CASE REPORT

Spastic Paraplegia with Amyotrophy of the Legs: A Rare Case of Motor and Sensory Neuropathy

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(Received for publication on August 20, 1994)

Abstract. A 36-year-old man who suffers from gait disturbance is reported. He noticed deformity of his feet at the age of 15. When he was 32 years old, he complained of heaviness in his lower extremities. Since then his legs have been always stiff. He had no previous illness or familial neuromuscular diseases. Neurological examination revealed no impairment of mental function or cranial nerves. Marked weakness and wasting of the feet were noted. The legs showed an inverted champagne bottle shape and pes cavus deformity was evident. Deep tendon reflexes were normal in the arms but abnormally brisk in the legs. Bilateral Babinski sign and ankle clonus were elicited. The patient tended to walk on his toes and the legs scissored. The motor nerve velocities were less than normal. Sural nerve biopsy showed reduced myelinated fiber density and increased endoneurial connective tissue. Electron microscopy showed axonal swellings filled with neurofilaments. Distal wasting and weakness involving the legs more than the arms resembled that of Charcot-Marie-Tooth disease. According to the classification by Dyck, this disorder could be referred to as hereditary motor and sensory neuropathy type V. Spastic paraplegia with amyotrophy is rare, but should be identified as a distinct disorder. Recognition of this disorder would imply the clinical and genetic heterogeneity of Charcot-Marie-Tooth disease. (Keio J Med 43 (4): 206–210, December 1994)

Key words: Charcot-Marie-Tooth disease, peroneal muscular atrophy, polyneuropathy, HMSN type V, axonal swelling

Introduction

Much confusion exists regarding the classification and characteristics of disorders manifesting neurogenic muscular atrophy. Charcot-Marie-Tooth disease usually has the following characteristics: Onset with foot or gait symptoms in the first or second decade, pes cavus, a variable amount of clinically apparent nerve enlargement, weakness and mild atrophy only in distal muscles of the limbs beginning in the peroneal muscle group, and areflexia or hyporeflexia. But it has been well recognized that occasional patients with Charcot-Marie-Tooth disease have extensor plantar response. The pyramidal features were first identified as a distinct subgroup in two families by Dyck and Lambert in 1968.^{1,2}

On the other hand, wasting of the leg muscles in association with hereditary spastic paraplegia has rarely been described. In 1883, Strümpell³ reported inherited spastic paraplegia with distal limb weakness. Subsequent reports of kinship with spastic paraplegia, some patients with which had distal limb weakness, were made by various authors.^{4,5} In 1984, Dyck⁶ used the more general term, hereditary motor and sensory neuropathy (HMSN) and proposed a classification into 9 subgroups.

The patient we present here clinically resembles Charcot-Marie-Tooth disease, with distal wasting and weakness involving the legs more than the arms. But he also has the characteristics of spastic paraplegia with brisk knee jerk and scissors gait. We performed sural nerve biopsy and on the basis of the histological find-

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ings we discuss the clinical entity to which this disorder belongs.

Case Report

The patient was a 36-year-old man who was thought to be normal until approximately 15 years of age, when he noticed deformity of his feet. Nevertheless, he could participate in physical education classes at school without difficulty. At the age of 27 he noticed he fell frequently and became unsteady when he turned rapidly. However, he could run and jump without difficulty. When he was 32 years old, he complained of heaviness in his lower extremities. Since then his legs have always been stiff. His gait was spastic with some degree of crossing of one leg in front of the other. Apart from his weak legs, he had no other complaints. He had slow progression of the spastic weakness of his lower limbs. He had noticed pollakisuria but had no fecal or urinary incontinence. He was admitted to the hospital at the age of 36. There was no prior history of other serious illness. He stated that his mother and father had never had any trouble in walking. He had four brothers and two sisters who are all healthy. He has a female child who is said to present no neurological symptoms.

