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One gene and different heart defects – how deep should we look?

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Introduction:
Most CHD are isolated cases. However in a few families there is a clear autosomal dominant inheritance. We present a family with GATA6 mutation and the role of Fetal Echocardiography and autopsy examination in establishing the final diagnosis.

Methods:
Fetal Echocardiography Examinations were performed in a Tertiary Referral Centre. Sequencing was performed using Illumina Hi-Seq (San Diego, CA) instruments after exome capture with the Sure Select All Human V6 design. Raw sequence data were post-processed using the bc-bio pipeline. Finally, ANNOVAR was used to annotate relevant information about gene names, predicted variant pathogenicity, reference allele frequencies and metadata from external resources.

Results:
A mother was operated on for ASD II and PDA during childhood and adolescence with good results. The first son was diagnosed tricuspid atresia in 22 weeks. During pregnancy the karyotyping with detection of 22q11 microdeletion with FISH techniques were performed excluding these aberrations. The cardiac surgery was performed at 9 months of age, however the baby died due to complications. In next two consecutive pregnancies the spontaneous pregnancy loss occurred about 8 weeks. During 4th pregnancy a common arterial trunk (TAC) with good truncal valve and well developed pulmonary arteries was diagnosed in 20 weeks. After the cordocentesis a routine karyotyping with detection of 22q11 microdeletion with FISH techniques excluded these aberrations. The baby was born by CS at 35 weeks of gestation due to fetal tachycardia. The baby died unexpectedly at 9 day of life. The diagnosis of TAC was confirmed and a pancreatic aplasia was diagnosed.
We have performed WES study the DNA from two born children, from mother and her non-affected parents. New stop mutation in GATA6 gene was identified in mother and both kids. In mother an MRI scan confirmed partial pancreatic aplasia.

Conclusions:
The standard G-band chromosome analysis and array analysis are not always sufficient to determine the cause of fetal congenital malformations. WES study allowed a molecular diagnosis in the family and revealed new stop mutation in GATA6 gene. The presence of heart defects and a pancreatic aplasia confirms the clinical phenotype of GATA6 mutation in our patients.