Amyotrophic Lateral Sclerosis Presenting with Respiratory Failure*

Diaphragmatic Paralysis and Dependence on Mechanical Ventilation in Two Patients

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Described are two patients whose initial symptom was acute respiratory failure requiring mechanical ventilation. Initially, the cause of the respiratory failure in each patient was obscure, but diaphragmatic paralysis was subsequently demonstrated fluoroscopically in each case. Further neurologic evaluation then supported the diagnosis of amyotrophic lateral sclerosis. Postmortem examination corroborated this diagnosis.

A cute respiratory failure requiring mechanical ventilatory support has many causes.1,2 In most large series of patients needing mechanical ventilation, there is a small group with neuromuscular diseases.1,3,4 Patients with amyotrophic lateral sclerosis are known to have respiratory complications, but these difficulties usually occur late in the course of the disease. A few cases of amyotrophic lateral sclerosis have been reported in which the original symptom was exertional dyspnea.5 To our knowledge, the two patients in this report represent the first two cases where acute respiratory failure requiring mechanical ventilation was the initial symptom of amyotrophic lateral sclerosis. The correct diagnosis was pursued only after multiple unsuccessful attempts to "wean" these two patients from mechanical ventilatory support.

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Case Reports

CASE 1

A 68-year-old white man was in seemingly excellent health until the spring of 1973, when he became short of breath and a diagnosis of congestive heart failure was made. On May 23, 1973, the patient became restless and tachypneic, a condition believed to be secondary to pulmonary edema. Mechanical ventilation was deemed necessary. With conservative management the patient improved; on May 28, 1973, he was alert and oriented. During the next four weeks, attempts to wean him from mechanical ventilatory support were unsuccessful, and the patient was transferred to the Shands Teaching Hospital of the University of Florida on June 29, 1973, to be weaned.

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of the corticospinal tracts was noted, and the cortex and the brain stem were normal.

Case 2

This patient was a 69-year-old white man with a past medical history of alcohol abuse, 50 pack-years of cigarette smoking, and reported chronic obstructive pulmonary disease. Results of pulmonary function tests performed at his local hospital six months before admission were thought to show airway obstruction and included the following values: forced vital capacity, 2.25 L; forced expiratory volume in one second, 1.72 L; PaO₂, 72 mm Hg; PaCO₂, 36 mm Hg; and pH, 7.47. On Nov 11, 1975, generalized weakness, pleuritic chest pain, and shortness of breath began and led the patient to seek medical attention on Nov 29, 1975.

The patient was believed to be in acute respiratory distress, and an endotracheal tube was placed. Initially, he was treated with a volume-controlled ventilator (Bennett MA-1), antibiotics, and with heparin for suspected pulmonary emboli. During the ensuing two weeks the patient's condition responded well; however, several attempts at weaning, even with equipment for IMV, were unsuccessful. The patient was transferred to the Gainesville (Fla) Veterans Administration Hospital on Dec 18, 1975, to be weaned from mechanical ventilatory support.

On admission the patient was alert, cooperative, in no distress, and on a ventilator (Emerson). Rales were heard at both bases of the lungs, but findings from the rest of the physical examination were normal. The neurologic examination revealed mild generalized weakness and muscular wasting, with normal sensation. Deep tendon reflexes were brisk, except for absent ankle reflexes, and the findings from the remainder of the examination were normal.

Laboratory data revealed levels of electrolytes, blood urea nitrogen, creatinine, calcium, phosphorus, transaminases, vitamin B₁₂, magnesium, and folate, as well as the results of urinalysis, to be normal. Arterial blood gas levels were as follows: PaO₂, 76 mm Hg; PaCO₂, 36 mm Hg; and pH, 7.45. The rate of IMV was 6/min and the FIO₂ was 0.4. A chest x-ray film disclosed bilateral infiltrates of the lower lobes compatible with pneumonia.

The patient was at first believed to have chronic obstructive pulmonary disease with acute respiratory pneumonia and possible pulmonary emboli. Within six hours of admission, his arterial blood gas levels were stable, despite a reduction of the respirator's rate of IMV to 2/min. At this point the patient himself removed the endotracheal tube. Over the next ten hours, his condition progressively deteriorated, with increasing dyspnea and severe respiratory acidosis. The patient was reintubated and again treated with a ventilator (Emerson).

