Diabetic neuropathic cachexia: report of a recurrent case

Carlayne E Jackson, Richard J Barohn

Abstract
Diabetic neuropathic cachexia is an uncommon peripheral neuropathy associated with diabetes mellitus and characterised by profound weight loss and painful dyasaesthesias over the limbs and trunk. The pathophysiological basis of this disorder remains unknown and there have been no published cases of recurrent episodes. A hispanic man who experienced two episodes of diabetic neuropathic cachexia over a seven year period is described.

(Keywords: diabetic neuropathic cachexia; diabetic neuropathy; acute painful neuropathy; peripheral neuropathy; diabetes; cachexia)

Diabetic neuropathic cachexia is an uncommon peripheral neuropathy associated with diabetes mellitus in which patients develop profound weight loss, a symmetric peripheral neuropathy, and painful dyasaesthesias over the limbs and trunk, without associated weakness. Unlike other neuropathies due to diabetes mellitus, diabetic neuropathic cachexia is reversible over a period of weeks to months. The eventual resolution of these symptoms, concomitant with weight gain, would suggest a primarily metabolic process; however, the pathophysiological basis of the disorder remains unknown. There have been no published cases in which a patient experienced recurrent episodes of diabetic neuropathic cachexia. We report on a hispanic man who experienced two episodes of diabetic neuropathic cachexia over a seven year period. Both episodes were associated with poor glucose control and profound weight loss.

Case report
A hispanic man at the age of 40 developed numbness and severe burning dyasaesthesias over his distal limbs and anterior trunk. Hyperaesthesias to touch was so pronounced that he was unable to wear a shirt. In addition, he experienced episodes of profuse sweating, impotence, and a 49 lb (22.2 kg) weight loss over three months. The patient's fasting blood sugar was 242 mg/dl and he was started on glipizide. The patient's painful dyasaesthesias however, did not improve, despite trials with amitriptyline, fluoxetine, lidocaine, carbamazepine, capsaicin, phenytoin, doxepin, TENS units, epiperidine and epidural injections.

Physical examination disclosed an emaciated cachetic hispanic man. Mental status and cranial nerve function were normal. Motor strength was Medical Research Council 2 grade impaired. Sensory examination disclosed very decreased vibratory sensation over the arms and the trunk. Pinprick sensation was diminished over the limbs, trunk, and face. Temperature sensation was greatly decreased to the level of the upper thighs and upper arms as well as across the chest and abdomen. Muscle stretch reflexes were grade 2 at the biceps, grade 2 at the triceps, grade 1 at the knee, and absent at the ankles with flexor plantar responses.

Laboratory evaluation including vitamin B12 concentration, venereal disease research laboratory, antinuclear antibody, RA, serum protein electrophoresis, thyroid function tests, creatine kinase, and heavy metal screen was normal. HGB A1c was 8.6% (normal 0–7%). Nerve conduction studies disclosed a sensorimotor neuropathy with a normal needle EMG (table). Sural nerve biopsy showed a severe loss of myelinated axons without ongoing axonal degeneration. Occasional clusters of thinly myelinated axons were seen surrounded by a Schwann cell indicating axonal regeneration. By contrast with the myelinated fibres, the small unmyelinated fibre population was not reduced.

The patient was placed on methadone for pain control and insulin therapy was initiated. He soon began to gain weight with gradual resolution of the truncal dyasaesthesias over the next nine months. The patient continued to experience numbness in his distal limbs.
Diabetic neuropathic cachexia can occur in both insulin and non-insulin dependent diabetic patients. Interestingly, there is a lack of correlation with other complications of diabetes such as nephropathy or retinopathy, suggesting that diabetic neuropathic cachexia is not due to microvascular disease, but due to an underlying dysmetabolic state.

Treatment of diabetic neuropathic cachexia can be difficult and strict diabetic control with insulin is usually necessary. Medications that can be given for symptomatic relief of the painful dysaesthesias include phenytoin, carbamazepine, clonazepam, and narcotic analgesics. A case report using combination therapy with amitriptyline and fluphenazine suggested excellent results, but this treatment was ineffective in our patient. The prognosis is usually good and patients typically recover their baseline weight with resolution of the painful sensory symptoms within one year. Our patient shows, however, that some symptoms may be prolonged for up to several years. A residual sensorimotor neuropathy is not uncommon. Our patient is the first case reported, however, who experienced a recurrent form of diabetic neuropathic cachexia, with an asymptomatic period of seven years between episodes. Both episodes occurred during periods of poor diabetic control, and it is interesting to speculate whether the patient would have experienced a relapse if he had been compliant with his diabetic medication after his initial episode of diabetic neuropathic cachexia.

