Endplate dysfunction causing respiratory failure in a patient with prior paralytic poliomyelitis

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A 56 year old man with late amyotrophic sequelae from poliomyelitis experienced progressive dyspnoea requiring intubation and artificial ventilation in the intensive care unit. Repetitive stimulation studies showed a marked decrement of the trapezius muscle response reversible with edrophonium. Ventilatory function considerably and lasting improved under anticholinesterase treatment. In the absence of biological evidence for autoimmune myasthenia gravis, it is suggested that a mechanism implying endplate dysfunction related to postpolio syndrome. Repetitive stimulation procedure should be considered in postpolio syndrome patients as some of them may benefit from anticholinesterase treatment.

Breathing disorders are common in patients with prior poliomyelitis. Such complications may be associated with degeneration of the motor neurons and the so called postpolio syndrome (PPS), which can be defined as any late motor event occurring in a formerly poliomyelitic patient. Clinical manifestations of the PPS commonly include non-specific symptoms such as fatigue, muscle weakness, myalgias, and cramps. In PPS, respiratory insufficiency may be associated with the sleep apnoea syndrome. Patients who develop chronic alveolar hypoventilation several decades after acute poliomyelitis have been described, but it was not clear whether these patients had PPS, and respiratory insufficiency is usually not reported as the unique symptom of PPS, such as in the following observation.

CASE REPORT
A 56 year old man with limb amyotrophy attributable to polio sequelae presented with rapidly progressive breathing discomfort. At the age of 11, he had suffered from a severe form of paralytic poliomyelitis, with tetraplegia and involvement of respiratory muscles requiring prolonged artificial ventilation. The disease was contracted in 1955 during the last epidemic polio outbreak in Geneva, just before introduction of vaccination. Progressive but partial recovery occurred, leaving the patient with severe paresis and amyotrophy of both lower limbs and of the distal muscles of upper limbs, but no conspicuous weakness of respiratory muscles. He was able to walk with braces and despite his motor handicap, could sustain a moderate light with artificial ventilation, requiring intubation and artificial ventilation.

On clinical examination, a severe amyotrophy of both legs and both hands with skeletal deformation and thoracic kyphoscoliosis was present. Manual testing of force showed a severe paresis of the most atrophic muscles, and a mild paresis (corresponding to M4 on the British Medical Council scale) of the limb girdle muscles including the trapezius. Pulmonary function tests (PFT) showed a restrictive disorder (total lung capacity: 3.45 litre, 54% of predicted) with markedly decreased inspiratory muscles strength (maximal mouth inspiratory pressure MIP: 53 cm H2O, 61% of predicted).

A standard repetitive stimulation test was performed. Low frequency (3/s) repetitive pulses were applied to the right spinal nerve at the neck behind the posterior border of the sternocleidomastoid muscle. The amplitude of the motor response recorded over the right trapezius muscle was 3.1 mV and showed a 28% decrement on the fifth shock (fig 1A), which decreased to 15% 10 minutes after intravenous injection of 10 mg of edrophonium chloride (fig 1B). High frequency repetitive stimulation and single fibre EMG were not undertaken at this time. A muscle response of normal latency but decreased amplitude was recorded through surface electrodes from the diaphragm after a single electrical stimulus of the phrenic nerve at the neck. A thoracic CT scan showed no mediastinal mass suggestive of a thymoma. Antibodies directed against the acetylcholine receptor and against the muscle specific receptor tyrosine kinase (MuSK), anti-striated muscle, and anti-ganglioside antibodies were negative in blood samples.

In suspicion of an immune mediated myasthenia gravis (MG), a five days course of intravenous immunoglobulins (0.4 g/kg) was given without noticeable effect. The patient was then given increasing doses of pyridostigmine (up to 240 mg/day), which considerably improved breathing, permitting extubation after two weeks and transfer to a rehabilitation unit, from where he was discharged three weeks later with nocturnal non-invasive ventilatory support. On follow up examinations, one month and one year after his acute respiratory failure, the patient was free from respiratory symptoms. However, he was pyridostigmine dependent and reported relapses of breathing discomfort on attempts to reduce this treatment. Under anticholinesterase treatment, PFT showed improved values of all parameters (forced vital capacity: +15%, MIP: +45%) and the PCO2, was normal at 5.8 kPa (43 mm Hg). Likewise, the 3 Hz repetitive stimulation test done one month and one year after his hospitalisation at the same recording site (right trapezius muscle) showed an increased initial amplitude (5.6 and 7.6 mV respectively) of the motor response and a marked reduction (to 8% and 11% respectively) of the decrement (fig 1C). No decrement was found in several other muscles (right abductor digiti minimi, gastrocnemius, and tibialis anterior) that were

