Successful Pregnancy in a 46, XY Gonadal Dysgenetic Woman Following Adnexectomy and Chemotherapy

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1. Abstract

1.1. Purpose: To describe a case of successful pregnancy following a unilateral adnexectomy and adjuvant chemotherapy in a 46, XY gonadal dysgenetic woman with a unilateral gonadoblastoma and endodermal sinus tumor.

1.2. Method: A case report was about a 17-year-old female with a 46 XY karyotype who underwent unilateral adnexectomy and adjuvant chemotherapy.

1.3. Results: The patient was free from tumor recurrence after 18 years’ follow-up. A successful pregnancy was achieved after oocyte donation and ICSI.

1.4. Conclusion: Following chemotherapy, 46, XY gonadal dysgenetic women with gonadoblastoma can maintain a normal pregnancy and delivery.

2. Introduction

Successful pregnancies in 46, XY patients with pure gonadal dysgenesis have been reported before, but so far there have been few reports of pregnancy in 46, XY patients with gonadal malignancy [1]. The occurrence of pregnancy in individual with malignant germ cell tumors who had a 46, XY karyotype has been reported [1]. However, it is important to note that in this particular case, the patient just underwent bilateral gonadectomy and did not get any chemotherapy treatment [1]. Here we present the case of a pure 46, XY gonadal dysgenetic female in whom an emergency left adnexectomy was performed due to the presence of rupture and hemorrhage of left gonadoblastoma and endodermal sinus tumor. After the operation, five cycles of chemotherapy were administered. After oocyte donation and ICSI, a successful pregnancy was obtained.

3. Case Report

A 17-year-old female patient was referred to a nearby hospital due to the presence of acute abdominal pain. Pelvic ultrasonography showed a small uterus (2.5 cm×2 cm×2 cm), presence of left adnexal tumors and pelvic hemorrhage. Based on the presence of tumor rupture and abdominal blood, the physician proceeded with an urgent laparotomy procedure. Exploratory laparotomy revealed an infantile uterus (3 cm×3 cm×2 cm), two normally appearing fallopian tubes, left adnexal tumors (7 cm×6 cm×5 cm) with a cauliflower-like laceration and blood oozing from the surface, and a normal right ovary. There was no observed evidence of local or distant metastases detected during the surgical procedure. Conse-
sequently, a left adnexectomy was done, and pathologic examinations revealed a gonadoblastoma accompanied by an endodermal sinus tumor and infiltration (1.3 cm) on the left fallopian tube. The patient and their family declined to undergo contralateral annex removal. After surgery, adjuvant chemotherapy was performed with 5 cycles of cisplatin, etoposide, and bleomycin. No evidence of recurrence was noted after a follow-up of 18 years.

Three years after chemotherapy, the patient still had no signs of menarche. Blood chromosome analysis demonstrated 46, XY. The patient received cyclic hormonal replacement therapy thereafter to achieve normal pubertal developments.

She first consulted for fertility concerns in our unit at the age of 29 years. Blood investigations done just prior to our first consultations showed the following results: low-normal anti-Müllerian hormone (AMH) level, <0.060ng/ml; follicle-stimulating hormone (FSH), 100.9 IU/L; luteinizing hormone (LH), 53.72 IU/L; estradiol (E2), 10.03 pg/mL; testosterone (T0), 33.0 ng/d; progesterone (P), 0.53 ng/mL, and prolactin (PRL), 12.54 ng/mL. Vaginal ultrasound showed an anteflexed uterus (uterine longitudinal diameter 66mm, anteroposterior diameter 27 mm, and transversal diameter 36mm), the left adnexa was absent, and the right adnexa was not clearly visualized. The patient and her husband were counseled regarding the donor cryopreserved oocytes program option.

For this XY gonadal dysgenesis patient, two fresh oocytes were donated to her four years after her first consultation. Sperm analysis of her husband showed a total sperm concentration of 4×10^6 /mL, with 25.9% motility. Both oocytes underwent intracytoplasmic sperm injection (ICSI) with frozen sperm from her husband (day 0). Both oocytes showed two pronuclei to be considered normally fertilized (day 1). One developed into a blastocyst (day 5) and was frozen.

