NEXT GENERATION SEQUENCING (NGS) IN PRENATAL SETTING, FROM GENO- TO PHENOTYPE: A CASE REPORT

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Abstract Body

Next generation sequencing (NGS) has shifted from a research setting to a clinical implementation, leading to an increased detection rate of potential causal genetic variations in pre- and postnatal settings. Specifically in a prenatal setting, identification of such variations may lead to a precise diagnosis, providing a more accurate prenatal counseling. We present a case, concerning a pregnant Moroccan consanguineous couple which presented themselves on a prenatal consultation because of ultrasound anomalies: encephalocele, intrauterine growth retardation (IUGR), hyperechogenic kidneys and an oligohydramnion. Aneuploïdy was ruled out by CGH array on amniotic fluid cells. The couple decided to carry on their pregnancy and a boy was born at 36 weeks of gestation, presenting features described prenatally. The baby died at 12 days of life, due to his critical health condition. Post-mortem exams such as a MRI or anatomic pathology examination were refused by the parents for religious reasons. Differential diagnosis of ciliopathy was suspected and NGS carried out on DNA collected pre-and postnatally. Three missense variants were found in genes involved in known ciliopathies: AHI1 c.2488C>T, p.Arg830Trp, APC c.3511C>T, p.Arg1171Cys, CCDC40 c.850G>C, p.Asp284His.
Segregation analysis was performed, showing that the mother carries the AHI1 c.2488C>T, p.Arg830Trp variant, whereas the father carries the CCDC40 c.850G>C, p.Asp284His variant. These findings may suggest that this baby suffered from an autosomal recessive ciliopathy, caused by digenic alterations in the primary cilia, giving this couple a recurrence risk of 25%. Unfortunately, there is no evidence available to support this possibility, so prenatal diagnosis in next pregnancy is not appropriate.
NGS technology will increasingly be applied in a prenatal setting, probably leading to a higher diagnostic rate of variants. However, further research is needed for the interpretation of these kind of variants, to determine their pathogenicity and geno-phenotype correlations.