

Article

Meiotic segregation of X-autosome translocation in two carriers and implications for assisted reproduction



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Abstract

The aim of this study was to analyse and compare the meiotic segregation of X-autosome translocation in two male carriers and to discuss couple-specific treatment modality before intracytoplasmic sperm injection (ICSI). Meiotic segregation was analysed by fluorescence in-situ hybridization (FISH) in spermatozoa of two men who were carriers of a X-autosome translocation: 46,Y,t(X;2)(p21;p25.3) (patient 1) and 46,Y,t(X;18)(q11;p11.1) (patient 2). The results indicated a majority of unbalanced spermatozoa (62.05%) for patient 1, but normal or balanced spermatozoa (54.36%) for patient 2. Moreover, the unbalanced gametes resulted from adjacent I, adjacent II and 3:1 segregation, in decreasing frequencies, for patient 1 but from 3:1, adjacent I, adjacent II segregation for patient 2. The results of the meiotic segregation analysis had different treatment implications for assisted reproduction. Couple 1 were advised against ICSI, due to the results of the meiotic segregation in spermatozoa from patient 1 and the age of his wife. For couple 2, the clinic viewed favourably an attempt with ICSI followed by conventional prenatal diagnosis. A 46,XY child was born without malformations.

Keywords: FISH, genetic counselling, meiotic segregation, spermatozoa, X-autosome translocation

Introduction

Cytogenetics has been an important diagnostic tool in male infertility since 1959, with the identification of a 47,XXY karyotype in patients with Klinefelter syndrome (Jacobs and Strong, 1959). The first studies found that the frequency of somatic chromosomal abnormalities was increased among infertile males (Chandley, 1979; De Braekeleer and Dao, 1991). Indeed, the frequency of chromosomal abnormalities at birth is approximately 0.85% (Nielsen and Wohler, 1991) whereas, in the infertile male population, it ranges from 2% to 20% (De Braekeleer and Dao, 1991; Baschat *et al.*, 1996;

Peschka *et al.*, 1999; Gekas *et al.*, 2001; Morel *et al.*, 2004a; Clementini *et al.*, 2005; De Braekeleer *et al.*, 2006).

Generally, the risk of carrying a somatic chromosomal abnormality increases with the severity of the spermogram, numeration being the best predictive parameter (Vegetti *et al.*, 2000; Vincent *et al.*, 2002). Moreover, males with oligozoospermia are more likely to have an autosomal rearrangement, including reciprocal or Robertsonian translocations or inversions, than those with azoospermia. On

the contrary, males with azoospermia are much more likely to have a sex chromosome numerical or structural abnormality than those with oligozoospermia (De Braekeleer *et al.*, 2006). Indeed, most of the males carrying a translocation involving a gonosome have azoospermia (Matsuda *et al.*, 1989; Buonadonna *et al.*, 2002; Ishikawa *et al.*, 2007) although a few have severe oligozoospermia (Mattei *et al.*, 1982; Alves *et al.*, 2002; Ma *et al.*, 2003).

Intracytoplasmic sperm injection (ICSI) is now a widely-accepted procedure to assist fertilization in couples with severe male infertility (Palermo *et al.*, 1992). However, as these carriers can produce a significant percentage of gametes with an unbalanced combination of the parental rearrangement, there is a potentially elevated genetic risk, according to cases, of chromosomal imbalances for their offspring (Morel *et al.*, 2004b, 2006). The aim of this study was to analyse and compare the meiotic segregation of X-autosome translocation in two male carriers and to discuss couple-specific treatment modality before ICSI.

Materials and methods

Patients

Couple 1 (woman 42 years old; man 44 years old) presented with a 2-year history of primary infertility. The female partner had a normal karyotype. Semen analysis showed an oligoasthenoteratozoospermia with $0.5\text{--}5 \times 10^6$ spermatozoa/ml, 40% mobile spermatozoa and 80% abnormal forms, according to the World Health Organization criteria (World

Health Organization, 1999) and the method proposed by David *et al.* (1975). The karyotype of peripheral blood lymphocytes of patient 1 was 46,Y,t(X;2)(p21;p25.3).

