A rare case of Primary Amenorrhea with Swyer Syndrome: a case report

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ABSTRACT

Background: Swyer syndrome is seen in females with primary amenorrhea, unambiguous female genital appearance, normal vagina, and cervix but XY karyotype. It is characterized by bilateral streaky ovaries, hypoplastic infantile uterus, normally developed Mullerian structures, and hypergonadotropic hypogonadism. The incidence of Swyer syndrome is about one in 80,000. It is a rare genetic condition affecting sexual organ development, classified as a disorder of sex development. Affected individuals usually have a uterus and fallopian tubes, but their gonads are not functional. Instead, the gonads are small and underdeveloped and contain little gonadal tissue.

This case report emphasizes the need for early detection and to start with treatment for both the physical and mental well being of the affected child.

Case Presentation: A 17-year-old girl presented with primary amenorrhea visited our clinic. Family history and the age at diagnosis were collected. After obtaining consent, a physical examination for secondary sexual characteristics was done. Initial laboratory tests like Thyroid profile, FSH, LH, and Estradiol for evaluating primary amenorrhea were investigated. Radio diagnosis to find uterine and ovaries size was done. Karyotyping and Fluorescent *In situ* Hybridization (FISH) tests were done to find the genotype of the girl.

Parents of the affected child have a history of second-degree consanguineous marriage. The child's height was 167 cm and weighed 44 kg. On examination, breasts were in tanner stage 2, with absent axillary hair but well-developed pubic hair. External genitalia was of the female type, per vaginal examination was normal and the cervix was small.

Conclusion: The purpose of reporting this case is rarest clinical condition and to know the importance of chromosome pattern XY female for appropriate management as there is a high chance of gonadal malignancies if undetected. Also to counsel about fertility-related problems.

Keywords: Primary amenorrhea, Swyer syndrome, hypogonadism, 46XY female, Case report.

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Background

Swyer syndrome or pure 46XY gonadal dysgenesis is a condition, in which the individuals have a female appearance [1]. They classically present as sexually infantile phenotypic females with primary amenorrhea. People with this disorder have female external genitalia but the uterus and fallopian tubes are underdeveloped. However, they do not have functional gonads (ovaries or testes). Instead, they have streaky gonads [1].

Complete gonadal dysgenesis or Swyer syndrome was first described by Jim Swyer in 1955; since then, a number of cases have been reported.[2] It is characterized by bilateral streak gonads, normally developed Mullerian structures, female-appearing external genitalia, and hypergonadotropic hypogonadism.[2] Patients usually present in adolescence with primary amenorrhea and with a lack of secondary sexual characteristics. The incidence of Swyer syndrome is 1:80,000 [3]. The purpose of reporting this case is its rarity and the importance of diagnosis of XY female for appropriate management as there is a high incidence of gonadal malignancies and also to counsel about fertility options.

Early diagnosis is critical as patients present with primary amenorrhea and lack of secondary sexual development, often leading to delayed recognition. Timely identification not only allows for appropriate hormone replacement therapy (HRT) to induce puberty and maintain bone and cardiovascular health but also plays a crucial role in reducing the risk of gonadal malignancy, which is significantly high (30%-40%). Additionally,

early diagnosis provides opportunities for fertility preservation counseling, as patients possess a functional uterus, making oocyte donation and assisted reproductive technologies viable options. Advances in genetic testing, imaging, and hormonal assessments continue to enhance clinical awareness, leading to improved patient outcomes [4].

A small number of successful pregnancies achieved with oocyte donation have been reported in patients with Swyer syndrome [3].

Case Report

A 17-year-old female patient (Figure 1) sought medical attention at S Nijalingappa Medical College and HSK Hospital in Bagalkote, Karnataka, India, due to the absence of menstruation. The patient had no notable surgical background. She reported no recurrent abdominal discomfort, exposure to hormones or radiation, or neurological symptoms like headaches or vision problems. She was the eldest child of parents who were second-degree relatives. Her younger sibling was a healthy male. Physical assessment revealed her height as 167 cm and a body mass index of 15.8 kg/m^2. Evaluation of her sexual development showed bilateral streaky ovary and Tanner stage 2 breast growths, underdeveloped secondary sexual characteristics like lack of axillary hair, but well-formed pubic hair.

Inspection of the external genitalia indicated female characteristics, with a visible vaginal opening. External genitalia shows unambiguously female, the vagina and uterus are present but underdeveloped. Importantly, there are no congenital anomalies or dysmorphic features beyond the lack of secondary sexual characteristics. Subsequent tests revealed elevated serum hormone levels: follicle-stimulating hormone at 47.3 mIU/l and luteinizing hormone at 34.96 mIU/l. Estradiol was measured at 66.969 mIU/l. Imaging studies showed abnormal reproductive organs: ultrasound detected a rudimentary uterus (Figure 2), while magnetic resonance imaging revealed an underdeveloped uterus lacking fallopian tubes and with streak-like ovaries, without distinct endometrial or myometrial layers. Both kidneys appeared normal.

