₁ (L)	2.42 (74%)
FVC (L)	3.34 (81%)
FEV ₁ /FVC	72.5 (95%)
Static lung volumes	
FRC (L)	4.32 (123%)
TLC (L)	6.07 (89%)
RV (L)	2.69 (115%)
RV/TLC	44.27 (120%)
Diffusion tests	
DlCO (mEq/min/mm Hg)	11.01 (117%)
VA (L)	5.79
KCO* (mEq/min/mm Hg/L)	1.90 (107%)

NOTE: Figures in parentheses indicate percentages predicted.

DlCO = lung carbon monoxide diffusing capacity; FEV₁ = forced expiratory volume in 1 second; FRC = functional residual capacity; FVC = forced vital capacity; KCO = transfer coefficient for carbon monoxide; RV = residual volume; TLC = total lung capacity; VA = alveolar volume.

*Corrected for hemoglobin.

power and jaw jerks were normal. Some fasciculations were found in the pectoralis, triceps, latissimus dorsi, and supraspinatus muscles, with relatively preserved muscle bulk. He exhibited wasting in the intercostal muscles, periscapular area, triceps, and first dorsal interosseous with dorsal guttering. Power in the upper limbs was normal. Reflexes generally were reduced. Coordination and sensations were normal. Lower limb examination was normal, with bilateral flexor plantar response. Investigations to exclude other possible causes of neuropathy, including liver function tests, bone profile, creatine kinase, thyroid function, autoantibodies, VDRL test, and immunoelectrophoresis, were normal or negative. Because there was no clinical suspicion, a heavy-metal screening test was not performed. A cervical spine radiograph was normal; magnetic resonance scanning was not performed because of the absence of long-tract signs.

Testing for muscle weakness revealed a sitting and lying vital capacity of 3.27 L and 2.13 L, respectively. The maximum inspiratory pressure and maximum expiratory pressure measured at the mouth with an occluded mouthpiece were -28 and +60 cm H₂O (best of 3 attempts), respectively.

A diagnosis of MND was made, presenting as chronic type 2 respiratory failure secondary to respiratory

muscle weakness. The diagnosis was confirmed by neurophysiologic studies showing a chronic, slightly active, diffuse neurogenic process involving the intercostal muscles and consistent with an indolent form of anterior horn cell disorder. The patient was placed on non-invasive nasal ventilation, which dramatically improved both his clinical condition and blood gas levels.

DISCUSSION

MND is a group of progressive degenerative disorders affecting the lower motor neurons (anterior horn cells of the spinal cord and their brainstem homologs innervating the bulbar muscles) and the upper motor neurons (motor cortex and descending corticospinal and corticobulbar tracts). MND frequently causes death within 5 years of diagnosis. Most deaths are due to pulmonary complications resulting from respiratory muscle weakness and bulbar involvement.

Respiratory Failure in MND

Respiratory failure often develops late in the course of MND, but respiratory muscle weakness often is present at diagnosis¹ and usually is asymptomatic at this stage.² Rarely, respiratory muscle weakness can be the presenting feature.^{3,4} More often, the course of MND involves insidious development of symptoms, slow deterioration, and eventually respiratory failure.²

Specific symptoms depend on the pattern of respiratory muscle involvement. Diaphragmatic weakness usually causes orthopnea, whereas global respiratory muscle weakness usually causes exertional dyspnea.² Exertional dyspnea can even be the first manifestation of MND, particularly when other significant cardiopulmonary conditions are present.⁵ "Difficulty taking a deep breath" can be a suggestive symptom.⁵ Symptom patterns depend on whether the inspiratory or expiratory muscles are predominantly involved (**Table 2**). (In global weakness of respiratory muscles, there is a combination of symptoms.) Severe dyspnea only when lying flat is a classic sign of bilateral diaphragmatic weakness.⁶ Unilateral diaphragmatic paralysis at presentation also has been reported,⁷ but these patients do not develop respiratory failure.⁸ Some of the symptoms that appear early in the course of MND can be mistakenly attributed to COPD, infection, heart failure, or psychologic causes unless respiratory muscle weakness specifically is sought.

