

Hyperandrogenism in a girl with Turner syndrome

A case report

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Abstract

Rationale: The gonads of patients with Turner syndrome (TS) were previously thought to be funicular. There was no increase in androgen level. The gonad that is testis should be taken into account when the patient's serum testosterone level was abnormal and hypothalamic-pituitary-adrenal disease was excepted.

Patient concerns: A 16-year-old girl was admitted to our hospital because of chromosomal abnormalities and elevated androgen levels.

Diagnosis: Turner syndrome could be diagnosed since her chromosome karyotype was 45, XO.

Interventions: The patient was given bilateral gonadectomy and hormone replacement therapies.

Outcome: The level of the patient's serum testosterone was <0.45 nmol/L 2 days after the operation. Postoperative pathology showed that her right gonad was testicular tissue. The patient's menstruation was normal after the treatment of hormone replacement therapy.

Lessons: All TS patients should get Y chromosome material screening. Gonadectomy could be done for Turner syndrome patients who have hyperandrogenism or Y chromosome material.

Abbreviations: CT = computed tomography, DNA = deoxyribonucleic acid, IVF-ET = in vitro fertilization and embryo transfer, PCR = polymerase chain reaction, SRY = sex-determining region on the Y chromosome, TS = Turner syndrome.

Keywords: hyperandrogenism, sex-determining region on the Y chromosome, Turner syndrome

1. Introduction

Turner syndrome (TS) also known as congenital ovarian dysplasia is a kind of disordered sex development disease. Its pathogenesis is absent of one X chromosome totally or partially. Previously the ovaries of patient with TS were thought to be funicular^[1] with no necessity to do surgical resection. However, in recent years, it is reported that 10% of TS patients^[2] have Y chromosome material. The presence of Y chromosome material increases the risk of gonadoblastoma.^[3] One study shows that 10% to 20% of TS patients who have Y chromosome material are at risk of gonadoblastoma.^[4] Therefore, we recommend all TS patients to

do Y chromosome material screening. If the result were positive, patients should have their bilateral gonads removed.

2. Case report

2.1. General information

A 16-year-old girl was admitted into our hospital in January 2017 due to chromosomal abnormalities and elevated androgen levels. Her karyotype was 45, XO when she was 13. Her androgen level was abnormally high, the level of her serum testosterone was 4.79 nmol/L. At the age of 16, SRY gene (Fig. 1) was found in her peripheral blood lymphocytes DNA genes by using polymerase chain reaction. She has never had menstruation. She was 152.7 cm high and weighed 47.7 kg. At that time, her limbs were bigger than that of her peers, the development of her breast was at 2nd tanner period. Gynecological examination showed that her vulva was normal while clitoris was enlarged about 2 cm long, which is able to erect after stimulation. And her hymen was visible.

2.2. Laboratory examination

The results of her serum level of 6 steroid sex hormones are the following: estradiol: <37.7 pmol/L, prolactin: 431.32 mIU/mL, gonadotropin: 58.54 IU/L, luteinizing: 26.01 IU/L, progesterone: <0.32 nmol/L, testosterone: 4.66 nmol/L.

Testosterone level did not decline after dexamethasone suppression test. The examinations of her head, chest, abdominal, and pelvic computed tomography (CT) scan were normal. The ultrasound of urinary system was normal. The ultrasound of reproductive system showed that the size of her uterus was about 3.3 cm × 1.6 cm × 1.2 cm, bilateral ovaries were not visible.

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This study meets the demands of medical ethics committee of affiliated hospital of Qingdao university and an agreement has been made on it. Before surgery, we had obtained written informed consent from the patient's families. Now, the patient has provided written informed consent to publish her case.

The authors have no conflicts of interest to disclose.

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Figure 1. PCR of the patient's SRY gene: ① marker ② men control ③ female control ④ the patient ⑤ water. The SRY gene in the patient's peripheral blood was similar to that in normal men. PCR=polymerase chain reaction, SRY=sex-determining region on the Y chromosome.

