Impact of reciprocal translocation t (18; 21) on male infertility and embryo development: lessons from an oocyte-donating ICSI cycle

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Received: 13 December 2010 / Accepted: 7 March 2011 / Published online: 1 April 2011
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Abstract

Purpose To report the outcome of intracytoplasmic sperm injection (ICSI) cycles of an oligozoospermic man with reciprocal translocation.

Methods Two ICSI cycles were given to a 29-year-old man with severe oligozoospermia and reciprocal translocation t (18;21)(p11;q21) and his wife. In the first cycle, no sperm were found in his semen and all 15 oocytes retrieved were donated to another infertile couple suffering from oligozoospermia and premature ovarian failure. In the second cycle, sperm from the husband's ejaculate were used to fertilize 13 retrieved oocytes.

Results Eleven embryos were acquired and a healthy girl was born in the oocyte-donated ICSI cycle. In the second cycle, 6 embryos were acquired and only biochemical pregnancy was achieved after three times of embryo transfer.

Conclusions By the unusual oocyte-donating ICSI procedures, impact of the new reported reciprocal translocation t (18; 21) (p11; q21) on male fertility and embryo development was suggested.

Keywords Biochemical pregnancy · Intracytoplasmic sperm injection · Oligozoospermia · Reciprocal translocation · t (18; 21)

Capsule Recurrent biochemical pregnancy after ICSI with sperm from an oligozoospermic man with reciprocal translocation t(18;21)(p11;q21), suggested the translocation as reason of oligozoospermia and ICSI failure.

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Introduction

Numerical or structural chromosome defects are important etiologic factors in male infertility [1, 2]. The frequency of chromosomal abnormalities in infertile males varies from 2.2% to 15.2% [3], among which robertsonian translocations and sex chromosome abnormalities are more frequent [4, 5]. Reciprocal translocations have been found in only less than 1% of oligozoospermic men [6].

In this study, we report the outcome of two ICSI cycles of a severe oligozoospermic man with a reciprocal translocation t (18; 21) (p11; q21).

Materials and methods

A couple with primary infertility of 5 years attended our infertility clinic. The husband was a 29-year-old man whose medical history was unremarkable for risk factors for infertility. His physical examination revealed a normally androgenized male. The size and consistency of both the testes and epididymises were normal. FSH, LH, and Testosterone levels were within the normal ranges. Semen analyses according to WHO criteria [7] revealed severe oligozoospermia: only 2–3 sperm found in a high-power field after centrifuged 3000 g for 15 min. Cytogenetic analysis was performed on peripheral blood lymphocytes and 20 GTG-banded metaphases analysis revealed a translocation t (18; 21) (p11; q21) in all the cells examined. His wife was 27 years old with no remarkable infertility factors. The couple requested to undergo in vitro fertilization with the husband's own sperm and refused to accept fluorescence in situ hybridization (FISH) screening to find out the percent of genetically normal sperm in his semen to predict the chance to father a healthy baby or undergo a

preimplantation genetic diagnosis (PGD) program to select genetically normal embryo to transfer.

After obtaining written informed consent from the patient, approved by the Ethics Committee of Tongji hospital, Wuhan, China, two ICSI cycles were performed. In both cycles, a same ovarian stimulation protocol was applied to retrieve oocytes from the wife. Briefly, 0.1 mg GnRH agonist (Triptorelin, Ferring, Kiel, Germany) was administered from the 21st day of the last menstrual cycle and 150 IU human menopause gonadotropin (HMG, Livzon, Zhuhai, China) 3 days after menstrual onset until oocyte retrieval. A dose of 5,000 IU HCG (Serono, Geneva, Switzerland) was administered when the follicles were 18–20 mm in diameter. Thirty-six hours later, oocyte retrieval was carried out by vaginal ultrasound-guided puncture.

