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Tracy I. George, MD, Chief Medical Officer

Patient Report

Patient Age/Sex: Female

Specimen Collected: 20-Dec-21 09:53

SNP Microarray, Products of Conception **|Received: 21-Dec-21 10:43** **Report/Verified: 21-Dec-21 10:46**

Procedure	Result	Units	Reference Interval
SNP Microarray, Products of Conception	**Abnormal** * f1 i1		Normal

Result Footnote

f1: SNP Microarray, Products of Conception
Test Performed: Genomic SNP Microarray, Products of Conception (ARRAY POC)
Specimen Type: Products of Conception (Tissue: Cord)
Indication for Testing: Fetal demise

RESULT SUMMARY
Abnormal Microarray Result (Female)

Allele Imbalance Consistent With Triploidy

Classification: Pathogenic

RESULT DESCRIPTION
This analysis showed genome-wide allelic imbalance. The pattern observed is most consistent with triploidy.

INTERPRETATION
This result is consistent with a diagnosis of triploidy (69,XXX), a frequent cytogenetic abnormality observed in pregnancy loss. The majority of cases are paternally derived (diandric), with morphologic features that may include partial hydatidiform mole, with a large, cystic placenta and mild, symmetrical growth restriction to normal growth. If maternally derived (digynic), phenotypic features may include severe growth retardation with marked head-body disproportion, macrocephaly, and a small non-molar, fibrotic placenta. Triploidy is typically a sporadic occurrence.

Additional testing by STR analysis to distinguish diandric from digynic triploidy may be considered.

NOTE: The presence of triploidy may impact the detection of CNVs below a size threshold of approximately 10-20 Mb. Therefore, only large genomic alterations are ruled out by this analysis.

Recommendation:
Genetic counseling

Health care providers with questions may contact an ARUP genetic counselor at (800) 242-2787 ext. 2141.

References:
1) Gardner and Amor. Gardner and Sutherland's Chromosome Abnormalities and Genetic Counseling. 5th edition. New York, NY: Oxford; 2018:239-241.
2) Zaragoza et al. Parental origin and phenotype of triploidy in spontaneous abortions: predominance of diandry and association with the partial hydatidiform mole. Am J Hum Genet. 2000 Jun;66(6):1807-20. PMID: 10801385.
3) Hui et al. Hydatidiform Moles: Genetic Basis and Precision Diagnosis. Annu Rev Pathol. 2017 Jan 24;12:449-485. PMID: 28135560.
4) McFadden and Robinson. Phenotype of triploid embryos. J Med Genet. 2006 Jul; 43(7): 609–612. PMID: 16236813.
5) Seckl et al. ESMO Guidelines Working Group. Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013 Oct;24 Suppl 6:vi39-50. PMID: 23999759.

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

Result Footnote

f1: SNP Microarray, Products of Conception

Cytogenomic Nomenclature (ISCN):
arr(X,1-22)x3

Technical Information
- This assay was performed using the CytoScan(TM) HD Suite (Thermo Fisher Scientific) according to validated protocols within the Genomic Microarray Laboratory at ARUP Laboratories
- This assay is designed to detect alterations to DNA copy number state (gains and losses) as well as copy-neutral alterations (regions of homozygosity; ROH) that indicate an absence- or loss-of-heterozygosity (AOH or LOH), and certain alterations to ploidy state due to errors at fertilization or early embryonic cell division (i.e. triploidy, molar pregnancy)
- AOH may be present due to molar pregnancy, parental relatedness (consanguinity) or uniparental disomy (UPD)
- LOH may be present due to acquired UPD (segmental or whole chromosome)
- The detection sensitivity (resolution) for any particular genomic region may vary dependent upon the number of probes (markers), probe spacing, and thresholds for copy number and ROH determination
- The CytoScan HD array contains 2.67 million markers across the genome with average probe spacing of 1.15 kb, including 750,000 SNP probes and 1.9 million non-polymorphic probes
- In general, the genome-wide resolution is approximately 25-50 kb for copy number changes and approximately 3 Mb for ROH (See reporting criteria)
- The limit of detection for mosaicism varies dependent upon the size and type of genomic imbalance. In general, genotype mixture due to mosaicism (distinct cell lines from the same individual) or chimerism (cell lines from different individuals) will be detected when present at greater than 20-30 percent in the sample
- Genomic coordinates correspond to the Genome Reference Consortium human genome build 37/human genome issue 19 (GRCh37/hg19)

Variant Classification and Reporting Criteria
- Copy number variant (CNV) analysis is performed in accordance with recommendations by the American College of Medical Genetics and Genomics (ACMG), using standard 5-tier CNV classification terminology: pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign
- CNVs classified as pathogenic, likely pathogenic, or variant of uncertain significance are generally reported, based on information available at the time of review
- Known or expected pathogenic CNVs affecting genes with known clinical significance but which are unrelated to the indication for testing will generally be reported
- Variants that do not fall within the standard 5-tier CNV classification categories may be reported with descriptive language specific to that variant
- In general, recessive disease risk and recurrent CNVs with established reduced penetrance will be reported
- For a list of databases used in CNV classification, please refer to ARUP Constitutional CNV Assertion Criteria, which can be found on ARUP's Genetics website at www.aruplab.com/genetics
- CNVs classified as likely benign or benign that are devoid of relevant gene content or reported as common findings in the general population, are generally not reported
- CNV reporting (size) criteria: losses greater than 50 kb and gains greater than 400 kb are generally reported, dependent on genomic content
- ROH are generally reported when a single terminal ROH is greater than 3 Mb and a single interstitial ROH is greater than 10-15 Mb (dependent upon chromosomal location and likelihood of imprinting disorder) or when total autosomal homozygosity is greater than 3 percent (only autosomal ROH greater than 3 Mb are considered for this estimate)

Limitations
This analysis cannot provide structural (positional) information associated with genomic imbalance. Therefore, additional cytogenetic testing by chromosome analysis or fluorescence in situ hybridization (FISH) may be recommended.

Result Footnote

f1: SNP Microarray, Products of Conception

Certain genomic alterations may not or cannot be detected by this technology. These alterations may include, but are not limited to:
- CNVs below the limit of resolution of this platform
- Sequence-level variants (mutations) including point mutations and indels
- Low-level mosaicism (generally, less than 20-30 percent)
- Balanced chromosomal rearrangements (translocations, inversions and insertions)
- Genomic imbalance in repetitive DNA regions (centromeres, telomeres, segmental duplications, and acrocentric chromosome short arms)
- Most cases of tetraploidy

This result has been reviewed and approved by Denise I. Quigley, PhD, FACMG

A portion of this analysis was performed at the following location(s):

[redacted]

Test Information

i1: SNP Microarray, Products of Conception

INTERPRETIVE DATA: Genomic SNP Microarray,
Products of Conception

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

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