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46,XY Gonadal Dysgenesis (Swyer Syndrome): A Case Report with Late Diagnosis

Fertilite İstemi Olan 46,XY Gonadal Disgenezi (Swyer Sendromu): Geç Tanı Almış Bir Olgu Sunumu

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ABSTRACT

The objective of this article is presenting the management of a case with late diagnosis of swyer syndrome and to evaluate the fertility request. A 31years old woman, married for 3years, G0P0 was diagnosed with pituitary insufficiency when she was admitted to the endocrinology clinic for hypoglycemia. The patient was consulted to the gynecology polyclinic with the complaints of not menstruating at the age of 13 and she was started hormone replacement therapy(HRT) that she is still using. No further analysis was performed for primer amenorrhea. After analysis; the patient was diagnosed with swyer syndrome and planned for gonadectomy. Bilateral salpengectomy and gonadectomy were performed. The patient was recommended to continue HRT. Patient with pregnancy request was explained that there were cases of healthy births with oocyte donation in the literature.

Keywords: Late diagnosis; swyer syndrome; 46,XY gonadal dysgenesis

ÖZET

Bu makalede geç tanı almış swyer sendromlu olgunun yönetimi ve fertilite isteminin değerlendirilmesi sunulmuştur. 31 yaşında, 3 yıllık evli, G0P0, ek hastalığı olmayan hasta hipoglisemik atak ile endokrinoloji polikliniğine başvurduğunda hastaya hipofizer yetmezlik tanısı kondu. Hastanın jinekolojik öyküsünde; 13 yaşında adet görememe şikayetiyle jinekoloji polikliniğine başvurduğu ve hala kullanmakta olduğu hormon replasman tedavisi başlandığı, primer amenoreye yönelik tahlil yapılmadığı öğrenildi. Hastaya yapılan tetkikler sonucunda swyer sendromu tanısı kondu ve gonadektomi planlandı. Bilateral laparoskopik salpenjektomi ve gonadektomi uygulandı. Hastanın hormon replasman tedavisine devamı önerildi. Gebelik istemi olan hastaya literatürde oosit donasyonu ile sağlıklı doğum ile sonuçlanmış örnekler olduğu anlatıldı.

Anahtar Kelimeler: Geç tanı; swyer sendromu; 46,XY gonadal disgenezi

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Swyer syndrome (46 XY Gonodal Dysgenesis) is a very rare form of gonadal dysgenesis. This syndrome is caused by a defect in gender determination during embryogenesis. The cases are phenotypically females but they have uterine hypoplasia, bilateral streak gonads and hypergonadotropic hypogonadism. Most of the time patients consult a doctor, due to the lack of pubertal signs and primary amenorrhea at puberty. They are diagnosed at an average age of 16-17 years. Streak gonads have a high risk of malignancy so they should be removed when diagnosed.

The purpose of this report is; presenting the management of a case with late diagnosis of swyer syndrome and to evaluate the fertility request.

CASE: REPORT

A 31 year old woman, married for 3 years, G0P0, was admitted to the endocrinology clinic for hypoglycaemic episodes. No pathology was found on physical examination. Height 170 cm, body weight 60 kg. As a result of the examinations, the patient was diagnosed with pituitary insufficiency and cortisol treatment was started. In addition to diagnosis of pituitary insufficiency, renal ultrasonography confirmed a horseshoe kidney. The gynecologic story of the patient was examined in detail when the rudimenter uterus and unclear ovaries were observed on the abdominal ultrasonography .

Medical story: the patient at the age of 13 was consulted to the gynecology polyclinic with the complaints of not menstruating and she was started hormone replacement therapy that she is still using. Patient stated that there was no additional analysis for the primary amenorrhea and that she did not come to regular checks at gynecology policlinic again because the menstrual cycles had been regulated with this treatment. The patient was negligent in this case.

Perineum, vulva, vagina were normal in the gynecologic examination. The corpus uteri was smaller than normal and the adnexes were non-palpable.

On the physical examination; breast development was normal, axillary and pubic hair was less than normal.

In laboratory tests; FSH: 113 mlU/mL, E2: 43 pg/mL, anti-mullerian hormone: <0,1.

In radiological imaging; the uterus was observed to be significantly smaller than normal for the age of the patient. In bilateral ovarian localization approximately 2x1 cm ovoid-shaped formations (might be ovaries) were observed. There was no solid mass lesion.

Chromosome analysis performed using the peripheral blood HRT banding method showed 46,XY genotype.

The patient was diagnosed with swyer syndrome and planned for gonadectomy. No additional pathology was found in preoperative preparation of the patient and tumor markers were observed in normal values.

Bilateral salpengectomy and bilateral gonadectomy were performed by laparoscopy. Laparoscopic abdominal observation showed normal fallopian tubes, streak gonads of 6-7 mm in the location of the ovaries (Figure 1, 2) and an atrophic uterus (Figure 3). The pathologic report of the material sent as right adnexa showed atrophic ovarian cortical tissue, fallopian tube, paratubal cyst, ectopic adrenal tissue, leydig cells and ductus deferens. The material sent as left adnexa showed fallopian tube, multiple paratubal cysts.

