In patients with neurological respiratory insufficiency it may be difficult to determine whether there is a neuromuscular problem, impaired central drive, or both. Phrenic nerve conduction studies and needle EMG of the diaphragm are well established methods in the diagnosis and prognosis of neuromuscular causes of diaphragmatic weakness.1 Transcortical and cervical magnetic stimulation with recording from the diaphragm and somatosensory evoked potentials of the phrenic nerve can assess the motor and sensory pathways of the central respiratory drive.2 We report the value of peripheral and central electrodiagnostic studies in a patient with acute high cervical spinal cord injury who developed secondary critical illness polyneuropathy.

This 76 year old previously healthy man had an acute onset of sharp, knife-like chest pain, and could not move his limbs a short time later. The pain lasted about an hour. On admission to hospital, three hours after onset of symptoms, his mental status and cranial nerves were intact. He was flaccidly quadriplegic with no voluntary movement except for elevation of both shoulders. Initially, he had diaphragmatic breathing clinically. Plantar responses were extensor. Pinprick, temperature, and light touch sensation were lost below C4 bilaterally. Vibratory sensation was lost in the limbs, but position sense was incompletely affected: passive movements were perceived in the toes on the left side, and at the knee on the right side. Within a few hours breathing became rapid and shallow. He was intubated and placed on a ventilator. The patient transiently worsened for about a week: he lost his ability to shrug his shoulders and the sensory level rose to below C3 bilaterally.

Spinal cord MRI showed abnormally increased signal anteriorly within the spinal cord signal from C4–T1 vertebral levels, and oedema ascending to C2. Examination of CSF was unremarkable. Serial electrophysiological studies for monitoring diaphragmatic muscle function were done (table). Phrenic nerve conduction studies were performed with electrical stimulations at the distal neck just posterior to the sternomastoid muscle.4 Transcortical magnetic stimulations were performed at the beginning of inspiration with a 90 mm circular coil positioned over Cz (determined by the 10–20 EEG system).2 No diaphragmatic compound muscle action potentials (CMAPs) were recorded after transcortical magnetic stimulation, and phrenic nerve conduction studies showed borderline onset latency and diaphragmatic CMAP amplitude at day 5 (figure). Transcortical magnetic stimulation on day 21 showed a delayed but recordable diaphragmatic CMAP, and normal phrenic nerve conduction. At this time he developed a septic syndrome due to pneumonia. The patient could not be weaned from the ventilator within the following weeks, and the necessity of a phrenic nerve pacemaker was raised. Subsequently, the sensory level descended distal to C6, and some movement was noted in the proximal left upper limb muscles (MRC 3).

Electrophysiological follow up study on day 51 showed complete recovery from both disorders.

Results of right phrenic nerve conduction (n = 25) and transcortical magnetic stimulation with recording of the right diaphragm (n = 35) in healthy subjects, and in the patient with cervical infarction and critical illness neuropathy

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Healthy subjects (Mean ± SD)</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phrenic nerve conduction:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>6.5 (0.8)</td>
<td>8.3 (5)</td>
</tr>
<tr>
<td>Amplitude (μV)</td>
<td>669 (159)</td>
<td>330 (5)</td>
</tr>
<tr>
<td>Cortical magnetic stimulation:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>13.5 (1.4)</td>
<td>No response (5)</td>
</tr>
<tr>
<td>Amplitude (μV)</td>
<td>263 (144)</td>
<td>No response (5)</td>
</tr>
</tbody>
</table>

For the patient, the day of examination after onset of illness is given in parentheses.

<table>
<thead>
<tr>
<th>Day 5</th>
<th>Magnetic stimulation</th>
<th>Acute cord ischaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 21</td>
<td>Improved cord ischaemia</td>
<td></td>
</tr>
<tr>
<td>Day 51</td>
<td>Developed critical illness neuropathy</td>
<td></td>
</tr>
<tr>
<td>Day 129</td>
<td>Full recovery from both disorders</td>
<td></td>
</tr>
</tbody>
</table>

Values of latencies and amplitudes of the right diaphragmatic compound muscle action potential.

