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Mixed Germ Cell Tumor Of Ovary And Clitoromegaly In Swyer’s Syndrome: A Case Report

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Abstract

Swyer syndrome is a type of pure gonadal dysgenesis correlating with 46 XY karyotype, primary amenorrhea, and female internal and external genitalia. It reveals a testicular differentiation abnormality.

A 16-year old girl admitted to our center with primary amenorrhea and abdominal mass. In spite of the absence of normal testis, clitoromegaly was noticed. Peripheral blood karyotype analysis showed 46 XY. Histopathology of the excised gonads determined mixed germ cell tumor in right ovary and streak left gonad without gonadoblastoma in left side.

In patients suffering from Swyer syndrome, high risk of gonadal neoplasia dictates early prophylactic gonadal excision to lengthen survival.

Keywords
gonadal dysgenesis, 46 XY, Swyer Syndrome, germ cell tumor

Introduction

Swyer’s syndrome as described in 1955 by Gim Swyer,(¹) is a kind of pure gonadal dysgenesis(²,³). Suffering persons revealing female phenotype with female external and internal genitalia have XY karyotype. Testicular differentiation is also abnormal(¹-⁴). Fibrous streaks usually replace the gonads(¹, ⁴). These patients usually present primary amenorrhea, tall or normal stature, normal vagina and cervix, hypoplastic uterus, absence of breast development and vice of secondary sexual characteristics(¹-⁴).

Enhanced gonadotropins and hypoplastic gonads with no germ cells are most often detected(⁵).

The exact incidence is unknown but is estimated at 1:100000 (⁴). The malignancy risk in such patients is almost 30% and the most common type detected is gonadoblastoma and dysgerminoma. Gonadoblastoma developing bilaterally is usually hormone dependent with estrogen and androgen(⁶, ⁷). Early diagnosis of Swyer Syndrome is more than principal due to increased risk of malignancy and decreased ability of survival lengthen by surgery and chemotherapy(⁴). In the present study we report of a young girl with Swyer syndrome with a large abdominal mass which was determined as a mixed germ cell tumor of dysgerminoma and embryonal carcinoma at stage III c on her right ovary.

Case Presentation

A 16-year old girl was admitted to our center in November 2008 with the chief complaint of primary amenorrhea and abdominal mass. She was 162 cm height and weighed 60 kg. She noticed her clitoromegaly since 5 years of age. On physical examination poor breast development (Tanner’s stage I, II) and clitoromegaly with clitoral size of 4 cm were distinguished. Her axillary and pubic hairs were sparse. The abdomen
was soft and non-tender with an abdominopelvic large mass above umbilicus. Under anesthesia examination revealed that vaginal and cervix length was normal and uterus was palpable in rectovaginal exam. Based on primary amenorrhea and abdominal mass, peripheral blood karyotype analysis was performed and revealed a genotype of nonmosaic 46 XY. The serum levels of Leutinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) as well as tumor markers were out of normal range, but Carcino embryonic Antigen (CEA) was within reference range.

The report on pelvic ultrasonography indicated a large lobulated solid mass measured 16 x 9 cm in pelvis with extension to abdomen.

Computerized Tomography (CT) scan of abdomino pelvic confirmed normal urinary system and a solid heterogen mass with the origin from posterior bladder to umbilicus. Abdomino pelvic Magnetic Resonance Imaging (MRI) showed CT scans findings and a rudimentary uterus with no documented testis tissue and right kidney hydronephrosis. (Figure 1)

The patient underwent laparotomy and peritoneal washing. Ovarian mass measured 20x20x5cm in right adnex and left streak gonad were detected. Right gonad tumor extended to the left side of pelvis, left streak gonad, para aortic and bilateral lymph nodes were excised. No gonadal lesion was detected in left adnex. Infantile uterus was preserved. The histopathology of the removed gonads confirmed mixed germ cell tumor including dysgerminoma (Figure 2) and embryonal carcinoma (Figure 3) in right gonad, tumoral internal iliac lymph node of right side and positive peritoneal cytology with tumor classification stage III C according to FIGO grading system. Ascitic fluid was negative for malignancy.

Subsequently, adjuvant chemotherapy including 4 cycles of Bleomycin, Etoposide and Cisplatin (BEP) was administered after surgery. Tumor markers such as CA-125, Alpha fetoprotein and β hCG returned to normal range after one course of chemotherapy.

