Chromosomal microarray: beyond copy number variations

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Background: CMA in pregnancy is the modality of choice for prenatal diagnosis of fetal malformations, diagnosing microdeletion/duplication syndromes. We demonstrate further utilities of CMA, by diagnosing monogenic diseases, imprinting disorders and uniparental disomy (UPD).

Methods: We performed CMA using Affymetrix CytoScan array for 6995 pregnancies for all indications since November 2013 in a tertiary referral hospital.

Results: Three fetuses had an unforeseen CMA result, shedding light on the clinical presentation. In fetus (1) examined due to intrauterine growth restriction, CMA revealed a 75kbp maternally inherited microdeletion encompassing the BLM gene. A diagnosis of Bloom syndrome was applied upon identifying a paternally inherited common founder Ashkenazi mutation. In fetus (2) extremely abnormal maternal serum analytes led to the identification of a deletion in 14q32.2q32.31, on the maternally inherited copy, diagnosing Kagami-Ogata syndrome known to be an imprinting disorder. Fetus (3) had amniocentesis following maternal CMV seroconversion. Maternal UPD of the entire long arm of chromosome 11 was detected.

Main points:
- Copy number changes discovered by CMA and single nucleotide polymorphism platform may diagnose monogenic recessive diseases, imprinting disorders and uniparental disomies.
- Extremely abnormal maternal serum analytes should direct diagnostic evaluation to the arena of imprinting disorders.
- A flowchart may aid evaluation of absence of heterozygosity (figure 1).

Conclusions: Prenatal CMA based on oligo and SNP platforms increases the yield and spectrum of diagnosed disorders beyond the determination of copy number changes.