Cortical magnetic stimulations were performed with a 90 mm circular coil positioned flat over the vertex (Cz). The phrenic nerve was stimulated electrically at the posterior border of the sternomastoid muscle in the supraclavicular fossa. The diaphragmatic compound muscle action potential was recorded bilaterally with surface electrodes from the xiphoid (active electrode) and the costal margin (reference electrode) for both magnetic and phrenic nerve stimulation. The table shows that there was no significant right-left differences.
recovery of the cortically evoked diaphragmatic response, but deterioration of the electrically evoked phrenic nerve response, showing prolonged onset latency and reduced diaphragmatic CMAP. Nerve conduction and needle EMG of the limbs showed a severe, symmetric, axonal, sensori-motor polyneuropathy. These findings were consistent with a critical illness polyneuropathy. This was not clinically apparent, as myelopathy masked neuropathy. These electrophysiological results showed that a phrenic nerve pacermaker was not necessary.

The patient recovered from critical illness neuropathy such that on day 121 he was extubated. Respiratory electrophysiological studies on day 129 showed normal diaphragmatic CMAPs after transcutaneous magnetic and electrical phrenic nerve stimulation. The patient was transferred to his home hospital five months after onset of the disease.

This study demonstrates the value of respiratory electrophysiological studies in localising the site of neurological causes of respiratory failure. An unusual feature occurred during the course of critical illness polyneuropathy. The diaphragmatic CMAP amplitude after phrenic nerve stimulation was lower than the CMAP amplitude evoked by peripheral magnetic stimulation. Submaximal stimulation was excluded as a cause. Central enhancement of somatosensory evoked potentials is known to occur in patients with peripheral neuropathy. This mechanism could be the explanation in our patient.

Moreover, the amplitude of magnetically evoked potentials increases in contracted muscles. The findings subjects magnetic stimulations during forced inspiration increase the diaphragmatic CMAP by about 100%. Possibly, the increased muscle tone leads to facilitation of the recording muscle resulting in increased CMAP amplitude. Further studies will be necessary to clarify the pathophysiological mechanisms of this phenomenon.

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Fulminant encephalopathy due to the cataclysmic primary antiphospholipid syndrome

The antiphospholipid antibody syndrome is characterised by recurrent arterial and venous thromboses associated with the presence of antiphospholipid antibodies.1 Neurological features can include cerebral ischaemia, multi-infarct dementia, migraine, epilepsy, transient ischaemic attacks, and chorea.2

We describe a patient with catastrophic primary antiphospholipid syndrome who presented with right hemispheric dysfunction which rapidly progressed to a fulminant encephalopathy associated with multiorgan failure.

A fifty-eight-year-old woman was admitted with a general malaise, headache, anorexia, and weight loss of four months. She had severe left lower limb deep venous thrombosis, and had been investigated for pleuritic chest pain for which no cause was established. She developed Graves’ disease at 45 years of age and was treated with radioiodine followed by thyroxine. She had no relevant family medical history.

On admission there were no significant abnormalities in the cardiovascular, respiratory, or gastrointestinal systems. She had a 5 cm skin ulcer on the right lateral malleolus. She was disorientated, restless, and unable to give a coherent history. There was no meningism and the optic fundi and eye movements were normal. She had a mild dysarthria and her upper motor neuron facial weakness and a mild left hemicerebralexsis with brisk tendon reflexes and a left extensor plantar response. She also had bilateral pinprick and pout reflexes, and left sided sensory inattention.

