

Clinical Heterogeneity of Autosomal Recessive Spastic Paraplegias

Analysis of 106 Patients in 46 Families

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Abstract

Background Hereditary spastic paraplegias (HSPs) are a heterogeneous group of neurodegenerative disorders characterized by progressive and predominant spasticity of the lower limbs, in which dominant, recessive, and X-linked forms have been described. While autosomal dominant HSP has been extensively studied, autosomal recessive HSP is less well known and is considered a rare condition.

Objective To analyze the clinical presentation in a large group of patients with autosomal recessive HSP from Portugal and Algeria to define homogeneous groups that could serve as a guide for future molecular studies.

Results Clinical features in 106 patients belonging to 46 Portuguese and Algerian families with autosomal recessive HSP are presented, as well as the results of molecular studies in 23 of these families. Five phenotypes are defined: (1) pure early-onset families, (2) pure late-onset families, (3) complex families with mental retardation, (4) complex families with mental retardation and peripheral neuropathy, and (5) complex families with cerebellar ataxia. Six additional families have specific complex presentations, each of which is unique in the present series. Pyramidal signs in the upper limbs and pes cavus are frequent findings, while pseudobulbar signs, including dysarthria, dysphagia, and brisk jaw jerks, are more frequent in the complex forms. The complex forms have a poorer prognosis, while pure forms, particularly those with early onset, are more benign. One Algerian pure early-onset kindred was linked to the locus on chromosome 8, previously reported in 4 Tunisian families. Two of the Portuguese kindreds with complex forms (one with mental retardation and the other associated with hypoplasia of the corpus callosum) showed linkage to the locus recently identified on chromosome 16.

Conclusions Although autosomal recessive HSP represents a heterogeneous group of diseases, some phenotypes can be defined by analyzing a large group of patients. The fact that only one Algerian family was linked to chromosome 8 suggests that this is a rare localization even in kindreds with the same ethnic background. Linkage to chromosome 16 was found in 2 clinically diverse Portuguese kindreds, illustrating that this locus is also rare and may correspond to different phenotypes.