Shortly thereafter, moderate distal muscular weakness, with prominent fasciculations, was noted. On Jan 6, 1976, fluoroscopic examination of the chest revealed paradoxical movement of the right diaphragm and no movement of the left. The result of a test with edrophonium chloride (Tensilon) was negative. Electrodiagnostic studies were performed and showed normal neural conduction and a normal evoked-potential electromyogram. Needle study of striated muscles showed fasciculations, fibrillations, and positive waves. The cell count, glucose level, and protein of the cerebrospinal fluid were normal. With the preceding findings the diagnosis of amyotrophic lateral sclerosis was made. Shortly thereafter, the patient died.

Postmortem examination of the lungs showed severe and extensive bronchopneumonia. Mild centriacinar emphysema was noted in both lungs.

The brain and spinal cord revealed no gross abnormalities. In the spinal cord, there was loss of anterior horn cells, which was most marked in the cervical segments (Fig 2). The lateral corticospinal tracts in the spinal cord and the pyramids in the medulla showed mild demyelination. A muscular section taken at autopsy revealed atrophy with fiber angulation.

Discussion

Segmental atrophy and weakness in the extremities are the initial manifestations of amyotrophic lateral sclerosis in most patients, although 25 percent of the patients will have bulbar paralysis.6 The patients with bulbar paralysis would be predisposed to respiratory complications earlier in the course of their illness because of respiratory tract infections and repeated aspiration. In those patients whose initial symptom is spinal muscular atrophy, respiratory complications usually occur with the onset of bulbar paralysis or intercostal muscular paralysis. Only rarely has dyspnea been reported as the initial symptom in patients with spinal muscular atrophy.5

We are unaware of previous reports with pathologic documentation of findings in patients with
acute respiratory failure as the first manifestation of amyotrophic lateral sclerosis. The two patients reported here were in acute respiratory failure and dependent on mechanical ventilatory support. After many unsuccessful attempts at weaning had been made, diaphragmatic paralysis was demonstrated, in addition to clinical and electrodiagnostic evidence of spinal muscular atrophy. The clinical diagnosis of amyotrophic lateral sclerosis was confirmed at autopsy by the loss of anterior horn cells, which was most severe in the cervical region. Respiratory paralysis was attributed to involvement of motor neurons innervating the diaphragm and intercostal muscles.

These patients were strikingly similar in initial symptoms and final clinical and pathologic diagnosis. We agree that bacterial infection, probably as a result of aspiration, accelerated respiratory compromise; however, subsequent chest x-ray films and determinations of arterial blood gas levels in each patient returned to nearly normal while the patients were being ventilated with low FIO2. During postmortem examination, minimal evidence of chronic obstructive pulmonary disease was found. Because of the severity of both patients' illnesses, routine testing of pulmonary function could not be performed. Goldstein and associates7 have suggested that maximum midinspiratory flow and maximum midexpiration flow may be used as tests to aid in the diagnosis of weakness of respiratory muscles. These tests may be of value and could be performed on patients with endotracheal tubes in place.

In patient 2, we were fortunate to have the results of pulmonary function tests performed six months before admission. These limited studies revealed evidence of a restrictive ventilatory defect. The pattern of the studies is compatible with many etiologies but was similar to studies reported by Goldstein and associates7 in a patient with respiratory insufficiency as the first manifestation of a peripheral neuropathy with involvement of the phrenic nerve. The values are also comparable to those reported by Miller and co-workers8 in three patients with exertional dyspnea as the initial complaint in progressive muscular atrophy and amyotrophic lateral sclerosis and also by McCredie and associates9 in a report of pulmonary function testing in patients with diaphragmatic paralysis. The patient of Goldstein et al10 had radiographic reports of "high diaphragms," probably representing diaphragmatic paralysis. Pontoppidan and associates11 have reported that patients receiving mechanical ventilation develop diaphragmatic palsy. The fluoroscopic patterns reveal discoordination and not the consistent paradoxical movement we report. Diaphragmatic paralysis can certainly lead to a restrictive pattern on pulmonary function tests and to respiratory compromise, and it was the major contributing factor in both of our patients' dependence on mechanical ventilation.

Our inability to wean these two patients from mechanical ventilation, in the face of what appeared to be limited intrinsic pulmonary or cardiovascular disease, prompted our thought that they might have a neuromuscular problem. Difficulty in weaning patients has been a problem since the inception of artificial ventilation and may be due to abnormal pulmonary mechanics and blood gas exchange, to low cardiac output, to a hypermetabolic state, or to muscular weakness.10 Recently, IMV has facilitated weaning of patients, but even this method was unsuccessful in our two patients.11 A disease of motor neurons, such as amyotrophic lateral sclerosis, that leads to respiratory muscular weakness and diaphragmatic paralysis should, therefore, be considered when respiratory support must be continued for unclear reasons.

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REFERENCES