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IDENTIFICATION OF A PATIENT WITH A CRYPTIC TRANSLOCATION VIA PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY: A CASE REPORT

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OBJECTIVE: One cause of recurrent pregnancy loss (RPL) is the presence of a balanced chromosome rearrangement in one of the biological parents. A standard RPL workup includes chromosomal analysis of both gamete sources via a karyotype¹. However, cryptic translocations can evade detection via karyotype due to being sub-microscopic or a high degree of visual homology between the translocated regions. We describe here a family with RPL and a previously undetected cryptic translocation detected via Preimplantation Genetic Testing for Aneuploidy (PGT-A) using next generation sequencing (NGS).

MATERIALS AND METHODS: A G₉P₁ female patient and her partner sought treatment of RPL. The couple reported eight pregnancy losses conceived naturally; most of the losses occurred at 6 weeks gestation and resolved spontaneously, preventing analysis of products of conception (POC). Previous karyotypes for the couple showed normal results (46,XX and 46,XY). The couple elected to proceed with in vitro fertilization (IVF) with PGT-A, which resulted in eleven blastocysts for trophoctoderm biopsy and cryopreservation. Biopsies were analyzed using a modified FAST-SeqS NGS-based PGT method and bioinformatics pipeline²⁻⁴.

RESULTS:

Of the 11 embryos tested, 3 were euploid and 8 were aneuploid. All 8 aneuploid embryos were found to have terminal chromosome deletions and duplications at the same breakpoints, 3p26.2 and 12p11.2, which was highly suggestive of a parental balanced translocation. The segments were similar in size and had similar banding patterns, making them difficult to differentiate from one another on karyotype and inhibiting detection of a translocation between these two regions via that methodology.

Subtelomeric FISH was recommended to evaluate for a potential translocation, and subsequent analysis using probes for 3p, 3q, 12p, and 12q confirmed the presence of the suspected reciprocal translocation in the female patient's sample when hybridization of the 3p probe to chromosome 12 and the 12p probe to chromosome 3 occurred. Using a combination of karyotype, FISH, and PGT-A results, the female patient's karyotype was adjusted to read 46,XX,t(3;12)(p26.2;p11.2).

CONCLUSIONS:

This case report demonstrates the utility of PGT-A in identifying chromosomal rearrangements that might not be detectable via traditional methods. The couple obtained a greater understanding about a contributing cause of their RPL. Furthermore, the couple's offspring and other family members will now be better able to assess their balanced translocation carrier status knowing detection will require FISH, rather than traditional karyotyping.

IMPACT STATEMENT: PGT-A enabled detection of a chromosome rearrangement that eluded detection via karyotype. This was possible due to the NGS methodology used for PGT-A, which



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counts the amount of chromosome material present directly instead of visual assessment on karyotype. In addition, PGT-A was able to identify unbalanced chromosome complements that would be unlikely to result in an ongoing unbalanced pregnancy and then be detected on either POC or prenatal chromosome analysis.

References:

1. ASRM Practice Committee. Evaluation and Treatment of RPL. *Fertil Steril*. 2012
2. Gole J et al. *Fertil Steril*. 2016;105(2):e25.
3. Umbarger MA et al. *Fertil Steril*. 2016;106(3):e152.
4. Umbarger MA et al. *Fertil Steril*. 2017; 108(3):e270.