Giving Birth After Fertility Sparing Treatment of Embryonal Carcinoma Figo III C: Case Report and Literature Review

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ABSTRACT

Introduction: Malignant ovarian germ cell tumors (MOGCTs) account for 2-5% of all ovarian cancers and among them pure embryonal cell cancer is rare condition (1, 2, 3, 4). Aim: To show successful pregnancy after unilateral salpingooopherectomy and chemotherapy in a girl with embryonal carcinoma of ovary (ECO). Case report: Patient had FIGO stage III c disease. After the surgical removal of the tumour, the patient underwent six cycles of adjuvant chemotherapy with bleomycin, etoposide and cisplatin (BEP). Eight years after chemotherapy she conceived spontaneously. The patient went through regular antenatal checkups in a consultation with a gynecological oncologist. In addition to all regular examinations and controls, monthly monitoring of carbohydrate antigen (CA) 125, human epididymis protein 4 (HE 4), Roma Index is also recommended. Congenital malformation excluded at 20 weeks of gestation by level III ultrasonography. At 39th gestational week, laparotomy as well as a C-section was done and the patient was managed successfully in giving birth to a healthy female baby. Three months after delivery, the woman was recurrence free and the infant did not show any problems. At the last follow-up visit (May 5, 2018), all the tumor markers were negative, and the control MRI and ultrasound examinations did not reveal tumor recurrence or pathological lymph nodes. Conclusion: Normal gonadal function and fertility are possible after fertility preservation surgery for ovarian germ cell malignancies, even with adjuvant chemotherapy.

Keywords: Carcinoma, Embryonal, Ovarian Germ Cell Cancer, Fertility preservation, Pregnancy.

1. INTRODUCTION

Malignant ovarian germ cell tumors (MOGCTs) account for 2-5% of all ovarian cancers and among them pure embryonal cell cancer is rare condition (1, 2, 3, 4). Embryonal carcinoma of ovary (ECO) was first described as a separate entity by Kurman and Norris in 1976 and often occurs mixed with other malignant germ cell tumour types(5). It is found predominantly in children, adolescents and in women in the reproductive age (average age 14 years) in contrast to perimenopausal or postmenopausal age associated with ovarian epithelial cancer (1, 2). Clinical presentation was related to hormonal disorders like a precocious puberty or menstrual irregularity (5). ECO produce serum tumor markers, beta-human chorionic gonadotropin (hCG), alpha-fetoprotein (AFP) and lactat dehydrogenase (LDH) that can provide prognostic information and can serve as a support for initial diagnosis, monitoring during therapy, and post-treatment surveillance (5, 6). Predominantly solid, but nonspecific imaging features on ultrasound, CT, and MRI, that overlap with other germ cell tumours of the ovary (7).

2. AIM

Aim of article was to present successful pregnancy after unilateral salpingooopherectomy and chemotherapy in a girl with embryonal carcinoma of ovary.

3. CASE REPORT

A 11 year old girl presented to the Clinic for Pediatrics, University Clinical Center Tuzla, Bosnia and Herzegovina in January 2008 with pain in abdomen and abdominal wall hardness. Physical examination showed a large abdominal mass. The patient did not have menarche. The basic laboratory findings were within normal limits. CT revealed a 12x10x11 cm heterodense, solid as
well as cystic mass. Left ovary was unremarkable. There was a large amount of ascites. Right sided salpingoophorectomy, omentectomy, biopsy left sided ovary was done. Postoperative serum AFP level was 765.64μg/L, CA-125 was 242.3U/mL, LDH was 1858U/L. Gross examination revealed a large mass of 11x10x7 cm, soft to firm consistency like a fish meat, lobular or nodular cut surface, with solid grayish white, cystic gelatinous areas with haemorrhage. Microscopic examination reveal tumor with infiltrative growth, polygonal cells with vesicular nuclei, prominent nucleoli focally. Cells are arranged in sheets and nests with focal gland differentiation.

Pathohistology diagnosis was: Carcinoma embrionale partim necroticum et haemorrhagicum infiltrativum textus fibroadiposae (Figure 1). Omental tissue was positive for tumor. Immunohistochemical analysis revealed positive staining for CD30, PLAP, kreatin wide, very focaly CK7, but negative staining for GFAP, vimentin, calretinin, EMA, CEA, Her 2, desmin which would also contribute to the embryonic carcinoma morphologically and by immunophenotypic cells (Figure 2). Ascites was negative for malignant cells on cytological examination. Biopsy of left sided ovary was negative for tumor. Patient had FIGO stage III c disease.

