CASE REPORT

One normal child and a chromosomally balanced/normal twin after intracytoplasmic sperm injection in a male with a de-novo t(Y;16) translocation

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A balanced translocation t(Y;16)(q11.21; q24) is described in a male with severe oligoasthenoteratozoospermia (OAT). Before having a chromosome investigation, the patient and his partner had undergone intracytoplasmic sperm injection (ICSI) treatment resulting in the birth of a healthy 46,XX child. After detection of the t(Y;16) translocation, the couple opted for further ICSI treatment, although they were extensively counselled on the risk of having chromosomally unbalanced offspring. This treatment resulted in a twin pregnancy, one with a 46,XX karyotype and the other a 46,X,t(Y;16) (q11.21; q24) karyotype, the same as the father. After an uncomplicated pregnancy two healthy children were born. We conclude that patients with a Y/autosome translocation as a cause of OAT can have chromosomally normal children after ICSI treatment.

Key words: chromosomal abnormalities/ICSI/male infertility/oligoasthenoteratozoospermia (OAT)/Y;autosome translocation

Introduction

Male infertility and subfertility can be caused by several factors, both acquired and genetic (Van Assche et al., 1996). However, the majority of cases remain unexplained.

The genetic factors that have been described include chromosome abnormalities (such as 47,XXY and balanced translocations), Y-chromosomal deletions (Reijo et al., 1995) and cystic fibrosis gene mutations (Van der Ven et al., 1996). In a recent screening of a consecutive series of men with less than 1×106 motile sperm cells per ml, 26% of them presented with one of these genetic risk factors (In’t Veld et al., 1997a).

Balanced chromosome translocations include Robertsonian translocations, reciprocal translocations and sex chromosome/autosome translocations. Y/autosome translocations can be divided into two categories. In the first there is a translocation of a Yq distal chromosomal fragment onto the short arm of an acrocentric chromosome as well as a normal Y chromosome. This type of translocation is without phenotypic effect.

The second category consists of translocations between the Y-chromosome and any autosome (excluding the short arm of the acrocentric chromosomes). Males with this type of translocation, which is almost exclusively de novo, are infertile in 80% of the cases (Hsu, 1994).

Here we present a normal healthy male with a t(Y;16) translocation belonging to this second category, and with severe oligoasthenoteratozoospermia (OAT). He and his partner were referred because of involuntary childlessness. Six intracytoplasmic sperm injection (ICSI) treatment cycles resulted in one pregnancy and birth of a normal 46,XX girl, one extrauterine pregnancy and one twin pregnancy with the birth of a normal 46,XX girl and a phenotypically normal 46,X,t(Y;16) (q11.21; q24) boy.

Case report

The patient is a normal healthy 43 year old male who was previously examined because of infertility. Repeated spermograms revealed a severe OAT (1×106 spermatozoa/ml of which only 10% were motile).

His family history revealed no abnormalities. His parents are from large families (the father and mother have 14 and 11 siblings respectively). He has two brothers and four sisters. Two of his sisters and two of his paternal uncles are involuntarily childless, for which no explanation was found.

There is no consanguinity between the patient and his partner. His partner is a healthy 35 year old female from a family of four siblings, all of whom have one or more children.

The first ICSI treatment, which was performed in an IVF centre abroad, yielded three embryos. Since all three embryos showed a developmental arrest, none of them was transferred. The second ICSI treatment (also performed abroad) yielded five embryos, two of which were transferred, resulting in a pregnancy with one fetus. A healthy girl was born after an uncomplicated pregnancy and delivery, with a birth weight of 3540 g. There were normal external genitalia, no dysmorphic features and on physical examination there were no abnormalities. Chromosome investigation was performed at the parents’ request because of the slightly increased risk of a sex chromosomal aneuploidy after ICSI. She appeared to have a normal 46,XX karyotype. She is now 28 months of age. Developmental milestones are within the normal range.

For further ICSI treatments, the couple visited Elisabeth Hospital, Tilburg, The Netherlands. As part of the routine diagnostic investigation, chromosome analysis was performed in the male partner. This revealed a 46,X,t(Y;16) (q11.21; q24) karyotype (Figure 1). His parents both had normal karyotypes.

