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Short communication

Two cases of complex balanced autosomal translocations associated with severe oligozoospermia

Yan-Wei Sha[a], Li-Bin Mei[a], Zhi-Yong Ji[a], Lu Ding[a], Yunsheng Ge[b], Qiong Wu[b], Hui Kong[b], Zhi-Ying Su[a], Ping Li[a,*]

[a] Department of Reproductive Medicine, Xiamen Maternity and Child Care Hospital, Xiamen, Fujian 361005, China
[b] Division of Genetics, Xiamen Maternity and Child Care Hospital, Xiamen, Fujian 361005, China

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ABSTRACT

Complex balanced autosomal translocation is rare and can lead to impaired spermatogenesis in males; however, its effects on oligozoospermia have rarely been reported. We report here two cases of rare complex balanced translocation in men with infertility. The karyotype of the first case was 46,XY,der(1)t(1;12)(p22;p11.2)ins(9;1)(p24;q25q23),der(9)ins(9;1),der(12)t(1;12)·ish der(1)t(1;12)(RP11-636B1+;RP11-659D23+)ins(9;1)(RP11-118P13+),der(9)ins(9;1),der(12)t(1;12). And the patient showed severe oligozoospermia with adult schizophrenia without other abnormalities. The karyotype of the second patient was 46,XY,der(5)t(5;11)(q14;p11.2),der(11)t(11;18)(p11.2;q11.2),der(18)t(5,18)(q14;p11.3)add(18)(q11.2?)·ish der(5)t(5;11)(RP11-846K3+,RP11-89B9+),der(11)t(11;18)(RP11-89B9-,RP11-170L12+,RP11-469N6+),der(18)t(5;18)(RP11-125L2+,RP11-29M13+)add(18)(q11.2?), and the patient displayed severe oligozoospermia without other abnormalities. The two cases were verified by fluorescent *in situ* hybridization, and no abnormalities were found by genome-wide copy number variation analysis. To our knowledge, these two cases of complex autosomal karyotypes have not been reported previously. Although rare, these cases suggest that complex balanced translocations may be important causes of oligozoospermia. We speculate that the balanced translocation hinders germ cell meiosis and causes impaired spermatogenesis. Accordingly, the two reported patients have very low probabilities of giving birth to a normal child; therefore, we suggest choosing donor semen or adopting a child.

1. Introduction

Chromosome abnormalities are common genetic factors that cause male infertility, with clinical manifestations including azoospermia, oligozoospermia, teratozoospermia, globozoospermia and recurrent miscarriage (Massart et al., 2012). Sex chromosome abnormalities are the major cause of male infertility, which are found in approximately 2% of all infertile males (Meschede et al., 1997), 5% of males with oligozoospermia, and 14% of males with azoospermia (Johnson, 1998), whereas only 0.7% of the general population have a chromosomal abnormality at birth. In infertile males, chromosomal abnormalities present as numerical and structural changes of sex chromosomes can cause impaired spermatogenesis. Furthermore, autosomal structural abnormalities such as balanced reciprocal translocations on chromosomes 1, 6, 12, and 22 can also lead to azoospermia or severe oligozoospermia (Lorda-Sanchez et al., 2001; Bianco et al., 2011; Zhang et al., 2015). In addition, complex balanced translocations, also known as complex chromosomal rearrangements (CCR), which mainly refer to balanced translocations that occur in at least two chromosomes with more than two breakpoints (Kleczkowska et al., 1982), are relatively rare structural chromosome aberrations that are another potential causes of male infertility (Rodriguez et al., 1985; Cai et al., 2001; Coco et al., 2004; Bartels et al., 2007; Loup et al., 2010; Kim et al., 2011; Pellestor et al., 2011; Madan, 2012; Li et al., 2013; Yakut et al., 2013; Asia et al., 2014; Chen et al., 2014; Hornak et al., 2014; Sadik and Seifeldin, 2014; Nguyen et al., 2015). The influence of balanced translocations on the resulting phenotype may vary (Pinho et al., 2005; Vialard et al., 2006; Perrin et al., 2008; Bianco et al., 2011; Zhang et al., 2016). Here we report two clinical cases of oligozoospermia caused by complex balanced autosomal translocations.

Abbreviations: CCR, complex chromosomal rearrangements; CNV, copy number variation; FISH, fluorescent *in situ* hybridization

* Corresponding author at: Department of Reproductive Medicine, Xiamen Maternity and Child Care Hospital, No. 10 Zhenhai Road, Xiamen, Fujian 361003, China.
E-mail address: saarc2001@sina.com (P. Li).

