

**Case Report**

**Swyers Syndrome: primary amenorrhoea with gonadal dysgenesis a rare cause**

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**Abstract**

Swyer syndrome is an uncommon form of gonadal dysgenesis, characterised by a 46, XY karyotype (1). In spite of presence of Y chromosome the affected individual has a female phenotype as the dysgenetic gonad produces neither AMH nor androgens. As a result of failure of masculinisation, the internal and external genitalia is that of a female. These cases generally present at puberty with primary amenorrhoea and lack to development of secondary sexual characteristics. We are reporting a case of partially developed breast, hypoplastic uterus and absent streak gonads. The patient was treated with hormone replacement therapy which resulted in breast and uterine development and establishment of regular menses. This case demonstrates a rare case of gonadal dysgenesis.

**Keywords:** Swyer syndrome, Gonadal dysgenesis, androgen, karyotype, SRY gene

**1. Introduction**

A 16-year-old girl presented with history of primary amenorrhoea and lack of development of breast. There was no history any chronic disease, chronic drug use, anosmia, radiation exposure, hirsutism, eating disorder or excessive physical activity or prior sexual exposure. Her school performance was good. Maternal menarche was 13 yrs and there was no history of delayed puberty in the family. Physical examination revealed a phenotypical female with eunuchoid habitus measuring height 165 cm, weight 54 kg, BMI 19.08kg/m<sup>2</sup> with no stigmata of Turner's syndrome. Breast development and pubic hair was detected to be consistent with Tanner stage II and I, respectively.

The blood examination revealed a very high follicle stimulating hormone (FSH) and luteinizing hormone (LH) and low oestrogens. Her testosterone levels were within normal range for females. Pelvic USG revealed a hypoplastic uterus with failure to visualise both ovaries. MRI abdomen and pelvis revealed a small hypoplastic uterus with no gonads. A karyotype analysis detected 46 XY chromosomes with SRY gene, thus confirming the diagnosis of Swyer syndrome. She was planned for laparoscopic gonadectomy.

Laparoscopic evaluation revealed streak gonads and hypoplastic uterus with fallopian tubes. Bilateral salphingo-gonadectomy was done. Pathological examination of gonads did not reveal any ovarian nor testicular tissue.

Patient was started on a daily equine oestrogen 1.25 mg daily along with medroxy progesterone acetate 5mg daily for last 12 days of the cycle for 6 months. She experienced regular menses with this therapy. She was switched to low dose oral contraceptive pills thereafter. Subsequent follow up after 4 yrs showed uterine enlargement on USG along with normal breast development. She was counseled about future fertility and prospects of ovum donation after marriage.

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**3. Discussion**

Swyer syndrome (46, XY pure gonadal dysgenesis) is rare cause of primary amenorrhoea. These patients are phenotypically females who often present with primary amenorrhoea and with completely normal female appearance and height. The common causes of primary amenorrhoea with completely female phenotype include Turners syndrome, Mullerian Agenesis (MRKH), Androgen insensitivity syndrome (AIS). Although most common karyotype of Turners syndrome is 45, X0, approximately 5% of women with Turners syndrome have a karyotype containing all or part of Y chromosome (3) and risk of gonadoblastoma is 5-10% in these patients. Mullerian agenesis is second common case of primary amenorrhoea (4). These individuals exhibit normal, symmetrical breast and pubic hair development, no visible vagina and rudimentary

uteri with no functional endometrium. Majority of patients have normal ovaries and a karyotype of 46, XX contrary to our case. AIS is the third most common cause of primary amenorrhoea. Affected individuals have a male karyotype 46, XY and testes produce both testosterone and AMH resulting in external genitalia that of a female with short or blind vagina and absent cervix and uterus as the target organs are insensitive to androgens. Serum testosterone levels in these individuals are normal or modestly elevated above the reference range observed in normal males and well above the normal levels of females. As in our case the testosterone levels are below normal range and the internal genitalia i.e. the uterus is present.

In Swyer syndrome, disturbances of gonadal differentiation during the early intrauterine developmental period result in insufficient secretion of testosterone and AMH and the evolution of internal and external genitalia as female. In 10-15% of the cases mutation in the SRY gene (Sex Determining Region of Y chromosome) is the cause (5). In rest of the cases no cause can be determined although mutations in SRY regulatory elements or genes involved in testes determining pathway have been implicated (6). We looked for signs of deletions at the SRY region in our patient and found no deletion type mutation. This condition further underlines the importance of the transcription factors other than SRY during the early developmental period of the testis. In the medical literature, patients with 46, XY pure gonadal dysgenesis have been reported as cases frequently having complications with gonadoblastoma. Therefore, owing to the tumour risk, it is recommended that bilateral fibrotic gonads are removed when such patients are diagnosed. Because 10-30% risk for gonadal tumour occurrence is reported with the presence of the Y chromosome. That risk, increases with age; it is reported that the risk is 50-70% in the third decade while being as high as 80% in the fourth (7). Among the tumours, gonadoblastoma and dysgerminoma are the most prevalent. Therefore, laparoscopic removal of the dysgenetic gonads is crucial in all cases with female phenotype and the Y chromosome even though the ovaries could not be shown with radiological techniques as in our case (8).

In this case report, we intend to highlight (i) the rarity of this case, (ii) the necessity of performing karyotype analysis in patients who present with primary amenorrhea, lack of secondary sex characteristics and female phenotype, (iii) early removal of the gonads owing to the risk for gonadal tumour development and (iv) successful restoration of menses and development of secondary sexual characters with appropriate treatment.

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