OLGU SUNUMU CASE REPORT

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# Swyer Syndrome: A Case Report

## Swyer Sendromu: Olgu Sunumu

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**ABSTRACT**

Disorders of sex development are congenital conditions in which the development of chromosomal, gonadal or anatomical sex is aytpical. Swyer syndrome is a pure gonadal dysgenesis associating with 46 XY karyotype, primary amenorrhea, delayed puberty and presence of female internal genital tract and bilateral streak gonads. 16 years old patient admitted to our clinic for no breast development and primary amenorrhea. She had female external genital organs and her breast-pubic hair development were Tanner Stage 2. Her ultrasonography showed a uterus of 3x1.5cm and ovaries were not visualized. Laboratory investigations revealed highly elevated serum levels of gonadotropins. Her chromosome analysis showed a 46, XY karyotype. Swyer syndrome is a rare condition that should be considered in women presenting with delayed puberty, primary amenorrhoea and high gonadotropins.The management of these patients is complex and requires a multidisciplinary team. Early diagnosis is important because of the increased risk of germ cell tumor.

**Keywords:** Swyer Syndrome, primary amenorrhoea, gonadal dysgenesis.

**ÖZET**

Cinsiyet gelişim bozuklukları, kromozomal, gonadal veya anatomik cinsiyet gelişiminin atipik olduğu kongenital patolojilerdir. Swyer syndrome dişi fenotipinde, dişi iç genital organ ve 2 taraflı çizgi gonadlar varlığında primer amenore ve 46,XY karyotipi ile ilişkili saf gonadal disgenezidir. 16 yaşındaki hasta kliniğimize primer amenore ve meme gelişiminin olmaması üzerine başvurdu. Hastanın fizik muayenesinde dişi dış genitaller mevcuttu. Meme ve pubik kıllanma Tanner evre 2 olarak değerlendirildi. Ultrasonografide 3x1.5 cm boyutunda uterus görüldü, overler görülmedi. Laboratuar bulgularınıda yüksek serum gonadotropin seviyeleri tespit edildi. Karyotip analizi 46 XY olarak raporlandı. Swyer sendromu, gecikmiş puberte, primer amenore ve yüksek gonadotropin ile başvuran kadınlarda dikkate alınması gereken nadir bir durumdur. Swyer sendromlu hastaların teşhisi ve yönetimi karmaşıktır ve optimum bakım, deneyimli bir multidisipliner ekip gerektirir. Artan germ hücreli tümör riski nedeniyle erken tanı önemlidir ve bilateral gonadektomi yapılmalıdır.

**Anahtar Kelimeler:** Swyer Sendromu, primer amenore, gonadal disgenezi.

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Swyer Syndrome is a pure gonadal dysgenesis and a disorder of sex development in which the patient is 46 XY in genotype, but external genital organs are phenotypically a female.[1] The syndrome was first defined in 1955 in two cases of sex reversal that differed from the known forms of what was then termed as "male pseudohermaphroditism". These two patients had primary amenorrhoea, female external genitalia and a 46 XY karyotype.[2] Swyer syndrome has been estimated to occur approximately 6,4 in 100,000 people.[3] Patients with Swyer syndrome have female phenotype. They usually present with delayed puberty or primary amenorrhea due to absence of functional gonads. 10-20% of women with the syndrome have a deletion in the DNA-binding region of the SRY (sex-determining region Y) gene, while remaining 80%-90% of cases, the SRY gene is normal and mutations in other testis determining factors are implicated.[4] In the remaining 80-90%, defects in genes including ARX, ATRX, CBX2, DHH, DMRT1, GATA4, MAMLD1, MAP3K1, NROB1, NR5A1, WNT4,WT1 and WWOX are detected.[5] The syndrome may also present in late adulthood with gonadal tumors, typically 25% of cases develop gonadoblastoma or dysgerminoma.[6]

The purpose of this report is; to present a case of a patient with Swyer syndrome and the management of this case.

## CASE REPORT

A 16 years old female patient admitted to our outpatient clinic for no breast development and primary amenorrhea. Her height was 172 cm and weight was 65 kg. On physical examination, she had female external genital organs and her breast and pubic hair development were Tanner stage 2. Her pelvis ultrasonography showed a uterus of 3x1.5cm and ovaries were not visualized (Figure 1). Laboratory investigations revealed highly elevated serum levels of gonadotropins with FSH 97 mIU/ml and LH 18.4 mIU/ml. Estradiol level was <10 pg/ml. Her chromosome analysis showed a 46, XY karyotype (Figure 2). For the treatment the patients was given combined oral contraceptives and laparoscopic gonadectomy was recommended.

