Mutations in the SPG7 gene encoding paraplegin are responsible for autosomal recessive SPG7 hereditary spastic paraplegia. We screened 134 unrelated index cases, selected in 4 different settings: 6 SPG7 patients identified during analyses of SPG31 using the MLPA kit containing SPG7 (n=7), previously reported ambiguous SPG7 cases (n=5), patients carefully selected on the basis of their phenotype (spastic paraparesis with cerebellar signs and/or cerebellar atrophy on MRI/CT scan and/or optic neuropathy and without other signs) (n=24) and hereditary spastic paraparesis patients referred consecutively from attending neurologists and the national reference center in a diagnostic setting (n=98). We indentified 23 SPG7-positive patients, 21% of the patients selected according to phenotype but only 8% of those referred directly. We confirm the pathogenicity of the Ala510Val mutation, previously identified as a variant of unknown significance. It was the most frequent mutation in our series (65%) that included a family with patients homozygous for this mutation.

Onset occurred late, at a median age of 39 years (range from 18 to 52 years). The disease progressed very slowly, with follow-ups as long as 17 years. The most frequent signs associated with SPG7 were cerebellar ataxia (9/23), cerebellar atrophy (9/19) and optic neuropathy or abnormalities revealed by Optical Coherence Tomography (10/10), which should be taken into account for genetic testing. Finally, 3 single heterozygous relatives had cerebellar signs or atrophy, or peripheral neuropathy, but no spastic paraplegia, suggesting that heterozygous mutations might predispose to cerebellar syndrome/atrophy or neuropathy.