Clinical relevance of screening for rare autosomal aneuploidies: a case of maternal uniparental disomy

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I. Introduction

Traditionally, fetal aneuploidy screening has focused on autosomal trisomies of chromosomes 21, 18, and 13. Subsequently, cell-free DNA (cfDNA) screening has expanded to include sex chromosome aneuploidies, select microdeletions, and recently genome-wide analysis. Though uncommon after the first trimester, aneuploidy of any autosomal fetus can occur in placental and fetal tissues. Some autosomal aneuploidies present at conception are rescued and restored to a euploid state. When this occurs with imprinted chromosomes, it can lead to a euploid fetus with a genetic syndrome due to uniparental disomy (UPD).

II. Methods

Maternal blood samples submitted to Sequenom Laboratories for MaterniT® GENOME testing were subjected to DNA extraction, library preparation, and whole-genome massively parallel sequencing as described by Jensen et al. Sequencing data were analyzed using a novel algorithm to detect aneuploidies and other subchromosomal events as described by Lefkowitz et al.

III. Results

A 42 year old patient elected genome-wide cfDNA screening after genetic counseling. Screening was positive, indicating an increased representation of chromosome 15, consistent with mosaic trisomy 15. The trisomy was predicted to be present at 35% mosaicism. The patient elected to pursue amniocentesis which returned a normal fetal karyotype, 46,XX. Subsequent testing of amniocytes detected maternal isodisomy of chromosome 15. Maternal UPD15 is a cause of Prader-Willi syndrome.

IV. Conclusion

This case illustrates the clinical relevance of screening for esoteric trisomies with cfDNA. Though the fetus did not have trisomy 15, the cfDNA test identified a trisomy in the placenta, presumably rescued in fetal tissue, which led to maternal UPD of chromosome 15 and a fetal diagnosis of Prader-Willi syndrome. Diagnosing Prader-Willi syndrome prenatally allows patients to make reproductive decisions, including pregnancy termination, adoption, and preparing for a child with disabilities.

V. References