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Case report

Respiratory failure in a patient with antecedent poliomyelitis: Amyotrophic lateral sclerosis or post-polio syndrome?

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Abstract

We report a 69-year-old man who developed paralytic poliomyelitis in childhood and then decades later suffered from fatal respiratory failure. Six months before this event, he had progressive weight loss and shortness of breath. He had severe muscular atrophy of the entire right leg as a sequela of the paralytic poliomyelitis. He showed mild weakness of the facial muscle and tongue, dysarthria, and severe muscle atrophy from the neck to proximal upper extremities and trunk, but no obvious pyramidal signs. Electromyogram revealed neurogenic changes in the right leg, and in the paraspinal, sternocleidomastoid, and lingual muscles. There was a slight increase in central motor conduction time from the motor cortex to the lumbar anterior horn. Pulmonary function showed restrictive ventilation dysfunction, which was the eventual cause of death. Some neuropathological features were suggestive of amyotrophic lateral sclerosis (ALS), namely Bunina bodies. In patients with a history of paralytic poliomyelitis who present after a long stable period with advanced fatal respiratory failure, one may consider not only respiratory impairment from post-polio syndrome but also the onset of ALS.

Keywords: Motor neuron disease; Neuropathological study; Postmortem study; Pulmonary functions

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease with selective and systematic involvement of the cortical and spinal motor neurons, causing systemic muscle atrophy including of the respiratory muscle [1–6]. Acute paralytic poliomyelitis is caused by infection with the poliovirus in childhood, which produces spinal motor neuron damage. This disease affects mainly the proximal muscles of the legs, and leads to asymmetric flaccid paralysis and atrophy. With the spread of the polio vaccine in the modern era, poliomyelitis has become uncommon. However, in acute paralytic poliomyelitis patients, various functional disorders sometimes appear decades after the initial disease. These disorders exacerbate motor, sensory, and respiratory dysfunction and are known collectively as post-polio syndrome (PPS) or post-polio muscular atrophy (PPMA) [7–10], which often mimics ALS symptoms. Conversely, ALS is rarely associated with antecedent paralytic polio, and mimics PPS [11–13]. About 1% of paralytic polio patients have been reported to develop ALS [14]. This rate is extremely high compared with the general prevalence of ALS. It is not yet clear whether the development of ALS is linked to paralytic polio [15–17].

We report a patient with severe residual paralysis in one leg from paralytic polio in childhood, who suffered fatal respiratory impairment in old age.

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2. Case report

The patient was a 69-year-old man. His history included febrile-associated acute motor palsy at the age of 4 years, and subsequent muscle atrophy and right leg paralysis. These conditions were arrested after the initial disease, with no relapse or progression. Other limb weakness and atrophy was not present. This clinical history strongly suggests that the patient suffered from poliomyelitis. His early acute anterior poliomyelitis did not seem to involve respiratory muscles. At 20 years of age his right upper lung was partially resected because of tuberculosis. He had a 40-year history of smoking. There was no history of neuromuscular disease in his family.

For 6 months before presentation, the patient had gradually progressing loss of weight and appetite, and noticed shortness of breath upon walking or exertion. For 3 months, he had gradually progressing general malaise, difficulty speaking, and a weak voice. He had difficulty in sleeping, but no snoring or apnea during sleep. He lost 10 kg in weight in 6 months, and visited our hospital because of breathing difficulty.

At the initial examination, he was alert and intelligent. His height was 158 cm, weight 37 kg, blood pressure 100/70 mmHg, body temperature 36.7 °C, and pulse rate 62 beats/min. He had no arrhythmia. Movement of the thorax was extremely limited on breathing. Severe muscle atrophy was seen from the right hip through the entire leg, and the right leg was 5 cm shorter than the left. There was mild weakness in the facial muscles, dysarthria, and mild paralysis and fasciculation of the tongue, but no dysphagia. Muscles from the neck through the proximal arms and trunk were severely atrophied, but there was no fasciculation. Grip strength was 27 kg in the right hand and 25 kg in the left. Limb weakness was minimal except for the right leg. Deep tendon reflexes in the limbs were decreased overall. Neither spasticity nor Babinski's sign were present. He had no sensory impairment.

