Key Summary of Conference Abstract

Detection of Fetal Prader-Willi/Angelman Microdeletion and Differentiation of Maternal Distal 15q Deletion by Prenatal Cell-free DNA Screening: Case Report

Background

- Prader-Willi and Angelman syndromes (PWS/AS) are rare disorders that are usually caused by genetic abnormalities called microdeletions.[1]
- Some commercial laboratories now offer detection in certain microdeletion regions as part of non-invasive prenatal cell-free (cfDNA) screening.
- However, because microdeletion syndromes are rare, the available data about their detection in clinical practice settings are limited.
- **Objective:** The investigators describe a case of PWS/AS microdeletion first identified by cfDNA screening and subsequently confirmed by prenatal diagnostic testing.

Methods

- cfDNA screening using the QNatal Advanced assay, which employs massively parallel shotgun sequencing (MPSS), was conducted on a submitted blood sample.
- Maternal and fetal karyotypes were also generated, and microarray analyses were conducted to confirm suspected microdeletions.

Results

- The patient was 35 years of age and at 12 weeks' gestation at the time of cfDNA screening.
- cfDNA screening results indicated microdeletion of chromosome 15 involving the PWS/AS critical region (z score = -8.41; fetal fraction = 16%).
- Review of the karyogram (a graphical representation of sequence reads) confirmed a microdeletion within the critical PWS/AS region and also identified a suspected microdeletion involving maternal cfDNA distal to the PWS/AS region.
- Since differentiating maternal and fetal contributions to the microdeletions was difficult with cfDNA screening alone, karyotype and microarray tests were ordered.
    - Maternal and fetal karyotypes displayed normal results.
    - Maternal microarray analysis confirmed a ~2-Mb deletion of chromosome 15q13.3-q14; the deletion was categorized as a variant of uncertain clinical significance.
    - Fetal microarray analysis confirmed a ~5-Mb deletion of chromosome 15q11.2-q13.1 and the same ~2-Mb deletion as the mother.
- These results indicated a diagnosis of PWS/AS and inheritance of the maternal microdeletion.

Conclusions

- To the investigators' knowledge, this is the first reported case in which a PWS/AS microdeletion was initially detected by NIPS cfDNA screening and subsequently confirmed by prenatal diagnostic testing.
- This case demonstrates the potential of cfDNA screening and follow-up testing to identify and differentiate fetal and maternal findings, which can help guide appropriate patient management.

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Reference

1. Adams JU. *Nature Education*. 2008;1:129.