Couple 2 (woman 24 years old; man 26 years old) presented with a 3-year history of primary infertility. The female partner had a normal karyotype. Semen analysis showed a very severe oligoasthenoteratozoospermia with 0.4×10^6 spermatozoa/ml, 95% immobile spermatozoa and 90% abnormal forms. The karyotype of patient 2 was 46,Y,t(X;18)(q11;p11.1).

Prior to this study, both patients were informed of the investigations and subsequently gave their consent.

Meiotic segregation analysis in spermatozoa

Four probes were used to analyse the sperm sample of patient 1: specific alphoid probes of chromosome 2 (spectrum red; Abbott, Rungis, France), X chromosome (spectrum aqua; Abbott) and Y chromosome (spectrum aqua; Abbott) and 2p subtelomere probe (tel 2p; spectrum green; Abbott). Ideograms showing the translocation and the probes' localization are schematized in **Figure 1**.

The sperm sample of patient 2 was analysed in triple FISH using a specific alphoid probe of chromosome 18 (D18Z1; spectrum aqua), an 18p subtelomere probe (tel 18p; spectrum green), and a Xq/Yq subtelomere probe (telXq/Yq; spectrum orange). Ideograms showing the translocation and the probes' localization have been previously described (Perrin *et al.*, 2008).

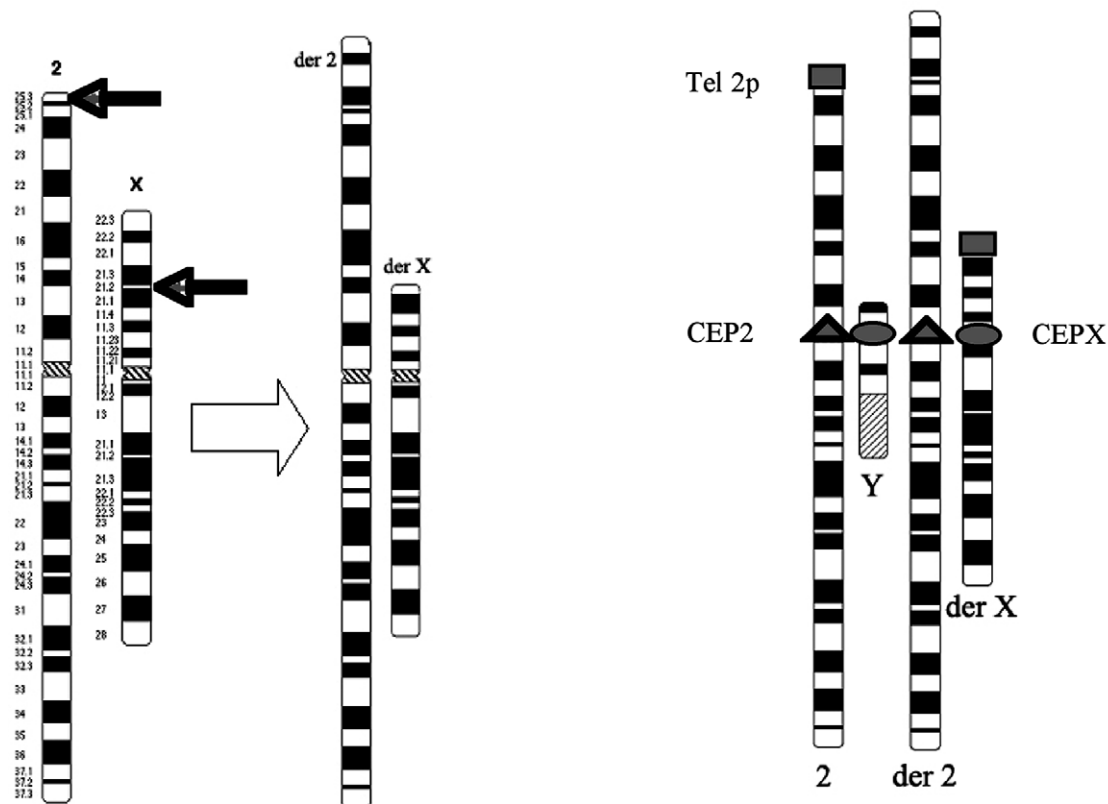


Figure 1. Ideograms showing the t(X;2)(p21;p25.3) and the localization of the probes.

