# A NOVEL MUTATION WIDENING THE SPECTRUM OF MUTATIONS IN SPG11 GENE

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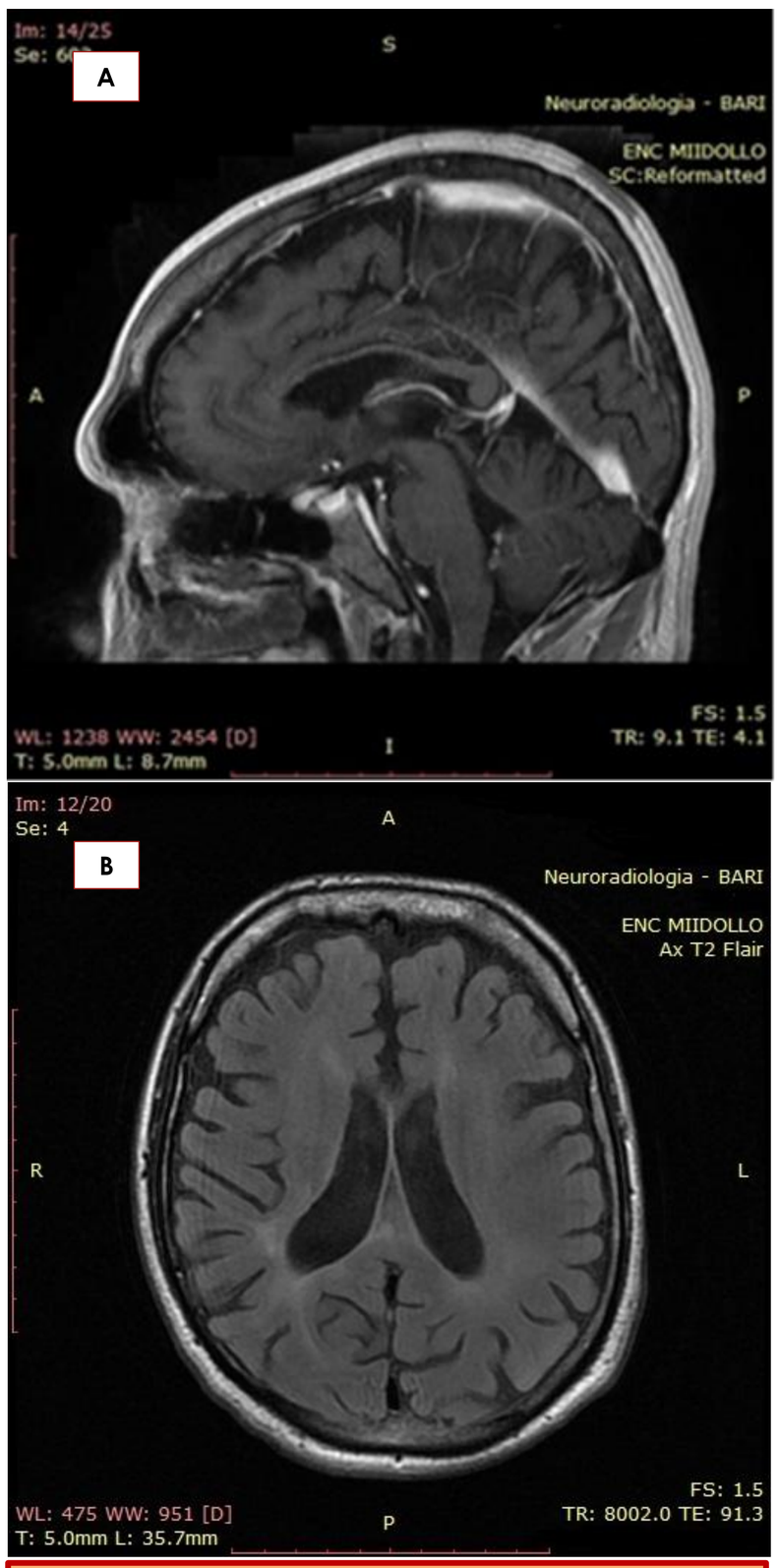


***Figure 1 . (A)*** *T1 MRI brain sagittal section showed considerable thinning of the anterior part and the body of corpus callosum: (B) Flair axial section showed periventricular and subcortical white matter hyperintensity*

