Structural fetal defects after preimplantation genetic diagnostics – a case report of unusual structural chromosome aberration

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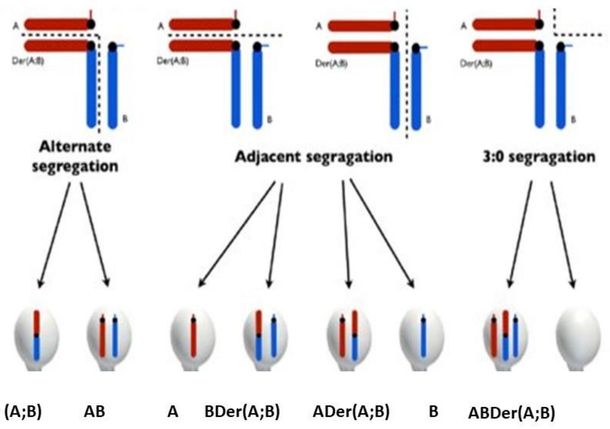
INTRODUCTION

Preimplantation genetic diagnostics (PGD) is a gold standard in eliminating chromosomal abnormalities of preimplantation embryos in balanced translocation carriers which may experience multiple pregnancy losses due to unbalanced segregation products formed in their gametes in relation to the involved chromosomes. This approach results in a significant reduction in spontaneous abortions and a significant increase in successful pregnancies. Robertsonian translocation (RT) is one of the most common balanced structural translocations in humans – it is a result of the centromeric fusion of two acrocentric chromosomes. Previous studies of the chromosomal patterns of embryos in RT carriers subjected to PGD have shown mixed results. Some have suggested that RT prompts abnormal chromosome segregation, resulting in high levels of mosaicism and chaotic embryos. Here we report a case of PGD in a couple attending reproductive clinics for two previous miscarriages. Cytogenetic analysis was performed in both partners. Results revealed Robertsonian translocation in the woman: karyotype 45, XX, der(14;22)(q10;q10). Because of the high risk for chromosomal abnormalities in the fetus, assisted reproduction with PGT-A was recommended. Screening for 24 chromosomes copy number was performed by Next Generation Sequencing (NGS) after Whole Genome Amplification (WGA) using Veriseq PGS (Illumina) protocol.



Only products of alternate segregation are balanced

RESULTS

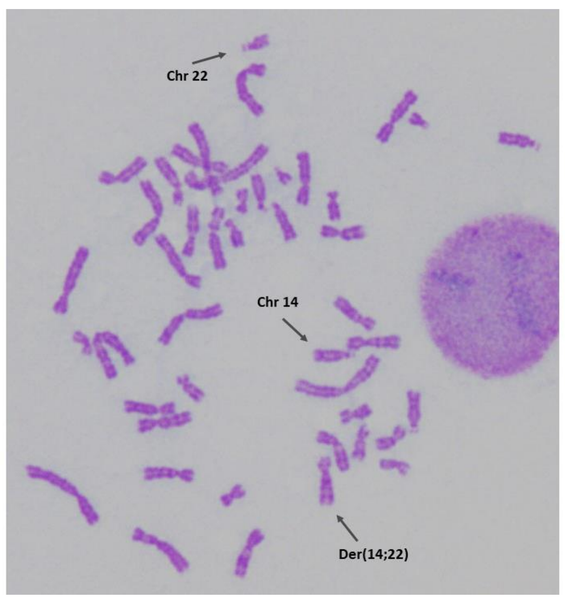


Figure 1. Karyotype of the mother: 45, XX, der(14;22)(q10;q10)

