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LETTER TO THE EDITOR

Male Infertility

Diagnosis of a Chinese man with 45,X/46,X,i(Y)(q10)/47,X,i(Y)(q10) ×2 mosaic Turner syndrome

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Dear Editor,

Turner syndrome (TS), characterized by the complete or partial absence of an X chromosome, is the only known viable chromosomal monosomy. It is one of the most common sex chromosome abnormalities in women, but it can also occur in men, with diverse chimeric phenotypes.[1]

We report here a case of a male TS patient with a rare karyotype. A 27-year-old Chinese man of short stature (140 cm) and his wife were referred to our hospital for a fertility evaluation. Despite 3 years of unprotected coitus with his wife, who had no evidence of subfertility, no pregnancy was achieved. The mental development, mammary glands, and genitals of this patient were normal, but sexual desire and testicular volume (about 12 ml for each testis) were low. After routine checkups, a series of auxiliary examinations were conducted according to the patient's request. Written informed consent was obtained from the patient for participating in the study.

Two semen samples were produced after 5-day abstinence; the average semen volume was 0.35 ml with pH 6.4. No spermatozoa were observed in either sample before or after centrifugation, so the patient was diagnosed as azoospermic according to the World Health Organization (WHO) Laboratory Manual for the Examination and Processing of Human Semen (2010).[2]

To examine sex hormone levels, peripheral blood was collected from the patient. We found that the level of testosterone (T) was still in the normal range (**Table 1**). To assess pituitary function, the gonadotropin-releasing hormone (GnRH) stimulation test was carried out. The result was "active response", which means that both the peak levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) had increased more than five times compared to the baseline levels (**Table 2**). The human chorionic gonadotropin (HCG) stimulation test was conducted to evaluate testicular tissue function. The result was "active response", which means the peak level of T had increased more than 50% compared to the baseline level (**Table 3**).

Chromosomal karyotyping and fluorescence *in situ* hybridization (FISH) were performed on the peripheral blood. Karyotyping was carried out following peripheral blood lymphocyte culture. A total of 20–100 metaphase cells were analyzed by the G-banding method, and the chromosome length included approximately 450–550 subbands. FISH was carried out using the sex-determining region Y protein (SRY), DNA probes specific for chromosomes X-1 (DXZ1), and DNA probes specific for chromosomes Y-3 (DYZ3) probes.

Three karyotypes were performed as shown in **Figure 1**. FISH results are shown in **Figure 2**. Histological examination of the testes included Hematoxylin and eosin staining (H&E) staining. Cell proliferation was observed in the seminiferous tubule, but the numbers of spermatogenic cells were reduced from normal, and no mature spermatozoa were observed. Moreover, the basement membrane showed thickening with hyaline degeneration. Mesenchymal cell presence was also decreased from normal (**Figure 3**).

On the basis of the above results, the patient was treated with testosterone undecanoate capsule (Andriol, Organon, 80 mg, bid p.o.). After 3-month treatment, the semen volume increased and the sexuality improved markedly, thereby achieving some of the psychological demands of the patient.

TS, also known as congenital gonadal/ovary dysgenesis, is characterized by abnormal sexual development due to the complete or partial absence of an X chromosome. The classical clinical features of TS include short stature, facial anomalies, webbed neck with low posterior hairline, aortic valve abnormality, and hearing impairment.

Table 1: Levels of sex hormones

Hormone	*Result*	*Reference range**
FSH (mIU ml^{-1})	3.75	1.27–19.26
LH (mIU ml^{-1})	2.19	1.24–8.62
T (ng ml^{-1})	1.82	1.75–7.81
E2 (pg ml^{-1})	<11.3	20–47

*The reference values were obtained from the enzyme-linked immunosorbent assay (ELISA) kit (Beckman Coulter, Inc., 250 S. Kraemer Boulevard Brea, CA 92821, USA) instructions. FSH: follicle-stimulating hormone; LH: luteinizing hormone; T: testosterone; E2: estradiol

Table 2: Results of GnRH stimulation test

Hormone	*–15 min*	*0 min*	*25 min*	*45 min*	*90 min*	*180 min*
FSH (mIU ml^{-1})	1.17	1.44	7.01	8.66	11.73	10.50
LH (mIU ml^{-1})	0.86	0.70	26.28	31.64	31.01	16.05