Genetic analysis through karyotyping (Figure 3) identified a 46XY genotype. To validate this finding and rule out potential false results, fluorescent *in situ* hybridization (FISH) (Figure 4) was performed, which confirmed the presence of one X and one Y chromosome in all examined cells. These findings were consistent with patients' presentations.

Mosaicism was specifically ruled out through karyotype and FISH analysis, as it can present with overlapping but distinct clinical features, such as asymmetry in gonadal development, mixed gonadal dysgenesis, and a higher risk of ambiguous genitalia or Turner-like features. Ruling out mosaicism is critical because it affects gonadal malignancy risk assessment and also aids in individual management decision which includes the timing of gonadectomy and long-term hormonal therapy.

Discussion

Swyer syndrome affects individuals with XY chromosomal make-up; nevertheless, they have a female appearance. The exact incidence is unknown. The diagnosis of Swyer syndrome is made based on thorough clinical evaluation, detailed patient history, identification of characteristic findings (e.g., amenorrhea and streaky gonads), and a variety of tests including karyotyping and FISH. Accurately differentiating Swyer syndrome (46, XY complete gonadal dysgenesis) from other disorders of sexual development is critical due to distinct implications for management, prognosis, and patient counseling. Several conditions, such as Turner syndrome (45X or mosaic variants), mixed gonadal dysgenesis (45X/46XY), and androgen insensitivity syndrome, can present with overlapping features but require additional investigations. The height

Figure 1. *17-year-old girl with primary amenorrhea suggestive of Swyer syndrome.*

of the patient is particularly helpful in distinguishing patients with pure 46XY gonadal dysgenesis from those with 45XO/46XY mosaicism but without the classic features of Turner syndrome [5]. The chromosomal analysis in Swyer syndrome shows a male karyotype (46XY) and FISH signals for males.

This female approached us at the appropriate age and time. This helped us with the proper workup and management. A study by Michala et al. [3] also shows that many females experienced delays in reaching accurate diagnosis, often several years after the presentation to their general practitioners. It is suggested that health professionals should update their scientific knowledge and be aware of sexual development disorders. Early diagnosis is important for a number of reasons: 1. Because of the risk of gonadal malignancy. 2. Early institution of hormonal therapy is vital for the induction of puberty. 3. HRT is required to prevent osteoporosis [1].

The risk of tumor development in Swyer syndrome is significant. A 20%-30% incidence of tumor in Swyer syndrome was reported [5]. The most common tumors involved in this condition are gonadoblastoma, dysgerminoma, and embryonal carcinoma were also reported [2]. Due to the risk of tumors, an extensive search for the rudimentary gonads is needed and bilateral gonadectomy is advisable. As for this patient, since we could not detect any rudimentary gonads, she requires a close follow-up in the long run. An interesting finding in this patient is that despite the late induction of puberty and non-compliance to hormonal treatment, there is marked improvement in her uterine development. However, her uterine size was smaller than in normal controls. This finding was similar to the study carried out by Michala et al. [3]. The small uterine size however does not appear to have an adverse effect on the fertility outcome in Swyer syndrome [2]. A small number of successful pregnancies have been reported in this group of patients [1,3]. Pregnancies were possible through oocyte donation and hormonal treatment. The presence of the XY genotype and the H-Y antigen does not affect the normal uterine and endometrial response. Thus, the possibility of maintaining normal pregnancy and delivery confirms the physiological ability of the uterus to accommodate and maintain successful pregnancy in patients with XY dysgenesis [6]. Swyer syndrome can be sporadic or linked to mutations in SRY, NR5A1, or MAP3K1, making genetic counseling valuable for family planning [4]. This case was considered significant due to the high risk of gonadal malignancy associated with Swyer syndrome,