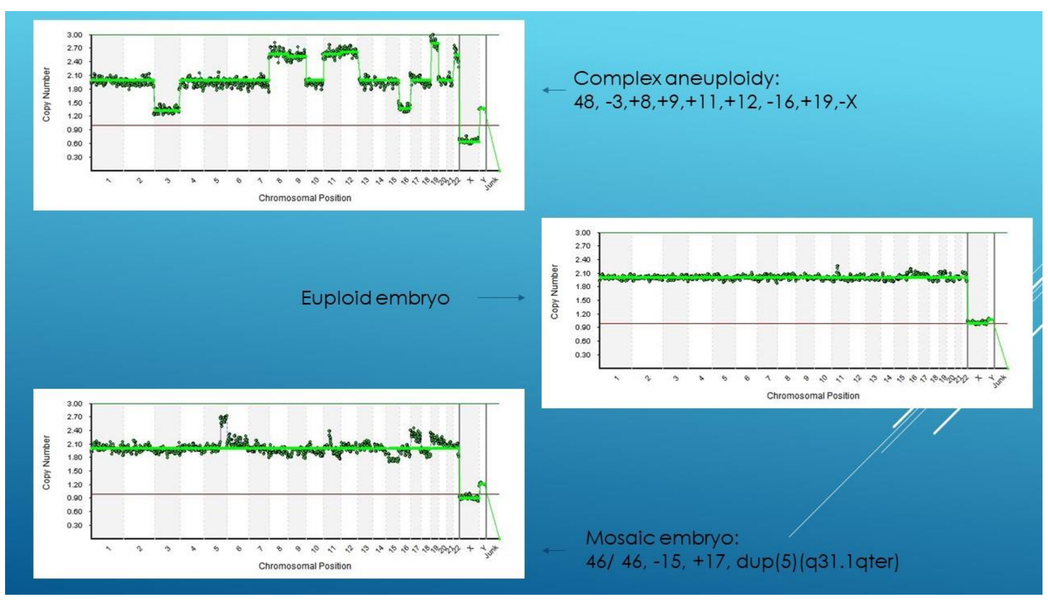


Figure 2. Results of three embryos tested at day 5

First transfer was done with the euploid embryo, but pregnancy was not realized. Mosaic embryo was transferred afterwards and pregnancy was detected. During first trimester screening ultrasound examination revealed severe cleft palate in the fetus and invasive prenatal testing (by CVS) was performed by array CGH analysis. Because suspicion of mosaicism, amniocentesis was performed as well, followed by Vista™ Chromosome Sequencing technology.

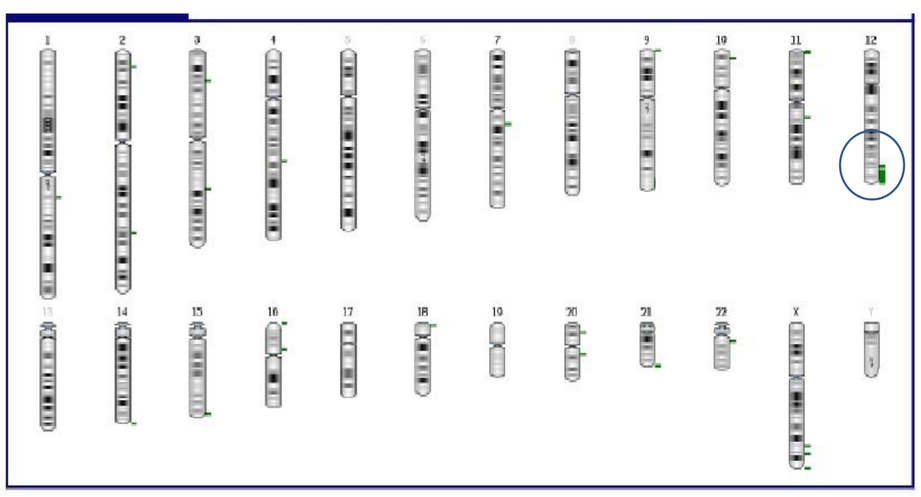


Figure 3. Result from aCGH analysis - terminal duplication of 12q - 46,XN,**dup(12q24.23q24.33)**, seq[GRCh37/hg19](120,686,369-133,841,515)×3; the aberration was not detected during PGT-A.

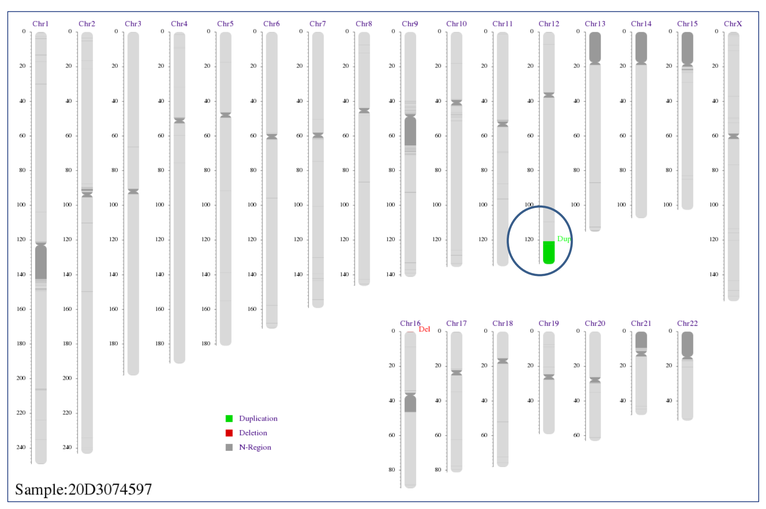


Figure 4. Result from Vista™ Chromosome Sequencing technology - confirmed **12q terminal duplication** and pregnancy was terminated.

Pregnancy was terminated based on the confirmed 12q terminal duplication and severe congenital malformation.

CONCLUSION

This case demonstrates the need for careful evaluation of pregnancies in which mosaic embryos are transferred, with an emphasize on the use of high-throughput whole genome techniques for copy number analysis.

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