Diabetic neuropathic cachexia: report of a recurrent case

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Abstract
Diabetic neuropathic cachexia is an uncommon peripheral neuropathy associated with diabetes mellitus and characterized by profound weight loss and painful dysesthesias 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 dysesthesias 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 dysesthesias in his legs associated with a 40 lb (18.1 kg) weight loss (figure) over two months. The diagnosis of diabetes mellitus was made and he was placed on chlorpropamide. Over the next five months, his sensory symptoms resolved and his weight gradually returned to baseline. The patient chose to discontinue his diabetic medication six years later and was lost to medical follow up. The next year, the patient developed numbness and burning dysesthesias over his distal limbs and anterior trunk. Hyperaesthesia 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 dysesthesias however, did not improve, despite trials with amitriptyline, fluoxetine, fluphenazine, carbamazepine, capsaicin, phenytoin, doxepin, TENS units, and epidural lidocaine injections.

Physical examination disclosed an emaciated and cachectic Hispanic man. Mental status and cranial nerve function were normal. Motor strength was Medical Research Council grade 5 in all proximal and distal limb muscles tested, with normal tone throughout. Sensory examination disclosed very decreased vibratory sensation in the toes. Proprioception was intact. There was hyperaesthesia to light touch sensation over all limbs 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 knees, 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 sensori-motor 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 dysesthesias over the next nine months. The patient continued to experience numbness in his distal limbs.
Table 1  Electrophysiological data

<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>3.9 (nl &lt; 4.5 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>6.6 (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; 1.1 µV)</td>
<td></td>
</tr>
<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.

Discussion

The patient in this case developed clinical features that are typical of diabetic neuropathic cachexia on two separate occasions. Both episodes were associated with poor glucose control. Diabetes mellitus was first diagnosed when the patient presented with the initial episode of diabetic neuropathic cachexia, which resolved after treatment with oral hypoglycaemic agents. Our case is unique in that recurrent episodes of diabetic neuropathic cachexia have not been reported. The second episode of diabetic neuropathic cachexia occurred after one year without antihyperglycaemic therapy due to medical non-compliance and required the initiation of insulin therapy. Diabetic neuropathic cachexia is a syndrome initially described by Ellenberg in 1973 and is characterised by a symmetric peripheral neuropathy associated with profound weight loss and painful dysaesthesias. Most reported patients have been men, usually in the sixth or seventh decades of life; there have been two cases described in women. All cases initially showed profound and precipitous weight loss up to 60% of total body weight, leading in many instances to an initially incorrect diagnosis of metastatic carcinoma or carcinomatous neuropathy. Weight gain typically occurs before resolution of the painful dysaesthesias, which are characteristically described as a constant, severe burning sensation. The dysaesthesias tend to be most severe in the distal lower limbs, but can occur in the proximal lower limbs, the hands, or the lower trunk.

Patients with diabetic neuropathic cachexia may experience intense contact hypersensitivity which may be provoked by clothing or bed-
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 Tönenfindungen als 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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