

THE ASSESSMENT OF THE CLINICAL PHENOMENA OF TWO NOVEL SPAST MUTATIONS

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Hereditary spastic paraplegia is heterogeneous group of genetically inherited disorders mainly characterized by spastic gait impairment. There are more than 50 mutations which can be responsible for the development of symptoms. Our aim was to present the genotype-phenotype correlation of a previously unpublished novel mutation site in the *SPAST* gene, and furthermore to report a *de novo* mutation leading to the development of characteristic symptoms in early childhood. The first case is a 47-year-old female patient with slight spasticity in her lower limbs considerably disturbing her gait and frequent urge to urinate and to have bowel functions. With regard to her family history, her father is wheelchair-bound because of a similar gait disorder. The genetic testing for a disease-causing mutation in the *SPAST* gene revealed heterozygous mutation in exon 17 (c.1732AT p.R578X) not only in our patient, but also in her father. The second case is an 8-year-old boy with spastic paraparesis. Genetic testing showed a *de novo* mutation in exon 11 of the *SPAST* gene (c.1334GC p.S445T). Although both genetic mutations affect the AAA domain of spastin – similarly to most of *SPAST* mutations – the clinical phenomenology is quite different. With regard to the first case, the closest known affected site by a nonsense mutation (c.1741CT p.R581X) causes similar symptoms, but slightly later disease onset. With regard to the second case, although the age at onset is quite different from the previously reported case of p.S445R amino acid change in spastin, the clinical course shows some similarities.