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

A Truffert, P H Lalive, J P Janssens, M Sinnreich, M R Magistris

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 lastingly 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.1 Such complications may be associated with the loss of respiratory muscles due to the so called postpolio syndrome (PPS), which can be defined as any late motor event occurring in a formerly poliomyelitic patient.1 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.2 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 some of them may benefit from anticholinesterase treatment.

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 anterior 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 professional activity as a psychiatrist in private practice. He was a non-smoker and had no history of chronic obstructive pulmonary disease. One year ago, about 45 years after his acute polio, he began to notice progressive breathing discomfort. Recently, he developed over two weeks a severe dyspnoea that led him to seek medical assistance. Several weeks before his admission, he noticed headaches and difficulties in concentration, but no unusual fatigue, decrease in limb muscles force, or muscle pain. On admission in the emergency room, the PCO₂ was 7.2 kPa (54 mm Hg) and deteriorated to 17.2 kPa (129 mm Hg) after oxygen administration, requiring intubation and artificial ventilation.

On clinical examination, a severe amyotrophy of both legs and both hands with skeletal deformation and thoracic kyphoscoliosis were 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 normal.

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
incidence of the sleep apnoea syndrome.

prior poliomyelitis.

tory decline with aging might be more marked in patients with
cle or joint pain, new muscle atrophy, functional loss and cold
ological mechanism.

PPS could nevertheless be considered, with new weakness of
the respiratory muscles as the only manifestation. Such clinical

Progressive breathing disorders developing insidiously over
years, are common in patients with late polio sequelae.\(^1\)\(^–\)\(^3\) Proposed explanations for this progressive decline of respiratory
function are usually unrelated to a new muscle weakness.\(^7\) They
include musculoskeletal deformation with kyphoscoliosis caus-
ing a restrictive syndrome, pulmonary hypertension, and poor
posture in the wheelchair bound patient. A central component
is also suspected to contribute to hypoventilation in postpolio
patients, when acute bulbar polio involved the reticular forma-
tion and the sleep regulatory centres,\(^1\) with an increased
incidence of the sleep apnoea syndrome.\(^8\) Additionally, respira-
tory decline with aging might be more marked in patients with
prior poliomyelitis.\(^1\) In our patient, respiratory failure
occurred over a short period, suggesting another pathophys-
iological mechanism.

Diagnostic criteria for the PPS include unusual fatigue, mus-
cle or joint pain, new muscle atrophy, functional loss and cold
intolerance beginning several decades after acute poliomyelitis.\(^4\)
Although our patient experienced none of these symptoms, a
PPS could nevertheless be considered, with new weakness of
the respiratory muscles as the only manifestation. Such clinical

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.\(^5\)

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 post-
synaptic, 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\(^6\) as well as in
patients with other chronic loss of motor units such as ALS.\(^9\)
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.\(^10\)
However, a large randomised trial of pyridostigmine in 126
PPS patients\(^11\) 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.\(^12\) 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 dener-
ervation and reinnervation of axons terminals resulting in immu-

nary endplates in a significant number of muscle fibres.\(^13\)\(^–\)\(^15\)

In our patient, an autoimmune myasthenia gravis (MG)
cannot be completely ruled out. MG sometimes starts with
acute ventilatory failure as the only manifestation.\(^14\)\(^–\)\(^15\) Antibodies
directed against acetylcholine receptors were negative, as often reported in MG with predominant
respiratory symptoms.\(^16\) Recently, Hoch et al demonstrated that
70% of these seronegative patients have serum autoantibodies
directed against the muscle specific receptor tyrosine kinase,
MuSK.\(^17\) 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 mecha-
nisms. The practical conclusion is that repetitive stimulation
tests in muscles affected by new weakness may help to iden-
tify patients with PPS who may benefit from an anti-
cholinesterase 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 a poster communication at the “XIIes Journées Francophones

Authors’ affiliations

A Truffert, PH Lalive, M Sinnreich, MR Magistris, Clinique de
Neurologie, Unité ENMG et des Affections Neuromusculaires, Hôpital

Figure 1 Repetitive stimulation test (3/s) on the trapezius muscle.
(A) At rest: 28% decrement of the response amplitude. (B) Ten
minutes after injection of 10 mg of edrophonium chloride (Tensilon):
reduction of the decrement to 15%. (C) One month later, under 240
mg/day of pyridostigmine (Mestinon), decrement is 8%. Note
increased amplitude of the initial response.
Cantonal Universitaire, Geneva, Switzerland.

JP Janssens, Division de Pneumologie, Hôpital Cantonal Universitaire

Competing interests: none declared.

Correspondence to: Dr A Truffert, Clinique de Neurologie, Unité ENMG et des Affections Neuromusculaires, Hôpital Cantonal Universitaire, Rue Michelli-Du-Crest 24, CH-1211 Geneva 14, Switzerland; andre.truffert@hcuge.ch

Received 6 June 2002
Accepted in revised form 21 November 2002

REFERENCES


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

A Truffert, P H Lalive, J P Janssens, M Sinnreich and M R Magistris

J Neurol Neurosurg Psychiatry 2003 74: 370-372
doi: 10.1136/jnnp.74.3.370

Updated information and services can be found at:
http://jnnp.bmj.com/content/74/3/370

These include:

References
This article cites 13 articles, 1 of which you can access for free at:
http://jnnp.bmj.com/content/74/3/370#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Infection (neurology) (494)
Neuromuscular disease (1311)
Spinal cord (542)
Tropical medicine (infectious diseases) (46)
Drugs: CNS (not psychiatric) (1945)
Immunology (including allergy) (1943)
Muscle disease (257)
Musculoskeletal syndromes (537)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/