The hybridization procedure and analysis have been described elsewhere (Morel *et al.*, 2004c; Douet-Guilbert *et al.*, 2005; Vialard *et al.*, 2007; Caer *et al.*, 2008).

Results

A total of 440 spermatozoa were analysed for patient 1. The frequency of normal or balanced spermatozoa, resulting from alternate segregation, was 37.95%. The majority of analysed spermatozoa (62.05%) showed unbalanced chromosomes resulting from adjacent I (21.59%), adjacent II (20.68%) and 3:1 (17.95%) segregation (**Table 1**). The remaining spermatozoa showed ambiguous signals or hybridization failure (0.91%) or were diploids or 4:0 segregation (0.91%).

A total of 447 spermatozoa were analysed for patient 2. The majority of the analysed nuclei (54.36%) showed normal or balanced chromosomes resulting from alternate segregation. All other spermatozoa (45.64%) were unbalanced (**Table 1**). The frequencies of adjacent I, adjacent II and 3:1 segregation were 8.28%, 5.15% and 22.37% respectively (Perrin *et al.*, 2008).

Discussion

Translocation is the most frequent structural abnormality in human. The majority of reciprocal translocations occur between two autosomes. Translocations involving gonosomes are rare (Lee *et al.*, 2003; Brisset *et al.*, 2005; Pinho *et al.*, 2005; Ishikawa *et al.*, 2007). Azoospermia is the common feature in male carriers of a X-autosome translocation (Kalz-Fuller *et al.*, 1999; Solari *et al.*, 2001; Ishikawa *et al.*, 2007), although severe oligozoospermia has been observed in a few patients (Ma *et al.*, 2003; Perrin *et al.*, 2008). Indeed, interaction between autosomal derivatives and sexual vesicle leads to meiotic disturbances and, consequently, to gametogenic arrest (Gabriel-Robez *et al.*, 1986; Delobel *et al.*, 1998; Pinho *et al.*, 2005).

The profiles of meiotic segregation are different between the two carriers studied here. The results indicated a majority of unbalanced spermatozoa for patient 1 but of normal or balanced spermatozoa for patient 2. Moreover, the unbalanced gametes resulted from adjacent I, adjacent II and 3:1 segregation, in decreasing frequencies, for patient 1 but from 3:1, adjacent I, adjacent II segregation for patient 2.

These different profiles confirm that, as for the translocations between two autosomes, the risk of meiotic imbalance varies according to the chromosomes involved in the translocation (chromosome X and autosome of group A for patient 1; chromosome X and autosome of group E for patient 2) and the breakpoint positions (telomeric for chromosome 2 and Xp21 for patient 1 and juxtacentromeric (Xq11, 18p11) for patient 2). Moreover, the configuration of quadrivalent at pachytene strongly determines the segregation mode that will preferentially follow during anaphase I (Perrin *et al.*, 2007). Adjacent I segregation occurs preferentially in translocations for which the sum of both centric segment lengths is greater than the two translocation segment lengths (as for patient 1) whereas the 3:1 segregation is likely if one of the chromosomes of the quadrivalent is small (as for patient 2) or is an acrocentric chromosome (Jalbert *et al.*, 1980).

The risk of producing a chromosomally unbalanced offspring related to the presence of the X-autosome translocation was 62.05% for patient 1 and 45.64% for patient 2 if it is considered that the unbalanced spermatozoa have the same fertilizing potential as the normal or balanced spermatozoa (Brugnon *et al.*, 2006). The risk of meiotic imbalance is primarily determined by the characteristics of the chromosomes involved and the breakpoint positions as well as survival rate. As many of these imbalances are incompatible with survival, the risk values change during pregnancy (Stengel-Rutkowski *et al.*, 1988). Thus, the offspring viability was evaluated according to different segregation modes based on the hypothesis that an embryo is unviable if monosomy accounts for more than 1% of his genome and trisomy for more than 3% (**Table 2**) (adapted from Cohen *et al.*, 1994).