GnRH: gonadotropin-releasing hormone; FSH: follicle-stimulating hormone; LH: luteinizing hormone

Table 3: Results of HCG stimulation test

Hormone	*–15 min*	*0 min*	*24 h*	*48 h*	*72 h*
T (ng dl^{-1})	782.89	655.70	1386.31	807.06	1009.69

HCG: human chorionic gonadotropin; T: testosterone

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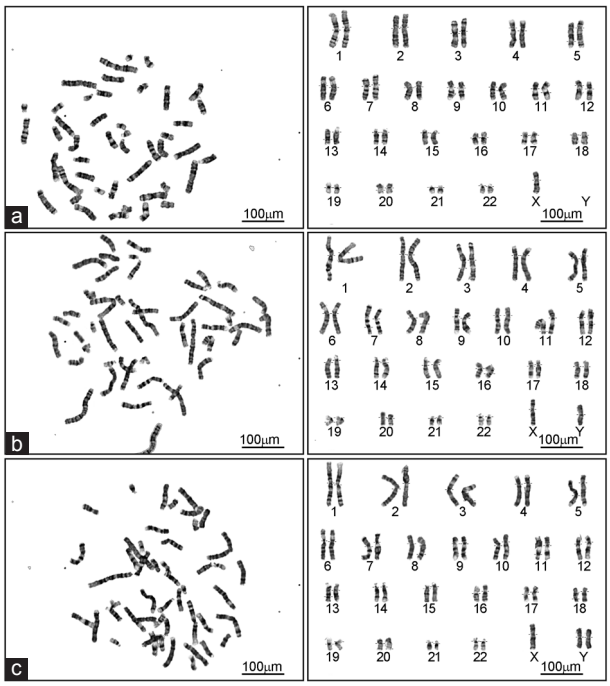

Figure 1: Results of routine karyotyping. (**a**) Routine karyotyping 45,X. (**b**) Routine karyotyping 46,X,i(Y)(q10). (**c**) Routine karyotyping 47,X,i(Y)(q10) ×2. Scale bars = 100 μm.

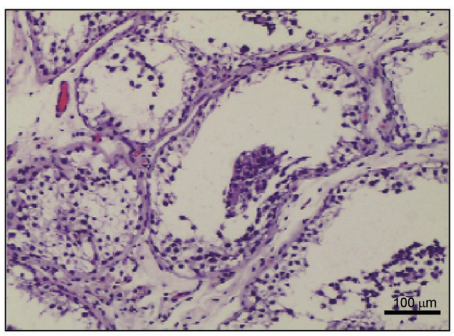

Figure 3: Pathological examination of testes. Scale bar = 100 μm.

The precise genetic basis of TS is not clear, but it appears that deletion of Xp (or loss of the Y) is sufficient to cause the full syndrome, thereby implicating haploinsufficiency of a variety of genes including short stature homeobox (*SHOX*). TS is not related to advanced maternal age and is more likely due to instability of the Y chromosome leading to its loss during male meiosis, since 75%–80% of X chromosomes in TS patients are maternal in origin.[3] Eunuchism may be found in male patients, and tuberculum majus may be detected in bilateral labium majus in female patients.[4] A case about a nonmosaic 46,X, isodicentric Yq female TS patient exhibited such phenotypes as craniofacial anomalies (epicanthal folds, broad nasal bridge, long philtrum, protruded tongue, low set ears, and short neck), genital ambiguity, with variable Turner stigmata and normal height.[5] TS patients with Y chromosome can also exhibit different sexual phenotypes. In chimeric individuals, the proportion of cells with abnormal karyotype can affect the clinical phenotype.[4,6] The chromosomal karyotype of our male patient, 45,X/46,X,i(Y)(q10)/47,X,i(Y)(q10) ×2, is unlike any similar TS cases reported in the literature. FISH results showed the detailed karyotype as 45,X,ish X (SRY−,DYZ3−,DXZ1+)(30)/47,X,ish

