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...
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 demylinating HSM 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. Electrolymographic and nerve conduction findings were in keeping with a severe mixed, predominantly demyelinating polyneuropathy. Protein in CSF was now 1.3 g/l. A nerve biopsy apparently showed a hypertrophic sural nerve, with striking onion bulb formation and occasional inflammatory infiltrates. No genetic studies for demylinating HSM I were available at the time.

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Hypertrophy of nerves in chronic inflammatory demyelinating neuropathy

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 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 propotosis and diplia 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.

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References