Blood tests revealed no anemia, and there were no abnormalities in biochemical test results. Thyroid function was normal, but tests were positive for HBs antigen and HCV antibody. There were no findings of pneumonia on chest radiograph, and no paresis of the diaphragm. Arterial blood gas analysis (room air) findings were PH 7.368, PaO_2 89.8 Torr, $PaCO_2$ 59.2 Torr, HCO_3 33.3 mEq/L, and SaO_2 97.0%. There were no abnormalities on electrocardiogram. Clinical respiratory symptoms showed no improvement with edrophonium. Motor, sensory and F-wave conduction velocities in the limbs were all within the normal range. Electromyogram revealed marked neurogenic changes in the right quadriceps femoris and tibialis anterior muscles. In addition, polyphasic and high amplitude potentials were observed in the paraspinal, sternocleidomastoid and lingual muscles. Repetitive stimulation was not performed with this patient. Measurement of central motor conduction was done using the technique of percutaneous magnetic stimulation of the brain and spinal cord. Central motor conduction time from the cerebral motor cortex to the cervical segment of the spinal cord (C-CMCT) was measured by subtracting the latency to onset of EMG activity of the thenar muscle after cervical stimulation from the latency to onset of EMG activity to the same muscle after scalp stimulation. The latencies to onset of the action potential of the

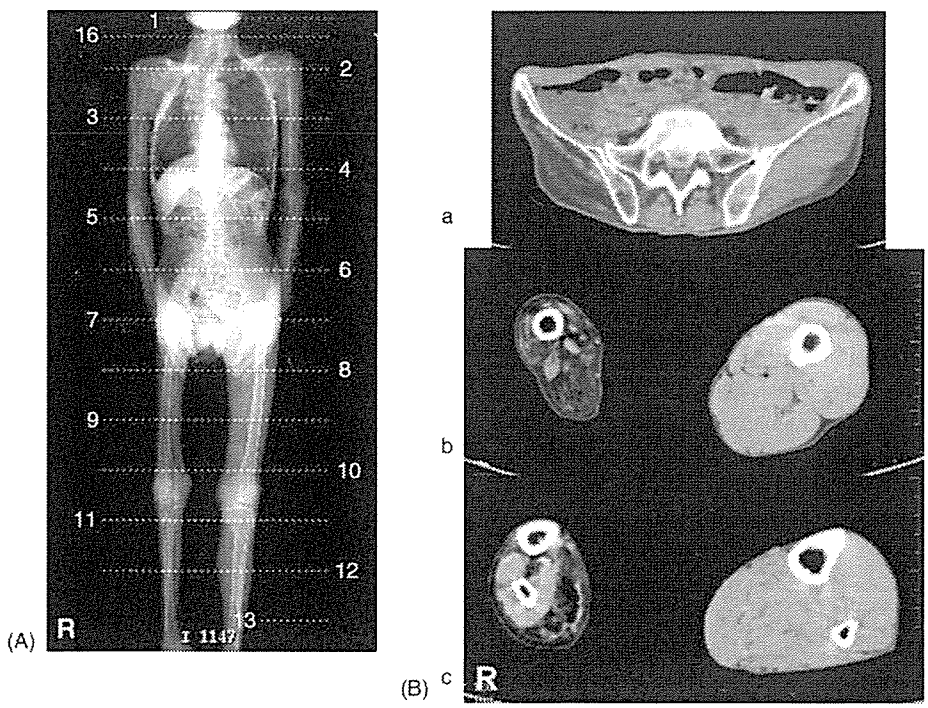

Fig. 1. CT findings. (A) Shows a full body image. (B) Shows transverse sections at the levels of the inferior pelvis (a), mid-thigh (b), and mid-calf (c). The right leg is shorter. Severe atrophy and fatty degeneration are seen from the right hip through the leg.

