LESSON OF THE MONTH

Hypertrophy of multiple cranial nerves and spinal roots in chronic inflammatory demyelinating neuropathy

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Hereditary motor and sensory neuropathy (HMSN) types I and III and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) in developed countries are the most frequent causes of enlargement of peripheral nerves, “hypertrophic neuropathy”, with clinically palpable thickened nerves, visible on MRI. They may even be the cause of spinal cord compression.

We report on a patient who developed clinical features that were interpreted elsewhere initially as a Guillain-Barré syndrome, and years later diagnosed as Dejerine-Sottas disease (HMSN III). We discuss the differential diagnosis between HMSN III and CIDP in this patient with a fluctuating but insidiously progressive 26 year history, in whom MRI demonstrated marked enlargement of multiple cranial nerves and spinal roots. We think that this is a dramatic example of cranial nerve and spinal root enlargement in a case of CIDP, and stress the importance of making a correct differential diagnosis when the disease presents in early childhood.

Case report
A 30 year old woman had had an upper respiratory infection at the age of 4; a few days later she had developed a rapidly progressive mixed motor and sensory distal impairment of all four limbs, more pronounced in lower limbs. Seen then in a children’s hospital, she was diagnosed as possibly having Guillain-Barré syndrome on the basis of altered electrophysiological studies, and an acellular CSF with high protein content (1.9 g/l). She remained stable for 3 months, improving slowly with physiotherapy, but never reached normality again.

Two years after the onset, she was again investigated because of progressive kyphoscoliosis, pes cavus, and hammer toes for which she had reconstructive surgery. By then there had been

Figure 1 Postcontrast T1 weighted sagittal images. Contrast enhancement of the anterior and posterior divisions of each cervical roots (arrows).
clear neurological progression with increased generalised muscle atrophy and weakness distally in all four limbs, more so in the lower limbs, with distal sensory loss (pain, temperature, and light touch), but only lower limb areflexia. Nerve conduction velocities had remained abnormally slow (9 and 10 m/s in the right peroneal and ulnar nerves and considerable delay of distal latencies), and the CSF protein was still high at 2.4 g/l. A nerve biopsy apparently showed a hypertrophic sural nerve, with striking onion bulb formation and occasional inflammatory infiltrates. No genetic studies for demyelinating HMSM I were available at the time.

She was seen by one of us (LEC) for the first time at the age of 8, confirming previous clinical signs, but she now had generalised areflexia and a left extensor plantar response. Electromyographic and nerve conduction findings were in keeping with a severe mixed, predominantly demyelinating polyneuropathy. Nerve conduction velocities had remained abnormally slow (9 and 10 m/s in the right peroneal and ulnar nerves and considerable delay of distal latencies), and the CSF protein was still high at 2.4 g/l. A nerve biopsy apparently showed a hypertrophic sural nerve, with striking onion bulb formation and occasional inflammatory infiltrates. No genetic studies for demyelinating HMSM I were available at the time.

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At the age of 22, she developed increasing difficulty in walking and her paraparesis evolved with bilateral extensor plantar response. An L2-L3 laminectomy at another hospital was performed because of spinal conus compression, but only enlarged thickened roots were found at surgery. Slight improvement occurred in the postoperative period, but 6 months later further motor and sensory deterioration occurred. MRI studies were performed before and after gadolinium DTPA administration. The spinal MRI showed thickening and contrast enhancement of nerve roots from their emergence from the spinal cord to the ganglia, both in the anterior and posterior segments (fig 1), with enlargement of the cauda equina, and widening of the intervertebral foramina. Cranial MRI showed both cavernous sinuses occupied by a mass-like lesion with a high signal intensity on the T2 weighted images (fig 2) and contrast enhancement. The first, second, and third divisions of the trigeminal nerves were clearly enlarged as they emerged through widened cranial foramina, with involvement of their frontal, supraorbital, and infraorbital branches. Contrast enhancement was seen in the more proximal segments involving the perineural aspects of the nerves. A 3 month trial of alternate day dexamethasone (4 mg) produced a remarkable motor improvement, which was sustained up to the age of 28 with a maintenance dose of dexamethasone (1 mg/alternate days). She was able to lead an independent life, walking with the support of one stick.

