Intron Variant Cause DICER1 Syndrome with Pleuropulmonary Blastoma

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Abstract

DICER1 syndrome (OMIM 601200) is a rare autosomal dominant familial tumor susceptibility disorder with heterozygous DICER1 germline mutations. The most common tumor in clinical practice is pleuropulmonary blastoma. Pleuropulmonary blastoma is a rare pediatric lung tumor that begins during fetal lung development and is part of an inherited tumor syndrome. We found a patient with pleuropulmonary blastoma in clinical practice and performed whole exome testing on him and his parents. The mutation is located at DICER1 gene, c. 1510-16G>A. The tested person has a heterozygous variation at this locus. The tested person's father has no variation at this locus, while the tested person's mother has a heterozygous variation at this locus. According to the ACMG guidelines, this mutation has been preliminarily determined as clinically significant (Uncertain) PM2_Supporting: The frequency of this Supporting variation in the normal population database is unknown; there is no report of correlation for this locus in the literature database, and the ClinVar database does not feature this locus. Point pathogenicity analysis results: Analysis of splicing was carried out by Sanger sequencing and RT-PCR from peripheral blood and a minigene splicing assay, both of which showed a deletion of exon 10 resulting from the c. 1510-16G>A variant at the mRNA level. Bioinformatic analysis of the reported c. 1510-16G>A variant suggests that the variant is pathogenic. Based on the clinical characteristics of the patient and the functional verification of the gene variants, our pediatricians have finally diagnosed the infant with pleuropulmonary blastoma (OMIM: 601200). Our findings expand the mutation spectrum leading to DICER1 deficiency-related diseases and provide accurate information for genetic counseling.

Keywords

DICER1 Syndrome, DICER1 Gene, Pleuropulmonary Blastoma, Minigene Splicing Assay