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Case Report /Vaka Raporu

Fertility preservation strategy in advanced ovarian cancer: A case repor

İlerlemiş over kanserinde doğurganlığı koruma stratejisi: Bir vaka raporu

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ABSTRACT

Ovarian germ cell tumors arise from the primary germ cells located within the ovary. These tumors may manifest as either non-malignant, exemplified by mature teratomas, or malignant, dysgerminomas, yolk sac tumors, and mixed germ cell neoplasms. In this case presentation, we describe a patient who, at the age of 24, underwent a fertility-preserving approach (egg and embryo freezing) due to the suspicion of malignancy in the remaining ovary during routine check-ups, while in remission from an immature teratoma (grade 2). The patient received in vitro fertilization treatment, and a random-start ovarian stimulation protocol was applied with GnRH antagonist and aromatase inhibitor. Subsequently, egg retrieval and embryo freezing procedures were performed. After the removal of the suspected cyst and left salpingectomy operation six months later, the patient underwent a frozen embryo transfer. Pregnancy and live birth occurred for a woman who had been in ovarian cancer remission for ten years. This case report demonstrates that patients with malignant ovarian germ cell tumors can become pregnant and give birth if they wish.

ÖZ

Over germ hücreli tümörler, ovaryumlarda bulunan primer germ hücrelerinden kaynaklanır. Bu tümörler ya non-malign (matür teratomlar) ya da malign (immatür teratomlar, yolk sac tümörleri ve karışık germ hücreli neoplazmlar) olarak ortaya çıkabilir. Bu vaka sunumunda, 24 yaşında, over immatür teratom (grade 2) remisyonunda olan ve kontrolleri sırasında overde malignensi şüphesi olan multiloküle, multiseptal kistik bir yapının görülmesi nedeniyle doğurganlığı koruyucu yaklaşım (yumurta ve embriyo dondurma) uygulanan hastayı tanımlıyoruz. Hastaya tüp bebek tedavisi, GnRH antagonisti ve aromataz inhibitörü ile rastgele başlangıçlı over stimülasyon protokolü uygulandı. Sonrasında yumurta toplama ve embriyo dondurma işlemi yapıldı. Şüpheli kistin çıkarılması ve sol salpenjektomi operasyonundan altı ay sonra hastaya dondurulmuş embriyo transferi yapıldı. On yıl boyunca over kanseri remisyonunda olan bir kadın için gebelik ve canlı doğum gerçekleşti. Bu vaka raporu, malign over germ hücreli tümörü olan hastaların istemeleri halinde gebe kalabileceklerini ve doğum yapabileceklerini göstermektedir.

ARTICLE INFO/MAKALE BİLGİSİ

Key Words: Immature Teratoma, Fertility Preservation, Pregnancy, Live Birth.

Anahtar Kelimeler: Olgunlaşmamış Teratom, Doğurganlığın Korunması, Gebelik, Canlı Doğum.

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INTRODUCTION

Ovarian germ cell tumors originate from the primordial germ cells found in the ovary. These tumors can either be non-cancerous, as in the case of mature teratomas, or malignant, encompassing immature teratomas, dysgerminomas, yolk sac tumors, and mixed germ cell neoplasms (1). The more common of these tumors is mature ovarian teratoma, also known as dermoid cyst. Immature ovarian teratoma is uncommon, comprising less than 1% of all ovarian teratomas (2). Patients typically present with an abdominal mass and range in age from 1-58 years old. Alpha-fetoprotein (AFP) is slightly increased in some people. These tumors often have a large median size of 18 cm, are unilateral and have zones of necrosis and bleeding. In rare cases, a developed cystic teratoma may be discovered in the ovary on the other side (3, 4).

According to current recommendations, young patients with early-stage malignant ovarian germ cell tumors (MOGCT) localized to one ovary can undergo fertility-sparing surgery (5). In this case, immature teratoma and

adult cystic teratoma—both rare—coexist. Therefore, we believe that this can add to the body of knowledge regarding fertility preservation strategies.

