ELECTROPHYSIOLOGICAL CHARACTERIZATION IN HEREDITARY SPASTIC PARAPLEGIA CAN EVENTUALLY ADDRESS MOLECULAR DIAGNOSIS?

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Introduction

The hereditary spastic paraplegia (HSP) are a heterogeneous group of disorders with common feature: length dependent axonopathy of the corticospinal motor neurons is the pathophysiological mechanism supposed to lead to gait spasticity. HSPs are among the most genetically-diverse neurologic disorders (mutation knowing over 90 genes)

Objective

To assess in SPG hereditary spastic paraparesis (HSP) the involvement of both PNS and CNS by a multimodal electrophysiological approach

Methods, subjects

A 20 years old boy (case1) and a 79 years old man (case2) of the same family are affected by spastic paraparesis: they underwent electrophysiological evaluation including EMG, NCS, MEPs by TMS and sensory EPs.

Results

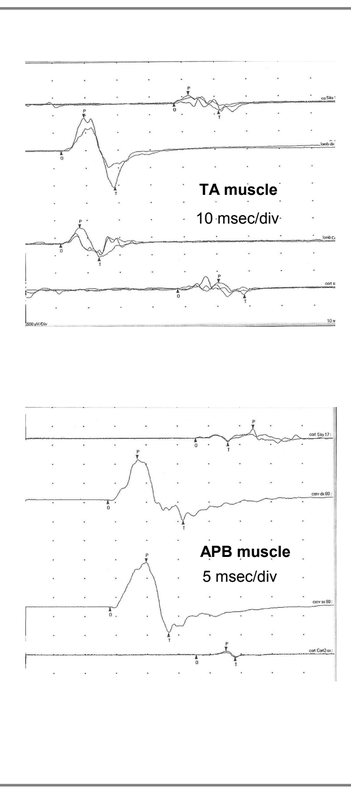
Case 1. Disease onset occurred in early childhood: pes cavus without spine deformity, progressive gait disturbance, muscle weakness and distal atrophy were observed. A first molecular DNA analysis did not reveal any mutation for CMT2A,CMT4A,CMT2D and CMTX.
He receive extracurricular assistance with reading and writing.
Actually, at the age of 21, neurological examination reveals a mild spastic hypertonia at the lower limbs with pyramidal signs. Sensory function is preserved, visual acuity is normal; the gait is possible without any support. Table for results case 1.
Case 2. Disease onset occurred in the middle sixties. The patient developed motor impairment to the lower limbs with increased muscle tone and spasticity: pyramidal signs, without atrophy, are associated to distal sensory defect. Actually, the gait is severely impaired and only possible with aid. . Table for results case 2.
In both cases spinal and brain MRI did not show any cause for the pyramidal syndrome.

Neurophysiological study

CASE1					
MCV LD AMPL	R med 48 4,5 4,8	R uln 45 4,5 5,8	R per 31 5,2 1,2	L per 27 6,5 0,8	L sur
SCV LD AMPL	 3,8 18,1	 3,5 15,8			37 3,3 8,7
MEPs UL	R CCT 15,0	L CCT 14,9	R PCT 13,8	L PCT 14,1	
MEPs LL	R CCT 36,5	L CCT 36,2	R CCT 12,5	L CCT 12,7	

CASE 2					
MCV LD AMPL	R med 51 3,5 7,1	R uln 56 3,0 8,3	R per 41 3,7 3,7	L per 41 4,1 3,7	
SCV LD AMPL	ABS	ABS			33 3,3 4,0
MEPs UL	R CCT 13,6	L CCT 13,3	R PCT 16,2	L PCT 15,9	
MEPs LL	R CCT 34,4	L CCT 15,9	R CCT 32,9	L CCT 15,3	

FIG 1



Conclusions

In these patients of the same family, both clinical and NCS a different involvement of the PNS: motor neuropathy (predominantly demyelinating) in case 1, and a sensory polyneuropathy (case 2). Motor evoked potentials showed similar abnormalities in both cases: overall a slowing of the central conduction was found both from lower and upper limbs (FIG 1)

Neurophysiological testing provides very useful information concerning the pathophysiology of the disease to eventually address the molecular diagnosis.
Inevitably in some cases, a single conclusively pathogenetic mutation cannot be identified and one or more candidate pathogenetic mutation remain (REEP2/MTPAP in our family).

Diverse clinical features have been reported with *SPG* mutations, including diversity in presentation and clinical course: comprehensive electrophysiological testing disclosed a more widespread affection of nervous system and could reflect different underlying pathomechanisms of HSP. (FIG 2)

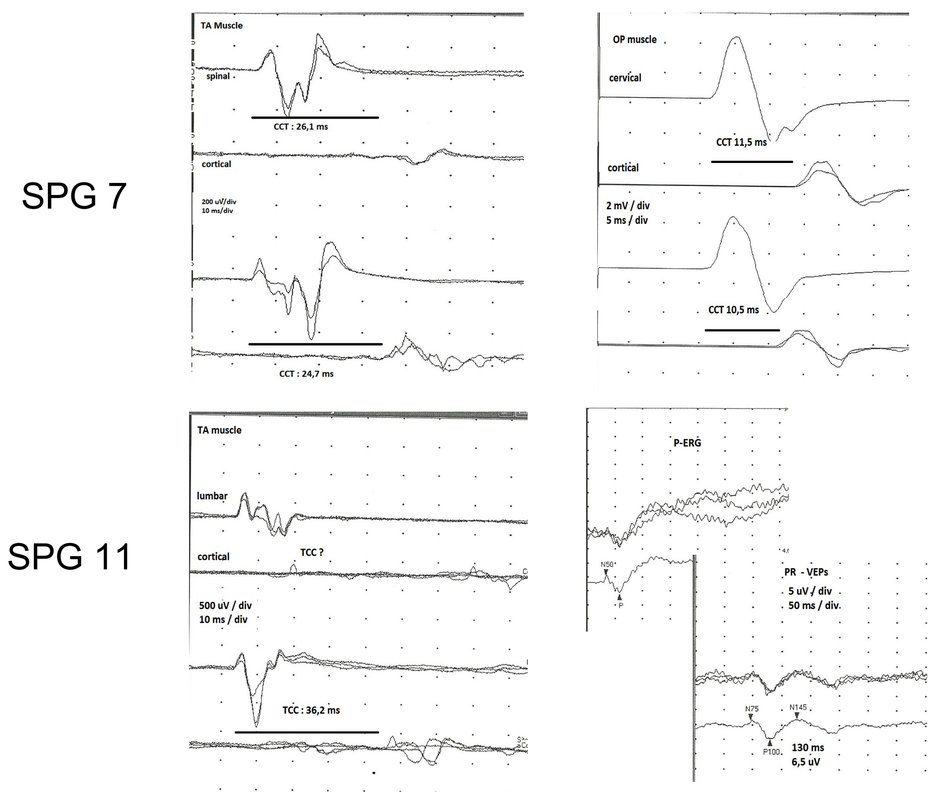


FIG 2

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