

Swyer Syndrome – Gonadectomy Performed 17 Years after Diagnosis: Case Report

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ABSTRACT

Swyer syndrome (46, XY) is caused by abnormal sex differentiation during the embryonic period. It results in undifferentiated gonads and normal female genitalia at birth. It is usually diagnosed in adolescence because of delayed puberty and amenorrhea. Spontaneous breast development and menstruation are very rare situations. Because of the risk of gonadoblastoma and dysgerminoma in women with Swyer syndrome, bilateral gonadectomy is

recommended to be performed as soon as the diagnosis is made. Our patient case presents a rare situation of gonadectomy performed many years after the diagnosis was made. The woman was diagnosed at the age of 18. The patient had gonadal dysgenesis with a reduced number of ovarian follicles. The gonadectomy was performed successfully at the age of 35. Despite late diagnosis and gonadectomy, we didn't find any signs of developing malignancy even many years after the procedure.

Key Words: *Swyer syndrome, Gonadectomy, Germ cell tumor, Gonadoblastoma, Dysgerminoma*

INTRODUCTION

Swyer syndrome is pure gonadal dysgenesis caused by abnormal sex Differentiation [1]. Patients with this condition present the failure of gonadal progression leading to deficiencies in the production of testosterone and Müllerian-inhibiting factors and an incomplete masculinization. It results in a female phenotype with a female genital appearance at birth and present Mullerian structures in people with 46, XY Genotype [2]. The condition is usually diagnosed in adolescence because of amenorrhoea being a consequence of no hormonal or reproductive potential of the gonads. A high incidence of tumor such as gonadoblastoma and germ cell malignancies have been reported. Because of this risk, bilateral gonadectomy is recommended to be performed as soon as the diagnosis is made [1]. We present a case of a patient who was diagnosed at the age of 18, but the gonadectomy was performed 17 years later.

CASE REPORT

An 18 years old female presented with amenorrhea and poorly developed secondary sexual characteristics in December 1989. On general examination, she was 169 cm high, 72 kg weight and her body mass index (BMI) was 25,21 (kg/m²). There was only a medical history of appendectomy. In 1990 a karyotype study confirmed the presence of the 46, XY genotype and diagnosis of the Swyer syndrome. Since the age of 19, she was prescribed hormone replacement therapy (HRT) which caused an appearance of menarche. Since that time she had scanty but regular bleedings.

In the check-up ultrasound examination dimensions of the uterus were decreased and gonads were vestigial. Breast development was assessed as stage 1/2, while pubic hair growth was described as stage 4 on Tanner scale. The successful gonadectomy was performed in 2007, 17 years after the diagnosis. The patient had refused the proposed treatment before that time. Histopathological examination confirmed the absence of neoplasm. In follow-up ultrasound examinations there were no signs of any disturbing changes. In 2009 the patient was admitted to the clinic because of HRT intolerance. Levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) remained increased during the break in HRT (FSH 79.35 IU/l and LH 34,62 IU/l). The oral glucose tolerance test showed increased levels of glucose (97 mg/dl; 146 mg/ml after 2 h). She continued the treatment with HRT composed of estradiol and dydrogesterone (1 mg, 10

mg, q.d.) and with metformin (850mg, t.i.d.). In 2020 hormone levels were normal and the patient had good control of her glucose levels.

DISCUSSION

Swyer syndrome is a genetically determined disease that affects people with the 46,XY karyotype who have the female phenotype [3]. It was first described in 1955 by Swyer, who reported two cases of male hermaphroditism, with features not previously reported [4]. This syndrome has a frequency of once in 80,000 births [1]. The genetic examination of the patients with 46, XY karyotype reveals mutations in the SRY gene in 10-20% of patients and mutations in other genes, such as DHH, NR5A1 [5]. In our case patient underwent a genetic test which confirmed 46,XY karyotype, however no SRY mutation was detected.

Because of gonadal dysgenesis, the production of sex hormones during the prenatal period and also after birth is reduced. The lack of androgens causes the development of female external genitals. Virilization is not presented. The fallopian tubes, uterus, and vagina develop due to the lack of AMH secretion, but they do not always develop properly [6]. Patients with Swyer syndrome are also distinguished by increased height, which applies also to our patient, who measures 169 cm. According to the literature, the increased height may be dependent on the presence of the Y chromosome and may be related to genes responsible for increased height [7,8]. Early detection of Swyer syndrome and its inclusion in the diagnosis of primary amenorrhea is crucial due to the subsequent risk. Patients may develop malignant neoplasms of the gonads like gonadoblastoma or dysgerminoma. Due to the decreased estrogen levels osteoporosis and delayed puberty appears [1]. Our patient was diagnosed at the age of 19. Administration of HRT was crucial to prevent diseases caused by decreased levels of sex hormones.

Swyer syndrome treatment is based mainly on the use of estrogens. It is necessary to induce pubescence and the development of secondary sexual characteristics. After the puberty induction, cyclic estrogen and progesterone therapy is applied. The use of estrogens in young women also influences bone remodeling, which decreases the risk of osteoporosis [1, 8, 9]. The results of studies carried out on patients with 46, XY genotype suggest that hormone therapy may have a beneficial effect on the lipid profile and reduce the concentration of makers of the endothelial dysfunction. This may possibly slow down the progression of atherosclerosis [10].

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Primary amenorrhea	•lack of period by the age 16
FSH level in blood	•elevated FSH level
Genital ultrasound	•streak gonads •normal or underdeveloped Mullerian structures
Karyotype	•46, XY •46,XX/46,XY
α-fetoprotein, beta human chorionic gonadotrophin, lactate dehydrogenase	•elevated levels make it possible to confirm the presence of cancer in dysgenetic gonads before surgery
Gonadectomy	• as soon as possible after diagnosis of Swyer syndrome

Women with Swyer syndrome have a 15-35% risk of developing dysgerminoma or gonadoblastoma, which most likely come from undifferentiated gonadal tissue from poorly developed ovaries, therefore gonadectomy is recommended as soon as the diagnosis is made [1]. Literature data report that neoplasms may occur at any age. The youngest patient with neoplasm was a 9-month-old girl [11]. According to studies by Ken Y. Lin the presence of the 46,XY karyotype in women did not affect the mean age of malignant ovarian germ cell tumor development comparing to women with the XX karyotype [12]. However, most patients with Swyer syndrome developed gonadal tumors at a young age. According to research by May Manuel et al., the frequency of cancer in people with gonadal dysgenesis increases with age [13]. He recommends the removal of gonads in this group of patients before puberty. Other studies show that the risk of a malignant tumor in a dysgenetic gonad may increase from 5% to 50% as the patient ages [14,15]. It should be emphasized that our patient underwent gonadectomy 17 years after the diagnosis at the age of 35 and she did not develop cancer. However, this was not a legitimate medical procedure. We emphasize the need of performing the gonadectomy as young as possible. It is crucial to avoid the risk of tumor development. The case of the described patient who, despite 17 years from the diagnosis of Swyer syndrome, did not develop cancer suggests an influence of other factors than the presence of dysgenetic gonads and age on tumor development.

CONFLICTS OF INTEREST

No

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