CHROMOSOMAL MICROARRAY ANALYSYS: BEYOND COPY NUMBER CHANGES, INTO THE ARENA OF MONOGENIC RECESSIVE DISEASES, IMPRINTING DISORDERS AND UNIPARENTAL DISOMY

Daum, Hagit[1]; Meiner, Vardiella[2]; Zvi, Naama[2]; Drai-Hasid, Revital[3]; Yagel, Simcha[3]; Zenvirt, Shamir[2]; Frumkin, Ayala[2]

[1]Hadassah medical center jerusalem, [2]Department for Genetics and metabolic diseases, Hadassah Hebrew University Medical Center Jerusalem, [3]OBGYN, Hadassah Hebrew University Medical Center Jerusalem

Objective: Chromosomal Microarray Analysis (CMA) is the modality of choice for prenatal diagnosis whenever fetal malformations are encountered. Microdeletion/microduplication syndromes diagnosed by CMA contribute to the diagnostic rate beyond that of chromosomal analysis by 3-8%.However, we would like to demonstrate further utilities of the CMA, as a platform by which we could diagnose monogenic diseases, imprinting disorders and uniparental disomy (UPD).Methods: Three unrelated expectant couples went through amniocentesis due to different reasons. IUGR of the first fetus, exceptional abnormal maternal serum analytes, and patient's request for the third fetus. Fetal genomic DNA was extracted from amniocytes and CMA analysis was performed using Affymetrix CytoScan array.Results: CMA analysis revealed in an IUGR fetus a microdeletion of 75kbp encompassing the BLM gene. Further investigation established fetal diagnosis of Bloom syndrome upon observation of maternal deletion of one allele of the gene and paternal founder Ashkenazi mutation on the other fetal allele. A 3.4-Mbp deletion in14q32.2q32.31 was found in a fetus referred due to exceptional abnormal maternal serum analytes. Further Single nucleotide polymorphism (SNP) analysis indicated that the deleted segment originated from the maternal copy of chromosome 14 leading to the diagnosis of 'Kagami-Ogata syndrome', an imprinting disorder. The third fetal CMA revealed maternal UPD of most of chromosome 11q without any clear clinical significance.Conclusions: Comprehensive CMA analysis including both platforms of oligo and SNP array may establish the diagnosis of a spectrum of disorders which is much wider than copy number changes.