Long-term Disease Free and Successful Pregnancy in a Woman with Gonadal Dysgenesis and Malignant Germ Cell Tumor

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Abstract

Objective: To report a case of long-term disease free and successful pregnancy after fertility sparing staging surgery with adjuvant chemotherapy in a 46,Xy gonadal dysgenetic with malignant germ cell tumor.

Materials and methods: A case report from a university hospital about a 19-year-old female with 46,XY karyotype (Swyer syndrome). The patient underwent bilateral gonadectomy and staging with uterus preservation. Six course adjuvant chemotherapy with VBP (Vinblastin, Bleomycin, Cisplatin) was given. The case got pregnant through IVF- embryo donation. Disease free period and successful pregnancy is reported.

Results: After treatment the patient is free of the disease after 11 years follow-up. She underwent in vitro fertilization treatment with oocyte donation and gave birth to a healthy ch.

Conclusion: Improved multimodality treatment, allowance for consideration of fertility options for some women with gynecologic cancers. Since major concern in women with XY gonadal dysgenesis is ovarian malignancy, even with stage II dysgerminoma hysterectomy may not be required in some cases considering the opportunity for childbearing with the use of embryo transfer.

Keywords: gonadal dysgenesis, dysgerminoma, adjuvant chemotherapy, successful pregnancy

Introduction

Pure gonadal dysgenesis is defined as the absence of differentiated gonads but with normally developed internal and external genitalia. The XY type is named Swyer after G.J.Swyer, the first person, described the syndrome (1). A major characteristic of a dysgenetic gonad carrying a Y chromosome is its propensity towards malignancy (2). Although successful pregnancies have been reported in women with Swyer syndrome (12_22) and there is a report of a 46XY female with malignant germ cell tumor, in early stage (IA) without receiving chemotherapy (3), we report the first case with advanced stage bilateral gonadal dysgerminoma whom underwent chemotherapy and successful term pregnancy with donation.

Case Report

A 19-year- old female (168 cm height and 65 kg

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weight) was referred to our hospital for primary amenorrhea and a histopathology report of dysgerminoma in January 2000. Prior to referring she had undergone a laparotomy procedure in a non academic hospital due to primary amenorrhea, lower abdominal pain and pelvic mass. According to the operation note, there was an infantile uterus, bilateral adnexal masses with extension to cul-de-sac and pelvic side walls adhesions. Only suboptimal mass resection and pelvic adhesion biopsies had been performed.

No hormonal, tumor marker or karyotype assessment was done before that surgery. After referring to our department further investigation was performed. Growth and secondary sexual characteristics were found to be normal on physical examination. Pelvic exam and ultrasound revealed bilateral pelvic masses. Computerized tomography scan revealed pelvic mass with pressure effect on right urethra, no ascites and no lymphadenopathy. Blood chromosome analysis demonstrated 46XY. Hormonal assays revealed elevated serum FSH (80mIU) and LH (48mIU) concentration and normal E_2 level. Histopathological review confirmed dysgerminoma diagnosis. Till preparation of mentioned paraclinical findings, she received one cycle chemotherapy with BEP (bleomycin, etoposide, cisplatin) regime. Then she underwent optimal debulking surgery (complete resection of bilateral gonadal and cul de sac masses, infracolic omentectomy with paraaortic and bilateral pelvic lymphadenectomy) with preservation the uterus in February 2000. Histopathologic report of the second surgery revealed necrotic tumoral tissue in right (8×6×2cm) and left (5×4×2) ovary. Omentum and lymph nodes were free of tumor and tumor was classified as stage IIC. After staging surgery, adjuvant chemotherapy consisted of 6 cycles of PVB (Cisplatin, Vinblastine, Bleomycin) was administered. Vinblastine was substituted for Etoposide due to hypersensitivity reaction at pre-operation chemotherapy. After that, she was on hormone replacement therapy (HRT) treatment and had menstrual flow. Seven years after her initial presentation, the patient and her husband sought after pregnancy using oocytes donation. Oocyte retrieval in the donor yielded 7 oocytes, 5 of which were fertilized by conventional in vitro fertilization using sperm obtained from the patient's husband. Three third-day embryos were transferred, and the patient conceived a twin pregnancy. One of the fetuses was missed at the second month. Because of preeclampcia, she underwent a cesarean delivery of a normal male infant (3000 grams weight) with good apgar score. She is receiving estrogen and progesterone and has periodic menstruation. After 11 years of her tumor treatment, she is healthy, has a 4-year-old son and trends to try second pregnancy.