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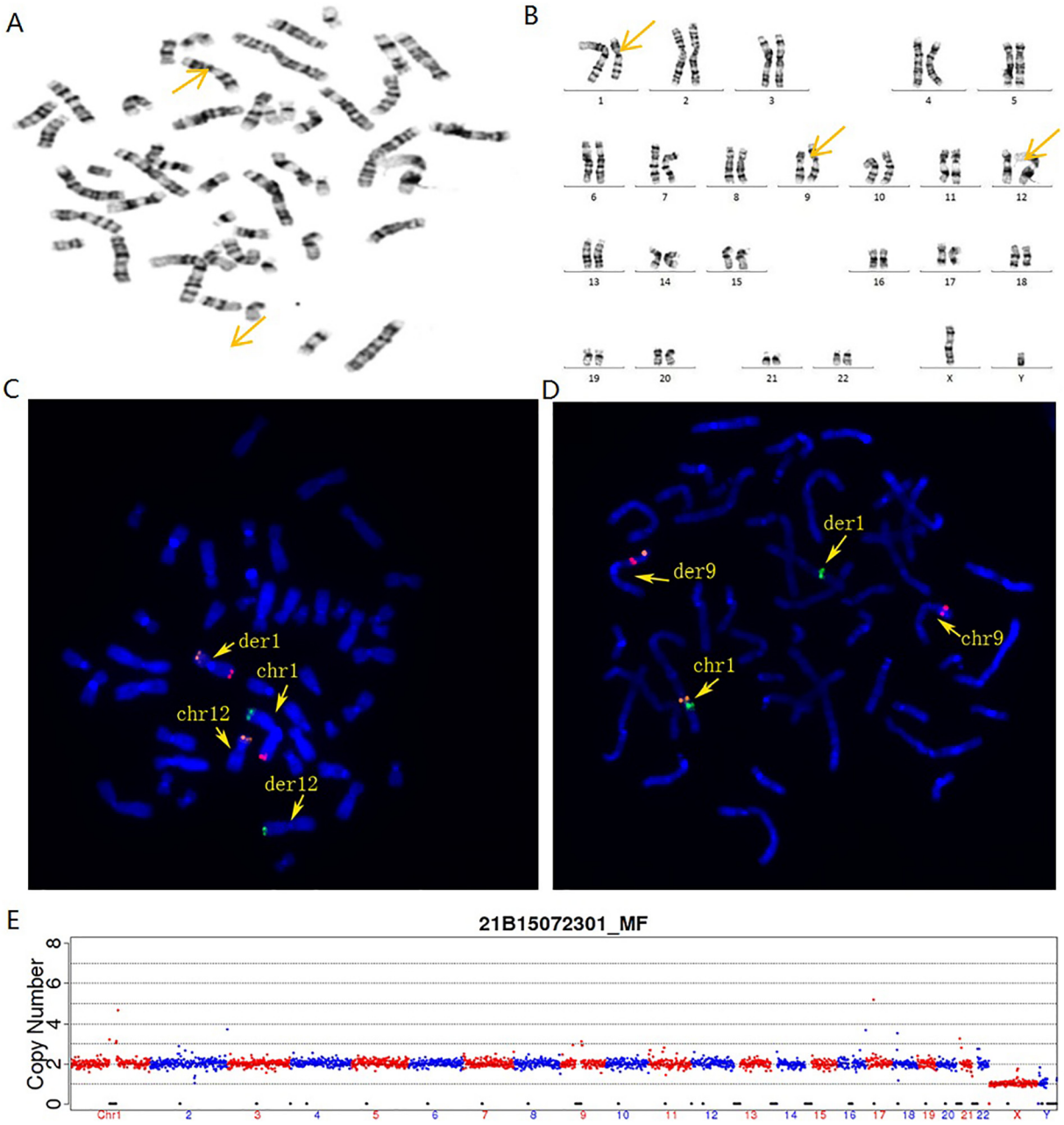

Fig. 1. Cytogenetic and molecular analysis results of patient 2. A and B, G-banding karyotype. C and D, fluorescence *in situ* hybridization (FISH) results showing reciprocal translocation between chr1p22 and chr12p13, and the chr1q25 translocation to chr9, respectively. E, copy number variation analysis for patient 2 did not reveal any abnormalities.

2. Material and methods

2.1. CNV sequencing

The CNV sequencing was performed as previously described (Liang et al., 2014). The average size of fragmented DNA was 200 bp. CNV-seq analysis of the extracted DNA was performed using the HiSeq 2000 (Illumina, San Diego, CA). The genome sequencing coverage was approximately 0.1-fold. The sequencing bins were 1 Mb of the genome.

2.2. Cytogenetic analysis

Cytogenetic analysis was performed on metaphase chromosomes derived from peripheral blood lymphocytes cultures from the patients and their parents. G-banding (400–550 bands) was performed first according to the standard procedure and guideline (ISCN2013). FISH analysis was performed as previously described (Ko et al., 2013) and carried out on metaphase or interphase chromosomes from the patients and their parents.

3. Results

3.1. Case 1

The patient is a 32-year-old male with a 3.5-year history of infertility. A Y chromosome microdeletion analysis did not reveal any abnormalities. His karyotype is 46,XY,der(1)t(1;12)(p22;p11.2)ins(9;1)(p24;q25q23),der(9)ins(9;1),der(12)t(1;12)·ish der(1)t(1;12)(RP11-636B1 + ;RP11-659D23 +)ins(9;1)(RP11-118P13 +),der(9)ins(9;1),der(12)t(1;12) (Fig. 1A and B). FISH validation results are shown in Fig. 1C