At the age of 28, further electrophysiological studies showed sporadic fasciculation and loss of motor units, surviving units being of increased amplitude. Decreased motor (20 m/s) and sensory conduction velocities (30 m/s), with reduced amplitude of sensory nerve action potentials, increased duration of motor and sensory evoked potentials, and conduction block of motor fibres on proximal stimulation in the tested nerve (median). No F response was registered. Transcranial magnetic stimulation evoked a long latency potential. Central motor conduction time, calculated by subtraction of latencies after vertex and radicular stimulation, was normal. There was an overall improvement in comparison with previous studies in the upper limbs, and a minor deterioration in the lower limbs. A possible diagnosis of CIDP was then considered. Intravenous immunoglobulin therapy (0.4 g/kg bodyweight/day) for five consecutive days was started. Two weeks later, she had improved markedly in both motor and sensory function, being able to walk without assistance, and her tremor decreased in intensity. Electrophysi-
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The onset of neuropathic symptoms in infancy usually suggests an inherited disorder, and therefore an acquired demyelinating neuropathy might not be considered. The diagnostic difficulty in recognising an inherited disorder is compounded by the apparent clinical and genetic heterogeneity of hereditary neuropathies in which autosomal dominant, recessive, and X-linked patterns of inheritance have been reported, as well as sporadic occurrences. It is only when the history and examination of relatives do not disclose evidence of neuropathy in the family that the possibility of an acquired and potentially treatable disorder tends to be considered.

Differentiating between CIDP and “spontaneous” HMSN is a common diagnostic problem in clinical neurology. Initially, the clinical features of our patient were interpreted elsewhere as a Guillain-Barré syndrome. Years later the diagnosis considered, despite the negative family history, was HMSN III on the basis of the neuropathological findings and skeletal deformities. Nevertheless, a detailed investigation of this patient, in particular at the age of 28, showed nerve conduction findings that suggested the possibility of CIDP of childhood onset, as the correct underlying diagnosis. Further support was provided by the MRI interpretation. Weakness persisted affecting both proximal and distal muscles, with universal areflexia. Motor nerve conduction velocities were low, and the CSF protein concentration remained increased. When CIDP develops slowly and its progression is more insidious, it may be difficult to distinguish it from a hereditary neuropathy, as occurred with our patient. There is a report of coexistent inflammatory demyelinating neuropathy in children of families with dominantly inherited neuropathy. Although there is considerable overlap in the range of characteristics encountered in the two groups of disorders, several clinical and laboratory features may be helpful in distinguishing CIDP from HMSN. Nerve conduction studies tend to be uniformly slow, although not always, in hereditary neuropathies, whereas in CIDP multifocal abnormalities may be detectable, as was found in our patient. MRI is a valuable complementary diagnostic tool in CIDP because pathological enhancement of the roots after intravenous gadolinium is indicative of blood-nerve barrier breakdown, suggesting inflammation.

There are few published references of CIDP, as opposed to HMSN, producing spinal cord compression syndromes. Indeed, as both disorders are hypertrophic neuropathies, they may develop syndromes of spinal cord compression at any level. Our patient presented bilateral proptosis and dipliaxia secondary to enlargement of cranial nerves in the cavernous sinuses and orbits, and a paraparesis due to the compression by enlarged and hypertrophic roots at the cauda equina and other levels of the spinal cord.

Nerve root enlargement in our case was striking and radiologically evident in MRI at both cavernous sinuses and orbits, of the trigeminal nerves and third portion of the facial nerve, and cervical, thoracic, and lumbar spinal nerve roots causing diffuse enlargement of the cauda equina. These findings are highly unusual in the same patient. Cranial nerve thickening has been reported before on cranial MRI in patients with HMSN, but not in patients with CIDP.

The remarkable improvement with steroids in our patient after such a long clinical history, and even more so with intravenous immunoglobulins, both clinically and electrophysiologically, would argue in favour of CIDP as the correct diagnosis.

We think, as did Ginsberg et al., that many of the case reports of secondary spinal cord compression syndromes classified as “hypertrophic neuropathy of Dejerine and Sottas” in the past might indeed be examples of CIDP. MRI together with electrophysiology studies, and treatment response may be necessary to establish a correct diagnosis.

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