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# Mutation in intron 5 of GTP cyclohydrolase 1 gene causes dopa-responsive dystonia (Segawa syndrome) in a Brazilian family

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**ABSTRACT.** Dopa-responsive dystonia (DRD), also known as Segawa syndrome or hereditary progressive dystonia with diurnal fluctuation, is clinically characterized by the occurrence of simultaneous or late Parkinsonism and by an excellent response to treatment with low doses of L-dopa. Diagnosis of DRD is essentially clinical. It is based on clinical history and the response to treatment with low doses of L-dopa. However, due to the low penetrance of the disease, asymptomatic carriers may exist. In these cases, mutational analysis of the GCH1 gene is an alternative to diagnose DRD. In the present study, we investigated a large DRD-carrier family in an attempt to identify the disease-causing mutation. The proband, a young woman diagnosed at the age of 13 years, is the daughter of a healthy non-consanguineous couple with history of several cases, on the maternal side of the family, of tip-toeing, disturbance of gait, Parkinsonism, rigidity and cramps in the lower limbs. Using single

 

strand conformational polymorphism and DNA sequencing techniques to analyze DNA extracted from blood samples, we identified a mutation in the GCH1 gene, IVS5+3insT, which would preclude the formation of the active enzyme due to the formation of truncated peptides.

**Key words:** Dopa-responsive dystonia; Segawa syndrome; GCH1 gene; GTP cyclohydrolase; Negative dominant effect; Hereditary progressive dystonia with diurnal fluctuation

 