CASE PRESENTATION

A 24-year-old married woman who had never given birth applied to our clinic with the desire to have a child. She was admitted to the hospital in 2012 with the complaint of abdominal pain. The patient had a right adnexal 12 cm mass and 5 cystic lesions of various sizes in the left ovary. After right salpingo-oophorectomy, right ovarian immature teratoma was reported pathologically as high grade (grade 2).

The left adnexal cysts were excised. Appendectomy, omentectomy and lymphadenectomy were performed. Then, the patient received 4 cycles of etoposide and cisplatin combination chemotherapy. Segmentectomy was performed in the 6th and 7th segments of the liver in 2013 due to liver metastasis. One year later, because a lobulated cystic structure was detected in the left ovary, cyst excision was performed and its pathology was reported as mature cystic teratoma.

In 2021, the patient applied to our center for preoperative oocyte and embryo freezing in order to protect her fertility after her ultrasonography revealed a multiloculated, multiseptal cyst (110x70 mm), which was suggestive for cancer. Following basal pelvic ultrasound, hormonal evaluation was performed. IVF treatment began with a random start-over stimulation protocol with GnRH antagonist and aromatase inhibitor. The patient's basal hormone panel is as shown in Table 1.

Oocyte pick up (OPU) was performed on the 12th day of stimulation under the guidance of transvaginal ultrasound 36 h after 10,000 IU human chorionic gonadotropin (hCG) injection to trigger ovulation. All ultrasonographically identifiable follicles larger than 14 mm were aspirated. Three metaphase II (MII), 1 metaphase I (MI), and 1 germinal vesicle (GV) oocytes were collected. One MII, 1 MI, and 1 GV oocyte were frozen and stored. ICSI was performed on two MII oocytes. The sperm parameters of the husband were as follows: the volume was 6.5 ml, the number was 15x106, and the motility was 60% (a+b motility). The patient's two oocytes, which underwent ICSI, were fertilized on the 1st day. On the 3rd day, two embryos of grade 2 were frozen and stored (6). After the follow-up and treatment in the obstetrics and oncology clinics, embryo transfer eligibility was given to the patient 6 months after the excision of the suspected cyst and left salpingectomy operation. Frozen embryo transfer was planned for the patient and an endometrial preparation protocol was performed according to hormonal replacement therapy (HRT). One embryo was thawed (Figure 1) and transferred to the patient.

Endometrial thickness was measured as 12 cm. Luteal support was given by vaginal, patch and oral progesterone treatment after embryo transfer. On the 12th and 14th days, the levels of hCG were found to be 238 mIU/ml and 655 mIU/ml, respectively. After five weeks and six days of pregnancy, a vaginal ultrasound revealed the presence of a fetal heartbeat. The patient was delivered by cesarean section at 38 weeks and 6 days in Ankara Bilkent City Hospital. A healthy baby boy with an Apgar score of 10-10, weighing 3750 kilograms, was born without any obvious abnormality.

Table 1. Patient's basal hormone values. The values in parentheses are the normal reference ranges.

Characteristics	*Hormone values*
AMH (µg/L)	*4.84*
Basal FSH (IU/mL)	*7.7 (3- 9)*
Basal E_2 (ng/ml)	*62 (27 – 161)*
E_2 level on ovuation trigger day (ng/ml)	*336*
Total dose of gonadotropin	*2925*
Progesterone on the day of oocyte pick up (mg)	*1.31*

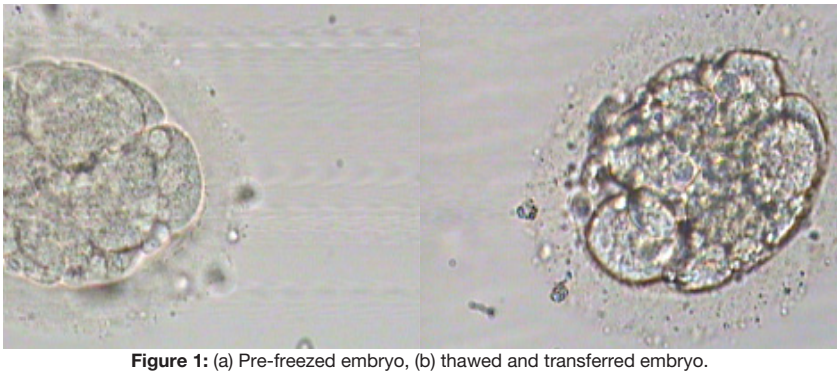

Figure 1: (a) Pre-freezed embryo, (b) thawed and transferred embryo.