On the day that oocytes were retrieved, semen was collected by masturbation after 5 days of abstinence. In the first cycle, no motile sperm was found in husband's ejaculation, and the couple decided to donate all the retrieved oocytes to another infertile couple suffering from premature ovarian failure and severe oligozoospermia. The recipient was 35 years old and her husband was 41, with infertility duration of 8 years. No abnormalities were found in genetic examination of the recipient couple. Motile sperm from the recipient husband's ejaculation were selected and micro-injected into donated oocytes in a standard ICSI procedure.

In the second ICSI cycle, the husband's semen was collected by masturbation after 6 days of abstinence. Motile sperm were found in his ejaculation and micro-injected into the retrieved oocytes in a standard ICSI procedure.

Results

In the first cycle, 15 oocytes were retrieved and 11 embryos were obtained after ICSI with the recipient husband's sperm. After cryopreserved for 6 months, 2 embryos were thawed and transferred into the recipient wife's uterus. Serum beta-HCG measured by Vidas HCG system (Biomerieux, Marcy L'Etoile, France) was found to rise to a level of above 500 IU/L 14 days later and clinical pregnancy was confirmed by transvaginal ultrasound 6 weeks after embryo transfer. A healthy girl was born 9 months later.

In the second cycle, 13 oocytes were retrieved and 6 embryos were achieved after ICSI. Two embryos were transferred and all the rest cryopreserved embryos were thawed and transferred in the subsequent two natural menstrual cycles. Serum beta-HCG rose to above 500 IU/L 14 days after all the 3 times of embryo transfer, however, no gestational sac was detected by transvaginal ultrasound examination 4 weeks after the rise of serum HCG.

Discussion

To our knowledge, this is the first case of reciprocal translocation t (18; 21) associated with male factor infertility and biochemical pregnancy after ICSI. Chromosome anomalies in males with oligozoospermia usually involve sex chromosomes and robertsonian translocations [6]; however, the rate of reciprocal translocations is also higher than in normal individuals [4]. The mechanism by which reciprocal translocations cause oligozoospermia is not completely clear. Some studies suggested that some specific genes could be damaged in the breakage and recombination of chromosome translocation among which there may be some genes critical to spermatogenesis [8]. On the other hand, the translocated chromosomes would form a pairing cross during meiosis, hindering the meiotic process and leading to spermatogenic arrest [9, 10], which may be another mechanism of the association between chromosome translocation and oligozoospermia.

It is well known that chromosomal translocations in man can cause meiotic disturbances and produce sperm with superabundant or insufficient genetic material, and the genetically defective sperm would consequently lead to pregnancy loss or abnormal offspring. Genetic material in embryo derived from unbalanced sperm would be excessive or insufficient, leading to partial trisomy or monosomy, and therefore result in obstacle in embryo development and showing biochemical pregnancy or early miscarriage [11, 12]. What is meaningful about this case is that, the comparison between the outcomes of ICSI cycles with sperm from two men with different chromosome type provided a much stronger evidence to show the impact of translocation on embryo development. In the two consequent assisted reproductive technology cycles, oocytes from the same female were micro-injected with ejaculated sperm from two different oligozoospermic men. The only remarkable difference between the two cycles was a chromosome translocation of proband. Fertilization rates of both cycles were comparable, but the outcomes after embryo transfer were completely different. Biochemical pregnancy was achieved every time after transfer with embryos derived from ejaculated sperm of the chromosomal translocation male, suggesting lethal development defects after implantation. Birth of healthy baby after transfer with embryo derived from sperm of oligozoospermic infertile man without chromosome abnormality suggested the embryo intrauterine development obstacle in the second cycle was resulted from the chromosome translocation.

With the development of genetic examination, technicians now can evaluate the percent of genetically normal sperm in a translocation carrier's ejaculation by FISH to predict the chance to father a healthy baby [13] and select genetically normal embryo to transfer by PGD. However, the couple refused to accept sperm FISH screening or PGD.

Although the application of PGD in reciprocal translocation patients remains to be controversial [14–17], we believe the technology would be helpful for the patients.

Conclusion

The reported reciprocal translocation t (18; 21) (p11; q21) may have a strong impact on spermatogenesis and embryo development, thus leading to severe oligozoospermia and failure after ICSI.

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