Chronic Inflammatory Demyelinating Polyneuropathy with Multiple Hypertrophic Nerves in Intracranial, and Intra- and Extra-Spinal Segments

Masaaki Niino, Sachiko Tsuji and Kunio Tashiro

Hypertrophic nerves have occasionally been seen in chronic inflammatory demyelinating polyneuropathy (CIDP), but most are in the cauda equina. We report a case with CIDP in whom magnetic resonance imaging (MRI) with gadolinium diethylene triamine penta-acetic acid (Gd-DTPA) enhancement demonstrated hypertrophy of various peripheral nerves including multiple cranial nerves. Interestingly, none showed neurological signs corresponding to the lesions, except for clinical signs consistent with CIDP. MRI can be useful for the detection of silent, but abnormal nerve involvement in CIDP. (Internal Medicine 38: 445-449, 1999)

Key words: nerve hypertrophy, magnetic resonance imaging (MRI), onion bulb formation

Introduction

Enlargement of the peripheral nerves has been reported in a variety of congenital and acquired neuropathies, for which the term "hypertrophic neuritis" has generally been used (1). Chronic inflammatory demyelinating polyneuropathy (CIDP) is now a well-established neurological disorder, the criteria of which has been proposed by the American Academy of Neurology (2). In CIDP, widespread nerve enlargement may occur (1); most are found in the lumbar region including the cauda equina (3-6). However, a few cases have shown hypertrophy of the cranial nerves (4, 7). Here, a patient with CIDP is presented, in whom magnetic resonance imaging (MRI) showed massive nerve root hypertrophy, including the gadolinium diethylene triamine penta-acetic acid (Gd-DTPA) enhancement of multiple cranial nerves.

Case Report

A 29-year-old man noticed slowly progressive muscle weakness and numbness of the bilateral lower limbs since age 17, followed by muscle atrophy and sensory disturbance of the lower extremities by age 27. He became unable to climb up the stairs, and visited our neurology department. There was no family history suggestive of polyneuropathy.

General physical examination on admission was within normal limits. Neurologically, mentation was normal, and mild bilateral facial paralysis was noted on the cranial nerve examination. In the upper extremities, strength was normal but moderate atrophy of the intrinsic hand muscles was noted. The lower extremities were hypotonic, and muscle weakness and atrophy were noted both proximally and distally, and much more severe in the distal part of legs with pes cavus. The deep tendon reflexes were diminished in the upper extremities and absent in the lower extremities with silent plantar responses. Mild stocking type sensory disturbance and markedly diminished vibration and position sense in both legs were noted. Romberg's sign was positive. Nerve trunks were not enlarged on palpation. Coordination was intact. He was able to stand with some difficulty and walk with severe steppage gait. There was no autonomic dysfunction.

The results of hemogram and urinalysis were normal. Serum chemistries were within normal limits with no evidence of serum cryoglobulin, M-protein, or Bence Jones protein in his urine. The glucose tolerance test was normal. Vitamin B1 was within normal limit. Autoantibody screenings, including anti-GM-1 antibody, were negative. Molecular genetic studies disclosed absence of 17p11.2 duplication. Cerebrospinal fluid showed 1 lymphocyte per microliter, and protein and immunoglobulin G (IgG) levels were markedly elevated at 315 and 46.1 mg/dl (IgG/albumin index 3.4), respectively. Motor nerve
Table 1. MCV Studies before and One Month after Steroid Therapies

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<th>CMAP-Amp (W/E) (mV)</th>
<th>Dur (W/E) (msec)</th>
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<td>9.0/8.8</td>
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<td>Right ulnar</td>
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<tr>
<td>One month after steroids</td>
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Discussion

Our patient had a long-standing sensory-motor neuropathy of 12 years' duration, without apparent inheritance. Polyneuropathy associated with paraproteinemia, collagen disease, vitamin B1 deficiency, and diabetic mellitus were excluded by laboratory studies. The important differential diagnoses include HMSN type I and type III. No family history, the absence of 17p11.2 duplication, and clinical and electrophysiological re-
Figure 2. MR images showing massively hypertrophied nerve roots compressing spinal cord at the C6-C7 level (arrows): (A) (sagittal image, TR=500 ms, TE=12 ms), (B) (axial image at C6/7 level, TR=600 ms, TE=15 ms), (C) (axial image at C6/7 level, TR=4,500 ms, TE=96 ms).

