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Male Infertility in Robertsonian Translocation: A Case Report

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Case series
Patients: Male, 34-year-old • Male, 35-year-old
Final Diagnosis: Primary infertility • Robertsonian translocation
Symptoms: Asymptomatic
Medication: —
Clinical Procedure: —
Specialty: Urology

Objective: Rare disease

Background: Translocations are the most common type of chromosomal structural anomalies. In balanced translocations, there is not an obvious loss of genetic material; they are usually phenotypically normal adults who present with reproductive issues. Male carriers of Robertsonian (ROB) translocation can have infertility and are shown to have abnormal semen analysis. Some patients have positive sperms in the ejaculate. Therefore, fertility management can be offered to couples to achieve pregnancy and delivery of healthy neonates.

Case Reports: We present 2 cases of 34- and 35-year-old males who presented to our tertiary care hospital because of primary infertility. Semen analysis showed nonobstructive cryptozoospermia and azoospermia, respectively. Genetic tests revealed ROB translocation (13;14). Fertility treatment was offered to both couples.

Conclusions: Males with ROB translocation can have positive sperms in the ejaculate. A multidisciplinary approach should be offered to the couples to help them achieve clinical pregnancy, reduce the risk of miscarriage, and increase the rates of delivery of healthy neonates.

MeSH Keywords: Infertility, Male • Semen Analysis • Translocation, Genetic

Abbreviations: **ROB** – Robertsonian; **ICSI** – intracytoplasmic sperm injection; **TESA** – testicular sperm aspiration; **Micro-TESE** – microsurgical testicular sperm extraction; **PGT-A** – preimplantation genetic testing for aneuploidies; **NGS** – next-generation sequencing

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/921616

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Background

Translocations are the most common type of chromosomal structural anomalies; they occur due to breaks in the DNA, followed by rearrangement of the fragments. The exchange in the genetic material can be balanced or unbalanced. In balanced translocations, there is not an obvious loss of genetic material; they are usually phenotypically normal adults who present with reproductive issues, recurrent abortion, and delivery of neonates with chromosomal abnormalities. In unbalanced rearrangement, on the other hand, the genetic material is lost and it results in partial trisomy or monosomy. Usually, monosomies and trisomies lead to spontaneous abortion and surviving fetuses will grow up with congenital and developmental disabilities.

Robertsonian (ROB) translocations are the most common balanced chromosome rearrangements, with a prevalence of 1 in 1000 individuals [1]. It is typically seen in acrocentric chromosomes 13, 14, 15, 21, and 22. These are chromosomes that have a short p-arm. The most common translocation is between chromosomes 13 and 14, found in 0.97 per thousand [2], which is the focus of our report. Male carriers of ROB translocation der (13;14) (q10;q10) can have problems with fertility and have abnormal semen analysis [3]. However, achieving clinical pregnancy and delivery of healthy neonates is possible [4]

We describe 2 males who presented to our tertiary care center with primary infertility, seeking fertility treatment. Their semen analysis showed nonobstructive cryptozoospermia and azoospermia. Karyotyping revealed ROB translocation (13;14). These 2 cases are reported to focus attention on the male fertility status in ROB translocation and to discuss methods of achieving pregnancy and delivery of healthy neonates.

Case Reports

Case 1

A 34-year-old Saudi male presented to our andrology and infertility clinic as a case of primary infertility for 2 years. Other than a venous malformation on the hand, the patient was healthy and had a normal sexual life, with normal erection, ejaculation, and libido. He was a nonsmoker, did not drink or use illicit drugs, and was not exposed to occupational hazards. He was married to a 32-year-old woman who had hypertension controlled with medications and had regular periods.

On examination, the patient did not show any dysmorphic features, and he had normal secondary male sexual characteristics. He had a normal penile shaft, normal meatus, and palpable bilateral vas deferens, with normal testicular size and consistency, with no clinical varicocele.

Table 1. Semen analysis of case 1.