## DISCUSSION

Swyer syndrome typically presents with delayed puberty and primary amenorrhea due to absence of hor-

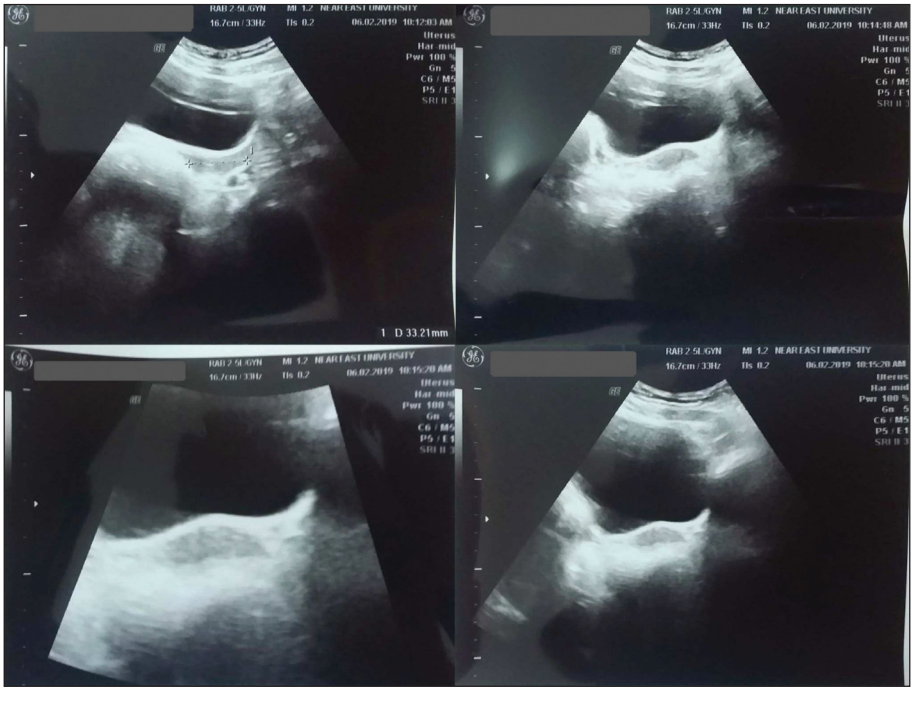

**FIGURE 1:** Ultrasonography findings of the case.

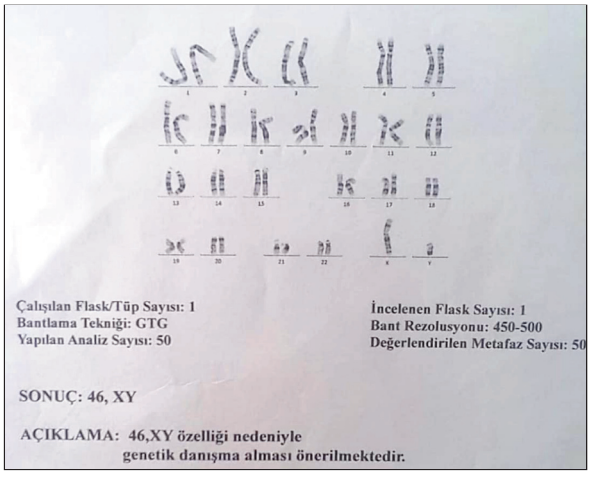


**FIGURE 2:** Genetic test result.

monal production from dysgenetic gonads. In this condition, the evaluation of the hormone profile is characterized by highly elevated serum concentration of luteinizing hormone and follicle-stimulating hormone with low circulating levels of gonadal steroids. These patients usually have little or no breast development but normal axillary and pubic hair.[1] Physical examination and pelvic imaging such as pelvic ultrasound and magnetic resonance imaging reveals normal female external genitalia, small prepubertal uterus, and bilateral streak gonads.

Sexual development begins with sex determination of the bipotential embryonic gonad, as either an ovary or testis, and this process is regulated by the chromosomal complement. Ovarian differentiation is the default pathway unless a Y chromosome with a normal sex-determining region on the Y (SRY) gene encodes a threshold level of transcription factor to trigger testis development. In the 46,XY fetus, secretion of anti-mullerian hormone (AMH) by sertoli cells results in mullerian duct regression, while testosterone secretion by leydig cells stabilizes wolffian ducts and induces their differentiation into epididymides, vas deferens, and seminal vesicles. External genital differentiation in the 46,XY fetus begins with the development of the phallus and genital swellings during the ninth week of gestation. Virilization of male structures is dependent on the presence of dihydrotestosterone (DHT), which is essential for fusion of urethral folds and labioscrotal swellings.[7]

Swyer syndrome is complete gonadal dysgenesis and the lack of secretion of AMH leading to the normal development of mullerian structures. This condition is thought to be caused by a mutation in the DNA-binding region of the SRY gene in 10-20% of cases, but there are other genes involved in sex determination that have been identified in the past years. The syndrome can be inherited in an autosomal dominant (NR5A1 mutations, heterozygous mutations in DHH, WNT4 duplications), autosomal recessive (homozygous [or compound heterozygous] mutations in DHH), X-linked (NR0B1 duplications) manner depending on the gene involved. The streak gonads fail to secrete testosterone. Without testosterone, the external genitalia fail to virilize, resulting in normal female external genitalia.

Differential diagnoses of patients with primary amenorrhea should consider various possibilities, including Mayer-Rokitansky-Kuster-Hauser syndrome (karyotype XX), which is the second most common cause of this condition; this syndrome is characterized by varying degrees of mullerian duct abnormalities and a rudimentary or absent uterus.[8] In addition, complete androgen insensitivity syndrome should be considered.[9]

The diagnosis and management of patients with Swyer syndrome is complex, and optimal care requires an experienced multidisciplinary team. Early diagnosis is important because of the increased risk of germ cell tumor and bilateral gonadectomy should be performed.[6] Early sex hormone treatment is necessary to induce and maintain typical pubertal development and to achieve optimal bone mineral density.

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***Declaration of Interest***

*No potential conflict of interest was reported by the authors.*

***Source of Finance***

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that pro-*

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### *Conflict of Interest*

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

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