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Case Report

# Turner Syndrome with 45,X/46,XY mosaicism underwent gonadectomy: Report of 3 cases

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**Abstract.** Turner syndrome (TS) is classically characterized by complete or partial absence of one X chromosome. A Y chromosome can be detected in some of the TS patients called mosaicism. In this study we report three cases of TS with a female phenotype and a 45,X/46,XY karyotype. All of the cases were referred or applied to our hospital for gonadectomy at third decade of their lives. They had many of the stigmata of TS. We performed gonadectomy to our patients. In one of them histopathology was suggestive for gonadoblastoma. Further genetic evaluation must be made in patients with TS for revealing a probable Y chromosome and these patients should be informed for gonadectomy.

Key words: Turner syndrome, mosaicism, gonadoblastoma

## 1. Introduction

Turner syndrome is a condition of unusual and asymmetrical gonadal development leading to sex chromosomal abnormality. TS occurs in 1 in 2500 to 1 in 3000 live-born females (1). It is typically characterized by the combination of physical features and genetics in females. The presenting clinical features can vary widely among affected individuals. However short stature and gonadal dysgenesis are prevalent in TS, many other organ systems can be affected at varying degrees and different stages of life. The syndrome was first described by Turner in 1938 consisted of short stature, primary amenorrhea, infantile uterus, vagina, and breasts, ovarian agenesis, pterygium colli, cubitus valgus, and low hair line at the back of the neck (2). The syndrome can be attributed to partial or complete monosomy of the X chromosome. In some cases, chromosome is missing in only some cells, is referred to mosaicism. The resulting phenotype depends on the proportions of each cell line present and on the locations of the breakpoints in chromosome Y (3). Also in cases without sexual ambiguity, the diagnosis is usually made at puberty. In this study we report three cases of TS with a female phenotype and a 45,X/46,XY karyotype.

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## 2. Case Reports

### *2. 1. Case 1*

The first patient was 23-year-old single female who referred to our clinic for gonadectomy. Her karyotyping had been showed 45,X/46,XY mosaicism before and she had been followed at an endocrinology clinic of another university hospital. She was primer amenoreic. The patient's height was 147 cm and her weight was 49 kg. On her physical examination she had a sternotomy scar because of pulmonary artery stenosis operation. External genitalia were noted as normal. Pubic and axillary hair with breast development was normal. Pelvic ultrasound revealed a 49*22 mm dimensioned hypoplastic uterus. Endometrium and ovaries were not visible on ultrasound scan. She was menstruating with intermittent hormone replacement therapy. On her laboratory testing E2: 36pg/mL, Total Testosterone: 0.981ng/mL, Free Testosteron: 3.08pg/mL, LH: 12.3mIU/mL, FSH: 29.8mIU/mL, β-hcg: 0, Hb: 10.4g/dL, WBC: 3200, PLT: 55.000, Crea: 0.6, Urea: 33, tumor markers were normal. Patient was operated via laparoscopically. Uterus was hypoplastic and ovaries were streak gonad. Gonadectomy was performed. Histological examination showed bilateral gonadoblastoma and fallopian tubes were identified bilaterally.

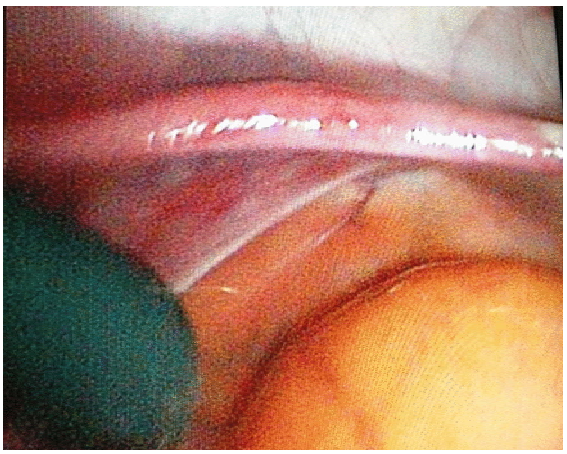

Fig. 1. Band shaped uterus.

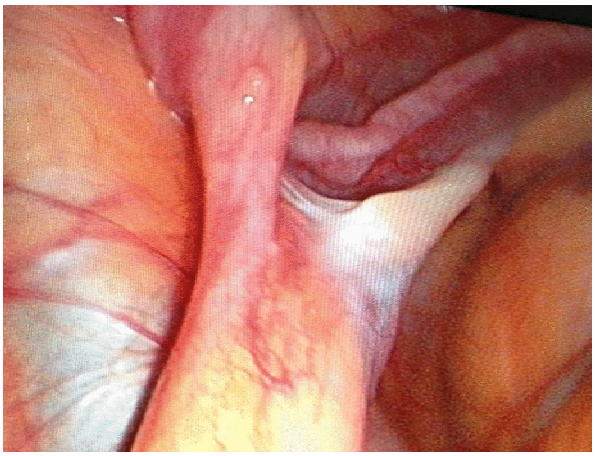

Fig. 2. Streak gonads.