Based on the analysis of the chromosomes involved in the translocation, patient 1 had a probability of 6.36% of producing a fetus with Turner syndrome and 1.14% with Klinefelter syndrome. He also had a 23.40% risk of producing a chromosomally unbalanced viable fetus (leading to the birth of a child with a polymalformation syndrome and/or mental retardation) and a 31.14% risk of producing an unviable fetus (leading to early pregnancy loss or spontaneous abortion). Thus, the risk of having an ongoing pregnancy associated with a chromosomally unbalanced fetus was 30.90%. Panasiuk *et al.* (2004), using the indirect method of risk estimates proposed by Stengel-Rutkowski *et al.* (1988), found that the probability of occurrence for unbalanced offspring at birth ranged from 2.1% to 17% in four families of reciprocal X:A translocation carriers involving the short arm of the X chromosome. Information about the magnitude of the individual figures at birth is different in comparison to data from sperm karyotyping; this should be considered during genetic counselling of families. Patient 2 had a probability of 7.61% of producing a fetus with Turner syndrome and 2.68% with Klinefelter syndrome. He also had a 24.61% risk of producing a chromosomally unbalanced viable fetus and 10.74% of producing an unviable fetus. Thus, the risk of having an ongoing pregnancy associated with a chromosomally unbalanced fetus was 34.90%.

The results of the meiotic segregation analysis had different treatment implications for assisted reproduction.

For couple 1, there was a high proportion of chromosomally unbalanced spermatozoa from the t(X;2)(p21;p25.3) carrier. Munné (2002) found that implantation rates in translocation carriers were directly correlated with the proportion of normal gametes and that pregnancy rates were inversely proportional to the number of abnormal gametes. Moreover, Escudero *et al.* (2003), analysing the outcome of preimplantation genetic diagnosis (PGD) from 11 couples in whom the male partner carried a translocation, found that, when the proportion of chromosomally unbalanced spermatozoa was higher than 63%, there were no pregnancies. Thus, due to the obtained results of the meiotic segregation in spermatozoa from patient 1 and the age of his wife (42 years), the clinic advised against ICSI during genetic counselling.

For couple 2, a majority of normal or balanced spermatozoa from the t(X;18)(q11;p11.1) carrier was found. This percentage was no higher than those found in carriers of autosome-autosome translocation (Morel *et al.*, 2004b; Nishikawa *et al.*,

Table 1. Results of the meiotic segregation of X-autosome translocation in two carriers.

Segregation mode	Chromosomal equipment	No. of spermatozoa (%)	
		Patient 1	Patient 2
Alternate	Y/A	167 (37.95)	243 (54.36)
Adjacent I	der(X)/der(A)		
	der(X)/A	44 (10.00)	16 (3.58)
Adjacent II	Y/der(A)	51 (11.59)	21 (4.70)
	der(X)/Y		
A/der(A)	46 (10.45)	0 (0.00)	
		35 (7.95)	12 (2.68)
3:1	Crossing-over	10 (2.27)	11 (2.46)
	A	28 (6.36)	34 (7.61)
	der(X)/Y/der(A)	5 (1.14)	12 (2.68)
	der(A)	6 (1.36)	30 (6.71)
	der(X)/Y/A	2 (0.45)	12 (2.68)
	der(X)	29 (6.60)	1 (0.22)
	Y/der(A)/A	3 (0.68)	6 (1.34)
	Y	4 (0.91)	3 (0.67)
4:0 or diploidy	der(X)/der(A)/A	2 (0.45)	2 (0.45)
	–	4 (0.91)	9 (2.01)
Others	–	4 (0.91)	35 (7.83)

A = Autosome involved in translocation (patient 1: A = 2, patient 2: A = 18).

