Juvenile ALS with long-term survival associated with *spastin* gene mutation

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Background: Juvenile ALS (JALS) is a form of chronic motor neuron disease presenting with upper and lower motor neuron symptoms prior to the age of 25 years. Rare cases of JALS with a survival of more than three decades have been described. Genetic risk factors of sporadic JALS are largely unknown.
Objective: to describe a male patient with apparently sporadic JALS at the age of 72 years with a natural history of ALS for 48 years.
Design: a case report, magnetic resonance imaging of the brain and mutation analysis of the *spastin* gene (SPG4).
Result: at the age of 24 years the patient developed a progressive lower motor neuron syndrome of the left hand followed by paresis and atrophy of the distal left lower limb. In the course of 2 years he showed a pyramidal syndrome of all extremities and a progressive bulbar and pseudobulbar syndrome. Since then he has fulfilled the diagnostic criteria for definite ALS. Recent magnetic resonance imaging of the brain has demonstrated severe occipital, parietal and insular atrophy in decreasing order. Mutation analysis of the locus SPG4 for hereditary spastic paraplegia (HSP) identified a heterozygous protein-changing mutation (c.304_309dupGCCTCG) within exon 1 of the *spastin* gene.
Conclusion: We report the first case of ALS demonstrating a mutation in the HSP-related *spastin* gene. We propose that sequence variants of spastin might serve as a previously unknown genetic risk factor for JALS. The finding implicates the potential involvement of the spastin gene in a greater spectrum of motor neuron disorders including clinical variants of ALS.