CASE REPORT

ACUTE RESPIRATORY FAILURE AS INITIAL PRESENTATION OF AMYOTROPHIC LATERAL SCLEROSIS ONSET

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SUMMARY

Amyotrophic lateral sclerosis (ALS) is a progressive, unrelenting and presently incurable neurodegenerative disorder. Respiratory muscle involvement is often a late complication of ALS. Only 1–3% of patients with ALS presenting to a tertiary care center had respiratory symptoms as their initial clinical symptom. In addition, only 14% of these individuals presented acutely and required emergency intubation. We report a 75-year-old female whose initial presentation at our emergency department was dyspnea. Dyspnea worsened and progressed to acute respiratory failure. There was no definite cause of respiratory failure found initially. However, ALS was diagnosed after physical and neurologic examination and electrodiagnostic studies. Respiratory muscle weakness was her first presentation of ALS. [International Journal of Gerontology 2008; 2(2): 72–75]

Key Words: amyotrophic lateral sclerosis, respiratory failure

Introduction

Amyotrophic lateral sclerosis (ALS) was first depicted by Charcot in the 19th century¹. This disorder affects anterior horn cells of the spinal cord and the motor cranial nuclei. It will cause muscle weakness, disability and eventually death, with a median survival of 3 to 5 years. ALS is relatively rare, although it is the third commonest neurodegenerative disease after Alzheimer’s and Parkinson’s diseases².³. ALS has an annual incidence of 1–3 cases in 100,000 population worldwide⁴. Asymmetric limb weakness is the most common initial presentation of ALS (80%). It is relatively rare that respiratory muscle weakness presents as the initial symptom of ALS. It accounts for only 1–3% of all ALS cases⁵. How to identify the respiratory onset of ALS in the beginning is worth investigating and discussing. We report a 75-year-old female with an unknown cause of acute respiratory failure.

Case Report

A 75-year-old female with a history of hypertension was discharged 1 month previously from another hospital after treatment for hypertrophy of the thyroid gland with external compression of the trachea, hyperthyroidism, diffuse bronchiolitis, and bronchiectasis. She was brought to our emergency department with dyspnea on September 8, 2007. Computed tomography did not show any lung mass, and lung function tests showed restrictive lung disease in our hospital. After treatment with anti-hyperthyroidism medicine, steroids and antibiotics, her condition improved and she was discharged on October 2, 2007.

On the night of discharge, she was brought to our emergency department because of cold sweats, chest tightness and progressive shortness of breath. Electrocardiogram and cardiac enzymes were all within normal limits. A chest X-ray showed cardiomegaly, atherosclerosis, and increased lung marking over both lung fields. After ipratropium and salbutamol inhalation...
and intravenous furosemide, her condition improved and she was discharged the next day. Unfortunately, she returned to our emergency department again on October 4, 2007 because of exacerbation of dyspnea. Her body temperature was 36°C, pulse rate was 105/minute, respiratory rate was 30/minute, and blood pressure was 133/77 mmHg. Physiologic monitoring and an oxygen mask with 100% oxygen were applied. She was alert but could not talk. Physical examination showed clear breathing sounds with a regular heartbeat. Ipratropium and salbutamol inhalation and intravenous hydrocortisone were administered immediately. The initial arterial blood gas showed: pH, 7.25; PCO2, 101.1 mmHg; PO2, 101.8 mmHg; HCO3, 34.9 mmol/L; and O2 saturation, 96.2%. However, she was drowsier after initial treatment, and subsequent follow-up of arterial blood gas showed an increase in CO2 retention of up to 143 mmHg. Due to severe respiratory acidosis with CO2 retention, an endotracheal tube was inserted for mechanical ventilation. During admission, the patient’s consciousness became clearer after correction of the CO2 level. The patient was alert with isocoric pupils and with normal light reflex. Extraocular movement was intact without limitation and the corneal reflex was normal. Muscle power of the bilateral extremities was around grade 4 without any sensory deficit or pain. There were upper motor neuron (UMN) signs with increased deep tendon reflex and jaw jerk, lower motor neuron (LMN) signs with muscle atrophy of the four limbs, and fasciculations of the tongue. Brain and cervical magnetic resonance imaging did not show any abnormality. Acetylcholine receptor antibody was negative. Serum thyrotropin, free thyroidine, corticotropin, cortisol and creatine kinase levels were all within normal limits. Paraneoplastic syndrome was once suspected, but tumor markers, including α-fetoprotein, CA-125, CA-153, carcinoembryonic antigen, CA-199 and squamous cells carcinoma antigen, were all negative. Vitamin B12 and folic acid levels were normal. Cerebrospinal fluid was clear in appearance with a normal cell count, but mildly elevated protein was found. Cerebrospinal fluid electrophoresis was done and no oligoclonal bands were detected.

