Abstract

A 19-year-old woman with a mixed germ cell tumor of the ovary, presented to our clinic and was treated by unilateral salpingo-oophorectomy, and adjuvant chemotherapy with bleomycin, etoposide, cisplatin (BEP) regimen. After successful management of the tumor, the patient gave birth to a healthy male baby. This mixed tumor consisted of yolk sac tumor, dysgerminoma, choriocarcinoma, polyembryoma and embryonal carcinoma. All these tumors are exceedingly rare germ cell tumors of the ovary, and to our knowledge, a mixed germ cell tumor containing all of these neoplastic components has not been described previously. We wish to report the case and present a review of the literature on the relevant subject.

Keywords: mixed germ cell tumor of the ovary, management, pregnancy

Introduction

Malignant ovarian germ cell tumors account for less than 5% of all ovarian malignancies (1). They occur primarily in young women with a median age of between 16 and 20 years (2). Ovarian germ cell malignancies are believed to originate from primordial germ cells (3) and they are classified according to their histological types by the World Health Organization (WHO) (2).

Mixed germ cell tumors comprise some 8% of all germ cells tumors (2) and contain two or more histological types. The onset of symptoms is at 18 years (3) and is usually indicated by rapidly enlarging abdominopelvic masses. Approximately one-third of patients have ascites, of which 10% present with peritonitis secondary to torsion, infection, or rupture of the ovarian tumor. Prepubertal patients may manifest signs of precocious puberty as a result of hormone production by the tumor (3). Prognosis of mixed germ cell tumors depends on tumor size, histological type and grade. These tumors are usually larger than 10 cm, and in more than one-third of cases the histological type consists of endodermal sinus elements, non-gestational choriocarcinoma or grade 3 immature teratoma (2).

This report describes a mixed germ cell tumor of the ovary containing yolk sac tumor, dysgerminoma, embryonal carcinoma, choriocarcinoma, and polyembryoma components presenting as a suspicious tubal ectopic pregnancy.

Case Report

A nulligravid 19-year-old woman was admitted to our clinic with complaints of lower abdominal pain and vaginal bleeding. She was referred to our emergency service with the suspicion of right tubal ectopic pregnancy. She had an unremarkable medical and family history without any risk factors for ovarian or malignant disease. She had normal...
secondary sex traits, regular menstruation, and no signs of virilization. Physical examination revealed a large, regular, mobile and firm mass occupying the right side of the lower abdomen. Ultrasonographic and computed tomographic examinations revealed a right-sided adnexal mass (Figure 1).

The serum levels of alpha-fetoprotein (AFP) was 2129.4 ng/ml (normal range: 0-15 ng/ml), β-subunit of human chorionic gonadotropin (β-hCG) was 42506.04 mIU/ml (normal range: under 5 mIU/ml), lactate dehydrogenase (LDH) was 1571 U/L (normal range: 220-450 U/L) and CA-125 was 67.62 U/ml (normal range: 0-35 U/ml).

After informing the patient, an emergency laparotomy was performed. There was a small amount of bloody ascites. The right ovary was diffusely enlarged to about 10 cm and had an irregular surface, but the uterus and the contralateral ovary had a normal appearance. The patient underwent right salpingo-oophorectomy followed by partial omentectomy. Due to suspicion of malignancy, a left ovarian wedge resection was performed. Because the laboratory was not available, a frozen section could not be performed at the time of the surgery.

In macroscopic pathological examination, the right ovarian tumor was found to be 12x9x4 cm in size and had a hemorrhagic and partially capsulated outer surface. The cut surface was greyish-tan in color, and was mainly solid with small cystic areas. The periphery of the tumor included areas of hemorrhage and cystic necrosis containing hemorrhagic fluid and was surrounded by a yellowish solid stroma. Microscopically, the tumor appeared as a mixed germ cell tumor, the most prominent components being yolk sac tumor (45%) and dysgerminoma (25%). In the peripheral area, the histology showed choriocarcinoma (9%), exhibiting neoplastic proliferation of cytotrophoblastic cells and syncytiotrophoblastic cells (Figure 2). The tumor also contained polyembryoma (1%) composed of numerous embryoid bodies. Solid aggregates of epithelium-like, polygonal or ovoid cells that contained ample amounts of somewhat pale eosinophilic granular cytoplasmic borders, and frequently formed a syncytial arrangement were detected in the embryonal carcinoma component (20%). The ascites fluid contained neoplastic cells.

Postoperatively, four courses of BEP (bleomycin, etoposide and cisplatin) chemotherapy regime were administered at 4-week intervals. The levels of AFP, β-hCG and CA-125 normalized after two courses of chemotherapy. After a postoperative disease-free period of 18 months, our patient conceived. Following the detection of her pregnancy, she received a routine pregnancy follow up. After an uneventful pregnancy, she gave birth to a healthy male baby weighing 3250 g by cesarean section due to cephalo-pelvic disproportion. Intraoperatively, the left ovary appeared normal, no adhesions were detected and there were no palpable retroperitoneal lymph nodes.

**Discussion**

According to the WHO classification, mixed germ cell tumors of the ovary that contain more than one neoplastic germ cell element, are one of the subcategories of germ cell tumors (3,4,6).

Ovarian germ cell tumors commonly occur in teenagers and in women in their twenties, who generally desire to preserve their reproductive and ovarian endocrine functions. Usually the disease can be diagnosed at stage I. The patients frequently have large adnexal tumors with a median diameter of 16 cm and, with the exception of dysgerminomas, are usually unilateral (2).