Table 1

<table>
<thead>
<tr>
<th>Nerve conduction study</th>
<th>Distal latency</th>
<th>Amplitude</th>
<th>Conduction velocity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulnar CMAP</td>
<td>3.9 (nl &lt; 3.6 ms)</td>
<td>6.2 (nl &gt; 5 mV)</td>
<td>42.6 (nl &gt; 48 m/s)</td>
</tr>
<tr>
<td>Median CMAP</td>
<td>3.0 (nl &lt; 3.5 ms)</td>
<td>5.0 (nl &gt; 3 mV)</td>
<td>42.7 (nl &gt; 48 m/s)</td>
</tr>
<tr>
<td>Peroneal CMAP</td>
<td>6.0 (nl &lt; 6.6 ms)</td>
<td>0.48 (nl &gt; 2 mV)</td>
<td>35.7 (nl &gt; 42 m/s)</td>
</tr>
<tr>
<td>Ulnar SNAP</td>
<td>NR (nl &lt; 2.1 ms)</td>
<td>NR (nl &gt; 11 µV)</td>
<td></td>
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<tr>
<td>Median SNAP</td>
<td>2.2 (nl &lt; 2.3 ms)</td>
<td>27.2 (nl &gt; 40 µV)</td>
<td></td>
</tr>
<tr>
<td>Sural SNAP</td>
<td>NR (nl &lt; 4.8 ms)</td>
<td>NR (nl &gt; 5 µV)</td>
<td></td>
</tr>
</tbody>
</table>

NR=no response; CMAP=compound muscle action potential; SNAP=sensory nerve action potential; nl=normal.
NEUROLOGICAL STAMP

Hermann von Helmholtz (1821–94)

The physician Hermann von Helmholtz, born in Potsdam, was, on his mother’s side, a descendent of William Penn, founder of Pennsylvania. His contributions to science—which included physiology, optics, electrodynamics, and meteorology—were numerous.

His doctoral thesis, begun in 1842, was on the connection between nerve fibres and nerve cells and he graduated from the Medical School in 1843. His demonstration in isolated preparations that muscles are the main source of animal heat, led him to his best known discovery, the law of conservation of energy and his paper in 1847 Über die Erhaltung der Kraft (On the Conservation of Force). In 1850 he became the first to measure the velocity of nerve impulses in the sciatic nerves of frogs using a pendulum myograph of his own invention. He invented the ophthalmoscope (1851) and was the first person to see the living human retina. This was followed by his phakoscope and ophthalmometer (1852). With the latter he was able to explain the mechanism of accommodation (1854), particularly the part played by the lens. His research on the eye and the result of his extensive research was his multivolume Handbuch der physiologischen Optik (Handbook of physiological optics) published in 1867, was one of the great contributions to medicine in the 19th century. The handbook was regarded as a classic and described by Von Graefe as “the Bible of the ophthalmologist. It remained for many decades the definitive study of the physiology and physics of vision. With Thomas Young (1773–1829) of London he developed a theory of colour vision and in studies of the ear Helmholtz showed how the cochlea resonates for different frequencies and analyses complex sounds into harmonic components. In 1863 he published Die Lehre von den Tönungsfundanden Physiologische Grundlage für die Theorie der Musik (The sensation of tone as a physiological basis for the theory of music). In this work he demonstrated that the aesthetics of music was a function of the ears’ mechanical ability to pick up wave motions of musical sounds. It became the handbook of not only audiologists, physiologists, and physicists, but musicians as well. Steinway, already famous for the quality of his grand pianos, tried out the improvements suggested by Helmholtz on the Helmholtz family grand piano.

With his close friend Sir William Thompson, afterwards Lord Kelvin, he estimated the age of the sun and calculated the energy radiated from its surface. Earlier, about 1840 with James Prescott Joule, he had demonstrated that electric circuits obey the laws of conservation of energy and that electricity is a form of energy.

He had been at various times Professor of Physiology at Königsberg University (appointed in 1849), Professor of Anatomy (1856–66) primarily at the University of Heidelberg, and in 1871 he was appointed Professor of Physics in Berlin where he spent the rest of his life. He then turned his attention to electrodynamics, and was assisted by Heinrich Hertz, whose discovery of “Hertzian waves” made modern wireless transmission possible. Had he done nothing else in his life but invent the ophthalmoscope, his name would not be forgotten. He became one of the greatest of scientists who did not forget that he was a physician. “Medicine”, he said “was once the intellectual home in which I grew up: and even the emigrant best understands and is best understood by his native land.”

He was honoured philately by Germany (West Berlin) in 1971 on the 150th anniversary of his birth (Stanley Gibbons B394, Scott GN314).

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