2.3. Surgery situation

Exploratory operation showed her uterus (in Fig. 2) was located slightly on the left side of the pelvic cavity with the size of about 3 cm × 2 cm × 2 cm. There was an egg green gonad tissue (Fig. 3) on the right side of the adnexal area, whose size was about 1 cm × 1 cm × 0.5 cm. There was a white funicular gonad tissue (Fig. 4) on the left side of the adnexal area, its size was about 0.5 cm × 0.3 cm. Both sides of the gonads appendage looked like normal fallopian tube. It is because the patient's SRY gene was positive that both side gonads and appendage could be completely excised under laparoscopy.

2.4. Postoperative results

Two days after the operation, the level of serum testosterone was <0.45 nmol/L. Postoperative pathology showed that there were hyperplasia of fibrous tissue and smooth muscle tissue in the left gonad. In the right gonad, there was testicular tissue without

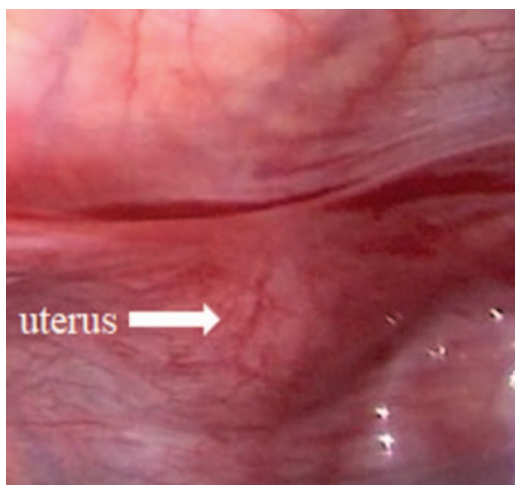


Figure 2. The patient's uterus. Exploratory operation showed the size of uterus was about 3 cm × 2 cm × 2 cm.

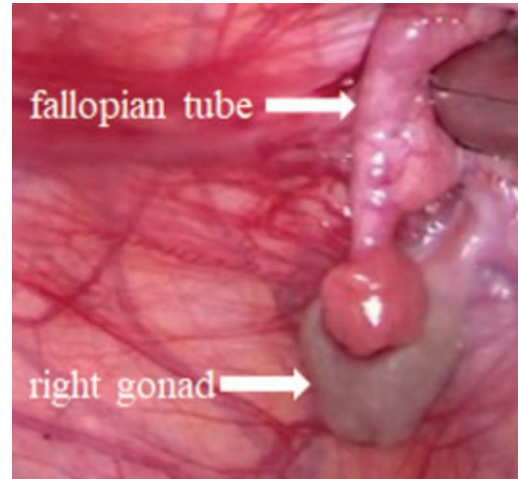


Figure 3. The patient's right side of gonad. Exploratory operation showed the right side of gonad was an egg green gonad tissue, the size was about 1 cm × 1 cm × 0.5 cm.

reproductive cells in seminiferous tubes. Therefore, she immediately received hormone replacement therapy after surgery. Six months later, gynecological examination showed that her clitoris was normal. One year after the surgery, the ultrasound of reproductive system showed that the size of her uterus was about 3.5 cm × 3.0 cm × 2.0 cm. And her menstruation is normal now.

3. Discussion

3.1. The necessity of bilateral gonads excision in TS patient with hyperandrogenism or SRY positive

It is generally known that patients whose social sex is female with abnormal sexual development and Y chromosome material facing the risk of gonadoblastoma should receive bilateral gonadectomy.

Y chromosome material^[2] has been reported existing in about 10% of TS patients. Patients who have signs of virilization or marker chromosome are suggested to do a test for Y chromosome

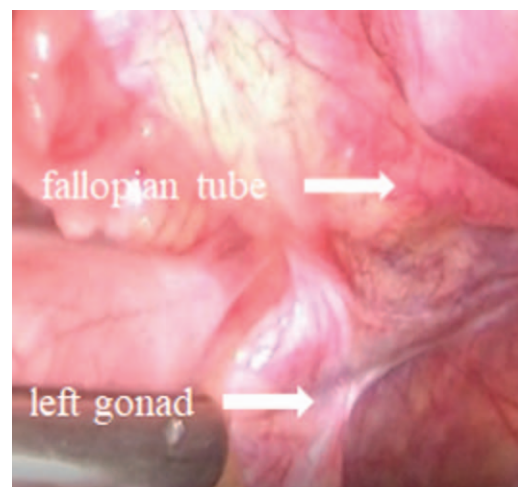


Figure 4. The patient's left side of gonad. Exploratory operation showed the left side of gonad was a white funicular gonad tissue, the size was about 0.5 cm × 0.3 cm.

