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Haplotype-based noninvasive prenatal testing for duchenne muscular dystrophy: a pilot study in South China

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Objective

To explore the accuracy and feasibility of a haplotype-based noninvasive prenatal testing (NIPT) for Duchenne Muscular Dystrophy (DMD).

Methods

Singleton pregnancies at 12-25 weeks of gestation from seventeen families, each with a proband affected by DMD were recruited in the antenatal clinic. The causative mutations in probands and their mothers were previously identified by multiplex ligation-dependent probe amplification (MLPA). Captured sequencing was performed on genomic DNA from parents and proband using customized hybridization probes targeted at highly heterozygous 2358 SNPs located within the 1M region flanking DMD gene and its coding region to acquire parental haplotypes and the linkage to pathogenic mutations. Maternal plasma DNA obtained at 12-25 weeks of gestation also underwent targeted sequencing to deduce fetal haplotypes assisted by parental haplotypes. The fetal genotypes in DMD gene were further validated by invasive procedures of prenatal diagnosis.

Results

The haplotype-based NIPT was successfully performed in all families. Four female and six male fetuses were identified to be normal. Four female fetuses were carriers and three male fetuses were DMD patients due to exons 49-52 deletion, exons 8-37 deletion and c. 628G>T, respectively. All these results were consistent with those of invasive procedures.

Conclusion

Haplotype-based noninvasive prenatal testing for DMD using targeted sequencing is promising and has potential for clinical implementation.