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Increased yield of exome sequencing in polihydramnios associated with growth restriction

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Objective

Fetal growth-restricted (FGR) fetuses are at higher risk of genetic disorders. In the past years, exome sequencing (ES) has demonstrated its usefulness in case of fetal malformations, although its diagnostic yield varies according to the anomaly type. Polyhydramnios is not considered a fetal abnormality but an ultrasound sign, and when associated with FGR it increases the likelihood of a genetic diagnosis at CMA. This study aimed to explore whether polyhydramnios results in an increased ES yield in FGR fetuses.

Methods

Cohort study including FGR fetuses followed up in our center from 2014 to 2020, in which ES was performed because of a research protocol. Maternal baseline characteristics, ultrasound examinations, and perinatal outcomes were retrospectively obtained from clinical records.

Results

ES was performed in 22 fetuses born at term with an birthweight < -2.5SD with normal Doppler studies and normal anatomy. A pathogenic variant was found in 7, and in 2 of them polyhydramnios was observed (40%: 2/5): in a Prader-Willi syndrome and in an X-linked Renpenning syndrome. Interestingly enough, difficulty to thrive and hypotonia are characteristic of both syndromes. None (0/17) of the cases with normal ES had a prenatal diagnosis of polyhydramnios.

Conclusion

ES diagnostic yield in FGR fetuses appears to increase when associated with polyhydramnios. Prenatal polyhydramnios may correspond to postnatal difficulty to thrive or hypotonia, and therefore it could be a useful sign for prenatal diagnosis of genetic disorders.