

## XY Female: Two Cases with Different Gonads presenting as Primary Amenorrhea

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### ABSTRACT

Two 18-year-old female patients admitted to the hospital with the complaints of primary amenorrhea. The clinical examination and investigations revealed one of them as complete androgen insensitivity syndrome and the other Swyer syndrome. Bilateral gonadectomy was performed and hormone replacement therapy started for both the patients. These two conditions should be considered in the differential diagnosis in every adolescent female patient with delayed puberty and the importance of early gonadectomy should be stressed in order to avoid the risk of gonadal tumor development.

**Keywords:** Complete androgen insensitivity syndrome, Swyer syndrome, Primary amenorrhea, Gonadectomy.

**How to cite this article:** Bhat BPR, Navada HM. XY Female: Two Cases with Different Gonads presenting as Primary Amenorrhea. *World J Endocr Surg* 2012;4(1):23-25.

**Source of support:** Nil

**Conflict of interest:** This is to certify that I, Badekai Poornima Ramachandra Bhat, the author of 'XY Female: Two Cases with Different Gonads presenting as Primary Amenorrhea' certify that there is no conflict of interest regarding the publication of this manuscript.

### INTRODUCTION

XY female is an intersex condition who has a chromosome composition of 46 XY and female phenotype. They may present in a variety of ways. It is the absence of testicular androgens or antimüllerian hormone production or an inability of the body to respond to these hormones that cause female phenotype to occur in XY females. These conditions are relatively rare and can be difficult to diagnose accurately and manage appropriately. Androgen insensitivity syndrome (AIS) is the most common cause of XY female and the incidence is probably around 1 in 40,000 to 60,000 births.<sup>1</sup> Complete androgen insensitivity syndrome (CAIS) occurs when there is no response to androgens. Partial androgen insensitivity syndrome occurs when the androgen receptors can partially respond to androgen stimulation. Swyer syndrome is the other rare cause of XY female and the incidence is 1 in 1,00,000 births.<sup>2</sup> Swyer syndrome also known as pure gonadal dysgenesis was first described by Gim Swyer, a London-based endocrinologist in 1955. There is testicular differentiation abnormality in Swyer syndrome. We are reporting cases of both these syndromes each showing different gonadal tissue presenting as primary amenorrhea.

### CASE REPORTS

#### Case 1

An 18-year-old unmarried girl came with complaint of primary amenorrhea. She had three sisters. Elder sister who was 21-year-old and her maternal aunt both have not attained menarche. They were not investigated. Other two sisters attained menarche at the age of 16. She was 152 cm tall and weighed 58 kg on examination. Breast development was Tanner stage 3. Axillary and pubic hairs were absent. Abdominal examination was normal. Local examination revealed normal female external genitalia with blindly ending vagina. Buccal smear did not show Barr bodies. Ultrasound abdomen showed absent uterus with hypoechoic structures in relation to iliac vessels suggestive of gonads (Fig. 1). Chromosome analysis by G banding showed 46 XY. Bilateral gonadectomy was performed through the inguinal incision (Fig. 2). Histopathology of right gonadal mass showed Sertoli cell adenoma and left gonadal mass showed Sertoli cell hyperplasia. Patient was advised estradiol valerate 2 mg daily as hormone replacement therapy (HRT).

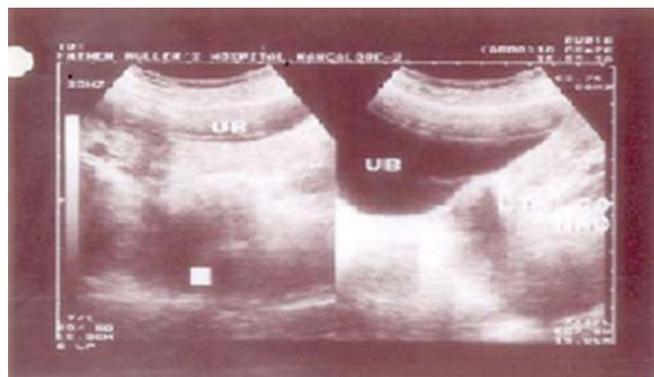


Fig. 1: Transabdominal ultrasound gonad near the iliac vessels



Fig. 2: Bilateral gonadectomy

## Case 2

An 18-year-old female came with complaints of primary amenorrhea and no breast development. There was no family history of similar complaints. She was 162 cm height and 48 kg weight. Her breast examination showed tanner stage 1. The axillary and pubic hairs were sparse. Abdominal examination was normal. The external genitalia appeared normal female type with normal vagina. Ultrasound revealed hypoplastic uterus 30 × 9 mm, right ovary 21 × 8 mm and left ovary 18 × 8 mm. Serum follicle stimulating hormone (FSH)—70.80 IU/ml (high), luteinizing hormone (LH)—31.61 IU/ml (high), serum prolactin—5.21 ng/ml (normal) serum estradiol (E2)—13.47 pg/ml (low). The chromosomal analysis showed 46 XY karyotype (Fig. 3). This was confirmed by two laboratories. Laparoscopic bilateral gonadectomy was performed. Histopathological examination was bilateral ovarian stroma with congested blood vessels and adipose tissue (Fig. 4). Subsequently, she was started on HRT with both estrogen and cyclical progesterone. She had menarche and her height and weight were increased to 166 cm and 53 kg respectively, with marginal breast development on follow-up.

