Fetal growth restriction (FGR) is a common complication of pregnancy that has been linked to a variety of adverse perinatal outcomes. Although the exact pathogenesis of FGR remains unclear, a strong association has been detected between FGR and chromosomal aberrations. Currently, karyotyping remains the gold standard for prenatal cytogenetic analysis; however, this technique tends to be time-consuming, expensive, subjective, and has poor resolution. Chromosomal microarray analysis (CMA), which is performed either by array comparative genomic hybridization or by using a single nucleotide polymorphism (SNP) array, can be used to diagnose genetic syndromes caused by chromosome deletions, chromosome duplications, or uniparental disomy (UPD), a potential cause of FGR. However, the effectiveness of CMA in detecting isolated FGR is still uncertain until now. This study aimed to investigate the genetic causes of isolated FGR by using CMA and karyotype analysis. Singleton FGR cases with the estimated fetal weight of < 10th percentile for gestational age and without structural anomalies at Nanfang Hospital of Southern Medical University and Fujian Provincial Maternity and Children’s Hospital from July 2015 to February 2016 were recruited, and those at high risk of noninvasive prenatal testing for trisomy 13, 18 and 21 were excluded. All study subjects were assigned into the early-onset group (< 24+0 weeks) and the late-onset group (24–33 weeks) according to the gestational age upon diagnosis. All subjects were given CMA and karyotype analysis. CMA detected 10 pathogenic copy number variants and 2 variant of uncertain significance case. CMA has a 5.5% (7/127) incremental yield of pathogenic chromosomal abnormalities over karyotyping. The positive detected rate was 9.6% (5/52) in early-onset group and 9.3% (7/75) in late-onset group, respectively. Our data demonstrate that CMA can identify a 5.5% (7/127) incremental detection rate of genetic causes of isolated FGR, which may affect clinical management for FGR. It is concluded that CMA as the first-line test plus karyotyping is effective and feasible as a combined prenatal testing for suspected FGR cases.

Abstract

Fetal growth restriction (FGR) is a common complication of pregnancy that has been linked to a variety of adverse perinatal outcomes. Although the exact pathogenesis of FGR remains unclear, a strong association has been detected between FGR and chromosomal aberrations. Currently, karyotyping remains the gold standard for prenatal cytogenetic analysis; however, this technique tends to be time-consuming, expensive, subjective, and has poor resolution. Chromosomal microarray analysis (CMA), which is performed either by array comparative genomic hybridization or by using a single nucleotide polymorphism (SNP) array, can be used to diagnose genetic syndromes caused by chromosome deletions, chromosome duplications, or uniparental disomy (UPD), a potential cause of FGR. However, the effectiveness of CMA in detecting isolated FGR is still uncertain until now. This study aimed to investigate the genetic causes of isolated FGR by using CMA and karyotype analysis. Singleton FGR cases with the estimated fetal weight of < 10th percentile for gestational age and without structural anomalies at Nanfang Hospital of Southern Medical University and Fujian Provincial Maternity and Children’s Hospital from July 2015 to February 2016 were recruited, and those at high risk of noninvasive prenatal testing for trisomy 13, 18 and 21 were excluded. All study subjects were assigned into the early-onset group (< 24+0 weeks) and the late-onset group (24–33 weeks) according to the gestational age upon diagnosis. All subjects were given CMA and karyotype analysis. CMA detected 10 pathogenic copy number variants and 2 variant of uncertain significance case. CMA has a 5.5% (7/127) incremental yield of pathogenic chromosomal abnormalities over karyotyping. The positive detected rate was 9.6% (5/52) in early-onset group and 9.3% (7/75) in late-onset group, respectively. Our data demonstrate that CMA can identify a 5.5% (7/127) incremental detection rate of genetic causes of isolated FGR, which may affect clinical management for FGR. It is concluded that CMA as the first-line test plus karyotyping is effective and feasible as a combined prenatal testing for suspected FGR cases.

Background

Fetal growth restriction (FGR) is a common complication of pregnancy that has been linked to a variety of adverse perinatal outcomes. Although the exact pathogenesis of FGR remains unclear, a strong association has been detected between FGR and chromosomal aberrations. Currently, karyotyping remains the gold standard for prenatal cytogenetic analysis; however, this technique tends to be time-consuming, expensive, subjective, and has poor resolution. Chromosomal microarray analysis (CMA), which is performed either by array comparative genomic hybridization or by using a single nucleotide polymorphism (SNP) array, can be used to diagnose genetic syndromes caused by chromosome deletions, chromosome duplications, or uniparental disomy (UPD), a potential cause of FGR.

Objective

To investigate the genetic causes of isolated FGR by using CMA and karyotype analysis.

Methods

A prospective multi-center cohort study was designed. Singleton FGR cases with the estimated fetal weight of < 10th percentile for gestational age and without structural anomalies at Nanfang Hospital of Southern Medical University and Fujian Provincial Maternity and Children’s Hospital from July 2015 to February 2016 were recruited, and those at high risk of noninvasive prenatal testing for trisomy 13, 18 and 21 were excluded. All study subjects were assigned into the early-onset group (< 24+0 weeks) and the late-onset group (24–33 weeks) according to the gestational age upon diagnosis. All subjects were given CMA and karyotype analysis.

Results

CMA detected 10 pathogenic copy number variants and 2 variant of uncertain significance case. CMA has a 5.5% (7/127) incremental yield of pathogenic chromosomal abnormalities over karyotyping. The positive detected rate was 9.6% (5/52) in early-onset group and 9.3% (7/75) in late-onset group, respectively.

Conclusions

CMA can identify a 5.5% (7/127) incremental detection rate of genetic causes of isolated FGR, which may affect clinical management for FGR. It is concluded that CMA as the first-line test plus karyotyping is effective and feasible as a combined prenatal testing for suspected FGR cases.

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