Fertility achieved through in vitro fertilization in a male patient with 48,XXYY syndrome

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Dear Editor,

The 48,XXYY syndrome is a rare sex chromosome aneuploidy with an incidence of 1:18 000–1:40 000 male births1 and is associated with hypergonadotropic hypogonadism as an endocrine disorder.2,3 Most men with this syndrome are never diagnosed in China. Due to sex chromosome aneuploidies and limited effective communication, these patients suffer from infertility.4

With a rare incidence rate, 48,XXYY syndrome is characterized by tall stature, abdominal adiposity, and small testicles; it often appears after puberty.5 These patients often present with azoospermia and have difficulty with fertility. However, the literature provides little information about the fertility issues resulting from this syndrome. Advances in assisted reproductive techniques have, in rare cases, allowed for the production of offspring by patients with certain diagnoses thought to be associated with universal infertility.6

Here, we report the case of a 30-year-old male patient with 48,XXYY syndrome who was referred to our hospital in April 2016 for fertility treatment. In his family history, he was the only child of healthy nonconsanguineous parent. His mother's pregnancy and delivery were normal. The patient was born at term with normal measurements. We noted that the patient had greater difficulties in understanding and developing social relationships. He married three years before presentation but did not have children at that time. However, there were no available data regarding his parent.

The patient had a height of 185 cm, a weight of 80 kg, a body mass index of 23.4 kg m−2, and a blood pressure of 125/75 mmHg. The secondary sexual characteristics of the patient are poorly developed, and he has some feminine characteristics, such as no beard, less hair, and breast development. In addition, he presents orbital hypertelorism, eunuchoid skeleton, reduced muscle mass, elongated arms and legs, and small testicles and penis.

Laboratory investigations showed a normal blood cell count, normal thyroid-stimulating hormone (TSH), iron and calcium levels, and abnormal hepatic, renal, and gonadal functions. Most biological data from urine were within normal limits, with the exception of urinary thyroid-stimulating hormone (TSH), iron and calcium levels, and small testicles and penis.

Table 1: Reproductive hormonal profile in the patient with 48,XXYY syndrome

| Hormone          | Blood  | Normal values |
|------------------|--------|---------------|
| FSH (mIU ml−1)   | 39.9   | 0.7–11.1      |
| LH (mIU ml−1)    | 26.4   | 0.8–7.6       |
| Testosterone (nmol l−1) | 1.9 | 3.0–8.5       |

FSH: follicle-stimulating hormone; LH: luteotrophic hormone

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was diagnosed, and the patient was hospitalized at our center to address this issue. A microdissection for testicular sperm extraction was performed for this patient with azoospermia. Ramasamy et al demonstrated that increased male age is associated with a trend toward a lower sperm retrieval rate in patients with Klinefelter’s syndrome, and that various types of preoperative hormonal therapies did not result in different sperm retrieval rates, but men with a normal baseline testosterone level had the best sperm retrieval rate of 86%. Fortunately, although the patient’s hormone levels were abnormal and his testosterone was low, normal sperm were nonetheless identified under the microscope after tearing of the seminiferous tubules. The entire search process was difficult, but it was a pleasant surprise that the screened sperm were nonprogressively motile and were normally shaped. With in vitro fertilization, the sperm and egg successfully combined, and embryonic development was progressing successfully at the time of the report.

Our case demonstrates the main typical features of 48,XXYY syndrome in a patient who suffers from infertility. The patient has a strong fertility requirement. How to help patients with 48,XXYY syndrome to have normal children has not been previously reported in the literature. Fortunately, normal sperm were found in our patient under high-magnification microscopy. Through the treatment of this case, it is proposed that microdissection testicular sperm extraction is an effective sperm retrieval technique for men with 48,XXYY syndrome.

COMPETING INTERESTS
All authors declare no competing interests.

AUTHOR CONTRIBUTIONS
DFL, KH, and HJ conceived the study, performed the operation, and drafted the article. KH, JMM, and LMZ performed the operation and participated in the acquisition of data. YZY and ZZ contributed to clinical follow-up of the patient and helped the review and editing of manuscript, and LMZ was responsible for the revision of the article. All authors read and approved the final manuscript.

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