General physical examination revealed a moderately well nourished man. There was no evidence of mental deterioration. Cranial nerve functions were intact. No nystagmus was present. Volitional movements of the uvula were intact and no lingual fasciculations or wasting were noticed. Marked weakness and wasting of the feet were apparent. Distal wasting was such that the legs resemble inverted champagne bottles and pes cavus foot deformity was evident (Fig 1). Although other skeletal muscles were well developed, no fasciculations were seen. Hypertonicity was present in the legs. Deep tendon reflexes were normal in the arms but abnormally brisk in the legs. Bilateral Babinski sign and ankle clonus were elicited. No cerebellar signs could be elicited. Light touch, pain and vibration senses were diminished in the distal parts of the lower extremities. Nerves were not palpably enlarged.

There were no abnormalities in serum, urinary electrolytes and other blood chemistry. Radiographs of the head and spine, head CT scan, myelogram, electroencephalogram and cerebrospinal fluid were normal. In the electromyogram, neuropathic motor unit potentials were slightly increased in the lower extremities. Conduction velocities of motor fibers of the right median, right peroneal and left peroneal nerves were 40.5, 26.5 and 27.0 meters/sec, respectively. Cystometry showed an uninhibited bladder.

Muscle biopsy from the quadriceps femoris showed some small angulated fibers, suggesting slight neuropathic changes. Sural nerve biopsy showed reduced myelinated

Fig 1 Typical wasting of distal muscles in the lower limbs, producing the inverted champagne bottle appearance. Pes cavus deformity is evident. Other skeletal muscles are well developed.

Fig 2 Transverse section of sural nerve stained with paraphenylenediamine. The numbers of myelinated fibers are reduced and some axons are markedly swollen.

fiber density and increased endoneurial connective tissue. Bodian staining revealed that the density of neurofibers was evidently reduced and axonal swelling was noticed.

Fig 3 Electron microscopy shows axonal swellings filled with neurofilaments. Demyelination and remyelination are not evident. Onion-bulb formation is not present.

Staining with para-phenylenediamine (Fig 2) showed that the numbers of myelinated fibers were decreased. Axonal swellings were often observed. Electron microscopy showed axonal swellings filled with neurofilaments (Fig 3). Demyelination and remyelination were not evident. Onion-bulb formation was not present. In the high-power electron micrograph, the increased neurofilaments, whose diameter was about 10nm, were seen to fill the axon.

Discussion

The patient reported here had slow progression of the weakness of his lower limbs. Distal wasting was such that the legs resembled inverted champagne bottles and pes cavus foot deformity was evident. The presenting symptoms resembled those of Charcot-Marie-Tooth disease. An important clue to the diagnosis of this patient was the suggestion of spasticity in the gait.

Charcot-Marie-Tooth disease is an inherited polyneuropathy described in 1886 almost simultaneously by Tooth⁷ in England and by Charcot and Marie⁸ in France. Essentially this is a chronic degeneration of the peripheral nerves and roots, resulting in distal muscle atrophy, beginning in the feet and legs and later involving the hands. The thin legs have been likened to those of a stork or, if the lower thigh muscles are affected, to an inverted champagne bottle. Paresthesia and cramps are invariably present to some degree and there is always

some impairment of deep and superficial sensation in the feet and hands, shading off proximally.

Dyck⁶ classified hereditary motor and sensory neuropathy (HMSN) into 9 groups in 1984 and this classification is now generally accepted. According to this, Charcot-Marie-Tooth disease corresponds to HMSN type I and type II. Measurement of nerve conduction velocities and sural nerve biopsy permit recognition of two distinct forms of Charcot-Marie-Tooth disease. Type I is the demyelination form. Nerve conduction velocities are less than 65% of normal and distal latencies are prolonged. Nerve biopsies show segmental demyelination, partial remyelination and onion-bulb formation.

Type II is the axonal form, which is less common than type I. Nerve conduction velocities exceed 65% of normal, but the amplitude of evoked responses is reduced. Nerve biopsies show axonal loss with little evidence of demyelination. Hypertrophic onion-bulb changes are observed only rarely. In type I, symptoms begin in the first or second decade of life with foot drop and steppage gait. The clinical features of type II resemble those of type I, but the onset of symptoms is generally later, in the second decade of life, and can be delayed until old age.⁹

Type III corresponds to Dejerine-Sottas disease.¹⁰ It resembles Charcot-Marie-Tooth disease but the onset is earlier and nerve hypertrophy is more prominent. Motor nerve conduction is extremely slow, falling to less than 12 m/sec. Nerve biopsies show extensive onion-bulb formation and marked thinning of the myelin sheaths surrounding axons of all diameters.