In our report, a 19 year old woman with a large right-sided adnexal mass was evaluated after clinical, ultrasonographic and computed tomographic examinations. The serum
levels of AFP, β-hCG, LDH and CA-125 were high. A fertility-sparing surgery was performed. The histological components of the tumor were determined as yolk sac, dysgerminoma, choriocarcinoma, polyembryoma and embryonal carcinoma. According to the FIGO classification (1988) the tumor was assumed to be at stage Ic. Pure polyembryoma of the ovary has never been recorded; although the mixed forms with some other germ cell tumors including immature teratoma, yolk sac tumor and embryonal carcinoma have been published. Ovarian choriocarcinoma is also rare, and to our knowledge, mixed germ cell tumors containing polyembryoma and choriocarcinoma have not been described (4, 5).

Patients referred with an incompletely staged dysgerminoma or low grade immature teratoma apparently confined to the ovary, are evaluated with tumor markers (lactate dehydrogenase, AFP and human chorionic gonadotropine) to detect nondysgerminomatous elements, and undergo a CT scan to detect any unsuspected residual tumor. If these studies are normal, restaging of the patient is not necessary and follow up with tumor markers and CT scans or ultrasonography is recommended. The safety of this approach is confirmed by the 98.2% recurrence free survival rate for patients with stage I disease and 88.9% for patients with advanced stage disease in the chemotherapy group (1, 7). In our case, the patient was re-evaluated with a postoperative CT scan, and no residual tumor was found.

It has been reported that endodermal sinus tumors, and tumors with AFP over 1000 IU/ml tend to be more aggressive than the other histological types (8). The normalization of AFP levels generally signifies cure in cases of endodermal sinus tumors and mixed tumors containing endodermal elements, particularly if the AFP remains normal over an extended period of time (9, 10). Nevertheless, there have been reports of residual tumors or recurrences despite negative AFP levels after therapy for AFP producing tumors (9). Normal serum tumor markers do not guarantee a total cure. The normalization of serum tumor markers in a mixed type tumor could be explained if only those cells which secreted AFP were chemosensitive while other malignant elements flourished, or simply if tumor cells lost their ability to synthesize or secrete those markers (8). In our case, all the serum markers after the operation were found to be within normal ranges.

Malignant germ cell tumors of the ovary (MGCTO) are often curable after conservative surgery and adjuvant chemotherapy. Many women are able to resume normal reproductive function after the therapy (8). A unilateral salpingo-oophorectomy with preservation of the contralateral ovary and the uterus is considered the appropriate surgical treatment for patients with malignant ovarian germ cell tumor (MOGCT) (1, 3). Subsequent experience over the past 15 years or so has further strengthened the principle of performing conservative surgery to preserve ovarian function and fertility for the majority of young patients with MOGCTs (1). During surgery, routine biopsy of the contralateral ovary should be avoided. Although occult bilaterality has been reported, biopsy of the contralateral ovary could lead to future infertility related the peritoneal adhesions or ovarian failure (1). However, our patient underwent right salpingo-oophorectomy followed by partial omentectomy and left ovarian wedge resection. The patient’s fertility status will be followed. The role of a second-look laparotomy for germ cell tumors has been debated in the literature and in the few reports published on the matter, it was found that after normalization of tumor markers, those patients with positive findings at second-look laparoscopy succumbed to their disease and thus did not benefit from the second surgical procedure (8). With effective systemic chemotherapy, the extent of the primary operation may be tailored to preserve reproductive functions (the uterus and one adnex) in the majority of women without compromising cure (2). In the presence of bilateral macroscopic involvement, unilateral or bilateral ovarian cystectomy is a good option, especially when combined with postoperative chemotherapy (3).

The PVB regime (cisplatin, vinblastine, and bleomycin) proved to be more effective than the VAC regime (vincristine, dactinomycin, and cyclophosphamide) in treating women with MOGCTs. Subsequently, the substitution of etoposide for vinblastine proved to be equally effective and less toxic, so it was incorporated into the treatment of MOGCTs, with bleomycin, etoposide, and cisplatin (BEP regimen) and has become the most widely used chemotherapeutic regime. Our patient was also treated with the BEP regimen. The overall survival of patients treated with platinum-based chemotherapy currently lies between 87% and 98% (1).

The long term impact of antineoplastic chemotherapy on ovarian function has been studied extensively. However, short term intensive chemotherapy particularly using antimetabolites such as methotrexate, vinca alkaloids such as vincristine, and anthracycline antibiotics such as dactinomycin appears to affect ovarian function less commonly. Factors such as cumulative drug dose, duration of therapy, and age at treatment have been mentioned in the literature as influencing the incidence of ovarian dysfunction in adult women. In a study, 62% of those undergoing chemotherapy were amenorrheic during treatment, but 92% resumed regular menses on completing chemotherapy (1).

In a retrospective study of 74 patients, fertility-sparing surgery was found to be the “procedure of choice” in young patients (10-35 years) with MOGCT confined to a single ovary. Advanced stages are not always accompanied by extensive pelvic disease and should not be a contraindication for preservation of the uterus and the contralateral ovary. With the appropriate addition of postoperative adjuvant platinum-based combination chemotherapy, these young patients have an excellent prognosis and can expect to maintain normal ovarian function and reproductive capacity (1).
Our case supports the idea that young patients with MOGCT can be treated by fertility-sparing surgery and adjuvant chemotherapy.

References