Table 2. Percentage of potential viability of a fetus according to segregation modes in spermatozoa in two carriers.

Segregation mode	Chromosomal equipment	Viability (%)	
		Patient 1	Patient 2
Alternate	Y/A	Normal	Normal
Adjacent I	der(X)/der(A)	Balanced (37.95)	Balanced (54.36)
	der(X)/A	Unbalanced viable (10.00)	Unbalanced viable (3.58)
Adjacent II	Y/der(A)	Unbalanced viable (11.59)	Unbalanced viable (4.70)
	der(X)/Y	Not viable (10.45)	Not viable (0)
	A/der(A)	Not viable (7.95)	Unbalanced viable (2.68)
	Crossing-over	Not viable (2.27)	Unbalanced viable (2.46)
3:1	A	Turner syndrome (6.36)	Turner syndrome (7.61)
	der(X)/Y/der(A)	Klinefelter syndrome (1.14)	Klinefelter syndrome (2.68)
	der(A)	Unbalanced viable (1.36)	Unbalanced viable (6.71)
	der(X)/Y/A	Unbalanced viable (0.45)	Unbalanced viable (2.68)
	der(X)	Not viable (6.60)	Not viable (0.22)
	Y/der(A)/A	Not viable (0.68)	Unbalanced viable (1.34)
	Y	Not viable (0.91)	Not viable (0.67)
	der(X)/der(A)/A	Not viable (0.46)	Unbalanced viable (0.45)
4:0 or diploidy	–	Not viable (0.91)	Not viable (2.01)
Others	–	Not viable (0.91)	Not viable (7.83)

A = Autosome involved in translocation (patient 1: A = 2, patient 2: A = 18).

2008). Therefore, during genetic counselling, PGD and prenatal diagnosis were discussed with the couple. As the waiting list for PGD is very long in France, the clinic favoured attempting ICSI followed by conventional prenatal diagnosis even if the risk of having an ongoing pregnancy associated with a chromosomally unbalanced fetus was high (34.89%). A total of 19 oocytes were collected, 12 were injected and six embryos were obtained.

One embryo was transferred, prenatal diagnosis revealed no chromosomal abnormality and a 46,XY child was born without malformations (Perrin *et al.*, 2008).

In conclusion, for both carriers of a balanced reciprocal translocation involving an X chromosome, the obtained profiles of meiotic segregation were different; frequencies of unbalanced

spermatozoa, which are predictive of the risk of chromosomally unbalanced offspring, were also notably different. FISH on spermatozoa allowed a personalized risk evaluation and led to a better genetic counselling with appropriate treatment.