Discussion

Swyer syndrome (pure gonadal dysgenesis) is a disorder of sexual differentiation characterized by mutations of the SRY gene responsible for male sex characteristics. This gene is located on the Y chromosome (p11.31); mutations at this site result in phenotypic females with mullerian external genitalia, underdeveloped (streak) internal gonads and amenorrhea (4).

Clinical diagnosis is difficult and usually made at later ages and as a result of certain clinical presentations such as evaluation of primary amenorrhea and possible lower abdominal pain.

However, early diagnosis is important because of the risk of gonadal malignancy, the early institution of estrogen therapy for induction of puberty and to allow for adequate hormone replacement to improve bone mineral density (5).

The exact incidence of the condition is unknown but is estimated to be 5: 100 000 births (6).

Female with pure gonadal dysgenesis (46,XY) have a high predisposition to gonadal tumors, such as gonadoblastomas and gonadal dysgerminomas. Gonadoblastomas are benign tumors with no metastatic potential; however they can be precursors to germ cell malignancies, such as dysgerminomas, which is the most commonly associated malignancy Dysgerminomas are the most common malignant germ cell tumor occurring in the ovary and the majority of cases (75 percent) arise in adolescents and young adults, in whom they account for about one-third of all ovarian malignancies. Approximately 5% of dysgerminomas are discovered in phenotypic females with abnormal gonads (7,8).

Most report that tumors occur in approximately 30% of all females with pure gonadal dysgenesis but some claim that the risk is as high as 75% (9). Whereas the risk of malignancy increases with age, bilateral gonadectomy must be done as soon as the diagnosis is made.

In patients with pelvic mass and primary amenorrhea, preoperative diagnosis is important in order to avoid multiple surgical procedures such as our patient, whom underwent two procedures.

The most frequently used chemotherapeutic regimen for germ cell tumors is BEP (Bleomycin, Etoposide, Cisplatin). In the past, PVB and VAC (Vincristin, Actinomycin, Cyclophosphamide) were commonly used but are rarely prescribed at present. Our case received PVB (due to hypersensitivity reaction to Etoposide) and had complete response without recurrence after 11 years. In an analysis of 148 women with malignant ovarian germ cell tumors (OGCT), 113 of whom received platinum-baced chemotherapy, five-year survival rates, were: 100%, 85%, 79%, and 71% for I, II, III and IV stages respectively. (10).

Although women with Swyer syndrome are considered sterile, but pregnancies can be obtained in the latter with the use of allogenic oocytes (11) even in patients with malignant tumors in their gonads(3). Therefore the immature uterus must be preserved during the procedure of staging and long-term hormone replacement therapy is necessary in the maintenance of endometrial cavity.

The first pregnancy and delivery by ovum donation was reported in 1984. So far, there are reported cases in the literature of pregnancies in females with the 46, XY karyotype (3,12-22).

This is the first case report of successful pregnancy in a female with Swyer syndrome and advanced-stage malignant germ cell tumor (dysgerminoma) who received adjuvant chemotherapy. The case reported by Chen et al., was in the early stage and did not receive adjuvant chemotherapy (3).

In summary, we presented a female 46, XY Swyer syndrome with stage IIc dysgerminoma, who underwent debulking staging surgery with uterus preservation and adjuvant chemotherapy. After that she had a successful pregnancy with oocytes donation and IVF. This case is a combination of the art of oncologic and assisted reproductive techniques.

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