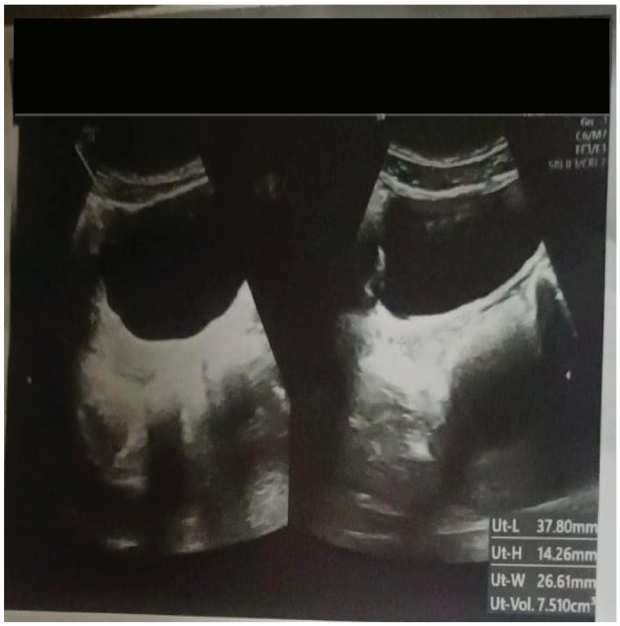

Figure 2. *Ultrasound image showing rudimentary uterus.*

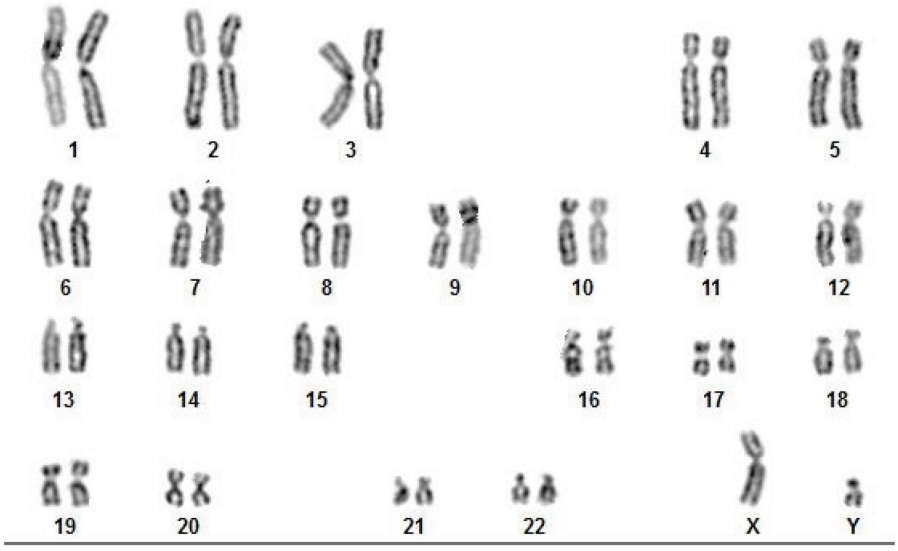

Figure 3. *Karyotype showing 46XY.*

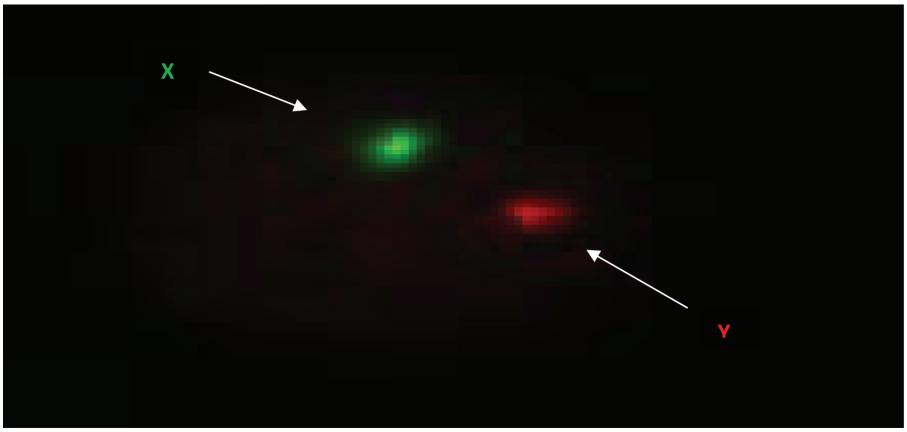

Figure 4. *Fluorescent in situ hybridization showing signals for XY.*

particularly the potential for gonadoblastoma and dysgerminoma in the dysgenetic gonads. Studies indicate that up to 30%-40% of individuals with Swyer syndrome develop gonadal tumors, with the risk increasing over time if the streak gonads are not removed. The malignancy risk is primarily due to the presence of Y chromosome material, which has been linked to oncogenic factors promoting abnormal cell proliferation in dysgenetic gonads.

A structured, multidisciplinary long-term follow-up plan ensures early detection of complications, optimization of hormone therapy, and overall well-being of patients with Swyer syndrome. Regular monitoring of hormone levels, bone health, and cardiovascular risks is critical for improving quality of life and long-term outcomes.

Conclusion

Swyer syndrome is extremely rare and invariably causes primary amenorrhea. Genetic testing plays a very important role in the diagnosis of Swyer syndrome. Early diagnosis is of crucial importance for various reasons, including the risk of gonadal malignancy and the need for removal of the gonads. Early institution of HRT for induction of puberty, improving bone mineral density and also counseling regarding fertility options.

What is new

Recent updates in Swyer syndrome include advances in early diagnosis and risk management, optimized hormone replacement therapy, emerging fertility prospects through assisted reproduction, and the importance of multidisciplinary care.

Conflicts of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

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Consent for publication

Written consent was obtained from the parents of the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of case

1	Patient (gender, age)	Female, 17
2	Final diagnosis	Swyer syndrome
3	Symptoms	Primary amenorrhea
4	Medications	HRT
5	Clinical procedure	NIL
6	Specialty	Endocrinology