After the surgical removal of the tumour, the patient underwent six cycles of adjuvant chemotherapy with BEP. After two years of laparotomy she got menarcha. Regular follow up was carried out with tumor marker, ultrasonography, CT and MRI. Seven years after chemotherapy the woman got married. Within six months she conceived spontaneously. Pregnancy was confirmed by positive urine pregnancy test as well as a dating ultrasound scan showing five weeks gestational sac. The patient went through regular antenatal checkups in a consultation with a gynecological oncologist. In addition to all regular examinations and controls, monthly monitoring of CA 125, HE 4, Roma Index is also recommended. Congenital malformation excluded at 20 weeks of gestation by level III ultrasonography.

Approximately eight year after the completion of chemotherapy, the woman spontaneously conceived. During the pregnancy patient had no clinical symptoms till the end of pregnancy. At 39th gestational week, laparotomy as well as a C-section was done and the patient was managed successfully in giving birth to a healthy female baby (birth weight and length 3,430 gm/53cm, Apgar score: 9 in first minute and 9 in fifth minute). Three months after delivery, the woman was recurrence free and the infant did not show any problems. At the last follow-up visit (May 5, 2018), all the tumor markers were negative, and the control MRI and ultrasound examinations did not reveal tumor recurrence or pathological lymph nodes.

4. DISCUSSION

ECO are rare MOGCTs that occur in young age and with almost allays unilateral presentation. For these cancers fertility preservation surgeries, like a staging laparotomy and unilateral adnexectomy, followed by chemotherapy are an accepted treatment (1, 2). Six cycles chemotherapy with BEP is regarded to be the gold-standard regimen for the treatment of germ cell tumors at all stages of disease (6, 4, 8, 1, 2).

In study Barton et al they noted an increased risk of infertility in cancer survivors at very young ages, even though most young female cancer survivors resume menstruation, showing that menstrual function does not equate to normal ovarian reserves and fecundity (9). Oncologist should refer cancer survivors of the risk of infertility to reproductive specialists for possible fertility preservation if they are not ready to attempt conception,
as soon as possible (9, 10). Modern reproductive medicine offers increased options for fertility preservation before cancer treatment and include oophoropexy and cryopreservation of oocytes, ovarian tissue, or embryos (9, 10). Markers of ovarian reserve are anti-Müllerian hormone and antral follicle count carried out in the first part of the menstrual cycle (10). The use of ovarian stimulation, before chemotherapy, like a gonadotropin and letrozole or tamoxifen is generally recommended for cancer patients (10).

Clinically, majority of patients with MOGCTs present with abdominal pain, abdominal distension or a pelvic mass as is the case with our patient (4). In our case, the patient had stage FIGO IIIc disease, although the patient appeared with suddenly and acute occurring symptoms.

The logical question is how long after chemotherapy could women conceive? In the literature, there is no unique attitude. Six months is needed for human oocyte maturation from dormant state (when oocytes was genetically undamaged despite chemotherapy) to fully mature. Because of that facts, cancer patients are advised not to conceive until 6 months from completion of chemotherapy (6). Many studies suggested that the right time is 24 months after the end of the last cycle of chemotherapy (6). Our patient got menarcha two years after chemotherapy and conceived spontaneously after 8 years.

Pregnancy rate is practically unaffected after chemotherapy for ECO(6). No significant increase in fetal malformations, miscarriage, genetic or chromosomal abnormalities after chemotherapy is noted (6). But it is still recommended for women to do accurate ultrasound examination and fetal echocardiography to rule out any abnormalities although these are rare (6).

There is no data reported in the literature about recurrence rate MOGCTs after pregnancy (6). There are no current guidelines for surveillance of patients with MOGCTs during pregnancy which is necessary (3).

In case report Hulewitz et al disease relapsed seven weeks later with peritoneal carcinomatosis, despite the fact that it was FIGO I A stage of the disease (11). In our case disease did not return even after 8 years, despite it was FIGO III C stage. This facts throws light on the use of chemotherapy and perhaps the need to change recommendations for the treatment of lower stages of the disease.

In study Kurman and Norris survival rate for the embryonal carcinoma was 39% (5). In study C Di Tucci cure rates for patients with early-stage MOGCTs approach 100% and even in advanced-stage disease, cure rates are at least 75% treated with fertility preserving surgery and chemotherapy (6).

5. CONCLUSION

Normal gonadal function, fertility and dramatically improved survival are possible after fertility preservation surgery with adjuvant chemotherapy for MOGCTs.

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