Prenatal diagnosis of FGF20 gene mutation associated with recurrent bilateral renal agenesis

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Objective
Bilateral renal agenesis (BKA) is the most serious expression of congenital anomalies of the kidneys and urinary tract, incompatible with extrauterine life, with an estimated incidence of 1 in 300 to 1 in 5000 births. The existence of a genetic component for urinary malformations was proposed based on the observation of familial and syndromic cases. A large range of genetic heterogeneity has been highlighted by the identification of mutations, mostly at the heterozygous state, in more than 50 genes, many of them encoding transcription factors with a crucial role during nephrogenesis. Although the pathophysiological mechanisms leading to BKA remain inconclusive, among these nearly 50 genes, few are associated with BKA in humans and mutations have been reported in ANOS1, EYA1, FGF20, ITGA8, and RET genes in some case subjects with isolated BKA. Our objective is to report a case of a patient who had two subsequent pregnancies with fetuses with BKA, and in the second, it was possible to identify the association with the mutation in the FGF20 gene.

Methods
Descriptive observational study, case report.

Results
A 29-year-old female patient, G2P1, 28-year-old partner, both without comorbidities, with no family history of renal disease and no known consanguinity. In their first gestation, a diagnosis of BKA was made in the second trimester by the morphological ultrasonography. It led to a cesarean delivery at 38 weeks of a female fetus, with neonatal death after two hours of life. No fetal karyotype or any other investigations were performed. In the second gestation, BKA was again diagnosed, in addition to a pericardial effusion. This time, at 25 weeks’ gestation, fetal blood was collected through cordocentesis for G-banded karyotype testing and fetal exome sequencing performed on the Illumina HiSeq 4000 New Generation Sequencer. The karyotype result was 46, XY, without structural or numerical changes. Sequence of fetal exome revealed a homozygous mutation for the FGF20 (fibroblast growth factor) gene, location chr8: 16,850,827 evidencing a C>T base exchange. Couple chose to continue gestation and an elective cesarean section was performed at 38 weeks of a male fetus, with death after three hours of life.

Conclusion
For recurrent cases of congenital anomalies, the genetic diagnosis is more relevant and should be offered to couples who seek answers for the occurrence of such anomalies. Data from the literature suggest that FGF20 gene would be essential for renal development and its loss would result in BKA in humans with an autosomal recessive familial inheritance pattern. FGF20 gene mutation is a hypothesis to be valued for the recurring BKA and our report corroborates as evidence with non consanguineous couple. There are still few cases described and new studies are needed to improve the approach during prenatal care, genetic counseling and to evaluate new therapeutic possibilities for congenital renal pathologies.