Hypoventilation from intercostal and accessory muscle weakness occurs first during sleep,⁹ and, in many patients, sleep-related hypoventilation occurs before dyspnea and causes daytime somnolence if severe enough.^{7,10} Upper-airway abnormalities also are an occasional feature of MND and can be associated with

obstructive events causing sleep disruption.¹¹ The diagnosis of chronic ventilatory failure usually is suggested by fatigability, lethargy, daytime somnolence, morning headaches, and difficulty concentrating. Other modes of presentation include acute respiratory failure or respiratory arrest^{12–15} or ventilator dependency,¹⁶ and these groups of patients usually have a bilaterally weakened diaphragm or bulbar muscle involvement with secondary pulmonary complications of aspiration and pneumonia.^{17,18}

In this case, the case patient had chronic respiratory failure with symptoms that suggested global weakness of the respiratory muscles, confirmed by respiratory muscle function tests. The absence of upper motor neuron signs pointed toward spinal muscular atrophy rather than amyotrophic lateral sclerosis. He had both inspiratory and expiratory muscle weakness, as shown by reductions in both maximum inspiratory pressure and maximum expiratory pressure, and more than a 30% decrease in the supine vital capacity, suggesting diaphragmatic paralysis.¹⁹ Residual volume was raised, probably because of expiratory muscle weakness.²⁰ Because he was unable to take adequate breaths, the alveoli were insufficiently ventilated and carbon monoxide diffusing capacity of the lung (DLCO) was reduced. However, when DLCO was corrected for lung volume and transfer coefficient for carbon monoxide was calculated, this was increased. Arterial blood gases also demonstrated florid type 2 respiratory failure. In fact, the patient also had right ventricular dysfunction secondary to chronic hypoxemia and polycythemia. It was considered, although not confirmed, that his daytime somnolence was due to nocturnal hypoventilation secondary to the muscle weakness,^{21,22} but because he already had significant daytime hypoxemia, no formal sleep studies or overnight oximetry tests were performed.

Of particular interest in this case were the indolent nature with which MND developed and the pattern of disease, which affected predominantly the intercostal muscles and diaphragm with relative sparing of the limb muscles. As a result, the neurologic signs were subtle and easily overlooked. In addition, paradoxical abdominal movement was absent because the forced vital capacity was not reduced significantly.²⁰ It has been shown that forced vital capacity correlates poorly with respiratory symptoms²⁰; maximum inspiratory pressure and nocturnal oximetry may be more sensitive measures of early respiratory insufficiency.

CONCLUSION

Selective axial and respiratory muscle weakness due to MND should be considered in the differential diagnosis

Table 2. Symptoms of Respiratory Muscle Weakness

Inspiratory muscle and diaphragmatic weakness

Breathlessness on exertion
Orthopnea
Breathlessness on leaning forward
Breathlessness when immersed in water

Expiratory muscle weakness

Difficulty coughing or expectorating
Difficulty clearing secretions

Hypoventilation

Daytime somnolence
Morning headache
Difficulty concentrating
Sleep fragmentation

of patients presenting with unexplained respiratory failure. It is important to diagnose respiratory muscle weakness early in patients with MND. Respiratory muscle weakness diminishes quality of life²³; moreover, the rate of decline in respiratory function may predict survival.¹ Increasing evidence shows that noninvasive ventilation extends life²⁴ and improves quality of life in patients with MND.^{23,25} Noninvasive nasal ventilation dramatically improved the case patient's clinical condition and blood gas levels. **HP**