She was thrombocytopenic (platelets 125 × 10^9/l) but her full blood count and peripheral blood film were otherwise normal. Her erythrocyte sedimentation rate was 89 mm/h and C reactive protein concentration was 386 mg/l. The prothrombin time was normal, but the activated partial thromboplastin time (APTT) was prolonged at 37.2 s (normal range 23.5–36.4 s). The D dimer assay was normal but her fibrinogen concentration was low (1:15 g/l, normal 1.5–4.0 g/l). Her plasma urea was slightly increased at 10 mmol/L and plasma electrolytes, creatinine, liver function tests, bone chemistry, thyroid function, and blood glucose were normal and a veneral disease research laboratory test was negative. Urine, blood, and CSF cultures were sterile and only skin commensal organisms were isolated from the foot ulcer. A chest radiograph, ECG, echocardiogram, and brain CT were unremarkable. Lumbar puncture disclosed clear CSF, with a normal opening pressure, 6 white blood cells/μl, and normal protein and glucose concentrations.

She was treated with broad spectrum antibiotics for a presumed infection of an unknown origin with a provisional diagnosis of right hemispheric ischaemic stroke. However, she became increasingly obtunded, developing signs of bilateral hemispheric dysfunction including pyramidal distribution weakness in all four limbs and bilateral extensor plantar responses. She developed livedo reticularis over her back and lower limbs along with a gorytolic murmur. She was noted at the cardiac apex. Her respiratory function deteriorated, she became hypotensive and oliguric, and required assisted ventilation and inotropic support.

Thyroid microsomal antibodies were present at a titre of 1 in 400, but other autoantibody titres were negative (including dsDNA-Ab, ANCA, and Anti-GBM-Ab). Her anticardiolipin antibody concentrations were raised (serum IgG aCL 41.5 GPL, IgM aCL 25.9 MPL, normal <10 GPL/MPL). Biopsies of the skin ulcer and an area of livedo reticularis disclosed widespread thrombosis within the small vessels but no vessel wall inflammation. Echocardiography now showed a vegetation on the mitral valve. Abdominal CT was normal and a repeat brain CT showed no abnormality. An EEG showed diffuse generalised slow wave activity.

After a diagnosis of catastrophic antiphospholipid syndrome was confirmed, she was managed with intravenous heparin and immunosuppressed with methylprednisolone (1 g intravenously/day), cyclophosphamide (500 mg, single dose), and plasmapheresis. Her urinary output increased over the next week and cardiorespiratory support was no longer needed. Her neurological condition did not improve and she remained unaware and unresponsive with no clinical evidence of cortical function but intact brainstem reflexes. She died 24 days after admission to hospital.

The most striking pathological finding at postmortem was of widespread small vessel thrombosis; the tissues involved included the brain, myocardium, lung, kidney, skin, bone marrow, uterus, ovary, bladder, pancreas, stomach, and small intestine. Examination of the heart showed marantic vegetations of the mitral valve which were Gram stain and culture negative. The larger veins and arteries, including the coronary arteries, were patent with only mild atheroma seen.

Macroscopic examination of the cerebral hemispheres showed extensive confluent areas of laminar cortical infarction in the watershed zones. The midbrain, brainstem, cerebellum, and spinal cord were macroscopically unremarkable. Microvascular changes included small arteriolar and venular thrombotic occlusion in the brain, brainstem, spinal cord, and meninges. There was no associated inflammatory reaction (figure).

In the absence of convincing evidence for infection, the evolution of multiorgan failure, together with livedo reticularis, suggested the possibility of a systemic vasculitis or a coagulopathy. Disseminated intravascular coagulation and the haemolytic uraemic syndrome were excluded by the absence of

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**Figure:** Oblusive vascular lesion in the corpus striatum showing an amorphous protein plug with perivascular endothelial and macrophage proliferation. The vessel seems to be dilated at the site of the lesion. The surrounding neuropil shows a pronounced gliosis. There is no evidence of vasculitis. Magnification bar = 100 μm.
Electrophysiological monitoring in neurological respiratory insufficiency.

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