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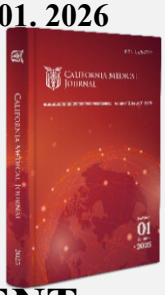

46 XY DISORDER OF SEX DEVELOPMENT DUE TO SWYER SYNDROME IN A 17-YEAR-OLD ADOLESCENT: A Rare Case Report

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ABSTRACT

Background: 46, XY Disorder of Sex Development (DSD) due to pure gonadal dysgenesis, known as Swyer syndrome, is a rare condition with an estimated incidence of approximately 1 in 80,000 live births. It is characterized by a 46 XY karyotype in phenotypic females with nonfunctional streak gonads, hypergonadotropic hypogonadism, and increased risk of gonadal malignancy.

Case Presentation: A 17-year-old phenotypic female presented with primary amenorrhea and absent breast development. Hormonal evaluation revealed low estradiol, markedly elevated FSH and LH, and low testosterone levels. Karyotype analysis demonstrated 46 XY. Pelvic MRI showed a streak uterus with a single cervix and vagina. Bone mineral density (BMD) assessment revealed a Z-score of −3.7 SD. The patient was diagnosed with delayed puberty due to 46 XY DSD consistent with Swyer syndrome, accompanied by overweight.

Laparoscopic gonadal exploration and staged estrogen replacement therapy were planned.

Conclusion: Swyer syndrome should be suspected in adolescents presenting with primary amenorrhea and hypergonadotropic hypogonadism. Early diagnosis is essential to prevent gonadal malignancy and long-term complications such as osteoporosis.

Keywords: 46 XY DSD, Swyer syndrome, primary amenorrhea, hypergonadotropic.

INTRODUCTION

Disorders of Sex Development (DSD) are congenital conditions involving atypical development of chromosomal, gonadal, or anatomical sex. One rare subtype is 46 XY DSD due to pure gonadal dysgenesis, commonly referred to as swyer syndrome. The estimated incidence is approximately 1 in 80,000 births. In swyer syndrome, individuals possess a 46 XY karyotype but fail to develop functional testes due to impaired gonadal differentiation during embryogenesis, often associated with mutations in the SRY gene or related pathways. As a result, streak gonads are formed, which do not produce sex steroids. Müllerian structures (uterus and fallopian tubes) persist due to the absence of anti-Müllerian hormone. Patients typically present during adolescence with primary amenorrhea and absent secondary sexual characteristics. This case report aims to describe the clinical presentation, diagnostic evaluation, and management plan of a 17-year-old adolescent diagnosed with swyer syndrome.

CASE PRESENTATION

A 17-year-old phenotypic female was referred from the general outpatient clinic to the Urology Surgery Department for planned laparoscopic gonadal exploration. The chief complaint was absence of menstruation. She also reported lack of breast development. Sparse pubic and axillary hair were present. The patient had previously sought medical evaluation at age 14 for delayed menarche but declined further referral at that time. Her mother experienced menarche at age 13. Since August 2025, the patient had been taking a combined oral contraceptive (Mycroginon® 1 tablet daily) prescribed by a gynecologist. She reported bilateral breast lumps with tenderness after starting the medication. There was no history of chronic illness, prolonged fever, tuberculosis exposure, bleeding disorders, seizures, or drug allergies. She was born at term via spontaneous vaginal delivery with a birth weight of 3.2 kg. Growth and developmental milestones were appropriate for age. She has been raised as female and reports heterosexual orientation.

Cytogenetic analysis performed on June 26, 2025, at the Biomedical Laboratory of Universitas Padjadjaran demonstrated a 46 XY karyotype without evidence of structural chromosomal abnormalities or mosaicism, confirming a genetically male chromosomal pattern.

