Assessment of the chromosomal segregation pattern based on the results of the PGT-SR in a family where both spouses carry an autosomal translocation

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INTRODUCTION

Autosomal reciprocal translocations (ART) represent exchanges of chromatin fragments between non-homologous chromosomes. Chromosomes involved form quadrivalent structures during the first meiotic division. Length of translocated and centric segments, asymmetry, and the presence of terminal breakpoints in quadrivalent influence segregation mode. We report a rare case of a family where both spouses carry different ARTs: 46,XY,t(3;6)(p22.2;p21.2) and 46,XX,t(2;17)(p16.1;p12). We evaluated segregation patterns in sperm and in embryos obtained after PGT-SR performed with FISH, aCGH, and NGS techniques.

CASE PRESENTATION

A nonconsanguineous couple with a two-year history of infertility, asthenozoospermia in the male, obesity in the female, and without other phenotypic features was referred to the International Centre for Reproductive Medicine for the first time in 2014, when the female was 28 and the male was 36 years of age. Karyotype analysis of each spouse revealed that both present with unique ARTs: 46,XY,t(3;6)(p22.2;p21.2) and 46,XX,t(2;17)(p16.1;p12). Couple then underwent 7 years (2014–2020) of treatment including 6 cycles of in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) and 3 balanced embryo transfers following PGT-SR evaluation by fluorescent in situ hybridization (FISH) or array comparative genomic hybridization (aCGH), resulting in a single pregnancy and the birth of a healthy son. Both spouses refused prenatal karyotyping and karyotype analysis of their son after birth revealed his inheritance of the maternal translocation: 46,XY,t(2;17)(p16.1;p12)mat

RESULTS

Based on the individual characteristics of quadrivalent we determined the theoretical segregation mode as adjacent-1 for both translocations. We identified an alternate segregation mode in 41.7% of the embryos regardless of translocation. Adjacent-1 was the predominant pathological segregation mode in both translocations (33.3% in female and 29.2% in male). The most common segregation mode in the sperm was also alternate (40.6%) following by adjacent-1 (35.3%). Segregation of 3:1 and adjacent-2 were detected in 18.8% and 5.3% of the sperm nuclei, respectively. The female ART presented with severe quadrivalent asymmetry while the male translocation induced mild asymmetry, both rearrangements were without terminal breakpoints. We detected 3:1 segregation in 12.5% of female ART embryos compared to 8.3% in male ART embryos, which is consistent with our evaluation of severe quadrivalent asymmetry in the female ART inducting pathological meiotic disjunctions.

CONCLUSION

Universal characteristics of quadrivalent may be used to predict pathological segregation mode and to assess the likelihood of success in IVF cycle. Such families may be advised to use a sperm or egg donor in the case of severe quadrivalent asymmetry, or advanced maternal age. At the same time, considering the frequency of alternate segregation, precise risk assessment for each family in pursuit of having a healthy offspring without the use of donor gametes is important.

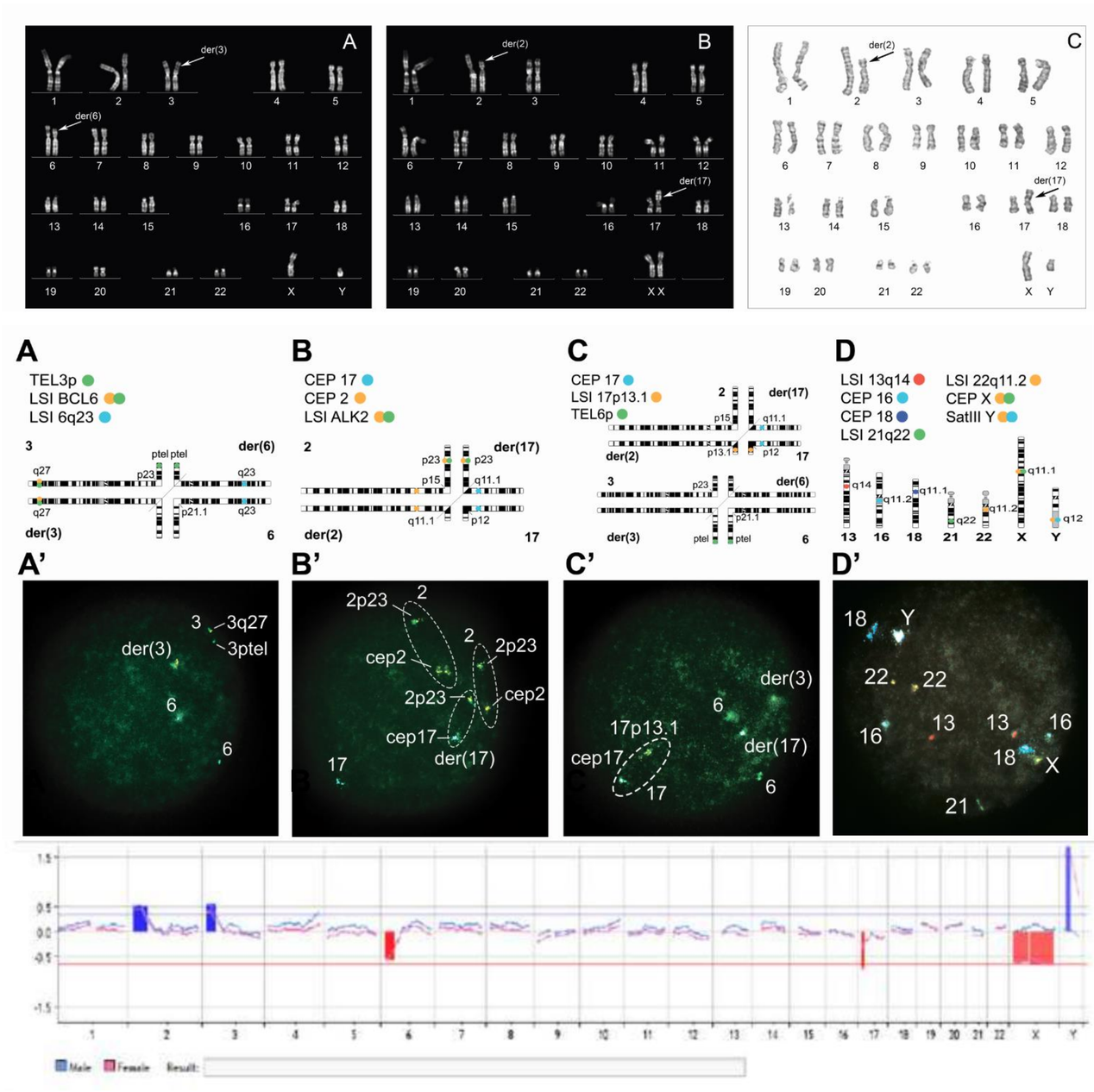

Figure: Karyograms (upper row) describing the karyotypes of the peripheral lymphocytes from the mother (A), father (B), and son (C) as evaluated by the QFH/Ac D (A, B) and GTG (C) banding techniques. The scheme of hybridization mixtures (A–D, 2nd row) and results of PGT-SR by FISH (A'–D', 3rd row) and a-CGH (bottom row).

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