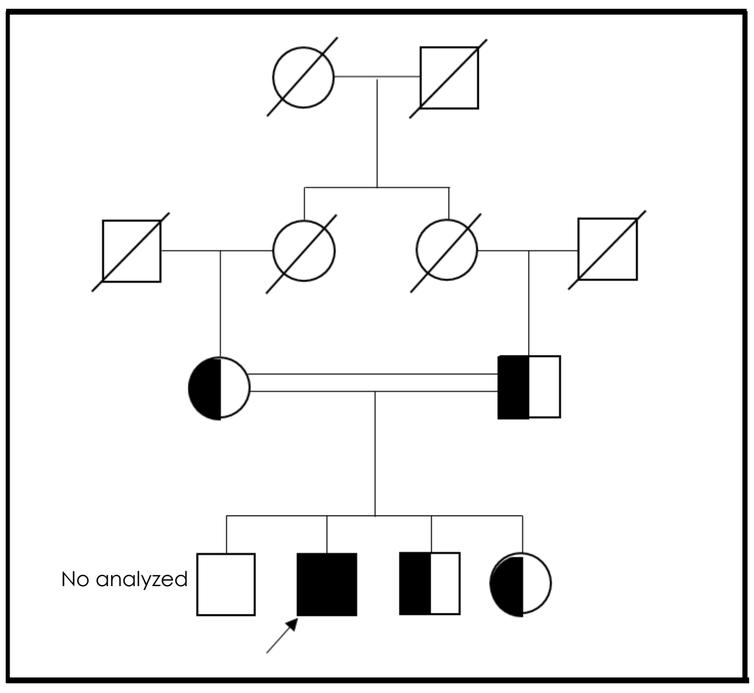


**Figure 2**: Arrow identify the proband. All relatives analized were healthy carriers.
Note that parents were consanguineous.

## Background

Hereditary spastic paraplegias (**HSPs**) are a heterogeneous group of inherited disorders with prevalence 4.8-13.9/100000 people, all characterized by progressive spastic paraparesis [1]. Different chromosomal loci have been identified, which are inherited as autosomal dominant, recessive and X-linked trait [2]. **HSPs** are classified into "pure forms", when isolated spasticity occurs and "complex forms", when additional neurological manifestations are present [3]. **SPG11** represents the most frequent autosomal recessive form of complex HSP, showing spasticity associated with thin corpus callosum (**ARHSP-TCC**) [1]. Several studies confirmed linkage to the 15q chromosome in **ARHSP-TCC** families [2]. All mutations induce the premature truncation of the gene encoding for the **spatacsin**, with a consequent loss of protein's function. A phenotypic variability suggests diverse roles played by spatacsin in the brain [4].

## Case Report

We describe a case of 27-year-old man came to our observation with a **spastic progressive paraparesis** history by several years. He was born by a consanguineous marriage. The motor and psychomotor developmental milestones were reached normally up to 12 years old, when he showed progressive gait difficulties, stiffness and clumsiness. Three years later he developed progressive dysarthria, learning disability, and spastic paraparesis, with loss of walking independence at the age of 25. At neurological examination he showed severe spastic paraparesis, diffuse muscle atrophy, sphinteric impairment and a MMSE score of 24/30. Pes cavus, scoliosis and seborrheic dermatitis were associated. Signs of peripheral axonal neuropathy were found at electrophysiological study. Brain MRI showed a cortical atrophy, more evident in fronto-parietal lobes, a thinning of the body of corpus callosum and a diffuse FLAIR periventricular and subcortical white matter hyperintensity ***(Figure 1 A-B)***. Spinal cord RMI was normal. Analysis of spatacsin gene on chromosome 15q21.1 of patient identified a **homozygous mutation (c.6463G>T) which results in a truncated protein (p.E2155X**), confirming the diagnosis of SPG11. All relatives analyzed (both the parents, the brother and the sister) were healthy carriers of the same patient's gene mutation in heterozygosis. ***(Figure 2)***

## Discussion

The study widens the spectrum of mutations in SPG11, showing a new mutation in the SPG11 genomic sequence. This mutation supports the concept that the role of spatacsin protein is essential to the function and the survival of different neuronal cell populations and a mutation or loss of this protein may induce neurodegeneration.

**REFERENCES:**

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