The endotracheal tube was removed smoothly after improvement in the patient’s condition. A bilevel positive pressure device and oxygen mask were used alternately. A sensory nerve conduction study (NCS) showed normal results. A motor NCS showed reduced compound motor action potentials of all sampled nerves and normal conduction velocity of all sampled nerves without conduction block. The electromyography (EMG) study suggested neuropathic change rather than myopathy.

ALS was diagnosed; because of the need for long-term noninvasive positive pressure ventilation support, she was transferred to a respiratory care center for further care.

Discussion

The term ALS is derived from the combination of the clinical finding of amyotrophy and the pathologic finding of lateral sclerosis6–10. The hallmark of ALS is the combination of UMN and LMN involvement6,11. The UMN signs include hyperreflexia, spasticity, and pathologic reflexes such as a jaw jerk or Hoffman’s sign. The LMN signs include weakness, atrophy, and fasciculations. Extraocular muscles and bladder and anal sphincter muscles typically are spared12. ALS has an age distribution that peaks in the seventh to eighth decade4. Ninety percent of all ALS cases are sporadic, and the rest are familial12. The only established risk factors for ALS are age and family history.

Differences in site and segment of onset, pattern and speed of spread, and the degree of UMN and LMN dysfunction produce a disorder that is extraordinarily variable between individuals. Asymmetric limb weakness is the most common initial presentation of ALS12. It accounts for 80% of all ALS cases. The manifestations are usually distal but gradually progress to involve the more proximal muscles. Upper extremity onset of ALS most often begins with hand weakness. Lower extremity onset is most often heralded by foot drop. Bulbar ALS onset is the next most common initial presentation (20%) and often presents as dysarthria or dysphagia.

In contrast, respiratory muscle weakness is a rare pattern of onset in ALS; it presents in only 1–3% of patients5. Patients with respiratory muscle weakness may initially complain of fatigue only but eventually note shortness of breath triggered by decreasing levels of activity or by lying flat. In addition, they may develop disturbed nocturnal sleep with frequent awakenings and excessive daytime sleepiness.

In our patient, diffuse bronchiolitis, bronchiectasis and hyperthyroidism were found in another hospital. She visited our hospital because of dyspnea. Bronchiectasis or congestive heart failure was suspected in the beginning, so we gave her ipratropium and salbutamol inhalation, and intravenous furosemide and...
hydrocortisone. However, dyspnea worsened and progressed to acute respiratory failure. Sensory examination including light touch, two-point discrimination, vibration sensation, joint position perception, temperature, and pain perception were checked and were all normal. Muscle power in the bilateral extremities was 4+ on the Medical Research Council scale. Pain, ocular dysmotility, ptosis, anal and bladder sphincter dysfunction, and tremor were absent in this patient. Both UMN and LMN signs were detected. UMN signs with increased deep tendon reflex and pathologic reflex, including jaw jerk and Hoffman’s sign, LMN signs with muscle atrophy in the four limbs, and fasciculation of the tongue were found. Therefore, diseases with both UMN and LMN signs could be the cause.