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References

- Alves C, Carvalho F, Cremades N *et al.* 2002 Unique (Y;13) translocation in a male with oligozoospermia: cytogenetic and molecular studies. *European Journal of Human Genetics* **10**, 467–474.
- Baschat AA, Kupker W, al. Hasani S *et al.* 1996 Results of cytogenetic analysis in men with severe subfertility prior to intracytoplasmic sperm injection. *Human Reproduction* **11**, 330–333.
- Brisset S, Izard V, Misrahi M *et al.* 2005 Cytogenetic, molecular and testicular tissue studies in an infertile 45,X male carrying an unbalanced (Y;22) translocation: case report. *Human Reproduction* **20**, 2168–2172.
- Brugnon F, Van Assche E, Verheyen G *et al.* 2006 Study of two markers of apoptosis and meiotic segregation in ejaculated sperm of chromosomal translocation carrier patients. *Human Reproduction* **21**, 685–693.
- Buonadonna AL, Cariola F, Caroppo E *et al.* 2002 Molecular and cytogenetic characterization of an azoospermic male with a de novo Y;14 translocation and alternate centromere inactivation. *Human Reproduction* **17**, 564–569.
- Caer E, Perrin A, Douet-Guilbert N *et al.* 2008 Different mechanisms of meiotic segregation in spermatozoa from three carriers of a pericentric inversion of chromosome 8. *Fertility and Sterility* **89**, 1637–1640.
- Chandley AC 1979 The chromosomal basis of human infertility. *British Medical Bulletin* **35**, 181–186.
- Clementini E, Palka C, Iezzi I *et al.* 2005 Prevalence of chromosomal abnormalities in 2078 infertile couples referred for assisted reproductive techniques. *Human Reproduction* **20**, 437–442.
- Cohen O, Cans C, Mermet MA *et al.* 1994 Viability thresholds for partial trisomies and monosomies. A study of 1,159 viable unbalanced reciprocal translocations. *Human Genetics* **93**, 188–194.
- David G, Bisson JP, Czyglick F *et al.* 1975 Anomalies morphologiques des spermatozoïdes humains. *Journal de Gynécologie, Obstétrique et Biologie de la Reproduction* **4**, 17–36.
- De Braekeleer M, Dao TN 1991 Cytogenetic studies in male infertility: a review. *Human Reproduction* **6**, 245–250.
- De Braekeleer M, Perrin A, Morel F 2006 Chromosomal abnormalities in male infertility. In: De Braekeleer M (ed.), *Cytogenetics and Infertility*. Transworld Research Network, Trivandrum (India), pp. 27–52.
- Delobel B, Djelati R, Gabriel-Robez O *et al.* 1998 Y-autosome translocation and infertility: usefulness of molecular, cytogenetic and meiotic studies. *Human Genetics* **102**, 98–102.
- Douet-Guilbert N, Le Bris MJ, Amice V *et al.* 2005 Interchromosomal effect in sperm of males with translocations: report of 6 cases and review of the literature. *International Journal of Andrology* **28**, 372–379.
- Escudero T, Abdelhadi I, Sandalinas M *et al.* 2003 Predictive value of sperm fluorescence in situ hybridization analysis on the outcome of preimplantation genetic diagnosis for translocations. *Fertility and Sterility* **79**, 1528–1534.
- Gabriel-Robez O, Ratomponirina C, Dutrillaux B *et al.* 1986 Meiotic association between the XY chromosomes and the autosomal quadrivalent of a reciprocal translocation in two infertile men, 46,XY,t(19;22) and 46,XY,t(17;21). *Cytogenetics and Cell Genetics* **43**, 154–160.
- Gekas J, Thépot F, Turleau C *et al.* 2001 Chromosomal factors of infertility in candidate couples for ICSI: an equal risk of constitutional aberrations in women and men. *Human Reproduction* **16**, 82–90.
- Ishikawa T, Konho Y, Yamaguchi K *et al.* 2007 An unusual reciprocal X-autosome translocation in an infertile azoospermic man. *Fertility and Sterility* **88**, 705.
- Jacobs PA, Strong JA 1959 A case of human intersexuality having a possible XXY sex-determining mechanism. *Nature* **183**, 302–303.
- Jalbert P, Sele B, Jalbert H 1980 Reciprocal translocations: a way to predict the mode of imbalanced segregation by pachytene-diagram drawing. *Human Genetics* **55**, 209–222.
- Kalz-Fuller B, Slegers E, Schwanitz G *et al.* 1999 Characterization, phenotypic manifestations and X-inactivation pattern in 14 patients with X-autosome translocations. *Clinical Genetics* **55**, 362–366.
- Lee S, Lee SH, Chung TG *et al.* 2003 Molecular and cytogenetic characterization of two azoospermic patients with X-autosome translocation. *Journal of Assisted Reproduction and Genetics* **20**, 385–389.
- Ma S, Ho Yuen B, Penaherrera M *et al.* 2003 ICSI and the transmission of X-autosomal translocation: a three-generation evaluation of X:20 translocation: case report. *Human Reproduction* **18**, 1377–1382.
- Matsuda T, Hayashi K, Nonomura M *et al.* 1989 Azoospermic male with a balanced Y-autosome translocation. *Urologia Internationalis* **44**, 43–46.
- Mattei MG, Mattei JF, Ayme S *et al.* 1982 X-autosome translocations: cytogenetic characteristics and their consequences. *Human Genetics* **61**, 295–309.
- Morel F, Douet-Guilbert N, Perrin A *et al.* 2006 Chromosomal abnormalities in spermatozoa. In: De Braekeleer M (ed.), *Cytogenetics and Infertility*. Transworld Research Network, Trivandrum (India), pp. 53–112.
- Morel F, Douet-Guilbert N, Le Bris MJ *et al.* 2004a Chromosomal abnormalities in couples undergoing intracytoplasmic sperm injection. A study of 370 couples and review of the literature. *International Journal of Andrology* **27**, 178–182.
- Morel F, Douet-Guilbert N, Le Bris MJ *et al.* 2004b Meiotic segregation of translocations during male gametogenesis. *International Journal of Andrology* **27**, 200–212.
- Morel F, Douet-Guilbert N, Roux C *et al.* 2004c Meiotic segregation of a t(7;8)(q11.21;cen) translocation in two carrier brothers. *Fertility and Sterility* **81**, 682–685.
- Munné S 2002 Preimplantation genetic diagnosis of numerical and structural chromosome abnormalities. *Reproductive BioMedicine Online* **4**, 183–196.
- Nielsen J, Wohler M 1991 Chromosome abnormalities found among 34,910 newborn children: results from a 13-year incidence study in Aarhus, Denmark. *Human Genetics* **87**, 81–83.
- Nishikawa N, Sato T, Suzumori N *et al.* 2008 Meiotic segregation analysis in male translocation carriers by using fluorescent in situ hybridization. *International Journal of Andrology* **31**, 60–66.
- Palermo G, Joris H, Devroey P *et al.* 1992 Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte. *Lancet* **340**, 17–18.
- Panasiuk B, Usinskiene R, Kostyk E *et al.* 2004 Genetic counselling in carriers of reciprocal chromosomal translocations involving short arm of chromosome X. *Annales de Génétique* **47**, 11–28.
- Perrin A, Douet-Guilbert N, Le Bris MJ *et al.* 2008 Segregation of chromosomes in sperm of a t(X;18)(q11;p11.1) carrier inherited from his mother: case report. *Human Reproduction* **23**, 227–230.
- Perrin A, Douet-Guilbert N, Laudier B *et al.* 2007 Meiotic segregation in spermatozoa of a 45,XY,-14,der(18)t(14;18)(q11;p11.3) translocation carrier: a case report. *Human Reproduction* **22**, 729–732.
- Peschka B, Leygraaf J, van der Ven K *et al.* 1999 Type and frequency of chromosome aberrations in 781 couples undergoing intracytoplasmic sperm injection. *Human Reproduction* **14**, 2257–2263.

