P-350

The importance of microarray in clarifying discrepant prenatal cytogenetic testing: A case study

Jovanni Cuevas, MS, CGC
Labcorp, New York, NY

Background

Prenatal chromosomal microarray (CMA) is used in prenatal diagnosis to identify both aneuploidy and smaller chromosomal insertions or deletions that could potentially diagnose a fetus with a genetic disorder. This case study highlights how microarray can be a tool for explaining results from chromosome analysis and prenatal FISH and may detect additional genetic findings.

Findings

The patient was referred to genetic counseling due to a positive cell free DNA (cfDNA) for trisomy 21 with a positive predictive value of 95%. After counseling, the patient decided to proceed with a CVS with FISH for common aneuploidies and standard karyotype performed on the sample. At the time, the patient was offered and declined CMA. The CVS results reported a normal female FISH (Figure 1), and a 47,XX,+21, consistent with trisomy 21 female on the chromosome analysis. The patient was offered amniocentesis to help clarify these discordant results. FISH for common aneuploidies and standard karyotype was ordered on the amnio sample. The FISH reported as normal female and the chromosome analysis reported 47,XX,+21, consistent with a trisomy 21 female. Microarray was ordered to try to find the cause of the discordant results. Microarray detected 47,XX,+21 with a 1.57 interstitial deletion of 21q22.11->21q22.12 on one of the three chromosome 21s. The deletion on the chromosome 21 included the location of the FISH probe. The presence of the 21q22 deletion was the underlying reason that the FISH analysis did not identify the trisomy 21 finding, which was ultimately diagnosed through both karyotype and microarray (Table 1). Parental follow-up testing revealed that neither patient nor father of pregnancy carried the deletion seen in the fetus.

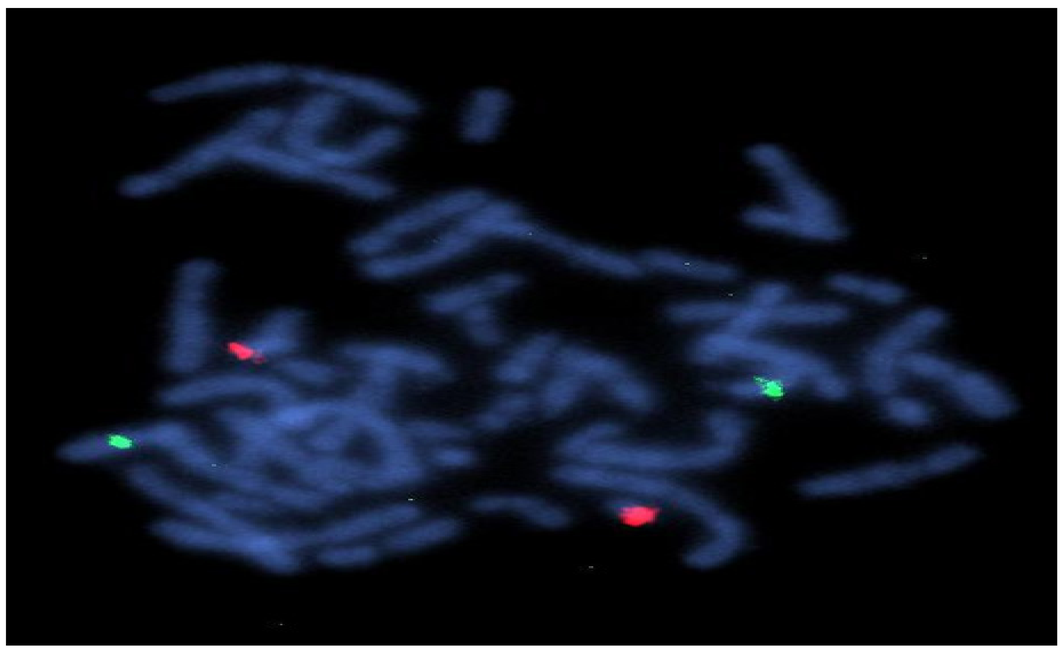

Figure 1. FISH probes used in CVS analysis. Image credit to Dr. Inder Gadi.

Test	Result
cfDNA	Trisomy 21
CVS FISH	Normal
CVS karyotype	Trisomy 21
Amnio FISH	Normal
Amnio karyotype	Trisomy 21
Amnio microarray	47,XX, +21 with deletion of 21q22.11->21q22.12

Table 1. Test results.

Conclusions

When discussing prenatal testing options with patients, discussion is often focused on conditions that can be detected and the potential limitations of each platform. When discussing the options for prenatal diagnosis following a positive cfDNA for a common trisomy, such as trisomy 21, patients often opt for standard karyotype. This case study reveals that consideration of microarray may be warranted in situations with a positive cfDNA test result. In addition to explaining the discordant FISH and chromosome analysis results, an additional genetic finding was detected. Results such as these could also prompt parental testing, which could change recurrence risk for future pregnancies. This case study highlights the potential need for further testing, even in what seems to be a routine indication.

NSGC 43rd Annual Conference; September 17-21, 2024; New Orleans, LA