Parameter	Case 1	Normal
Semen volume (mL)	2	≥1.5
Semen color	Gray-white	Gray-white
Semen appearance	Turbid	Turbid
Semen viscosity	Viscous	Slightly viscus
Semen pH	7.6	≥7.2
Sperm concentration	No sperms seen	≥15
Sperm motility (%)	0	≥40
Progressive motility (%)	0	≥32
Sperm kinetics	0	
Semen WBC	Negative	Negative
Semen RBC	Negative	Negative
Semen mucus	2+	Negative
Sperm agglutination	Negative	Negative
Semen analysis diagnosis	Crypto-zoospermia	
Volume post wash (mL)	0.1	
Sperm count post wash (10^6/mL)	0.009200	
Sperm kinetics post wash	0–1	
Total motility post wash (10^6/mL)	0.000212	
Progressive motility post wash	2	

Semen analysis, hormonal profile, and an ultrasound of the scrotum were ordered. Semen analysis showed normal volume cryptozoospermia (Table 1) with a total count of 9200 sperms, of which 212 were motile. The hormonal profile showed testosterone level of 9.210 nmol/L (normal range is 9.9-26.8 nmol/L) (Table 2). Since the patient had cryptozoospermia, chromosomal analysis was done using GTW banding technique, which revealed ROB translocation (13;14), and the karyotype was 45, XY, der (13;14) (q10;q10) (Figure 1).

On ultrasound, both testes were normal in size and echogenicity. The right testicle measured 3.8×1.5×2.3 cm and the left testicle measured 3.7×1.7×2.2 cm. No focal lesions or varicocele were seen. There was a small 0.3×0.4×0.3 cm right epididymal head cyst. No hydrocele or varicocele were noted.

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Table 2. Hormonal profile of case 1.

Parameter	Case 1	Normal
E2 (pmol/L)	67.6	28–156
FSH (IU/L)	4.8	1.5–12.4
LH (IU/L)	4.9	1.7–9.6
Prolactin ug/L	9.3	4.1–18.4
Testosterone (nmol/L)	9.210	≥17 yrs, 9.9–26.8
TSH (mU/L)	2.620	0.270–4.2

The results were discussed with the patient in the follow-up appointment. The couple was referred to the IVF clinic for pre-IVF genetic counseling with an emphasis on the low success rate when using the husband's sperms. After extensive counseling, the couple did not wish to adopt or use donor gametes, and preferred IVF treatment using the husband's own sperms. Therefore, informed consent was obtained, and the patient was scheduled for intracytoplasmic sperm injection (ICSI) with ejaculate and backup testicular sperm aspiration (TESA). Informed consent was also obtained for IVF and preimplantation genetic testing for aneuploidies (PGT-A) following embryo fertilization and at the blastocyst stage. It was explained to the couple that only normal euploid pattern embryos are considered for transfer, as per the hospital's protocol. A collaborative effort between andrologists, IVF specialists, geneticists, and embryologists to help couples with male factor infertility due to ROB translocation to establish pregnancy and delivery of healthy neonates.

Case 2

A 35-year-old Saudi male presented to our andrology and infertility clinic as a case of primary infertility for 10 years. He was healthy and had a normal sex life, with normal erection, ejaculation, and libido. He was a lifelong nonsmoker, did not drink alcohol, never used illicit drugs, and was not exposed to occupational hazards. He reported having occasional epididymal pain. He denied any history of pelvic trauma, epididymo-orchitis, or lower urinary tract symptoms. On examination, there was bilateral palpable vas difference. Both testes were smaller than average size. His wife was a 27-year-old healthy woman, but with irregular menstrual cycles. The couple had a normal sex life.

Semen analysis, hormonal profile, and chromosomal analysis were ordered. Semen analysis showed normal volume azoospermia (Table 3). The hormonal profile revealed low testosterone 8.93 nmol/L, (normal range is 9.9-26.8 nmol/L) and high FSH 23.4 IU/L (normal range is 1.5-12.4 IU/L) (Table 4).

Chromosomal analysis was done using GTW banding technique. It showed balanced ROB translocation. The karyotype was 45, XY, der (13;14) (q10;q10) (Figure 2).

As with the first case, the couple was referred to the IVF clinic for pre-IVF genetic counseling. In the follow-up appointment, the couple decided to try IVF. PGT-A and the process of choosing embryos were further explained to the couple. Therefore, the patient was scheduled for microsurgical testicular sperm extraction (micro-TESE) and sperm retrieval.