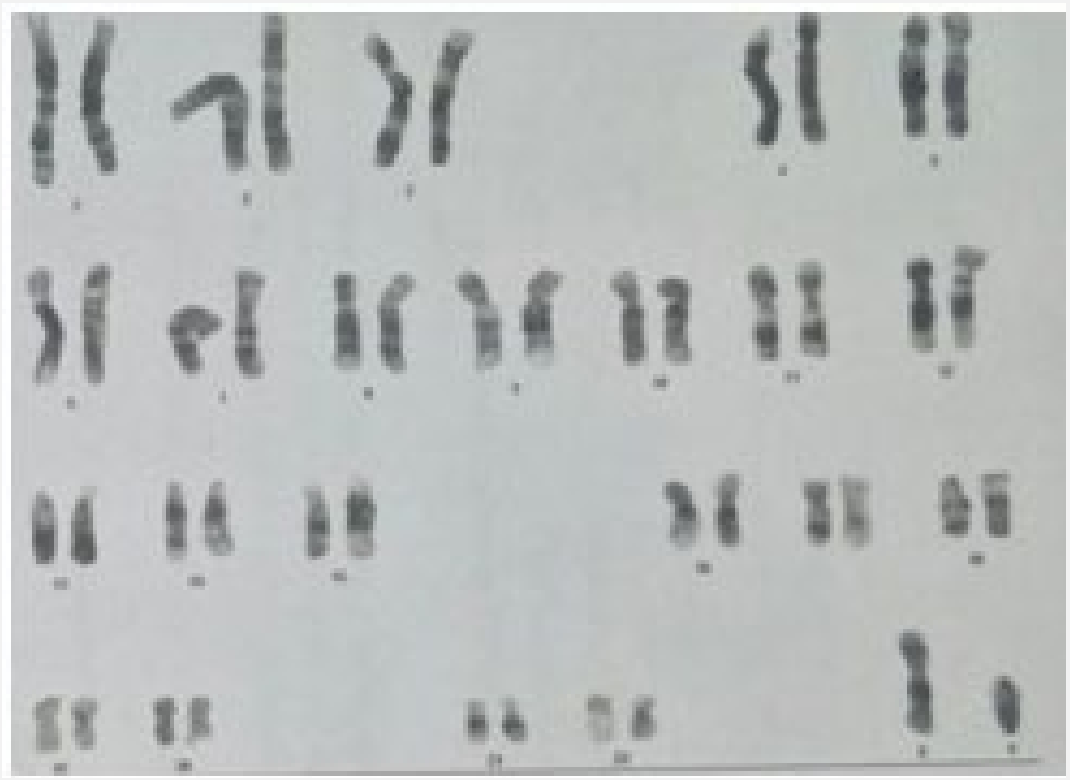

Figure 1. Cytogenetic analysis demonstrated a 46 XY karyotype. Note: The analysis result shows a male karyotype. No abnormal chromosome structures or mosaic conditions were found.

Hormonal evaluation revealed markedly elevated gonadotropins, with follicle-stimulating hormone (FSH) level of 62.98 mIU/mL and luteinizing hormone (LH) level of 20.44 mIU/mL, accompanied by low estradiol level (14.67 pg/mL). Serum testosterone was <2.50 ng/dL, which is within the female reference range and significantly lower than expected male levels. Prolactin and lactate dehydrogenase (LDH) levels were within normal limits. These findings are consistent with hypergonadotropic hypogonadism secondary to primary gonadal failure.

Routine hematologic and biochemical investigations showed hemoglobin 13.3 g/dL, leukocyte count 4,890/μL, and platelet count 334,000/μL, all within normal limits. Renal function, fasting blood glucose, coagulation profile, and electrolyte levels were unremarkable.

Pelvic magnetic resonance imaging (MRI) with contrast performed on August 2, 2025, demonstrated the presence of a hypoplastic uterus with a single cervix and a single vaginal canal. The uterine size was smaller than expected for the patient's chronological age, consistent with hypoestrogenic status. Bilateral fallopian tubes were visualized, indicating intact Müllerian structures. No obvious ovarian tissue was identified, and the gonadal structures appeared as streak-like formations suggestive of streak gonads. There was no evidence of pelvic lymphadenopathy involving the obturator, internal iliac, external iliac, common iliac, presacral, perirectal, or inguinal regions. No mass lesion suggestive of gonadal malignancy was detected on imaging.

