P-48

Lessons from exome sequencing in prenatally diagnosed heart defects – a basis for prenatal testing

Westphal D.S. (1,2), Leszinski G.S. (1), Rieger-Fackeldey E. (3), Graf E. (2), Weirich G. (4), Meitinger T. (1,2), Ostermayer E. (5), Oberhoffer R. (6), Wagner M. (1,2,7)
Institute of Human Genetics, Technical University of Munich, Munich, Germany (1); Institute of Human Genetics, Helmholtz Zentrum Munich, Neuherberg, Germany (2); Department of Pediatrics, Technical University of Munich, Munich, Germany (3); Institute of Pathology, Technical University of Munich, Munich, Germany (4); Department of Gynecology and Obstetrics, Technical University of Munich, Munich, Germany (5); Department of Pediatric Cardiology and Congenital Heart Disease, Deutsches Herzzentrum München, Technical University of Munich, Munich, Germany (6); Institute of Neurogenomics, Helmholtz Zentrum Munich, Neuherberg, Germany (7)

Objectives: We aimed to illuminate the clinical utility of exome sequencing (ES) in cases with prenatally diagnosed congenital heart defects (CHDs).
Methods: In the present study, we retrospectively analysed the diagnostic yield as well as the percentage of non-conclusive findings and incidental findings in 30 cases with prenatally diagnosed CHDs in which we performed ES. In most cases, ES was done as parent-child trios.
Results: A definite genetic diagnosis was established in 20% (6/30) of cases. Non-conclusive results were found in 13.3% (4/30) of cases. Incidental findings were reported in 10% (3/30) of cases. There was a phenotypic discrepancy between the reported prenatal and postnatal extracardiac findings in 40% (8/20) of individuals. However, none of these additional, postnatal findings altered the genetic diagnosis.
Conclusion: Our study shows that ES in prenatally diagnosed CHDs results in a comparably high diagnostic yield. There was a significant proportion of cases in which incidental findings and variants of unknown significance in known disease genes were found, as well as potentially pathogenic variants in novel disease genes. These kind of findings can bedevil genetic counselling and decision making for pregnancy termination. Our findings also contribute to the range of prenatal findings in genetic disorders, which are unknown in most cases.