The daily dose of oral estradiol tablets (Femoston, Abbott Biologicals B.V.) was 4 mg for seven days, followed by 6 mg for five days. On day 12, serum LH, E2, and P levels, as well as an ultrasound examination (LH, 19.30 IU/L; E2, 211.0 pg/mL; P, < 0.05 ng/mL and endometrial thickness, 1.1 cm) and 10000 IU human chorionic gonadotropin (hCG) was administered. From day 13, progesterone was administered both orally (20mg/day; Femoston, Abbott Biologicals B.V.) and vaginally (90 mg/day; 8% Crinone vaginal gel, Fleet Laboratories Limited) along with oral estradiol tablets 6 mg (Femoston, Abbott Biologicals B.V.). Blastocyst transfer was conducted five days after progesterone administration.

The level of serum β-hCG was 781.90 mIU/mL on the 12th day after embryo transfer (ET). Four weeks after ET, the intrauterine presence of a gestational sac was noted during ultrasound examination. A month later, there was a fetus with registered heart action. The pregnancy was continuously monitored (Figure 1). A healthy baby with an Apgar score of 10 was delivered by cesarean section at the 39th week of gestation. During the cesarean section, low amniotic fluid (<500 mL) and a short umbilical cord (<25 cm) were found. The cesarean delivery was performed to remove the remaining lateral gonad concurrently (Figure 2). Histopathological examination of the gonad showed fibrous connective tissue hyperplasia with collagen hyperplasia and calcificatio
4. Discussion

Gim Swyer first described Swyer’s syndrome in 1955. Affected individuals have an XY karyotype but have female external and internal genitalia [2]. Pure gonadal dysgenesis is an uncommon condition. The incidence of pure gonadal dysgenesis syndrome is approximately 5 per 100,000 infants. Most patients are diagnosed for the first time during puberty, when they present with primary amenorrhea.

Females with pure gonadal dysgenesis exhibit a notable inclination towards the development of gonadal tumors, specifically gonadoblastomas and gonadal dysgerminomas [3]. Because of the high risk of neoplastic transformation, it is generally recommended that dysgenetic gonads undergo gonadectomy promptly upon diagnosis [4]. Additionally, a subset of patients have unfortunately experienced the development of malignant degeneration in either one or both of their gonadal glands at the time of diagnosis. Successful pregnancies in 46, XY patients with pure gonadal dysgenesis have been reported before, but so far there have been few reports of pregnancy in 46, XY patients with gonadal malignancy [1]. We are the first to present the results of 46, XY women’s pregnancy following adjuvant chemotherapy. At that point, the patient presented with urgent medical symptoms, including tumor rupture and pelvic hematoma, necessitating the need for immediate surgical intervention. Due to the absence of chromosome examination during the aforementioned period, the patient and her family declined to undergo contralateral annexation and hysterectomy procedures in order to maintain her fertility. After a complete discussion between doctors and the patient as well as the families, adjuvant chemotherapy was administered due to the highly malignant nature of the yolk sac tumor and the infiltration (1.3 cm) on her left fallopian tube. As to the NCCN guidelines pertaining to malignant germ cell tumors (MGCTs) [5], it is recommended that chemotherapy be administered following surgical intervention for all MGCT, with the exception of Stage I dysgerminoma or Stage I Grade 1 immature teratoma. The BEP (cisplatin/etoposide/bleomycin) regimen is currently the primary chemotherapy for malignant germ cell tumors. Fortunately, the patient achieved a pregnancy uneventfully thereafter and has been free from tumor recurrence until now.

It is recommended that pure XY patients need continuous hormone therapy, especially after gonadectomy. This intervention aims to address the deficiency of sexual hormones and promote the onset of regular menarche in individuals with pure gonadal dysgenesis, hence serving as a preventive measure against malignancies [4]. Furthermore, hormones can prevent osteoporosis and cardiovascular diseases [6, 7]. Frequently, larger hormone dosages are required to treat XY females compared to those used to treat normal menopausal women. If the pregnancy is desired, hormone therapy will prepare the uterus for embryo implantation and should be maintained throughout the first trimester.

In conclusion, we describe a case of successful pregnancy following a unilateral adnexectomy and adjuvant chemotherapy in a 46, XY gonadal dysgenetic woman with a unilateral gonadoblastoma and endodermal sinus tumor. A successful pregnancy was achieved after oocyte donation and ICSI. The patient was free from tumor recurrence after 18 years’ follow-up.

References