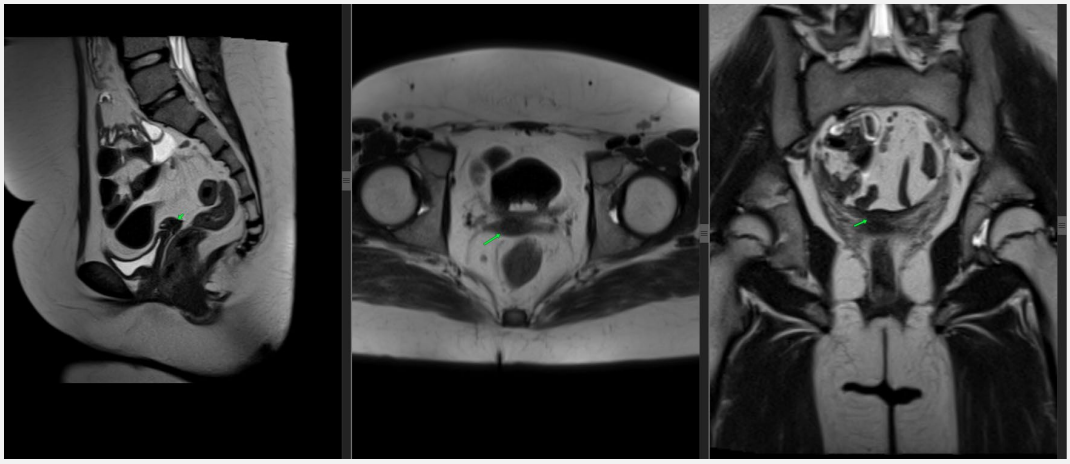

Figure 2. Hypoplastic uterus with a single cervix and a single vaginal canal

Bone mineral density assessment demonstrated significantly decreased bone mass, with a Z-score of −3.7 SD, which is categorized as "below the expected range for age" according to WHO and ISCD criteria. Bone age assessment using the Greulich-Pyle method revealed skeletal maturation appropriate for chronological age.

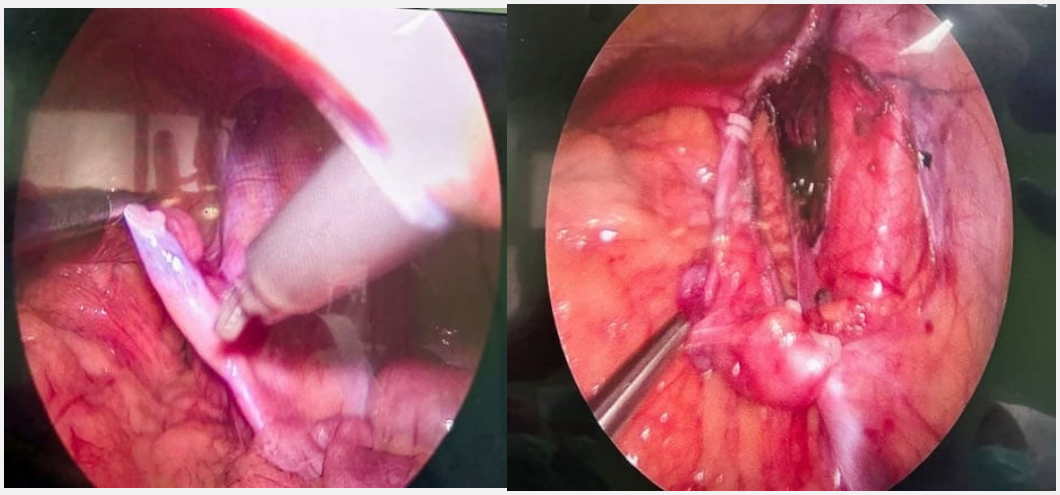

Figure 3. Exploratory laparoscopy reveals bilateral streak gonads

DISCUSSION

Swyer syndrome is a rare form of 46 XY Disorder of Sex Development (DSD) characterized by complete gonadal dysgenesis in individuals with a 46 XY karyotype and female phenotype. The estimated incidence is approximately 1 in 80,000 live births, making it a rare cause of primary amenorrhea. Early recognition is essential due to the associated oncologic risk and long-term metabolic consequences. Normal male sex differentiation requires functional expression of the SRY gene located on the Y chromosome, which initiates testicular differentiation from the bipotential gonadal ridge. In Swyer syndrome, mutations in SRY or other genes involved in testicular development (e.g., SOX9, NR5A1, DHH) may impair this process. As a result, the gonads fail to develop into functional testes and instead form fibrous streak gonads. The absence of functional Sertoli cells leads to lack of anti-Müllerian hormone (AMH) production, allowing Müllerian structures (uterus, fallopian tubes, and upper vagina) to develop normally. Simultaneously, absence of Leydig cell function results in insufficient testosterone production, preventing masculinization of the external genitalia. Therefore, patients present with normal female external genitalia despite a 46 XY karyotype. The streak gonads lack steroidogenic activity, resulting in estrogen deficiency. Consequently, the hypothalamic–pituitary axis increases gonadotropin secretion (FSH and LH), leading to the characteristic picture of hypergonadotropic hypogonadism observed

