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abstract

The germline genetic testing in children with DICER1-associated benign and malignant tumors: A 6-year single-center experience

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abstract

The germline genetic testing in children with DICER1-associated benign and malignant tumors: A 6-year single-center experience

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Introduction: DICER1 syndrome is characterized by predisposition to a tumour growth during the lifetime. The syndrome is caused by germline pathogenic variants (PVs) in the DICER1 gene. We present the results of germline molecular genetic testing of the DICER1 gene in children with DICER1-associated malignant and benign tumors during a 6-year period in our Center (2019 – 2024).

Methodology: The retrospective analysis of 28 probands suspected of DICER1 syndrome was performed. The DNA was isolated from the blood. Next generation sequencing (NGS) with a custom panel and Sanger method were used to detect single nucleotide variants (SNVs), and MLPA was used to detect whole exon/gene deletions. The germline PVs in the DICER1 gene were confirmed in 17 probands. The relatives (parents and siblings) were also tested if their DNA was available.

Results: In 6 families, we observed two siblings with DICER1 syndrome, and in 3 of them siblings were asymptomatic at the moment of investigation. Totally, in 20 children with DICER1-associated tumors, the median age at the time of tumor diagnosis was 2,5 years. Cystic nephroma was the most common tumor (7/20, or 35%), followed by pleuropulmonary blastoma (PPB) (6/20, or 30%). Five probands had two synchronous or metachronous tumors.

Totally, 15 different SNVs and 2 large deletions were found. The syndrome was inherited from one of the parents in most cases (11/20, or 55%). In one unique case, a patient had two syndromes – DICER1 inherited from the mother and Legius (caused by a PV in the SPRED1 gene) inherited from the father.

Conclusion: The genetic testing for DICER1 syndrome is strongly indicated in children with PPB and cystic nephroma. DICER1 syndrome in children is inherited in most cases. NGS is effective in revealing the cause as most germline PVs are SNVs rather than large deletions.