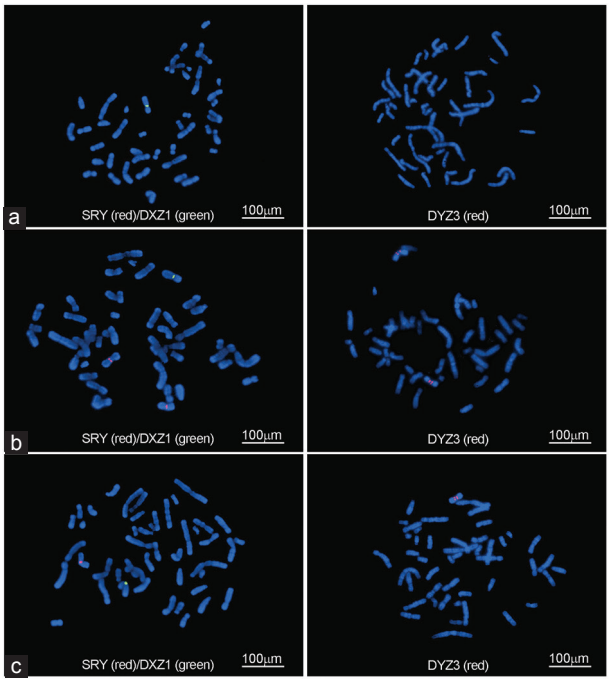

Figure 2: FISH results. (**a**) 45,X,ish X (SRY−,DYZ3−,DXZ1+)(30). (**b**) 47,X,ish psu dic(Y)(p11.3)(SRY+,DYZ3+,DXZ1−) ×2(49). (**c**) 46,X,ish Y (SRY+,DYZ3+,DXZ1−)(21). FISH: fluorescence *in situ* hybridization. Scale bars = 100 μm.

psu dic(Y)(p11.3)(SRY+,DYZ3+, DXZ1−)×2(49)/46,X,ish Y (SRY+,DYZ3+,DXZ1−)(21). This mosaic TS male patient had acceptable pituitary function and obvious male characteristics (both testes could be palpated). However, he exhibited obviously short stature and spermatogenic dysfunction. The abnormal karyotype for the Y chromosome may also contribute to the phenotype.

For patients seeking treatment for fertility problems, advice on the use of donor semen for assisted reproduction or adoption should not be excluded if long-term reproductive function of the male patient is not satisfactory. Meanwhile, clinicians should also pay attention to the higher risk of sex gland tumors, especially the gonad germ cell tumor, in this group of patients.[7]

AUTHOR CONTRIBUTIONS

YWS conceived of the study and carried out the stimulation tests. LD drafted the manuscript. ZYJ carried out the routine analysis of semen samples. YSG and HK carried out the chromosomal karyotyping and FISH. QZ carried out the hormone level tests in peripheral blood. YLZ participated in the genetic analysis and PL coordinated and helped draft the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declare no competing interests.

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REFERENCES

1 Grynberg M, Bidet M, Benard J, Poulain M, Sonigo C, *et al*. Fertility preservation in

Turner syndrome. *Fertil Steril* 2016; 105: 13–9.
2 World Health Organization. WHO laboratory manual for the examination and processing of human semen. 5th ed. Geneva: World Health Organization; 2010.
3 Zhong Q, Layman LC. Genetic considerations in the patient with Turner syndrome-45,X with or without mosaicism. *Fertil Steril* 2012; 98: 775–9.
4 Saenger P, Wikland KA, Conway GS, Davenport M, Gravholt CH, *et al*. Recommendations for the diagnosis and management of Turner syndrome. *J Clin Endocrinol Metab* 2001; 86: 3061–9.
5 El-Bassyouni HT, El-Gerzawy A, Eid O, El-Ruby MO. Clinical and cytogenetic study of a non mosaic 46, X, isodicentric Yq in an Egyptian patient with Turner syndrome. *Genet Couns* 2013; 24: 37–44.
6 Nadeem M, Roche EF. Turner syndrome: awareness of health issues. *Ir Med J* 2014; 107: 222.
7 Kavoussi SK, Christman GM, Smith YR. Healthcare for adolescents with Turner syndrome. *J Pediatr Adolesc Gynecol* 2006; 19: 257–65.