abductor hallucis muscle after scalp stimulation and to onset of the action potential of the same muscle after lumbar stimulation were also measured, and the difference between the two latencies was estimated as central motor conduction time from the cortex to the lumbar segment of the spinal cord (L-CMCT). The C-CMCT for the right thenar muscle was 9.4 ms (normal: up to 10 ms). The L-CMCT for the abductor hallucis muscle was 15.8 ms, showing a slight increase (normal: up to 15 ms). On spirometry, forced vital capacity (FVC) was 1.87 L, % predicted value (%VC) was 59.8%, and forced expiratory volume (FEV) 1.0% was 81.7%, showing restrictive ventilation dysfunction. There were no abnormalities in cerebrospinal fluid, which tested negative for type I poliovirus antibodies. CT showed diffuse severe muscular atrophy and fatty degeneration from the right hip through the entire leg (Fig. 1A and B). Atrophy of the paraspinal and intercostal muscles was also seen. Brain MRI showed mild atrophy, but no abnormal signals were seen along the corticospinal tract.

Two months after admission he required non-invasive positive pressure ventilation by nasal mask for his sleep disorder. After 4 months he could not orally ingest food sufficiently because of his breathing difficulty. After 5 months his pulmonary function showed an FVC of 0.99 L, %VC of 38.1%, and FEV 1.0% of 41.3%. In arterial blood gas analysis (room air), both PaO_2 and $PaCO_2$ continued to be about 60 Torr. After 6 months the patient died from respiratory failure. The clinical diagnosis was a residue of paralytic polio and ALS presenting as respiratory failure. An autopsy was performed about 8 h after death.

Brain weight was 1370 g. No marked changes were seen in the brain grossly, but there was atrophy of the spinal ventral roots. Histologically, motor neuron loss in the spinal ventral horn was seen. In the anterior horn of the left lumbar cord, active degeneration was seen, including atrophied motor neurons with Bunina bodies, appearance of macrophages, axonal spheroids, and hypertrophic astrocytes (Figs. 2–4). On the right side, atrophy of the ventral horn, extensive neuronal loss, and gliosis were seen, but there were few findings of active degeneration (Fig. 3). At the cervical and thoracic levels, there was not a clear difference between motor neuron lesions on the right and left sides. Mild cell loss in the hypoglossal nuclei was present. Bunina bodies were also seen in remaining motor neurons of the cervical anterior horn and the hypoglossal nuclei. There was mild loss of Betz cells in the motor cortex. In the spinal cord, the lateral column demonstrated a slight pallor bilaterally with Klüver–Barrera stain (Fig. 2), and the presence of macrophages. Glial bundles were seen on the right side, particularly in the lumbar ventral roots. Neurogenic atrophy was also seen in the intercostal muscles and diaphragm.

