Mol Biol Rep. 2012 Jan 5.

A missense mutation (p.G274R) in gene ASPA causes Canavan disease in a Pakistani family.

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Source: Department of Biotechnology and Informatics, BUITEMS, Quetta, Pakistan.

Abstract

Canavan disease (OMIM 271900) is an autosomal recessive lethal neurodegenerative disorder characterized by spongy degeneration of the brain. A highly consanguineous Pakistani family with Canavan disease was enrolled on the basis of diagnosis. All the affected individuals have mental retardation, megalocephaly and degradation of motor skills, poor head control, partial vision loss, weakness of the muscles and raised urinary concentration of N-acetyl aspartic acid in the urine. Blood samples were collected from affected as well as normal siblings and processed for DNA purification. Linkage analysis was performed by typing three short tandem repeat markers D17S1583 (7.19 cM), D17S1828 (10.02 cM) and D17S919 (14.69 cM) for an already-reported gene/locus ASPA at chromosome 17p13.2 causing Canavan disease. During linkage analysis, all the affected individuals were homozygous for short tandem repeat markers while the normal siblings were heterozygous showing co-segregation of the disease. Gene ASPA (NM_000049) was undertaken to sequence for mutation analysis. As a result of sequence analysis, we found missense substitution 740A→G (p.G274R) in exon 6 of gene ASPA. To our knowledge, this is the first report about Canavan disease on a Pakistani family.

PMID: 22219087 [PubMed - as supplied by publisher]