Case Report

A Rare Case of Swyer Syndrome

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Abstract

Swyer syndrome is caused by abnormal sex differentiation during the embryonic period, resulting in incomplete intrauterine masculinization and undifferentiated gonads. The present case report describes a patient with Swyer syndrome associated with gonadoblastoma. At age of 16 years, this patient reported with primary amenorrhea at Gynae Department of the BIRDEM general Hospital. A physical examination revealed that the patient was at Tanner stage 4 with respect to axillary hair, breasts and pubic hair; she had normal vagina and a small cervix. As her examination findings revealed normal, she was referred to Endocrine outpatient (OPD) for further evaluation. Her karyotyping revealed 46XXY, abdominal ultrasonography revealed adnexal tumor in both sides. On laparotomy, complex tumor was found in both adnexal regions and both ovaries were resected and histopathology revealed gonadoblastoma. The patient was subjected to subsequent chemotherapy. She was treated with a combination of estrogens and progestogens to induce cyclical bleeding, which she discontinued after 3 years. She was lost to follow up for 16 years and again reported to endocrine OPD with irregular menstrual bleeding. Presence of any residual gonadal functional tissue was searched both biochemically and by imaging and the result was negative. Her menstruation was stopped by progestogens and which later on withdrawn successfully without any further onset of menstruation. In conclusion, this report describes an extremely rare case of Swyer syndrome with gonadoblastoma and spontaneous menstruation after a long period of discontinuation of hormone replacement treatment.

Key words: *Disorders of sex development, gonadoblastoma, Swyer syndrome.*

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Introduction

Disorders of sex development (DSD) are congenital conditions characterized by atypical chromosomal, gonadal or anatomical sex development.[1] In 2006, a consensus statement was issued that recommended the use of the DSD classification to replace various terms that are no longer used, such as pseudohermaphrodite, intersex and sex reversal.[2] Complete gonadal dysgenesis is characterized by a female phenotype, nonambiguous genitalia and presence of Müllerian derivatives, gonadal dysgenesis and a normal karyotype.[3] Swyer syndrome is a type of gonadal dysgenesis and a rare cause of DSD with an incidence of 1:80,000. This syndrome, which was described by Swyer in 1955, is caused by an error in sex determination during the course of embryogenesis. These people are with 46XY, have a female appearance, usually tall, typically raised as females, with typical female external genitalia, normal axillary and pubic hair and a normal uterus and Fallopian tubes. The gonads are dysgenetic strips, composed of only fibrous tissue; they do not exhibit hormonal function, gametogenesis or any structure that allows them to be identified as either ovaries or testes. Most Swyer syndrome patients first seek medical attention in adolescence for primary amenorrhea and/or the absence of secondary sex characteristics.[4] The gonads are at high risk for gonadal tumors, which are typically gonadoblastomas and/or dysgerminomas,[3,5] and they are usually surgically removed as early as possible. In addition to removal of streak gonads, treatment includes hormone replacement therapy from puberty onward. Patients with Swyer syndrome present with an incomplete masculinization due to deficiencies in the production of testosterone and Müllerian-inhibiting factors that result in the failure of gonadal progression.[5]

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Case Report

The patient first reported at the Gynae and Obstetric Department of BIRDEM General Hospital in the year 2005 at age of 16 years for amenorrhea. On physical examination, the patient's height was 158 cm and her axillary hair, breasts and pubic hair were consistent with Tanner stage 4. There was no genital ambiguity, vagina was normal.

Laboratory tests revealed: follicle-stimulating hormone (FSH) levels of 81 mIU/ml, luteinizing hormone (LH) levels of 22 mIU/ml, estradiol levels 21.00 ng/ml, serum testosterone 0.44 ng/ml unit. As a diagnosis of primary gonadal failure, the patient was refereed to Endocrine OPD for further evaluation. Further evaluation revealed normal thyroid function and serum prolactin and a karyotype of 46,XY. Ultrasonogram of abdomen revealed normal uterus, cervix and vaginal structures with adnexal tumor in both sides.

On laparotomy, complex tumor was found in both adnexal regions and both ovaries were resected and histopathology revealed gonadoblastoma. The patient was subjected to subsequent chemotherapy. A combined estrogens-progestogens pill was prescribed for regular menstrual bleeding.