Type IV is equivalent to Refsum disease.¹¹ It resembles Dejerine-Sottas disease in the distal motor and sensory abnormalities. But it also has retinitis pigmentosa, progressive neurogenic hearing loss and scaly skin. Serum phytanic acid content is markedly elevated.

Type V is HMSN with spastic paraplegia.⁶ Hereditary spastic paraplegia can be subdivided into two groups depending on whether the disorder is a pure spastic paraplegia or a more complex syndrome with other associated features.¹²⁻¹⁴ Complicated forms of hereditary spastic paraplegia are all rare. Silver¹⁵ reported a distinct disorder in which dominantly inherited spastic paraplegia was associated with moderate or severe wasting and weakness of the small hand muscles. Symptoms referable to the legs were minimal or absent. The Troyer syndrome¹⁶ is autosomal recessive and comprises delayed development, spastic quadriplegia, pseudobulbar palsy, distal wasting in the limbs, dystonia and short stature. Harding and Thomas¹⁷ reported twenty-five cases of peroneal muscular atrophy with pyramidal features from 15 families. It differs from Charcot-Marie-Tooth disease in that the knee jerks are usually brisk, the plantar responses are extensor, and the patient's gait often exhibits spasticity.

It has been recognized that occasional patients with Charcot-Marie-Tooth disease have extensor plantar responses. These pyramidal features were first delineated in 1968 by Dyck and Lambert,^{1,2} who described patients from two families who all had pyramidal signs in the legs as well as peroneal muscular atrophy. Pyramidal signs may occasionally develop as a result of hypertrophied nerve roots compressing the spinal cord.¹⁸

There have been few reports on peripheral nerve histology in HMSN type V. Dyck¹⁹ has reported loss of large myelinated fibers in older patients. Behse and Buchthal²⁰ found a slight loss of large myelinated fibers in two out of five patients stated to have hereditary spastic paraplegia with peroneal muscular atrophy. In our case, histological findings show axonal swellings filled with neurofilaments. Demyelination and onion-bulb changes were not evident. The changes resemble those of HMSN type II more than those of type I.

Our case did not show a contributory family history. However, HMSN includes sporadic cases which have been generally interpreted as being recessively inherited.^{9,21} Even if family history is reported as negative, relatives might have mild neurologic deficits of which they are unaware, or which they have ignored. The severity of the disease varies and it may be so mild as to be asymptomatic.

There are important clinical differences between Charcot-Marie-Tooth disease and HMSN type V. In post-mortem study of four typical cases of Charcot-Marie-Tooth disease, Hughes and Brownell²² demonstrated severe atrophy of peripheral nerves, both motor and sensory, with degenerative changes and loss of neurons in the anterior horns and posterior root ganglia and corresponding degeneration of the posterior columns. The pyramidal tracts appeared intact. Those findings agree with those reported in the older literature. In the most cases of Charcot-Marie-Tooth disease the knee jerks are absent or depressed. Whereas in HMSN type V, the knee jerks are always increased and symptoms most frequently begin in the legs with a progressive spastic gait disturbance. Clinically it should be stressed that HMSN with spastic paraplegia is quite distinct from Charcot-Marie-Tooth disease. According to the classification of Dyck,⁶ our case can be regarded as HMSN type V.

On post-mortem examination of familial spastic paraplegia, Strümpell²³ found degeneration of the pyramidal tracts, beginning below their decussation and most definite in the lower thoracic and lumbar segments. Within single families, there are wide variations in age of onset, severity of symptoms, and associated disabilities. In some cases, spasticity and weakness are followed by loss of motor neurons and amyotrophy. According to the classification of Harding and Thomas,¹⁴ this case can be made classified among the complicated forms of hereditary

spastic paraplegia associated with amyotrophy. Spastic paraplegia with amyotrophy is rare but should be identified as a distinct disorder. Recognition of this disorder would imply the clinical and genetic heterogeneity of Charcot-Marie-Tooth disease.

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