Variants in BRCA1/2 and MMR genes in children with cancer

August 24 2022, by Stefan Zorn

Professor Dr. Christian Kratz, initiator of the international study that investigated the cancer risk of disease-relevant variants in BRCA1/2 and MMR genes in children. Credit: Maike Isfort/MHH

Pathogenic variants in BRCA1/2 genes are associated with an increased risk of breast and ovarian cancer in adults, and variants in mismatch repair (MMR) genes increase the risk of gastrointestinal and other cancers. Until now, the role of such variants in children and adolescents with cancer was unclear. An international study initiated by the Department of Pediatric Hematology and Oncology at Hannover Medical School (MHH) has now revealed that pathogenic variants in BRCA1/2 and the MMR genes may also contribute to the risk of cancer in individuals below age 18 years.

"Children and adolescents with BRCA1/2 or MMR gene variants were mainly affected by brain tumors but also other solid tumors," says Professor Christian Kratz, initiator of the study published in the *Journal of the National Cancer Institute*. "A statistically significant association with malignant diseases of the blood system, such as leukemias, could not be established so far," adds the Director of the MHH Clinic for Pediatric Hematology and Oncology.

The international research team conducted a meta-analysis based on 11 studies that included results on germline testing of a total of 3,775 children and adolescents suffering from cancer. Another cohort of children and adolescents with cancer was analyzed to validate the results. "Only with the large number of patients it become possible to demonstrate a statistically significant enrichment of variants in the BRCA1/2 or MMR genes in children and adolescents with cancer compared to two control populations," Kratz explains. "Further studies are necessary to independently confirm the results and to investigate the exact tumor spectrum in children and adolescents."

Early genetic testing is not necessary

According to the pediatric oncologist, there is no need to adapt current genetic tests or surveillance practices: "In children and adolescents, the

absolute risk that variants in BRCA1/2 or an MMR gene lead to childhood cancer is statistically significantly increased, but still in such a low range that the detection of such a variant in a healthy child would currently not justify any immediate medical consequences," Professor Kratz says. "Our results therefore give no reason to change the current practice of predictive testing. It consists of testing healthy individuals for BRCA1/2 and MMR gene variants only from adulthood onwards, should such a variant be known in the family."

However, detection of these gene changes may be of immediate importance for the child with cancer and the family: "Such variants may influence the choice of therapy when treating a child with cancer and the type of follow-up care after treatment has been completed," says Professor Kratz. "The detection of BRCA1/2 or MMR gene variants in an affected child with cancer also offers adult family members the opportunity for genetic counseling and genetic testing to clarify their own risk of developing the disease."

More information: Christian P Kratz et al, Heterozygous BRCA1/2 and Mismatch Repair Gene Pathogenic Variants in Children and Adolescents with Cancer, *JNCI: Journal of the National Cancer Institute* (2022). DOI: 10.1093/jnci/djac151

Provided by Medizinische Hochschule Hannover