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

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

Ceren SANCAR,* Nuri YILDIRIM,a,b Sevinj MAMMADOVA,* Ahmet Mete ERGENOĞLU,a Nedim KARADADAŞ a

aDepartment of Obstetrics and Gynecology, bDivision of Gynecologic Oncology, Ege University Faculty of Medicine, İzmir, Turkey

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 31 years old woman, married for 3 years, 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 oğlunun 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 jinekolojide poliklinikte başvurduğu ve hala kullanılmakta olduğu hormon replasman tedavisi başlandığı, primer amenoreye yönelik tahil yapılmadığı öğrenildi. Hasta yapılan tıbbi tedivinin sonucunda swyer sendromu tanıtıldı ve gonadektomi planlandı. bilateral laparoskopik salpenjektomi ve gonadektomi uygulandı. Hastanın hormon replasman tedavisine devam etmesi öncelikli idi. Gebelik istemi olan hasta literatürde oosit donasyonu ile sağlıklı doğum ile sonuçlanmış örnekler olduğu anlatıldı.

Anahtar Kelimeler: Geç tan; swyer sendrom; 46,XY gonadal dysgenezi

TJRMS 2018:2(3):120-3

Geliş Tarihi/Received: 15.07.2018 Kabul Tarihi/Accepted: 15.10.2018

Yazıma Adresi/Correspondence:
Ceren SANCAR
Ege University Faculty of Medicine, Department of Obstetrics and Gynecology, İzmir, TURKEY/TÜRKİYE
cerensancar@gmail.com

Published as a poster in the ‘19th World Congress on In Vitro Fertilization in conjunction with VI. Society of Reproductive Medicine and Surgery Congress’, October 2017, Antalya, Turkey.

Copyright © 2018 by Üreme Tıbbı Cerrahi Eğitim Araştırma ve Uygulama Vakfı

TJRMS 2018:2(3) 120
Swer syndrome (46 XY Gonadal 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 rudimentary 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 polyclinic 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 mU/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 salpingectomy 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.
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 gonadal 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.

Swyer Syndrome originates from a pathogenesis occurring 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
REFERENCES

1. Swyer Gl. Male pseudohermaphroditism: a hitherto undescribed form. British medical journal 1955;2(4941):709.

2. Berglund A, Johannsen TH, Stochholm K, Vium MH, Fedder J, Main KM, et al. Incidence, prevalence, diagnostic delay, and clinical presentation of female 46, XY disorders of sex development. J Clin Endocrinol Metab 2016;101(12):4532-40.

3. Michala L, Goswami D, Creighton S, Conway G. Swyer syndrome: presentation and outcomes. BJOG 2008;115:737-41.

4. Chrysostomou A. Swyer Syndrome in a Woman with Pure 46, XY Gonadal Dysgenesis, A Rare Disorder, Late Presentation: Case Report. Women’s Health & Gynecology 2017;3(3).

5. Keskin M, Savaş-Erdeve Ş, Kurnaz E, Çetinkaya S, Karaman A, Apaydın S, et al. Gonadoblastoma in a patient with 46, XY complete gonadal dysgenesis. The Turkish journal of pediatrics 2016;58(5):538.

6. Berg FD, Küzi R, Hinrichsen MJ, Zander J. Familial 46, XY pure gonadal dysgenesis and gonadoblastoma/dysgerminoma: case report. Gynecol Oncol 1989;32(2):261-7.

7. Morsy AH, al-Fadly A, Mokhtar S, el-Aasar EM, Farag TI. Swyer syndrome: an unusual presentation, Int J Gynaecol Obstet 1995;49(2):185-6.

8. Chen MJ, Yang JH, Mao TL, Ho HN, Yang YS. Successful pregnancy in a gonadectomized woman with 46, XY gonadal dysgenesis and gonadoblastoma. Fertil Steril 2005;84(1):217.

9. Bardeguez AD, De Ziegler D, Weiss G. Multifetal pregnancy in a gonadal dysgenesis mosaic. Obstet Gynecol 1990;76(3 Pt 2):502-4.

10. Kan AK, Abdalla Hl, Oskarsson T. Two successful pregnancies in a 46, XY patient. Hum Reprod 1997;12(7):1434-5.

11. Cornet D, Alvarez S, Antoine JM, Tibi C, Mandelbaum J, Plachot M, et al. Pregnancies following ovum donation in gonadal dysgenesis. Hum Reprod 1990;5(3):291-3.

12. Sauer MV, Lobo RA, Paulson RJ. Successful twin pregnancy after embryo donation to a patient with XY gonadal dysgenesis. Am J Obstet Gynecol 1989;161(2):380-1.

13. Ko PC, Peng HH, Soong YK, Chang SD. Triplet pregnancy complicated with one hydatidiform mole and preeclampsia in a 46, XY female with gonadal dysgenesis. Taiwan J Obstet Gynecol 2007;46(3):276-80.

14. Dirnfeld M, Bider D, Abramovica H, Calderon I, Blumentfeld Z. Subsequent successful pregnancy and delivery after intracytoplasmic sperm injection in a patient with XY gonadal dysgenesis. Eur J Obstet Gynecol Reprod Biol 2000;88(1):101-2.

15. Plante BJ, Fritz MA. A case report of successful pregnancy in a patient with pure 46, XY gonadal dysgenesis. Fertil Steril 2008;90(5):2013.e1-2.

16. Tulic I, Tulic L, Milic J. Pregnancy in patient with Swyer syndrome. Fertil Steril 2011;95(5):1789.e1-2.

17. Taneja J, Ogutu D, Ah-Moye M. Rare successful pregnancy in a patient with Swyer Syndrome. Case Rep Womens Health 2016;12:1-2.