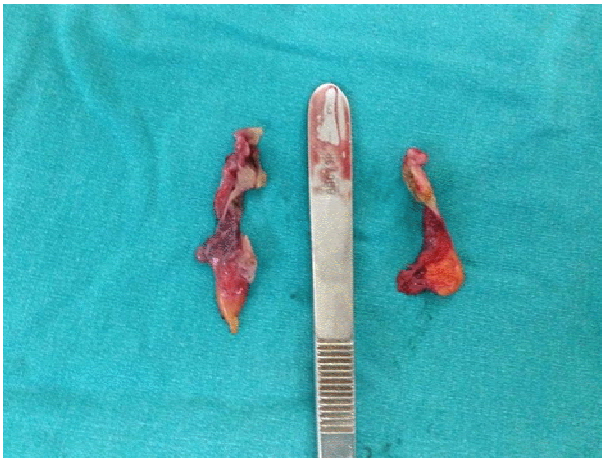

Fig. 3. Pathologic specimen of the removed gonads.

*2. 2. Case 2*

23-year-old female admitted to our clinic for gonadectomy. On her genetic consultation gonadectomy was recommended to her because of 45X/46,XY mosaic karyotyping. She was primer amenoreic and unmarried. She was an epilepsy patient and congenital deafness was presence. The patient's height was 149 cm and her weight was 48 kg. On her pelvic ultrasound there were no uterus and no ovaries, but ectopic pelvic kidney was seen. Serum levels of E2: 41pg/mL, Total Testosterone: 0.426ng/mL, Free Testosterone: 1.6pg/mL, LH: 32.3mIU/mL, FSH: 69.1mIU/mL, β-hcg: 0, Hb: 13.2g/dL, WBC: 6100, PLT: 254000, urea: 31, crea: 0.9, tumor markers were normal. Bilateral ovarian cortex with rudimentary sex cord and fallopian tubes were viewed at histological examination. The postoperative course was good and the patient is receiving estrogen replacement therapy.

*2. 3. Case 3*

The patient was 24-year-old who followed by endocrinology clinic of another hospital. Her height was 151cm and her weight was 54kg. When she was at 17 year-old, TS syndrome (45 XO) was determined on cytogenetic analysis from the material of blood and skin. Following this procedure, Y chromosome was investigated by PCR and gonadectomy was recommended after detecting 45XO/46XY karyotype. At that time patient and her family had rejected an operation. They accepted operation 7 years later. She was primer amenoreic and unmarried. On physical examination she had broad chest, absent breast development, normal external genitalia and pubic hair growth. Uterus and ovaries were not seen on her pelvic ultrasound and magnetic resonance imaging. Laboratory analysis showed that Estradiol 45pg/mL, FSH 115 mIU/mL, LH 29.3mIU/mL, Total Testosterone 0.514ng/dL, Free Testosterone 1.8pg/dL, β-hcg: 0, Hb: 11.2g/dL, WBC: 8.200, PLT: 240.000, urea: 20, crea: 0.6, tumor markers were normal. After the initial work up, operative laparoscopy was performed. The band shaped uterus and streak gonads were visualized during the operation

(Figure 1,2,3). Gonadectomy was performed; fallopian tubes and ovarian cortex without germ cell were shown at histological examination.

## 3. Discussion

Turner Syndrome is classically characterized by complete or partial absence of one X chromosome. Data obtained from the screening of consecutive newborn babies indicate that the incidence at birth is of the order of 3 per 10.000 female live births (4). The first reported case was amenorrhea in seven adolescent and young adult females with sexual infantilism, short stature, a webbed neck and cubitus valgus (2). 45,X/46,XY mosaicism is associated with a broad spectrum of phenotypes ranging from apparently normal male development to individuals with incomplete sexual differentiation and clinical signs of TS in both males and females. The most common presentation among individuals with a 45,X/46,XY karyotype is sexual ambiguity, accounting for approximately 60% of cases, while the least common category of 45,X/46,XY patients consists of those with bilaterally descended testes, found in 11-12% (5). The resulting phenotype depends on the proportions of each cell line present and on the locations of the breakpoints in chromosome Y (6). Male phenotypic patients intend to have more anomalies than female ones. In cases without sexual ambiguity first diagnosis is most commonly made at puberty. If evident growth restriction or adjunct anomalies are present, the diagnosis can be made in early childhood. Different genotypes and phenotypes were defined on mosaic TS syndrome in the literature (7). Our patients were carrying clinical features both of stigmata of TS and congenital anomalies associated with this syndrome like cardiac, renal, hearing defects, skeletal anomalies. The laboratory parameters were undefined. But in the first patient with gonadoblastoma total and free testosterone level was at the upper reference value. In a report of case series 4.8% patients with TS carried a 45,X/46,XY karyotype. Gonadoblastoma can be evident even at an early age in streak gonads with Y mosaicism and may be bilateral. So they recommended prophylactic laparoscopic gonadectomy of streak gonads in patients with TS who carry a Y mosaic genotype, because fertility is not an issue, surgical morbidity is minor and there may be a high potential for malignant transformation of gonadoblastomas in this population (8).

## 4. Conclusion

In conclusion TS have different cytogenetic and chromosomal subtypes including Y chromosome mosaicism. In cases suspected clinically and confirmed genetically as TS, a Y chromosome presence must be investigated. Gonadectomy should be offered and performed to these patients as soon as possible because of high risk of gonadoblastoma. Afterwards proper hormonal therapy like growth hormone and sex steroids should be initiated.

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