Figure 3. T1-weighted axial image after the injection of Gd-DTPA at Th7 level shows intercostal nerves with enlargement and peripheries of nerves are slightly enhanced with Gd-DTPA (arrows) (TR= 660 ms, TE=15 ms).

Responses for steroid therapy may favor the diagnosis for CIDP over HMSN type I. In HMSN type III, a remarkable increase in the protein content of the cerebrospinal fluid (CSF) may be present (8), and clinically, gait is severely impaired because of generalized limb and truncal weakness from childhood. The present patient had normal motor development during childhood, and his neurological signs and symptoms started in adulthood. His clinical signs, symptoms and laboratory data were compatible with CIDP defined by the American Academy of Neurology (2).

The widespread nerve enlargement has been reported in CIDP, but usually occurring in the cauda equina (3-6). The present case showed marked hypertrophy of not only the cauda equina, but also the cervical and thoracic nerve roots, intercostal nerves and cranial nerves. Symonds and Blackwood reported a case of spinal cord compression by root hypertrophy with Babinski's sign (9). In our case, although definite cord compression was seen on MRI, no neurological evidence was noted indicating cord involvement.

The nerve hypertrophy in CIDP is chiefly attributable to the proliferation of Schwann cells caused by repeated demyelination and remyelination (10). The mucopolysaccharides in the endoneurium as secondary products associated with nerve degeneration (11) and edema (12) may also be contributed to nerve swelling in CIDP. In other reports, neither onion bulb formation nor inflammatory findings was detected in the sural nerves, while remarkable onion bulb formation and inflammatory cell infiltration were present in the hypertrophied nerves (13, 14). In the right sural nerve of the present case, severe loss of myelinated fibers with slight proliferation of interstitial tissue and
Figure 4. T2-weighted sagittal image shows hypertrophy of the cauda equina (TR=2,052.5 ms, TE=70 ms).

Figure 5. 1 μ section of right sural nerve biopsy (toluidine blue, ×230). Severe loss of myelinated fibers and slight edema under the perineurium are present without inflammatory cell infiltration.

edema were present, suggesting that the hypertrophy of the nerves in our case might be associated with onion bulb formation. Prednisolone, plasma exchange, intravenous immune globulin and cyclosporine are choices of therapy for CIDP, but most have not been proven to be effective for nerve hypertrophy (4, 5), except for a case report stating steroid responsiveness (12). The present patient was treated with oral prednisolone with some clinical improvement, but no improvement for hypertrophy of peripheral nerves including cranial nerves was noted.

The cranial nerve involvement was clinically detected in the facial nerves, and was supported by the prolonged facial nerve conduction time and blink reflexes. Involvement of other cranial nerves was suggested by the results of BAEPs and MRI. Schady et al reported enlargement of the cranial nerves VII and the cauda equina (4), and Castillo and Mukherji showed enlargement and contrast enhancement of the cranial nerves III, V, VI, VII, VIII, IX, X and XI on MRI (6). In another report of CIDP, the enhancement of cranial nerve VIII was reported (7), and abnormal enhancement of the cauda equina was also reported (3). In our case, cranial nerves V, VI, VII and VIII were thickened, with Gd-DTPA enhancement of the cranial nerves III, V, VI and VIII. The mechanism for enhancement seen with inflammatory processes is considered to be due to breakdown of the blood-nerve barrier (15, 16).

In 66% of patients with CIDP, a slow monophasic progressive course was observed (17), as seen in our case. Nerve hypertrophy, the mild response to steroid therapy and absent inflammatory cell infiltration in the sural nerve biopsy in our patient might be explained by his long-standing progressive course.

Although the enlargement and enhancement of peripheral nerves and cranial nerves in CIDP have been reported by several others (3–7, 9, 10), to our knowledge, this is the first report to demonstrate the enlargement of multiple cranial nerves, together in the multiple nerve roots and intercostal nerve in the same patient. Multiple hypertrophic nerves in the intracranial, and intra- and extra-spinal segments might be identified by neuroimaging studies, without the corresponding clinical signs and symptoms.

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References


2) Research criteria for diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP). Report from an Ad Hoc Subcommittee of the