In the sixth month after surgery and chemotherapy, clinical examination and lab tests as well as imaging results showed the patient being tumor free.

The patient inclining to be a man was referred to a team consisting of endocrinologist, psychiatrist and plastic surgeon for consultation.
Discussion

Swyer syndrome as a 46 XY gonadal dysgenesis correlates with primary amenorrhea, normal or tall stature, female internal genitalia tract and external genitalia, hypoplastic and streak gonads and hypoplastic uterus in phenotypic females \(^8\), \(^9\). Deletion of short arm Y chromosome including SRY or other genes’ mutation leading to inhibition of SRY function or mutation in SRY function are assumed to be the etiology of gonadal dysgenesis in Swyer syndrome \(^9\).

To date SRY mutation or deletion is described as the cause of 46 XY pure gonad dysgenesis in just 20% of cases and normal SRY are detected in 80%. Female phenotype with XY karyotype having mullerian system, normal levels of female testosterone and vice of sexual development could be considered as Swyer syndrome \(^4\). Gonadotropins are increased in such patients \(^5\). The patients with Swyer syndrome are at high risk of ovarian cancer with most histotypes of gonadoblastoma and dysgerminoma \(^10\)-\(^12\). Germ cells of dysgerminoma could be the source of hCG. \(^4\). In the patients who are diagnosed as the Swyer syndrome cases, bilateral gonadal excision is highly recommended which could be followed by chemotherapy to prevent malignancy \(^2\)-\(^4\), \(^13\). Malignant tumors of ovaries in girls and teenagers have demonstrated 75% of affected cases by left ovary involvement with most frequent of dysgerminoma (56%) \(^14\). Correlation of two varied histotypes in one patient is unusual \(^10\), \(^11\).

In our 16-year old patient with complaint of primary amenorrhea and abdominal mass, Karyotype analysis was performed. Physical examination of the patient revealed poor breast development and Clitoromegaly with Clitorol size of 4cm. Based on her symptoms and karyotype analysis of 46 XY, Swyer syndrome was diagnosed.

Tumor markers and hormonal assessment showed increased serum levels of LH, FSH, CA-125, Alpha- FP, β hCG and CA19-9. 17Hydroxy progesterone was increased, ACTH test was done by cosyntropin and negative for Congenital Adrenal Hyperplasia (CAH). CA-125 increase was caused by ascitis and peritoenal stimulation. Embryonal carcinoma caused AFP rise. In laparotomy, right ovary which was affected by tumor with streak left gonad, paraaortic and bilateral lymph nodes were removed. Histopathology of excised right gonad determined mixed germ cell tumor of dysgerminoma and embryonal carcinoma, tumoral right internal iliac lymph node and positive cytology of peritoneum which led to put the patient at stage IIIc based on FIGO staging system. Adjuvant chemotherapy was administered following surgery. Although correlation of two different histotypes in one patient has been rarely reported \(^10\)-\(^12\), but mixed germ cell tumor of dysgerminoma and embryonal carcinoma was detected in our case. Clitoromegaly is not a usual sign in Swyer syndrome while it was found in our patient. Despite detection of germ cell tumors in early stage, our patient was diagnosed at stage IIIc. However Swyer patients undergo gonadectomy, but they could have normal sexual relations as well as Invitro fertilization followed by pregnancy with conception by donor oocytes and successful delivery \(^15\)-\(^17\). Hormone replacement therapy is suggested at the puberty onset to prevent complications of chronic estrogen lack and to induce female sexual characteristics, although breast development and secondary sexual characteristics tends to be poor \(^1\), \(^2\). Our patient tended to be a man therefore estrogen and progesterone replacement therapy weren’t administered and she was referred to a team comprising of a psychiatrist, endocrinologist and plastic surgeon for more evaluation. In summary, Swyer syndrome as a rare genetic disease is important to be diagnosed and remedied early due to increased risk of gonadal malignancy. Inspite of detection of germ cell tumors in early stage it could rarely be determined at a later stage. Early surgical excision of gonads which could be followed by chemotherapy will lengthen survival.
Mixed Germ Cell Tumor Of Ovary, S.Aminimoghaddam, et. al.

References