VALIDATION OF A 1-MB INHERITED CNV DETECTED BY PGT-A USING TARGETED NGS AND SNP-BASED ANALYSIS: A CASE REPORT

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Abstract

Background: Preimplantation genetic testing for aneuploidy (PGT-A) is routinely used to detect chromosomal abnormalities and improve embryo selection in assisted reproductive treatments. Next-generation sequencing (NGS) based PGT-A provides high accuracy for identifying whole-chromosome and large segmental abnormalities but still have limited resolution for smaller copy number variants (CNVs). Recent targeted sequencing approaches, such as PGTseq, allow detection of small CNVs down to approximately 3 Mb, expanding the scope of embryo chromosomal assessment. However, interpretation of these small CNVs remains challenging due to limited clinical evidence and difficulty in distinguishing inherited variants from de novo events. Here, the inheritance and pathogenicity of a small copy number variant detected by a targeted NGS based PGT-A was validated.

Methods: A ~1 Mb CNV was detected in an embryo using targeted NGS with SNP-based analysis on the Juno PGTseq platform. The size and location of CNV detected in embryos was validated by high-resolution microarray analysis. Parental microarray testing was performed to determine inheritance, origin, and classify the pathogenicity of the variant.

Results: The recurrent 1-Mb CNV was detected in 2 of 4 embryos derived from the same couple. Two embryos exhibited duplications on chromosome 17, spanning approximately chr17:5,672,387–6,985,477, with estimated breakpoints between 1–4 Mbs. Microarray confirmed the CNV at the same genomic locus identified by PGTseq-A. Parental microarray identified a paternal duplication, arr[GCRh37]17p13.32p13.1(5,600,947–6,740,551)x3. This small CNV was classified as a variant of uncertain significance (VUS) and likely benign.

Conclusions: Our study highlights the accuracy and reliability of PGTseq in detecting small CNVs below the standard resolution of NGS based-PGT-A. Integration of confirmatory microarray and parental testing enhances interpretive accuracy and supports informed embryo transfer decisions, reinforcing the clinical value of PGTseq in comprehensive embryo genetic evaluation.

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