

Case Report

Donor Screening: Level of Sensitivity in Karyotype with GTG banding vs PGT-A with NGS

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INTRODUCTION

The development of assisted reproductive technology (ART) is intricately intertwined with the evolution of genetic testing to aid in the identification of individuals who may be susceptible to genetic conditions or miscarriages. There are several different methods of genetic analysis, including karyotyping with Giemsa banding (GTG banding) which has played an integral role in routine screening. GTG banding can be cost-effective, but has a limited resolution of approximately 550 bands per haploid chromosome set, making it less sensitive to subtle abnormalities (Di Gregorio et al. 2014). In contrast, next-generation sequencing (NGS) has emerged as a more sensitive modality for detecting chromosomal abnormalities (Tamura et al. 2020). It can detect base pairs up to 800 bands per haploid chromosome set (Niederberger 2020). The increasing prevalence of donor gamete utilization necessitates a closer examination of the sensitivity of screening methods, given that GTG karyotyping has historically been considered the gold standard (Cheng, Fei, and Xiao 2023). However, due to its lower sensitivity, it may miss subtle chromosomal abnormalities.

Our case report identifies a case which delineates disparities in chromosomal error detection between traditional karyotyping with GTG banding and NGS. We present a case where both maternal and paternal karyotypes were normal, however PGT-A with NGS revealed multiple chromosomal abnormalities in embryos during an IVF cycle. Our case underscores the importance of adopting more sensitive screening platforms in the realm of ART.

CASE PRESENTATION

We describe a case of a 37-year-old primigravid woman with a history of late-term termination at 29 weeks due to multiple chromosomal abnormalities. She sought in-vitro fertilization (IVF) using donor sperm and opted for preimplantation genetic testing for aneuploidy (PGT-A). The patient had a normal karyotype with GTG banding obtained previously due to her prior history of genetic abnormalities. However, PGT-A during this cycle with donor sperm revealed two embryos with identical deletion/duplication abnormalities in chromosome 8 as shown in [Image 1](#). Furthermore, as part of routine screening, the donor also had

a normal karyotype. This discrepancy between the normal karyotypes and the abnormalities detected prompted further investigation into parental origin.

Labs:

- PGT-A findings: Two embryos with identical deletion/duplication abnormalities in chromosome 8
- Maternal findings: Normal karyotype; Normal single nucleotide polymorphism of chromosome 8
- Paternal findings: Normal karyotype
 - Per donor bank, has multiple ongoing pregnancies using this donor sperm, initially raising concern about potential transmission of genetic abnormalities. Thus, PGT complete was obtained.
- PGT complete with single nucleotide polymorphism matching: inconclusive
 - Parent of origin could not be matched to the deletion abnormality due to its size of less than 10mb pairs. However, in full karyomapping the duplication abnormality was found to be maternally inherited in one embryo and paternally inherited in the other embryo.

The patient subsequently made the decision to terminate her IVF cycle due to aneuploid embryos. She then opted for another cycle with an alternate donor, which ultimately did result in euploid embryos.

DISCUSSION

Patients who rely on donor sperm aspire to conceive healthy children and therefore, donor banks utilize widespread genetic testing. GTG-karyotyping is widely accepted as the gold-standard for donor sperm genetic testing. However, as mentioned above, the sensitivity of it compared to NGS reveals a disparity.

This case sheds light on a scenario where a patient using donor sperm during an IVF cycle produced embryos with identical chromosomal abnormalities in chromosome 8. The unexpected identification of abnormalities, despite the donor's prior normal GTG-karyotype, underscores the limitations of traditional screening methods. While this method can be proficient in detecting larger chromosomal

Sample ID	Sample Barcode	Result	Sex	Chromosomes Impacted	Interpretation
KB1	2022083744	Aneuploid	XY	del(8)(pter-p23.1),dup(8)(p22-qter)	Abnormal
KB2	2022083744	Aneuploid	XY	+2,del(8)(pter-p23.1),dup(8)(p22-qter)	Complex Abnormal

Image 1.

abnormalities, it may overlook more subtle genetic changes.

Additionally, the heightened risk of segmental aneuploidies stemming from paternal chromosomes, as documented in prior investigations, underscores the necessity for more sensitive screening platforms in reproductive genetic testing (Kubicek et al. 2019). Consequently, this case prompts a reevaluation of current genetic screening practices during IVF, suggesting that a normal GTG-karyotype may not eliminate the possibility of genetic abnormalities being passed down to the embryo.

CONCLUSION

Our case report emphasizes the need for advanced genetic screening in ART. The discrepancy between traditional karyotyping and NGS in detecting chromosomal abnormalities, particularly in donor sperm utilization, underscores the limitations of conventional methods. Moving forward, a shift toward comprehensive and more sensitive genetic testing methods may be warranted for improved outcomes in ART.

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