- Pinho MJ, Neves R, Costa P *et al.* 2005 Unique t(Y;1)(q12;q12) reciprocal translocation with loss of the heterochromatic region of chromosome 1 in a male with azoospermia due to meiotic arrest: a case report. *Human Reproduction* **20**, 689–696.
- Solari AJ, Rahn IM, Ferreyra ME *et al.* 2001 The behavior of sex chromosomes in two human X-autosome translocations: failure of extensive X-inactivation spreading. *Biocell* **25**, 155–166.
- Stengel-Rutkowski S, Stene S, Gallano P 1988 *Risk estimates in balanced parental reciprocal translocations*. Monographie des Annales de Génétique, Expansion Scientifique Française, Paris.
- Vegetti W, Van Assche E, Frias A *et al.* 2000 Correlation between semen parameters and sperm aneuploidy rates investigated by fluorescence in situ hybridization in infertile men. *Human Reproduction* **15**, 351–365.
- Vialard F, Delanete A, Clement P *et al.* 2007 Sperm chromosome analysis in two cases of paracentric inversion. *Fertility and Sterility* **87**, 418.
- Vincent MC, Daudin M, De MP *et al.* 2002 Cytogenetic investigations of infertile men with low sperm counts: a 25-year experience. *Journal of Andrology* **23**, 18–22.
- World Health Organization 1999 *Laboratory Manual For the Examination of Human Semen and Semen-Cervical Mucus Interaction*. Cambridge University Press, New York.
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