Abbreviations: ALS, amyotrophic lateral sclerosis; EMG, electromyography; MIP, maximal mouth inspiratory pressure; MG, myasthenia gravis; MuSK, muscle specific receptor tyrosine kinase; PFT, pulmonary function tests; PPS, postpolio syndrome
presentation of PPS seems uncommon, and a breathing problem was the least frequently (6%) new symptom reported in a series of 79 patients followed up in a postpolio clinic. In our patient, electrodiagnosis demonstrated a partial block of neuromuscular transmission. This was attested by (1) the low amplitude motor responses recorded over the diaphragm and trapezius muscles, (2) the decrement on repetitive shocks, and (3) the reduction of the decrement and the increased response under anticholinesterase treatment. Moreover, the absence of incremental response with tetanic stimulation suggests a postsynaptic, rather than a pre-synaptic disorder such as observed in the Lambert-Eaton myasthenic syndrome. The disorder could not be demonstrated in skeletal muscles that seemed spared by any recent weakness. Clinically, the hypothesis that a neurotransmission defect played a significant part in the patient’s respiratory symptoms, is further supported by favourable outcome and significant improvement of the restrictive syndrome with pyridostigmine, and by relapse of dyspnoea upon withdrawal of this treatment. Nocturnal ventilatory support probably also contributed to improvement of alveolar hypoventilation.

Disorders of neuromuscular transmission, and beneficial effects of anticholinesterase drugs have been recognised by early investigators in patients with poliomyelitis as well as in patients with other chronic loss of motor units such as ALS. In ALS patients, efficiency of this treatment is seldom lasting as it was in our patient. Anticholinesterase drugs have been shown to improve fatigue in some patients with PPS. However, a large randomised trial of pyridostigmine in 126 PPS patients failed to demonstrate a significant benefit of this drug, suggesting that a defect of neuromuscular transmission was not the main mechanism for PPS symptoms in this group of patients.

Neuromuscular junction dysfunction is known to increase linearly with the time elapsed since acute polio. These changes are believed to reflect inability of the enlarged motor units to sustain the metabolic demand of neurotransmission in an increased number of endplates over a prolonged period of time. Other possible mechanisms include permanent ongoing denervation and reinervation of axons terminals resulting in immature endplates in a significant number of muscle fibres.

In our patient, an autoimmune myasthenia gravis (MG) cannot be completely ruled out. MG sometimes starts with acute ventilatory failure as the only manifestation. Antibodies directed against acetylcholine receptors were negative, as often reported in MG with predominant respiratory symptoms. Recently, Hoch et al demonstrated that 70% of these seronegative patients have serum autoantibodies directed against the muscle specific receptor tyrosine kinase, MuSK. In our patient, the anti-MuSK antibody assay was negative and intravenous Ig treatment was ineffective, rendering the hypothesis of MG unlikely.

In conclusion, this case report illustrates the possibility of acute respiratory events many years after an acute paralytic poliomyelitis. This may represent a particular form of PPS, perhaps related to exacerbation of chronic asymptomatic end-plate dysfunction. Thus, PPS as a clinical entity shows a wide variety of manifestations and pathophysiological mechanisms. The practical conclusion is that repetitive stimulation tests in muscles affected by new weakness may help to identify patients with PPS who may benefit from an anticholinesterase treatment.

ACKNOWLEDGEMENTS

We wish to thank Dr Angela Vincent for having performed anti-MuSK antibodies assay in our patient. This observation has been presented as poster communication at the “XIIes Journées Francophones d’Electroneuromyographie” in Toulouse, France, on 5–7 June 2002.

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Received 6 June 2002
Accepted in revised form 21 November 2002

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