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To further characterize this translocation, fluorescence in-situ hybridization (FISH) was performed, using whole chromosome paints for chromosome 16 and the Y. As expected, the Y paint hybridized to the derivative Y (der Y) as well as to the translocated Y fragment on the derivative 16 (der 16) chromosome. Paint 16 only stained the der 16 chromosome, the normal chromosome 16, and did not detect any material derived from 16q attached to der Y (data not shown). The fragment derived from the 16q telomere, which is expected to be present on the der Y, was not detected by paint 16 either because it is too small to be visualized or because it is under-represented in this paint.

The couple was extensively counselled on the potential risks of ICSI treatment, without any precise estimate being given, since such data are not available from the literature. Nevertheless they chose to undergo further treatment.

The third ICSI treatment yielded nine embryos, two of which were transferred, again resulting in a pregnancy. However, this pregnancy, which turned out to have been an extraterine one, was complicated by a bleeding in the lower abdomen necessitating laparotomy and termination of the pregnancy.

The fourth and fifth treatments yielded five and three embryos respectively, of which two and three were transferred. Neither of these treatments resulted in a pregnancy. In the sixth treatment four embryos of poor quality were obtained. One grade 3 embryo (uneven blastomeres with <10% fragmentation; Steer et al., 1992) with six blastomeres and two grade 2 embryos (10–50% blastomeric fragmentation) both containing six blastomeres were transferred 3 days after oocyte recovery. Despite the poor embryo quality, a twin pregnancy was established. Chromosome analysis in amniotic fluid showed that one twin had a 46,XX karyotype and the other a 46,X,Y(16) (q11.21;q24) karyotype. Extensive ultrasound investigations of the twins revealed no abnormalities. In particular, there were no abnormalities of the internal and external genitalia. After an uneventful pregnancy two healthy children were born: a girl with a birth weight of 3050 g and a boy with a birth weight of 2070 g. The boy had to undergo a partial exchange transfusion due to a high blood viscosity. On physical examination the newborns showed no abnormalities.

**Discussion**

Reciprocal Y/autosome translocations, such as the de-novo translocation 46,X,Y(16) (q11.21;q24) described in this patient (Figure 1) are rare. There are only a few reports of men with these translocations having offspring. There is one report of a subfertile man who transmitted a Y/Y translocation to his healthy (subfertile) son (Teyssier et al., 1993), and there are two reports of children with an unbalanced Y/autosome translocation whose fathers had a balanced Y/autosome translocation (Laurie et al., 1984; Nikolis et al., 1991). Although theoretically the meiotic segregation products in the patient described here would include normal X spermatozoa, as well as balanced der(Y)/der(16) spermatozoa, the birth of a chromosomally normal child to a carrier of a reciprocal Y/autosome translocation appears to be uncommon, since we could not find similar cases in the literature. However, it is important to note that the two previous reports on children with unbalanced Y/autosome translocations have an ascertainment bias, since these children were karyotyped because of phenotypic abnormalities. So it is possible that there are other chromosomally normal or balanced offspring of Y/autosome translocation carriers who have not been detected due to a lack of phenotypic abnormalities. Therefore, the outcome of pregnancies of Y/autosome translocation carriers may not be essentially different from that of autosomal translocation carriers (Laurie et al., 1984; Pellestor et al., 1997).

After diagnosis of severe OA T, the patient and his partner asked for ICSI treatment. The risk of a chromosome abnormality in a child born after ICSI treatment is difficult to assess. A 1% risk of sex chromosome abnormalities was reported (Liebaers et al., 1995). The risk of autosomal chromosome abnormalities in ICSI conceptions from oligozoospermic men with balanced translocations remains unknown, but may be significantly higher than for natural conceptions (Wilkins-Haug et al., 1997). Therefore, many reports (Wilkins-Haug et al., 1997; In’t Veld et al., 1997a; Harrison, 1997; Pauer et al., 1997) advise chromosome analysis in males with OAT prior to ICSI. In general, if a couple wants to have ICSI treatment, the detection of a chromosome abnormality in the male partner may be considered a strong argument to advise the couple to refrain...
from the treatment, because of the risk of having a chromosomally unbalanced child. Support for this advice was presented by In’t Veld et al. (1997b) who published a case report of a couple with a male Robertsonian translocation carrier in whom ICSI treatment yielded a chromosomally unbalanced child.

The present case illustrates that, although this advice may be justified in many cases, subfertile translocation carriers can have chromosomally normal spermatozoa, and thus produce normal children after ICSI treatment.

References