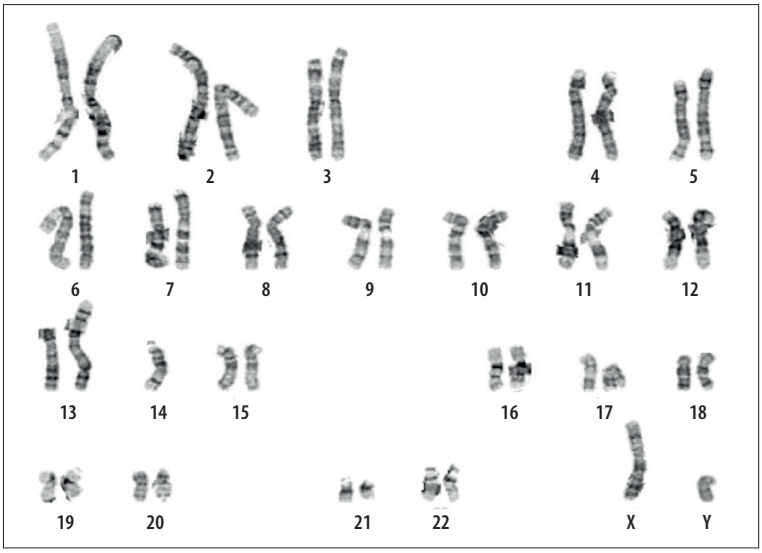

Figure 1. Robertsonian translocation involving acrocentric chromosomes 13 and 14; Male 45, XY, der (13;14) (q10;q10).

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Table 3. Semen analysis of case 2.

Parameter	Case 2	Normal
Semen volume (mL)	2.5	≥1.5
Semen color	Gray-white	Gray-white
Semen appearance	Turbid	Turbid
Semen viscosity	Watery	Slightly viscus
Semen pH	8.6	≥7.2
Sperm concentration	No sperms seen	≥15.00000
Sperm motility (%)	0	≥40
Progressive motility (%)	0	≥32
Sperm kinetics	0	
Semen WBC	2+	Negative
Semen RBC	Negative	Negative
Semen mucus	2+	Negative
Sperm agglutination	Negative	Negative
Semen analysis diagnosis	Azoospermia	
Volume post wash (mL)	0.1	
Sperm count post wash (10^6/mL)	0	
Sperm kinetics post wash	0	
Total motility post wash (10^6/mL)	0	
Progressive motility post wash	0	

Table 4. Hormonal profile of case 2.

Parameter	Case 2	Normal
E2 (pmol/L)	95.7	28–156
FSH (IU/L)	23.4	1.5–12.4
LH (IU/L)	8.7	1.7–9.6
Prolactin ug/L	7.85	4.1–18.4
Testosterone (nmol/L)	8.93	≥17 yrs, 9.9–26.8
TSH (mU/L)	2.62	0.270–4.2

Discussion

Translocations are the most common type of chromosomal structural anomalies. Chromosomal translocations are known to reduce fertility in men and women. A study of 1056 infertile men showed that 16.1% had chromosomal abnormalities and 2.1% had chromosomal translocation [5]. It has been reported that the reorganization of chromosome architecture, including ROB translocations, were 6–10 times higher among infertile males compared to the general population [6,7].

There are few studies and published reports focusing on the semen analysis results and sperm quality in male carriers of ROB translocation. In one study including 13 male carriers of ROB translocation, normal semen parameters were found in 30.8% of males [8]. A retrospective study of sperm parameters in infertile men with balanced chromosomal translocation showed that 11.5% of ROB translocation carriers had cryptozoospermia, 3.8% had azoospermia, and 84.6% had oligozoospermia [9]. ROB translocations were found to be more frequent in oligospermic males with infertility (0.9%) than in azoospermic males (0.3%) [4]. A study on 14 male carriers of ROB translocation, of whom 7 had (13;14) translocation, showed that the sperm count in those patients ranged from 500 to 1032 [3]. Semen analysis of 3 infertile male carriers of (13;14) ROB translocation showed that sperm counts ranged between 4 and 8×10^6 spermatozoa/mL. Progressive motility ranged from 4% to10% of spermatozoa, and 3% to 10% of spermatozoa had normal forms according to the David classification [10].

Few reports have described detailed cases of male carriers of ROB translocation from the physical examination findings, family history, and fertility potential. A study including 7 males with ROB translocation showed that the patients with chromosomal translocation tended to have small testicular volume compared to fertile males, but no significant differences in hormonal levels, with the exception of testosterone, which was found to be significantly lower in patients with ROB translocation [5]. Their findings on testicular size and testosterone were consistent with the present cases. However, in the second case we presented, the patient had high FSH level. It was suggested in this study that the reduction in the testicular volume and testosterone caused by the translocation may be the reason for impaired spermatogenesis and infertility in those males [5].

Family studies on male carriers of ROB translocations show that infertile males often have relatives with the same translocation, yet are fertile [11]. However, in the present cases, it was unknown whether the translocations were *de novo* or transmitted from carrier parents. This suggests that translocations might not be the only contributing factor to infertility in those individuals. Further research is needed to confirm this and to identify those factors.