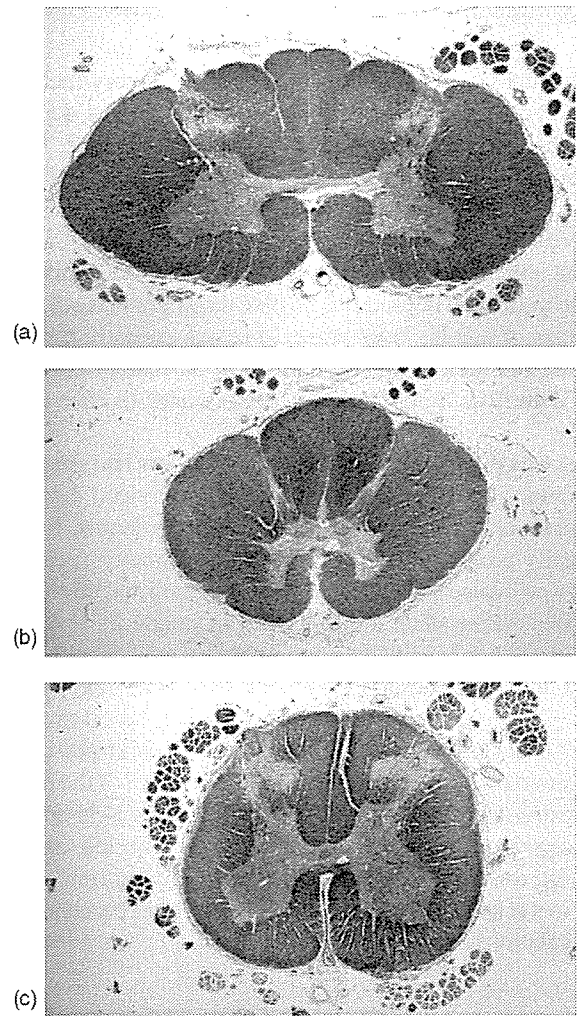

Fig. 2. Spinal cord findings. Transverse section at the spinal level ((a) cervical, (b) thoracic, and (c) lumbar). Mild pallor is seen in the lateral columns at the lumbar level. Klüver–Barrera stain (×3).

3. Discussion

The present patient had a history of paralytic polio in childhood. After a stable period of about 65 years, he suffered severe weight loss and a respiratory disorder. This was a rare case in which the lower motor neuron symptoms and signs were in the foreground, and the condition rapidly progressed to fatal respiratory failure. The findings included some atypical features for ALS, namely, absence of the obvious clinical pyramidal signs.

Typical symptoms of PPS and PPMA include new deterioration of muscle strength, general fatigue, speech and vocal impairment, dysphagia, and depression.

Rather than a reinfection or reactivation of the poliovirus or a new progressive degenerative process, PPS may be a secondary functional disorder from the addition of age-related changes to existing functional failure [7–10]. Among PPS cases, progressive ventilation failure such as chronic alveolar hypoventilation, progressive respiratory failure, and sleep apnea syndrome have been reported [18,19]. The clinicopathological diagnosis of our patient was more likely ALS presenting as respiratory failure or dyspnea-fasciculation syndrome [20], rather than respiratory disorder due to PPS or PPMA.

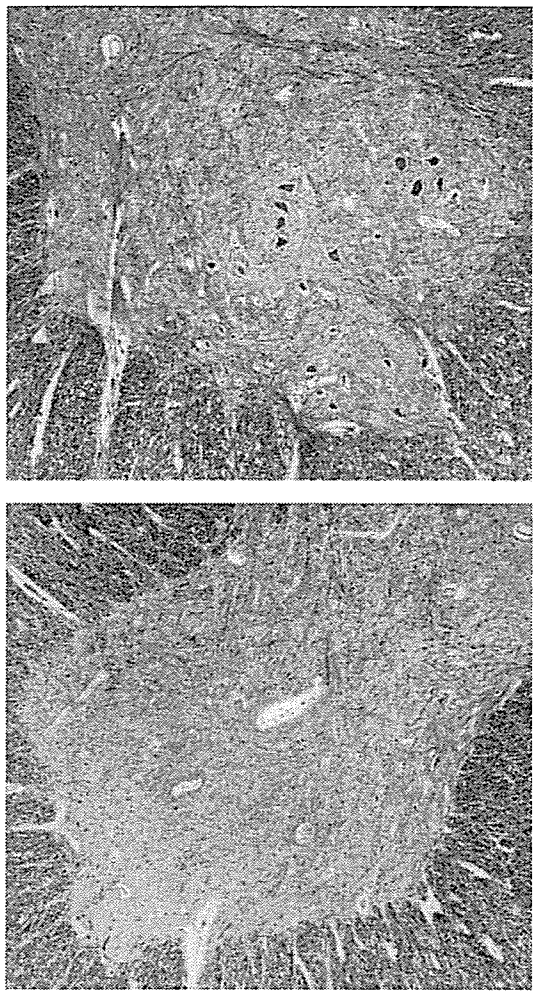

Fig. 3. Spinal ventral horn findings. Transverse sections of the lumbar ventral horn. Mild to moderate loss of motor neurons is seen on the left side (a). On the right side (b), ventral horn atrophy, severe motor neuron loss, and gliosis are seen. Klüver–Barrera stain (× 10).