REFERENCES

- Schiffman PL, Belsh JM. Pulmonary function at diagnosis of amyotrophic lateral sclerosis. Rate of deterioration. *Chest* 1993;103:508–13.
- Mustfa N, Moxham J. Respiratory muscle assessment in motor neurone disease. *QJM* 2001;94:497–502.
- Al-Shaikh B, Kinnear W, Higenbottam TW, et al. Motor neurone disease presenting as respiratory failure. *Br Med J (Clin Res Ed)* 1986;292:1325–6.
- Chen R, Grand'Maison F, Strong MJ, et al. Motor neuron disease presenting as acute respiratory failure: a clinical and pathological study. *J Neurol Neurosurg Psychiatry* 1996;60:455–8.
- Nightingale S, Bates D, Bateman DE, et al. Enigmatic dyspnoea: an unusual presentation of motor-neurone disease. *Lancet* 1982;1:933–5.
- Davison A, Mulvey D. Idiopathic diaphragmatic weakness. *BMJ* 1992;304:492–4.
- Howard RS, Wiles CM, Loh L. Respiratory complications and their management in motor neuron disease. *Brain* 1989;112(Pt 5):1155–70.
- Laroche CM, Carroll N, Moxham J, Green M. Clinical significance of severe isolated diaphragm weakness. *Am Rev Respir Dis* 1988;138:862–6.
- White JE, Drinnam MJ, Smithson AJ, et al. Respiratory

- muscle activity and oxygenation during sleep in patients with muscle weakness. *Eur Respir J* 1995;8:807–14.
10. Arnulf I, Similowski T, Salachas F, et al. Sleep disorders and diaphragmatic function in patients with amyotrophic lateral sclerosis. *Am J Respir Crit Care Med* 2000;161 (3 Pt 1):849–56.
 11. Garcia-Pachon E, Marti J, Mayos M, et al. Clinical significance of upper airway dysfunction in motor neurone disease. *Thorax* 1994;49:896–900.
 12. Fromm GB, Wisdom PJ, Block AJ. Amyotrophic lateral sclerosis presenting with respiratory failure. Diaphragmatic paralysis and dependence on mechanical ventilation in two patients. *Chest* 1977;71:612–4.
 13. Al-Shaikh B, Kinnear W, Higenbottam TW, et al. Motor neurone disease presenting as respiratory failure. *Br Med J (Clin Res Ed)* 1986;292:1325–6.
 14. Meyrignac C, Poirier J, Degos JD. Amyotrophic lateral sclerosis presenting with respiratory insufficiency as the primary complaint. Clinicopathological study of a case. *Eur Neurol* 1985;24:115–20.
 15. Hill R, Martin J, Hakim A. Acute respiratory failure in motor neuron disease. *Arch Neurol* 1983;40:30–2.
 16. Hostetler J, Ludwin S, Saly V, Zochodne D. Motor neuron disease presenting as ventilator dependency [abstract]. *Can J Neurol Sci* 1992;19:280–1.
 17. de Carvalho M, Matias T, Coelho F, et al. Motor neuron disease presenting with respiratory failure. *J Neurol Sci* 1996;139(Suppl):117–22.
 18. Chen R, Grand'Maison F, Strong MJ, et al. Motor neuron disease presenting as acute respiratory failure: a clinical and pathological study. *J Neurol Neurosurg Psychiatry* 1996;60:455–8.
 19. Allen SM, Hunt B, Green M. Fall in vital capacity with posture. *Br J Dis Chest* 1985;79:267–71.
 20. Fallat RJ, Jewitt B, Bass M, et al. Spirometry in amyotrophic lateral sclerosis. *Arch Neurol* 1979;36:74–80.
 21. Skatrud J, Iber C, McHush W, et al. Determinants of hypoventilation during wakefulness and sleep in diaphragmatic paralysis. *Am Rev Respir Dis* 1980;121:587–93.
 22. Sivak ED, Shefner JM, Sexton J. Neuromuscular disease and hypoventilation. *Curr Opin Pulm Med* 1999;5:355–62.
 23. Bourke SC, Shaw PJ, Gibson GJ. Respiratory function vs sleep-disordered breathing as predictors of QOL in ALS. *Neurology* 2001;57:2040–4.
 24. Pinto AC, Evangelista T, Carvalho M, et al. Respiratory assistance with a non-invasive ventilator (Bipap) in MND/ALS patients: survival rates in a controlled trial. *J Neurol Sci* 1995;129(Suppl):19–26.
 25. Lyall RA, Donaldson N, Flemming T, et al. A prospective study of quality of life in ALS patients treated with non-invasive ventilation. *Neurology* 2001;57:153–6.

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