The relative rarity of ROB translocation makes it difficult for researchers to conduct case-control studies to increase understanding of fertility treatment outcomes in those patients.

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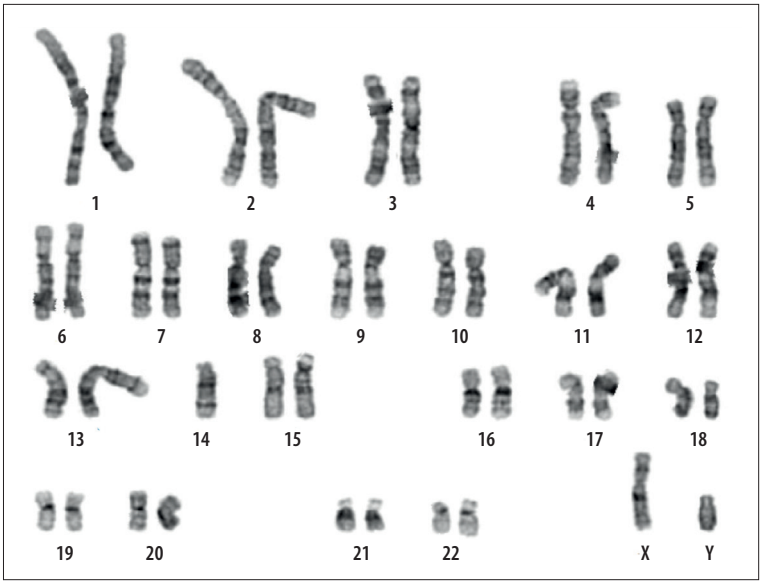

Figure 2. Robertsonian translocation involving acrocentric chromosomes 13 and 14. Male 45, XY, der (13;14) (q10;q10).

A series of 3 cases of males carrying ROB translocation showed that pregnancy was achieved, and delivery of a healthy carrier was achieved in 1 out of the 3 couples, where the male was a carrier of translocation (13;14) [4]. Another study on preimplantation genetic diagnosis (PGD) outcome in ROB translocation carriers showed that out of 10 oligozoospermic males, 5 were able to deliver a healthy child [12]. A study of the pregnancy outcome in male and female carriers of ROB translocation showed higher rates of pregnancies that led to the birth of a healthy child in male carriers than in female carriers – 61.8% versus 52.7%, respectively [13]. Despite the low success rate in most published papers, it is worth providing fertility treatment, especially in cases similar to ours where couples do not have other options to conceive and deliver healthy offspring.

PGD is a technique used to detect possible embryos with aneuploidies, genetic defects, and congenital disorders. It is recommended for carriers of ROB translocation to achieve birth of neonates unaffected by the translocation.

Studies have shown that PGD significantly reduced miscarriage in pregnancies in carriers of translocations. Studies on PGD for balanced translocation carriers showed a strong positive impact on reproductive outcomes in terms of achieving clinical pregnancies, pregnancies resulting in healthy deliveries, and reduction of spontaneous abortions [14]. There was also a reduction in the rate of spontaneous abortion with the use of PGD, from 87.8% to 17.8%, and an increase in take-home baby rate, from 11.5% to 81.4% [14].

Taking into account the risk of having devastating pregnancy outcomes for carriers of ROB translocation and the promising outcomes of PGD in those patients, in the present case, PGD was recommended to the patients, along with other prenatal diagnostic approaches to achieve successful pregnancy and deliver healthy neonates. In our center, when patients are referred for IVF treatment, the cycles are backed up with PGT-A following embryo fertilization and at the blastocyst stage, by utilizing next-generation sequencing (NGS) to ensure that only normal euploid pattern embryos are considered for transfer. Patients, therefore, sign an informed consent and a management plan is made.

Conclusions

This is a report of 2 cases of male factor infertility. Both men were carriers of ROB translocation (13;14). Our report highlights the fertility status in ROB translocation carrier men, the possibility of having positive ejaculate sperms, and methods of achieving pregnancy and delivery of healthy neonates. Therefore, a multidisciplinary approach including andrologists, IVF specialists, geneticists, and embryologists should be offered to couples to help them achieve clinical pregnancy, reduced the risk of miscarriage, and increase the rates of delivery of healthy neonates.

More studies are needed on sperm quality, fertility treatment, and pregnancy outcome in male carriers of ROB translocation to improve understanding of the clinical pattern and possible outcomes and limitations in treating such couples who wish to achieve pregnancy.

Conflict of interest

None.

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