The patient was recommended to continue hormone replacement therapy.

We explained the patient that there were cases of healthy births with oocyte donation in the literature since she had a pregnancy request.

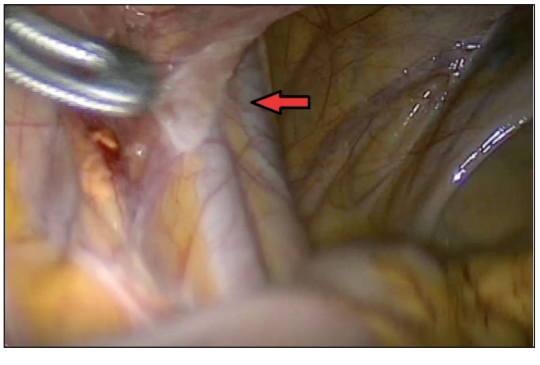

FIGURE 1: Right adnexa, streak gonad.

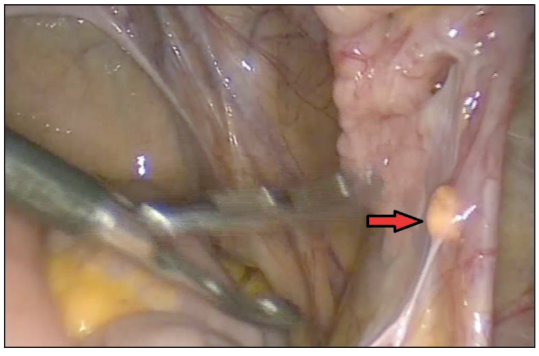

FIGURE 2: Left adnexa, streak gonad.

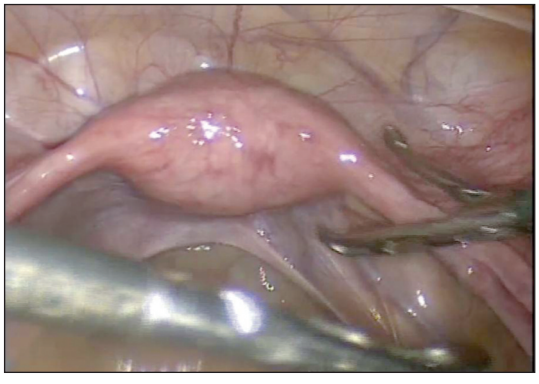

FIGURE 3: Uterine hypoplasia.

DISCUSSION

Swyer syndrome was first recognized in 1955 when Gim Swyer presented two cases with primary amenorrhoea diagnosed as a type undescribed in the literature of male pseudohermaphrodites.[1]

Swyer syndrome (46 XY gonodal dysgenesis) is a very rare form of gonadal dysgenesis. Prevalence of 46,XY females is 6.4 per 100 000 liveborn females.[2] It is characterized by a 46,XY karyotype, normal female external genitalia, completely undeveloped (streak) gonads, no sperm production, hypergonadotropic hypogonadism (secondary to gonadal failure) and presence of normal mullerian structures (uterus, fallopian tubes, and vagina).[3] Patients with swyer syndrome usually come at the age of puberty with primary amenorrhea and lack of sexual development. Early diagnosis is only possible when karyotype analysis is performed for another reason or if the patient has a sibling with similar complaints because findings were normal during prepuberty. Like our patient; diagnosis may be delayed until late ages when patient has no other complaints after hormone therapy is given for amenorrhea.

Sywer Syndrome originates from a pathogenesis occuring during embryogenesis, where the early stages of genital development are similar in the male and female. Normal development in women consists of the development of mullerian structures and atrophy of wolffian structures. In swyer syndrome the indifferent gonads fail to differentiate into testes in a XY (genetically male) fetus. In the absence of testes, no testosterone or anti-müllerian hormone (AMH) is produced. Without testosterone, the external genitalia fail to virilize, resulting in normal female genitalia. The wolffian duct fail to develop, so no internal male organs are present. Without AMH, the mullerian ducts develop into normal internal female organs (uterus, fallopian tubes, cervix and vagina).[4]

10-20% of the patients diagnosed with complete gonadal dysgenesis has deletion at the SRY gene DNA-binding site. In the remaining 80-90%, defects in genes including ARX, ATRX, CBX2, DHH, DMRT1, GATA4, MAMLD1, MAP3K1, NROB1, NR5A1, WNT4, WT1 and WWOX which are effective in testis development, probably caused complete gonadal dysgenesis in patients with normal SRY gene.[5]

Gonadectomy should be done when diagnosed because it is likely to cause malignancy. Fibrotic gonadal tissue may develop gonadoblastomas, disgerminomas and less frequently embryonal carcinomas. The risk of gonadoblastoma in female XY individuals can range from 25% to 75%. Risk increases with age. This risk increases to 50-70% at 30 years old, to 80% at 40 years old.[6,7]

The intellectual and physical development of swyer syndrome patients is normal, and there is no increase in any specific medical problem. Hormone replacement treatment should be started. Oocyte donation can be recommended to patients with pregnancy request, and there are no complications in pregnancy of these patients other than normal pregnancies. In the published literature there are many cases of patients with swyer syndrome giving live birth.[8-17]

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