Microarray-based analysis in prenatal diagnosis of submicroscopic chromosomal aberrations in fetuses with CHD

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Objective
To assess the value of chromosomal microarray analysis (CMA) in fetuses with congenital heart diseases (CHDs) with or without other abnormalities.

Methods
All the two hundred fetuses with CHD enrolled in the study received invasive prenatal diagnosis including both CMA and chromosome karyotype. The samples were divided into three groups as follows: Group I: samples with isolated structural anomalies; Group II: cases with multiple cardiovascular anomalies; Group III: cases of cardiovascular anomalies complicated with other systemic abnormalities.

Results
Among the 200 pregnancies with CHDs, CMA revealed 5 fetuses with chromosomal aneuploidy, which is consistent with the results showed by karyotyping. In the other 195 pregnancies with normal karyotype, CMA revealed 130 copy number variants (CNVs). Eleven pathogenic CNVs were detected in 11 fetuses (5.6%). The proportion of variants of unknown significance was 2.1% (4/195). Other CNVs were all benign or like benign. The three groups contained 131, 32 and 37 cases respectively. The pathogenic CNVs detection rates among the three groups were 3.8% (5/131), 15.6% (5/32) and 2.7% (1/37), respectively. The detection rate of pathogenic CNVs in Group II was significantly higher than that in Group I(15.6%, 5/32 vs. 3.8%, 5/131, P=0.013). However, there is no significant difference between the detection rate of pathogenic CNVs in other groups (Group I, 3.8%, 5/32 vs. Group III, 2.7%, 1/37, P=1.00; Group II, 15.6%, 5/32 vs. Group III, 2.7%, 1/37, P=0.089).

Conclusion
Chromosomal microarray analysis is useful in the prenatal diagnosis of CHDs. The multiple cardiovascular anomalies enhanced the frequency of pathogenic CNVs compared with isolated CHDs.