Because of her previous history of hyperthyroidism, blood thyrotrpin, free thyroxine, corticotropin and cortisol levels were checked and were all within the normal range. Brain and cervical magnetic resonance imaging did not show any abnormality, so cervical spondylosis, spinal cord compression or spinal tumor was not the cause. Cerebrospinal fluid examination showed no central nervous system infection or inflammation. Acetylcholine receptor antibody was checked to exclude the possibility of neuromuscular junction disorder such as myasthenia gravis, which also turned out to be negative. Neither did the patient present with ptosis or diurnal variation of symptoms, and myasthenia gravis was excluded. The EMG and NCS revealed denervated and re-innervated polyphasic motor unit action potentials in all sampled muscles, suggesting neuropathic change rather than myopathy, so myopathy was excluded. Diseases of the brain, spinal cord, neuromuscular junction and muscle had been excluded.

According to the patient’s neurologic examination and clinical course, ALS or multifocal motor neuropathy with conduction block should be considered. Multifocal motor neuropathy with conduction block usually manifests slowly with the mean age of onset between 20 and 50 years. In addition, deep tendon reflexes may be absent or normal, and motor NCS should show conduction block. However, our patient was 75 years old; thus, her deep tendon reflex was increased and the mode of disease onset was very acute. Also, sensory NCS showed normal results, and motor NCS showed reduced compound motor action potentials in all sampled nerves and normal conduction velocity in all sampled nerves without conduction block. Therefore, multifocal motor neuropathy with conduction block was excluded.

This is an important finding, because multifocal motor neuropathy with conduction block responds well to immunoglobulin.

EMG and NCS are most helpful when clinical evidence supporting the diagnosis of ALS is limited or conflicting. The EMG findings in ALS contain features of acute and chronic denervation. Signs of active denervation include fibrillation potentials and positive sharp waves, whereas signs of chronic denervation include large amplitude, long duration, and polyphasic motor unit potentials. Sensory and motor NCS are often normal in ALS, although compound motor action potential amplitudes may be reduced in severely atrophic and denervated muscles. Motor conduction block should not be observed. In our case, EMG and NCS supported the diagnosis of ALS. In summary, based on the presence of UMN and LMN symptoms, NCS and EMG reports, and the absence of an alternative explanation, ALS was diagnosed.

In the study of Shoesmith et al., the survival time of patients with respiratory onset ALS was not significantly different from general ALS in a large case series. Thus, they concluded that ALS with respiratory onset does not necessarily mean a rapidly progressive course. The mean age of symptom onset in patients with respiratory onset was slightly greater than the average age of ALS reported in the literature. Only 14% of these individuals present acutely and require emergency intubation.

No cure for ALS is known at present. Medical care in ALS is primarily palliative. Riluzole is the only drug licensed for the treatment of ALS. It is designed as a specific glutamate antagonist and can prolong tracheostomy-free survival by 3–6 months. Respiratory failure will be anticipated in all ALS patients. Current recommendations are that noninvasive positive pressure ventilation should be offered to any patient with respiratory symptoms and vital capacity of less than 50%. Noninvasive positive pressure ventilation will improve survival in ALS, reduce the work of breathing, promote good gas exchange, and improve quality of sleep. Some patients may require ventilatory support for increasing periods while awake or even continuously and may choose to undergo tracheostomy. Tracheostomy may lead to prolonged survival in the face of severe disability. End of life should be clarified early.

Although neurologists readily recognize ALS and its variants, about 10% of patients are misdiagnosed and delays in diagnosis are common. The delay from onset...
of the disease to confirmation of the diagnosis can vary between 13 and 18 months\textsuperscript{25}. No single diagnostic test can confirm or entirely exclude the diagnosis of ALS. A careful history and physical and neurologic examinations are always important, especially when the full clinical features are not manifested.

In conclusion, acute respiratory failure is often a late complication of ALS, but it could occur as an initial manifestation of ALS onset and is easily misdiagnosed. Confirming the diagnosis of ALS may initially be difficult until the full clinical features are manifested. It is a good reminder that while such a complaint is common, we should be alert for the occasional patient who presents with an unexpected disorder. Therefore, a careful history and physical and neurologic examination are important, particularly in the elderly or those who have a family history of ALS.

References