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Case report: Incidental diagnosis of Mulchandani-Bhoj-Conlin syndrome by prenatal microarray

Lauren Petrarca, MS, CGC; Labcorp, New York, NY

Background

Chromosomal microarray is routinely offered to patients undergoing prenatal diagnosis. The increased diagnostic yield of microarray compared to karyotype is well established in the prenatal setting. Single nucleotide polymorphism (SNP) microarray is a valuable tool for detecting gains and losses of chromosomal material and can also provide other information that can benefit patients, such as detecting regions of homozygosity. We present a case where chromosomal microarray, performed after karyotype resulted as 47, XXX, identified regions of homozygosity on chromosome 20. This case highlights the benefits of microarray testing in cases where aneuploidy is identified.

Case presentation

A 47-year-old, G1P0 patient presented for genetic counseling at 12 weeks gestation following a high-risk prenatal cell-free DNA screening result suggestive of 47, XXX. The patient reported this was a spontaneous pregnancy after multiple rounds of unsuccessful in vitro fertilization.

Diagnostic workup

Chorionic villus sampling was performed and karyotype resulted as 47, XXX. The patient chose to proceed with microarray testing, and in addition to a gain of an X chromosome, it identified a long contiguous region of homozygosity on chromosome 20 (Figure 1). Uniparental disomy (UPD) analysis by SNP array was subsequently performed and revealed maternal heterodisomy of chromosome 20 consistent with Mulchandani-Bhoj-Conlin syndrome (MBCS). These results are summarized in Table 1. The patient chose pregnancy termination given the dual diagnosis of 47, XXX and MBCS. The recurrence risk for UPD 20 in future pregnancies is expected to be low; however, the risk for aneuploidy is increased given the patient's age and history of a 47, XXX pregnancy.

Discussion

MBCS is characterized by prenatal and postnatal growth retardation, premature birth, short stature and prominent feeding difficulties with failure to thrive. This syndrome has been reported as having a Silver-Russell syndrome-like phenotype. Maternal UPD 20 results in the loss of the expressed paternal allele of the GNAS locus at 20q13.22.[1] Maternal heterodisomy is often due to nondisjunction in meiosis 1, followed by a trisomy rescue in which the paternal chromosome is lost. Regions of isodisomy (which can be detected on SNP microarray) typically result from meiotic recombination.

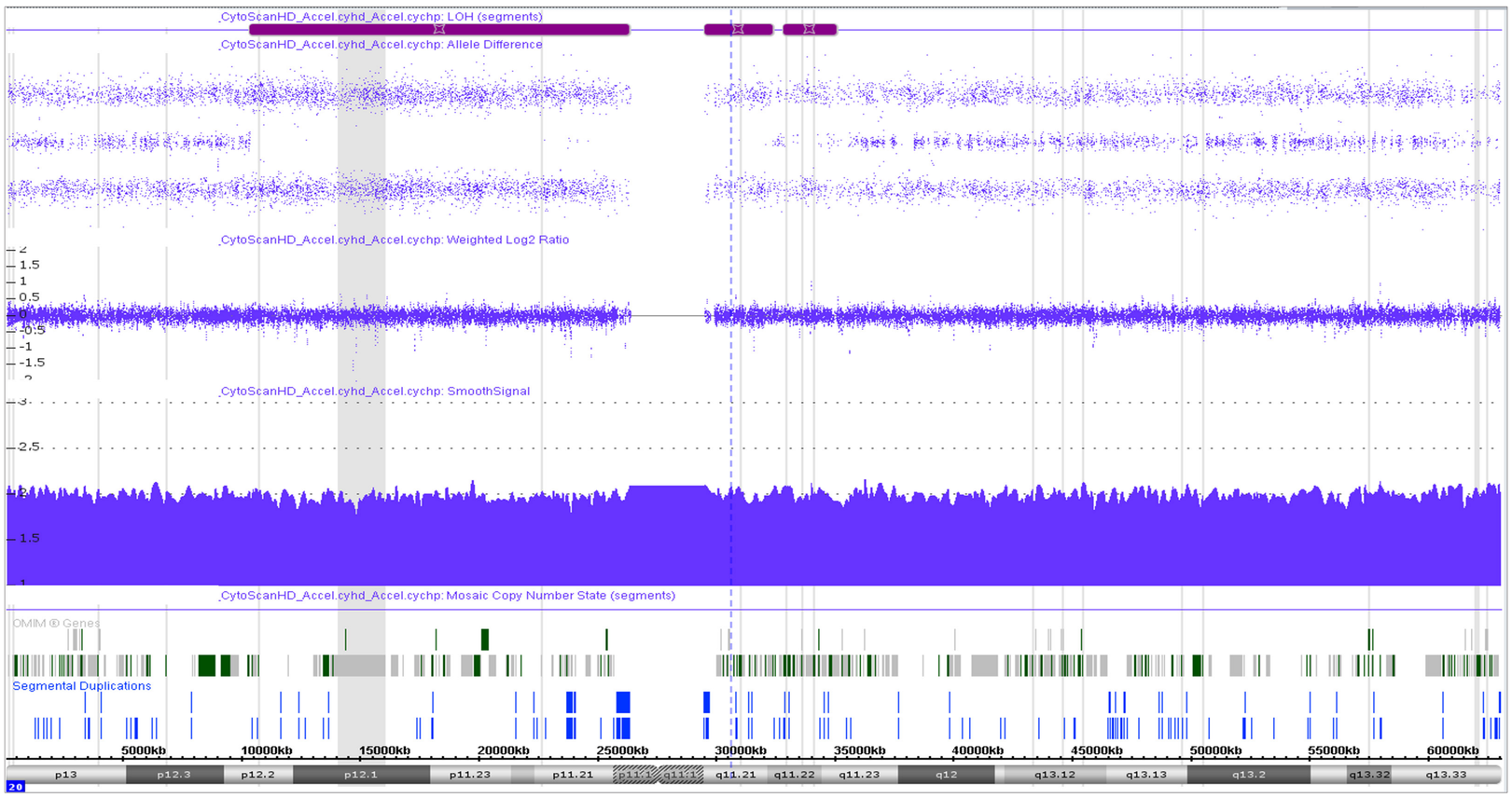

Figure 1. Microarray consistent with homozygosity on chromosome 20.

Test performed on CVS sample	Result
Karyotype	47, XXX
Microarray	Long contiguous region of homozygosity on chromosome 20 and gain of X chromosome
UPD 20	Maternal heterodisomy for chromosome 20; consistent with diagnosis of MBCS

Table 1. Summary of diagnostic testing results.

Conclusions

In this case, microarray analysis provided additional clinical information that assisted the patient with making reproductive decisions. Microarray testing should be considered in cases when an abnormal fetal karyotype is identified.

Reference

1. Tannorella P, Minervino D, Guzzetti S, et al. Maternal Uniparental Disomy of Chromosome 20 (UPD(20)mat) as Differential Diagnosis of Silver Russell Syndrome: Identification of Three New Cases. *Genes (Basel).* 2021 Apr 17;12(4):588. doi: 10.3390/genes12040588. PMID: 33920573; PMCID: PMC8073552.

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