material. The presence of Y chromosome material in patients with TS increases the risk of gonadoblastoma of 10% to 20%.^[4] So we recommend all patients with TS to do Y chromosome material screening. If patients are tested positive, bilateral gonadectomy should be done to prevent the occurrence of tumor.

Androgens is mainly secreted by the gonad and adrenal glands. A few estrogens can be converted into androgen in peripheral tissues. Androgens come from adrenal glands. So normally, peripheral tissue is too little to cause hyperandrogenism. For patients with TS syndrome, the excessive androgen may come from gonad after excluding adrenal disease. The content of Y chromosome material in peripheral blood is different from that of the gonads or other body tissues,^[2] so it does not matter that the screen of Y chromosome material is positive or negative, when combining with hyperandrogenism, it's necessary to do bilateral adnexectomy.

3.2. Aspects should be paid attention to in the surgery

The anatomical location of dysplastic gonads is often different from normal gonads. During the operation, the first step is to do comprehensive exploration of pelvic region to determine whether there is a uterus in pelvic cavity and the position, shape and size of the uterus, and whether there are gonads and appendage in both sides of pelvic cavity. If there are no gonads to be found in pelvic cavity, search the gonads, streak gonads, and appendage in bilateral iliac fossa, groin, and labia majora. Second, complete resection of the gonads is very important. If the gonads are streak, the scope of resection should include part of the peritoneal tissues surrounding the gonads. If the gonads are testicular tissue and are located in the inguinal canal, you can pull the gonads into abdominal cavity from inguinal canal, and remove it. Then, repair the inguinal canal mouth to prevent the happening of hernia. Finally, due to the abnormal position of gonad and the change of anatomical structure, we should always remember to avoid ureteral injury during the operation.

During the surgery of this patient, we found that her uterus was small and slightly on the left side of the pelvic cavity. The left gonad was streak, the right gonad was testes. The ultrasound showed that her uterus was long and narrow rather than pear-shaped. We considered that the right side gonad might inhibit the growth of the same side gyneduct which lead to unicornuate uterus.

3.3. The possibility of fertility of patients with TS

One study^[5] showed that, germ cells can be found in the gonads in about 68% patients who have disorders of sex development. The ratio of germ cells in different gonad tissue is not the same, germ cells may be in any forms of gonads tissues. The reproductive ability of these germ cells requires further evaluation. The fertility of these patients should be taken into account when they are going to receive gonads resection. If possible, it is necessary to preserve the fertility of these patients.

The development of uterus in most of the TS patients is not mature. The patients tend to be getting old when they go see a doctor as a result of amenorrhea. At this time, to start hormone replacement therapy is relatively late. Part of the previous view was that the uterus was very difficult to get the best state of development with conventional hormone dose. However, a new study^[6] shows that, the finally size of the uterus is associated with the duration of hormone replacement rather than the patient's age of starting hormone replacement and chromosome karyotype. Most patients with TS will have a mature uterus after having enough doses and duration of hormone replacement therapy. They also can be pregnant successfully. So it is never too late to start hormone replacement therapy.

Because the preservation of germ cells in patients with disorders of sex development has never been carried out, the reproductive ability of these germ cells is unable to be evaluated. Now, the main methods for TS patients to be pregnant are through donor eggs and in vitro fertilization and embryo transfer (IVF-ET) technology.^[7]

In conclusion, we recommend all TS patients to get Y chromosome material screening. Surgical removal of the bilateral glands can prevent tumor of gonads if the results are positive or hyperandrogenism. Hormone replacement therapy should be actively carried out to promote the development of uterus, and fertility may be achieved through assisted reproductive technology.

Author contributions

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