Prenatal high resolution array CGH in fetuses with ultrasound anomalies in first trimester screening

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Objective

To study the high resolution array comparative genomic hybridization (aCGH) in fetuses with ultrasound anomalies in the first trimester screening.

Methods

We enrolled a total of 3043 women at the time of their first trimester screening for aneuploidies in China. There were 101 high-risk cases undergoing aCGH using a 60K oligonucleotide array, Agilent, ISCA. The anomalies or ultrasound soft makers found in the first trimester scan included increased nuchal translucency (NT), absent/hypoplastic nasal bone, tricuspid regurgitation and reversed a wave in the ductus venosus, echogenic bowel, hydrocephalus, megacystis, cardiac defects, and limbs defects. Each sample was divided into two: standard karyotyping was performed on one portion and the other was sent to the laboratory for chromosomal microarray analysis. Copy Number Variations (CNVs) were excluded when they were known non-pathogenic variants after parental survey. The pathogenic CNVs were reported and the association with NT and other ultrasound findings described.

Results

We enrolled a total of 101 women undergoing aCGH analysis. The indications for prenatal diagnosis were abnormal results from the Down's syndrome screening test in 20 cases (19. 8%), structural anomalies on ultrasonography in 37 cases (36. 6%), advanced maternal age in 27 cases (26. 7%), family history in 10 cases (9. 9%), and other indications in 7 cases (7. 0%). Microarray analysis was successful in all the fetal samples. There were six cases of de novo micro-duplication/deletion associated with mental retardation, 6 structural anomalies, and one case of each trisomy 21, 18 and 13 respectively. Six cases of micro-duplication were inherited from the parents. In fifteen cases major congenital anomalies or syndromes were non-associated neither with karyotype nor with aCGH results. In samples with a normal karyotype, microarray analysis revealed clinically relevant deletions or duplications in 6. 0% of cases with a structural anomaly and in 1. 5% of those whose indications were advanced maternal age or positive screening results.

Conclusion

aCGH allows detection of submicroscopic chromosomal abnormalities of which the prevalence may be increased in fetuses with ultrasound abnormalities.