Unfortunately, the patient lost to follow up. By this time, she get married and adjusted her life with her husband agreeing the condition of infertility. In August 2018, at her age of 29 years, the patient reported with irregular menstrual bleeding for 2 months on and off. History revealed she stopped taking hormones by herself since 2008. Her concern was the irregular menstrual bleeding in spite of any estrogen and progesterone replacement. Thorough physical examination revealed small uterus and nulliparous cervix. Biochemical tests in search for presence of any functional ovarian tissue revealed undetectable anti-Mularian hormone, estradiol levels 26.5 ng/ml, βHCG and alpha fetoprotein reveal normal. Her bleeding stopped with progesterone pill and no withdrwal bleeding started with dicontinution of oral progesterone. Bone densitometry tests revealed osteopenia; no abnormalities were detected at pelvic ultrasound and mammogram.

Discussion

Individuals with Swyer syndrome exhibit female phenotypes and are typically raised as girls; they usually report with primary amenorrhea and the absence of secondary sex characteristics.[4] The breast development among adolescents are consistent with Tanner stage 4.[6] Their vagina are usually found to be normal and cervix and uterus usually found to be small.[3]

Patients with suspected Swyer syndrome are first subjected to laboratory testing for diagnostic confirmation. These tests include measurements of serum electrolytes and FSH, LH, prolactin, TSH, free T_4, sex hormone-binding globulin, androstenedione, estradiol and testosterone.[1] In the present case, the patient presented with high LH, FSH and low estradiol level indicating primary gonadal failure. As a rule, Swyer syndrome patients exhibit low androgen levels and low or undetectable levels of androgen precursors. Cytogenetic analyses of these patients reveal a karyotype of 46,XY. These findings were consistent with the reports of the present case.

Differential diagnoses of patients with primary amenorrhea should consider various possibilities, including Mayer-Rokitansky-Küster-Hauser syndrome (XX), which is the second most common cause of this condition; this syndrome is characterized by varying degrees of Müllerian duct abnormalities and a rudimentary or absent uterus.[7] In addition, complete androgen insensitivity syndrome should be considered where XY individuals with primary amenorrhea had normal breast and vaginal development, but with no uterus.[8] Karyotyping should be performed in any individual with elevated gonadotropins and pubertal delay.

Once gonadal dysgenesis is confirmed, the tumor markers like alpha-fetoprotein, beta-human chorionic gonadotropin, lactate dehydrogenase and alkaline phosphatase should be tested; however, according to certain authors, these markers should only be measured in cases involving gonadal tumors.[1] Transabdominal ultrasound is the first-choice diagnostic imaging method for investigating such lesions, with magnetic resonance imaging restricted to cases in which ultrasound fails to clearly reveal Müllerian structures or urinary tract abnormalities.[1,2] In the case described in the current report, ultrasonography of abdomen revealed normal uterus, cervix and vaginal structures with adnexal tumor in both sides.

In cases of Swyer syndrome, after surgical removal of gonads, hormone replacement therapy to induce puberty

and the development of secondary sex characteristics is indicated.[5] Estrogen therapy should be administered as quickly as possible to ensure adequate bone mass formation and prevent reductions of bone mineral density that lead to osteopenia and osteoporosis. Cyclic estrogen and progesterone replacement is indicated until 50 years of age, when hormonal therapy may be discontinued.[1,2] In the case described in this report, hormonal treatment advised but patient did not follow the advice and lost to follow up.

Patients with Swyer syndrome should be subjected to surgery for gonad removal as soon as the diagnosis has been established because of their high risk for tumors such as dysgerminomas, which are the most common type of tumor found among these patients.[5] The objective of this surgery is to concurrently diagnose, stage and treat the patient. In the present case gonad removal surgery was performed and histopathology revealed gonadoblastoma which was later treated by chemotherapy and radiotherapy.

The survival rates of patients with XY gonadal dysgenesis and dysgerminoma largely dependent on tumor stage.[9] Reports regarding these patients largely reflect 5 years of follow-up but have seldom examined 10-year survival.[10,11] The described case is a rare situation of having a healthy life without any tumor recurrence after 14 years of diagnosis. The dilemma of the present case remains the spontaneous per-vaginal bleeding without any hormonal supplement.

In summary, the current case report is a rare case and needs attention to the need to subject women with primary amenorrhea to thorough investigation to exclude Swyer syndrome and other chromosomal abnormalities associated with high rates of incidence of malignant gonadal tumors.

Conflict of interest: Nothing to declare.

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