Recently, Truffert et al. [21] have reported that a 56-year-old man with prior paralytic poliomyelitis developed progressive respiratory failure caused by endplate dysfunction. Repetitive stimulation studies showed a marked decrement of the trapezius muscle response, which was reversible with edrophonium. In the absence of biological evidence for autoimmune myasthenia gravis, it may be that some kind of endplate dysfunction mechanism is related to postpolio syndrome. The repetitive stimulation procedure should be considered in postpolio syndrome patients as some of them may benefit from anticholineesterase treatment. In our patient the negative result from the edrophonium test was rather unsuggestive of significant endplate dysfunction. Truffert et al. reported a patient whose presentation was quite similar to the present case, but who improved with anticholinesterase therapy, contrary to our patient.

Neuropathological reports on ALS patients with antecedent paralytic polio are rare. Roos et al. [12] reported an ALS patient who had contracted poliomyelitis at the age of 15 years. This patient had weakness of the right hand at the age of 45, and died 3 years later. These authors noted that, neuropathologically, this case presented a classical picture of ALS. Shimada et al. [13] reported a woman who had leg paralysis from acute poliomyelitis at the age of 2 years, onset of progressive weakness of the left hand at the age of 75, and respiratory failure causing death at the age of 80.

Neuropathologically, there were findings of old poliomyelitis in the lumbar ventral horn, together with ALS pathology presenting cortical and spinal motor neuron damage. However, they described several atypical findings that differed from classical ALS [22], including the preservation of the hypoglossal nucleus, no Bunina bodies in the remaining motor neurons, and no ubiquitin-positive inclusions. Pezeshkpour et al. [23] reported local, asymmetric spinal anterior horn motor neuron degeneration and a well-preserved corticospinal tract. Miller [24] indicated that PPMA patients presented spinal motor neuron loss and axon spheroids, and mild spinal lateral funiculus damage and loss of Betz cells in the motor cortex.

In the present case, there was atrophy in the right lumbar anterior horn, and severe loss of cells of all sizes, from large alpha motor neurons to small interneurons. This was quite different from the size-dependent selective pattern of

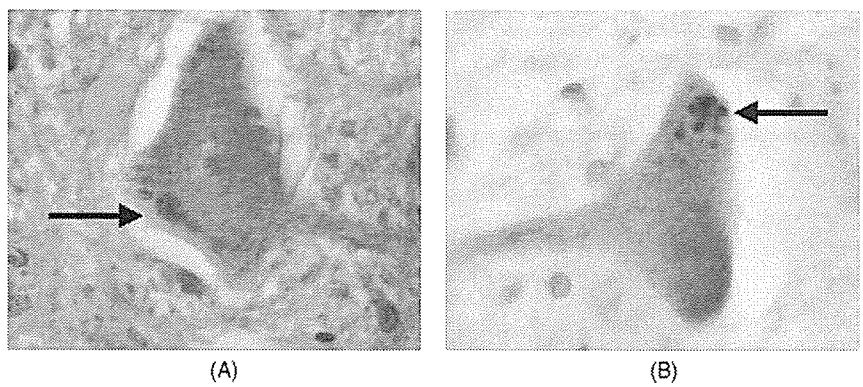

Fig. 4. Bunina body findings. (A) Shows Bunina bodies (arrows) in motor neurons of the lumbar ventral horn with hematoxylin-eosin stain (× 100). (B) Shows cystacin-C stain (× 100).

motor neuron loss in ALS [25–28]. The glial bundles present predominantly in the right lumbar spinal roots were those from paralytic polio [29]. Otherwise, the pathophysiological findings were indistinguishable from those of sporadic ALS. The extremely rapid progression of motor neuron dysfunction resulting in respiratory failure may reflect the underlying dormant pathophysiological process due to antecedent poliovirus infection, since antecedent poliovirus infection would have spread far beyond the lesions of apparent motor neuron loss [18,19].

In patients with a history of paralytic poliomyelitis who present progressive respiratory failure after a long and stable course, one may consider not only respiratory disorder due to PPS but also, in rare cases, the development of ALS.

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