Progressive spastic paraparesis with cerebellar ataxia: a case of hereditary spastic paraplegia caused by mutation in the SPG7 gene

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BACKGROUND

Hereditary spastic paraplegias (HSP) are a group of clinically and genetically heterogeneous neurodegenerative diseases. They are characterized by lower limb weakness and spasticity with subtle onset and slowly progressive course, that could be associated with additional neurological (such as epilepsy, parkinsonism, ataxia) and systemic features, so HSP can be classified as pure or complicated forms (table 1).

Harding's classification, based on signs and symptoms	
Pure HSP	Spastic paraparesis with sphincter disturbances and mild to moderate sensory loss
Complicated HSP	Spastic paraparesis plus additional neurological and systemic signs and symptoms

Table 1

HSP can be inherited as autosomal dominant, autosomal recessive, X-linked, or maternal pattern traits disorders (table 2).

Classification based on pattern of inheritance	
Autosomal dominant HSP	SPG3A, SPG4, SPG6, SPG8, SPG9, SPG10, SPG12, SPG13, SPG17,SPG19, SPG29, SPG31, SPG33, SPG36, SPG37, SPG38, SPG41, SPG42,SPG72, SPG73
Autosomal recessive HSP	SPG5, SPG7, SPG11, SPG14, SPG15, SPG18, SPG20, SPG21, SPG23,SPG24, SPG25, SPG26, SPG27, SPG28, SPG30, SPG32, SPG35, SPG39,SPG43, SPG44, SPG45/SPG65, SPG46, SPG47, SPG48, SPG49, SPG50, SPG51, SPG52, SPG53, SPG54, SPG55, SPG56, SPG57, SPG58, SPG59, SPG60, SPG61, SPG62, SPG63, SPG64, SPG66, SPG67, SPG68, SPG69, SPG70, SPG71, SPG72, SPG74
X linked HSP	SPG1, SPG2, SPG16, SPG22, SPG34
Mitochondrial HSP	MT-ATP6, MT-TI, MT-CO3, MT-ND4

Table 2

CASE REPORT

A 50 years old man started complaining about gait disturbance associated with leg stiffness and urinary urgency.
He was admitted to a Neurology Unit at another Hospital where a spastic paraparesis with hyperreflexia in lower limbs were revealed; he did blood tests, with autoantibodies and serological investigations for neurotropic viruses, a MRI of the brain, a lumbar puncture and an electromyography that didn't show any abnormalities. He also underwent motor evoked potentials and sensory evoked potentials, which were altered in lower limbs.
A MRI of the cervical and thoracic spine showed a cervical disc herniation (C5-C6) with slight compression of the dural sac, that was treated with neurosurgery through cage positioning, without clinical benefits.
During the following years, the patient worsened and, seven years after the appearance of signs and symptoms, he was admitted to the center for Rare Neurological Diseases at the Neurology Department, Careggi University Hospital, Florence.

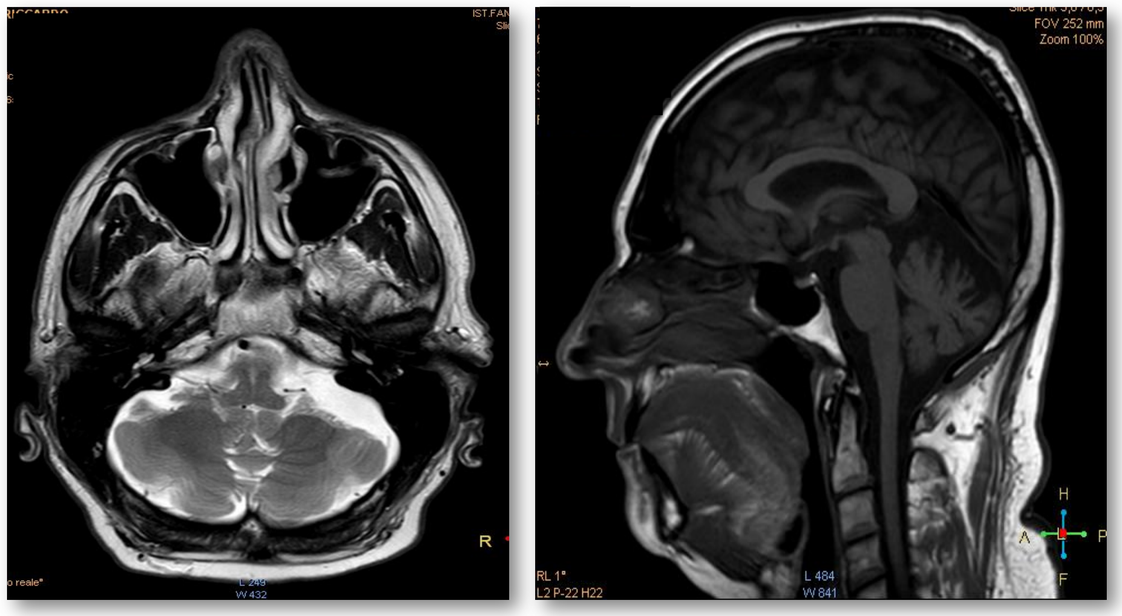

Figure 1

At neurological examination the patient had a parapareto-ataxic gait, clonus, Babinski sign bilaterally, spasticity, hyperreflexia and dysmetria in the lower limbs. Bilateral pes cavus was observed.
He underwent a new MRI of the brain that showed marked cerebellar atrophy (Fig. 1).
In the suspicion of a hereditary spastic paraplegia, genetic tests for SPG4 and SPG7 were performed, although he had not familiar history for neurological diseases.
Test for SPG4 was negative, while a compound heterozygous mutation c.1529C>T (p.A510V) e c.2216dupA in SPG7 was identified.

CONCLUSIONS

- Hereditary spastic paraplegias represent a challenge in clinical practice because of its clinical differential diagnosis and heterogeneity in clinical presentation that should be considered in patients with spastic paraparesis with or without other neurological features, after the exclusion of other acquired and inherited causes of spastic paraparesis.

- SPG7 mutation leads to a complicated HSP with interfamilial variability characterized by adult onset spastic paraparesis, ataxia, pes cavus and sphincter disturbances.

References:
-Paulo Victor Sgobbi de Souza et al., Hereditary spastic Paraplegia: Clinical and Genetic Hallmarks, Cerebellum, 2017
- Ingrid Faber et al., Clinical features and management oh hereditary spastic paraplegias, Arq Neuropsiquiatr, 2014
- Rebecca Schule, Genetics of hereditary spastic paraplegias, Seminars in Neurology, 2011

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