SPG31: a rather frequent form of autosomal dominant HSP?

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Hereditary spastic paraplegia (HSP) is a clinically and genetically heterogeneous disorder characterized by progressive spasticity, weakness and hyperreflexia of the lower limbs. It is divided into a 'pure' form with progressive spasticity as an isolated symptom and 'complicated' forms accompanied by other neurological abnormalities.

In ~55% of families with the 'pure' autosomal dominant form of HSP, DNA sequence analysis identifies a mutation (including gross deletions) in the *SPG4* gene (spastin) and in ~9% a mutation in the *SPG3* gene (atlastin). Mutations in the *SPG31* gene (REEP1) were exclusively analysed in a single study, and pathogenic mutations were then identified in 6.5% of cases. We, therefore, determined the frequency of mutations in the *SPG31* gene in a second cohort of patients with the 'pure' autosomal dominant form of HSP. We analysed blood samples from 162 patients with positive family history (symptoms of 'pure' HSP present in ≥2 persons) for mutations in the *SPG31* genes using DHPLC and direct sequencing analysis.

We found pathogenic mutations (small insertions/deletions, nonsense-, splice-site and 3'UTR exchanges) in ~4.3% of cases and novel variants (missense and splice sites) in ~1.9% of cases. Thus, mutation analysis in the *SPG31* gene must be included in the comprehensive care for patients with the 'pure' autosomal dominant form of HSP.