in this patient. The most common presentation is primary amenorrhea with absent or minimal secondary sexual characteristics. In this case, the patient presented at 17 years of age with primary amenorrhea and poor breast development. Sparse pubic and axillary hair were present, which may be attributed to minimal adrenal androgen production. Differential diagnoses of primary amenorrhea with hypergonadotropic hypogonadism include, Turner syndrome (45 X or mosaic variants), 46 XX pure gonadal dysgenesis, Autoimmune ovarian failure, Gonadal dysgenesis with Y chromosome material (including Swyer syndrome)

Turner syndrome was unlikely in this patient due to the absence of characteristic phenotypic features (short stature, webbed neck, shield chest) and the confirmed 46 XY karyotype. The presence of a uterus and absence of virilization further supported the diagnosis of Swyer syndrome rather than complete androgen insensitivity syndrome (CAIS), in which Müllerian structures are absent due to intact AMH production.

One of the most critical aspects of Swyer syndrome is the increased risk of gonadal tumors. Dysgenetic gonads containing Y chromosome material are associated with a 20–30% lifetime risk of gonadoblastoma, which may progress to dysgerminoma. The risk increases with age, particularly after puberty. Therefore, prophylactic bilateral gonadectomy is strongly recommended once the diagnosis is established, even in asymptomatic individuals. In this case, laparoscopic gonadal exploration was planned to evaluate and remove dysgenetic gonadal tissue. A notable feature in this case was severe reduction in bone mineral density (Z-score −3.7 SD). Adolescence is a critical period for achieving peak bone mass, and estrogen plays a fundamental role in bone maturation and epiphyseal closure. Chronic estrogen deficiency in Swyer syndrome disrupts bone remodeling, leading to decreased bone mineral density and increased future fracture risk. The patient's bone age corresponded to chronological age, indicating that skeletal maturation had progressed despite estrogen deficiency. However, failure to achieve adequate peak bone mass places her at long-term risk of osteoporosis. Early initiation of estrogen replacement therapy is therefore essential not only for induction of secondary sexual characteristics but also for optimization of bone health. Pubertal induction should mimic physiological puberty. Current recommendations suggest initiating

low-dose estrogen therapy and gradually increasing the dose over 2–3 years. Cyclic progestin should be added after adequate estrogen priming or once breakthrough bleeding occurs to protect the endometrium. In this case, estradiol 0.5 mg daily was planned as initial therapy. Gradual dose escalation will promote breast development, uterine growth, and improved bone mineralization.

Patients with Swyer syndrome are typically raised as female and identify as female, as seen in this case. Disclosure of chromosomal findings requires sensitive counseling. Multidisciplinary management involving endocrinology, urology, genetics, and psychological services is crucial to address identity, fertility counseling, and long-term health monitoring. Although spontaneous fertility is not possible due to nonfunctional gonads, pregnancy can be achieved through assisted reproductive technology using donor oocytes, provided the uterus is functional. This case is considered rare due to, low prevalence of Swyer syndrome, diagnosis made in late adolescence despite earlier symptoms, Presence of severe low bone mineral density at presentation. It underscores the importance of early evaluation of primary amenorrhea to prevent delayed diagnosis and associated complications.

CONCLUSION

This case highlights a typical presentation of 46 XY complete gonadal dysgenesis diagnosed during adolescence due to primary amenorrhea. Cytogenetic confirmation, imaging evaluation, and hormonal assessment are essential for diagnosis. Early laparoscopic bilateral gonadectomy is crucial to prevent malignant transformation. Multidisciplinary management ensures optimal endocrine, reproductive, skeletal, and psychosocial outcomes.

DISCLOSURE OF POTENTIAL CONFLICT OF INTEREST

- The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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