## DISCUSSION

XY females have male genotype 46 XY with varied female phenotype ranging from female external genitalia to that with some features of virilism. XY female can be due to a variety of genetic defects that affect hormone-dependent formation of the male external genitalia. Sexual differentiation follows a sequential pattern *in utero*. After fertilization, there is establishment of the genotype of the embryo and the primordial gonads differentiate into ovaries

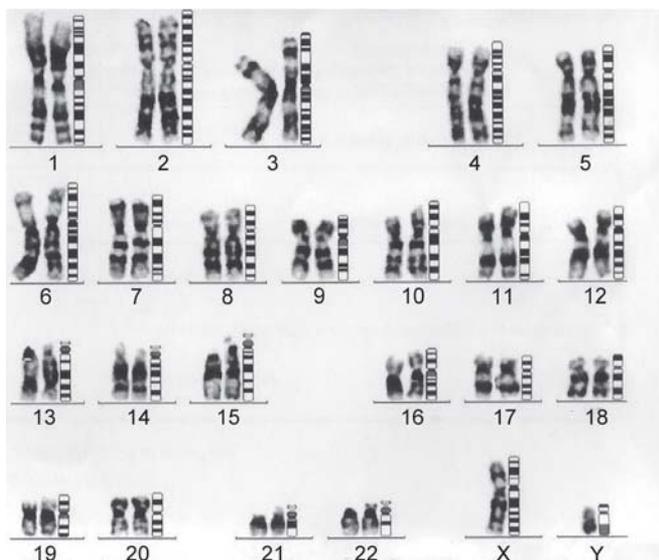


Fig. 3: Karyotype with 46 XY

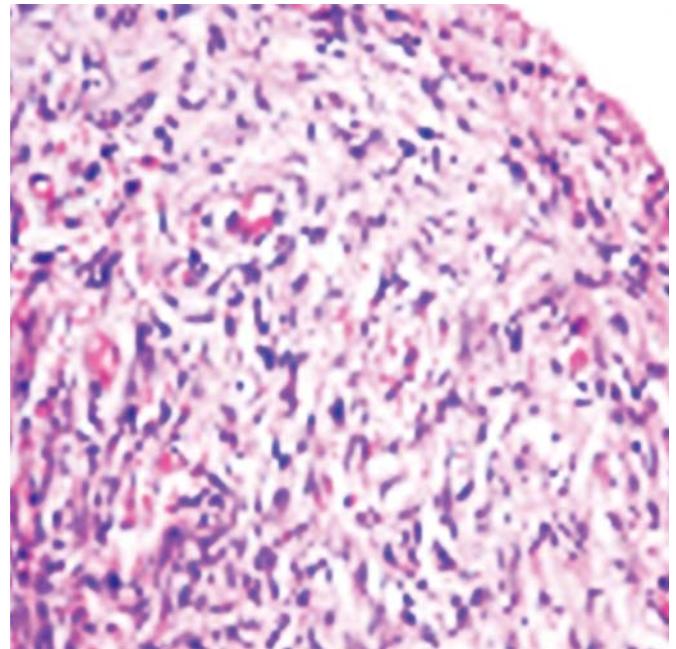


Fig. 4: Ovarian stroma (40 × H&E)

by default in the absence or nonfunctioning of the Y chromosome. Under the influence of the single gene determinant (testes determining factor) on the short arm of the Y chromosome, they differentiate to testes. This differentiation of the primordial gonads into the testes or ovary will lead to an alteration of the hormonal milieu of the fetus, which in turn results in the corresponding differentiation of the internal and external genitalia. The external genitalia also develops into female external genitalia by default in the absence of effective male sex hormones.

In our first case, we made the diagnosis of CAIS as she presented with primary amenorrhea with underdeveloped female external genitalia, better developed breast, absence of pubic, axillary hairs and uterus. The most important is the presence of testis instead of ovaries with XY karyotype. This X-linked inherited disease is the result of absent or qualitative or quantitative abnormalities of androgen receptors.<sup>3</sup> The gene is located in the q11-12 region of Y chromosome.<sup>4</sup> Detection of AIS demands careful investigations of other affected family members, since it may also occur in other family members.

Our second patient was a female with normal stature, presented with primary amenorrhea, sexual infantilism, hypoplastic uterus, with pure XY genotype and the gonadal tissue showing the features of ovarian stromal tissue. Hence, the diagnosis of Swyer syndrome was made. The main differential diagnosis of Swyer syndrome is mixed gonadal dysgenesis which is more frequently seen than the former. In this condition, the gonads on histopathology will also show testicular differentiation.

The etiology of this 46 XY gonadal dysgenesis is thought to be a short arm Y chromosome deletion involving sex determining region of Y chromosome (SRY), a mutation in other genes that leads to inhibition of SRY function or mutation of SRY function.<sup>5</sup> These inhibit testicular differentiation and inhibit antimullerian hormone production.

Management of XY female involves the following:

- i. Making the correct diagnosis.
- ii. Communicating the diagnosis to the patient and the parents along with expert psychological support.
- iii. Need of early gonadectomy since the risk of malignancy is 5 to 10% in childhood rising to 30% by the age of 50 years.<sup>6</sup>
- iv. Lifelong HRT is essential after gonadectomy for many aspects of health and well being which may include induction of puberty and to maintain bone mineral density. Presence of uterus in Swyer syndrome requires cyclical HRT with progesterone to induce menstruation.
- v. Treatment for vaginal hypoplasia may be required in these XY females to have coital function.
- vi. Females with Swyer syndrome are able to conceive with *in vitro* fertilization and donor oocyte.<sup>7</sup>

## CONCLUSION

Early diagnosis and prompt follow-up is important for the risk of gonadal malignancy and for the adequate HRT to improve bone mineral density.

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