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Role of prenatal next generaition sequencing in the etiological diagnosis of fetal renal dysplasias

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Objective

To assess the diagnostic yield of Next Generation Sequencing (NGS) gene panel including targeted genes involved in congenital anomalies of the kidneys and urinary tract (CAKUT) applied to the prenatal etiologic diagnosis of fetal renal dysplasias.

Methods

Fetuses with sonographic suspicion of renal dysplasia (including hyperechogenic, hypoplastic, polycystic, multicystic kidneys and bilateral agenesis) and normal microarray analysis (CMA), detected by prenatal ultrasound in our Fetal Nephrourological Unit in the last 8 years. The fetal exome was sequenced and CAKUT genes were interpreted, prenatally or post-mortem in terminated pregnancies.

Results

Among the 26 CAKUT gene panels performed, 17 (65%) monogenic disorders responsible of different most of them ciliopathies were found: autosomal recessive polycystic kidney disease (PKHD1) (n=4), autosomal dominant polycystic kidney disease (PKD1)(n=2) nephronopthisis (HNF1B) (n=2), Bardet-Biedl syndrome (BBS1, TTC8) (n=2), reno-hepatic-pancreatic dysplasia (NEK8, NPHP3) (n=2), Joubert syndrome (KIF7, TMEM138) (n=2), Fraser syndrome (FRAS1) (n=1), Multicystic dysplastic kidneys (PAX2) (n=1) and glutaric acidemia IIB (ETBF) (n=1). An adverse perinatal outcome was observed in 18 cases: 15 terminations of pregnancy and 3 neonatal demises with palliative perinatal care. In six cases babies were born alive: five of them unevently and followed-up in the pediatric nephrology Unit, one was lost to follow-up and the remaining two are still ongoing pregnancies.

Conclusion

CAKUT gene panels can find the causative genetic variant in two thirds of congenital renal dysplasias and provide valuable information for prenatal counseling, both in prognosis, which can be a dilemma especially in cases that present with a normal volume of amniotic fluid, and in genetic counseling regarding subsequent pregnancies.