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Clinical and molecular determinants of ataxia-telangiectasia in Pakistani ethnicity

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Abstract

Cerebellar ataxia is characterized by nystagmus, tremor, dysarthria, and cognitive impairment. An autosomal recessive condition called ataxia-telangiectasia (AT) is characterized by immune system abnormalities, telangiectases, cerebellar ataxia, and a propensity for cancer. It results from a homozygous or compound heterozygous mutation in the ATM gene at chromosome 11q22. The *ATM* encodes for the ATM protein, which is one of the proteins that phosphorylates important substrates involved in cell cycle regulation and/or DNA repair in response to damage to DNA. Due to a lack of integrated registries and genetic testing capabilities, prevalence data for cerebellar ataxia are sparse in some Asian countries, most notably Pakistan. The purpose of this research is to shed more light on the genetic and clinical signs of hereditary ataxia in a family from Pakistan. We investigated a Pakistani family that displayed clinical signs of ataxia telangiectasia using whole exome sequencing. On the family members that were available, a segregation analysis was done. The proband's symptoms began at the age of five years old and included muscular weakness, telangiectasia, severe dysarthria, slurred speech, and difficulty walking. We identified a homozygous frameshift variation c.3503dup (p.Cys1168TrpfsTer11) in *ATM*. The findings of this study contribute to a better knowledge of the genetic architecture and phenotypic diversity of the illness in the Pakistani community.

Keywords: *Cerebellar Ataxias; Whole exome sequencing; Pakistan; Consanguity*