DISCUSSION

Infertility is a common side effect of cancer treatment and current medications may have harmful effects on gamete activity. Approximately 90% of men and women who are diagnosed with cancer may be at risk of irreversible infertility depending on the location and stage of the illness, the patient's age, and the type of therapy (7). Postoperative chemotherapy is used to treat almost all MOGCT types, with the exception of stage I dysgerminoma and stage I grade IA immature teratoma. The survival rate in MOGCT cases has dramatically increased with chemotherapy treatment Most women with MOGCT may want to preserve their fertility because its occurrence is highest in women who are fertile. The afflicted ovary is surgically removed as part of the standard management of MOGCT and adjuvant chemotherapy is given. Even for women with advanced cancer, overall survival rates are favorable due to the susceptibility of these tumors to platinum-based chemotherapy. The gold standard has been determined to be fertility-sparing surgery (unilateral salpingo-oophorectomy and uterine preservation) for patients with early-stage illness (8). In a recent multivariate analysis, Jorge et al. found that 90% of patients with immature teratoma were between the ages of 18 and 39 years. Three-quarters of these patients were in an early stage and might be treated conservatively with chemotherapy and fertility-sparing surgery. Age, stage, and grade are unfavorable prognosis indicators (9).

There are now a few options for fertility preservation (FP), but two tried-and-true procedures—oocyte and embryo cryopreservation—require ovarian stimulation (10). It has been suggested that the technique randomly starts ovarian stimulation in patients undergoing FP, independent of the menstrual cycle phase. For patients who need to begin gonadotoxic anticancer therapy immediately, this regimen is helpful (11). The random-start controlled ovarian stimulation (COS) in the context of FP indicated by a cancer diagnosis was linked to a shorter time between ovarian stimulation and oocyte retrieval, according to a systematic review by Danis et al.. Additionally, the yield of mature oocytes and cryopreserved embryos was comparable to conventional stimulation protocols (12). Some studies have shown that the total number of oocytes collected does not change. However, there is inconclusive information on the oocyte quality, pregnancy rate, and live birth rates in these randomly initiated COS cycles (13).

It is essential to keep educating female patients about fertility preservation options because many of them may experience a reduction in their window of fertility after therapy. As early in the diagnostic procedure as possible, patients and families should receive a personalized assessment of the risk of gonadotoxicity and information regarding fertility preservation (14).

Numerous studies have demonstrated that despite the use of chemotherapy and surgery, a successful pregnancy is still achievable following treatment for an immature teratoma (15). In their retrospective analysis, Alwazzan et al. demonstrated that 10 pregnancies—eight of them following chemotherapy—came from 12 of 27 patients who attempted to conceive. To determine recurrence rates and salvaging options, long-term follow-up of patients with immature teratoma treated conservatively is crucial (16). In this case, we report a pregnancy that occurred ten years after a unilateral salpingo-oophorectomy with a diagnosis of an immature teratoma and chemotherapy. Due to liver metastases, our patient also underwent liver resection. She was diagnosed with mature cystic teratoma in the left ovary. Fertility-sparing surgery and a multidisciplinary approach are advised for these individuals due to the rarity of the illness and the significance of early detection of malignant ovarian tumors in improving patient survival.

Pregnancy was achieved by embryo transfer after the freeze thaw cycle of a patient with liver metastasis who received surgery and chemotherapy treatment for immature cystic teratoma. Achieving successful pregnancies with a good treatment protocol in infertile patients is satisfactory for both patients and clinicians. Fertility-preserving treatments in this field are very important.

Ethics approval

This study was written with the patient's ethical approval.

Conflict of interest

No author has any potential conflict of interest.

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