Case Report

A favorable maternal and neonatal outcome following chemotherapy with etoposide, bleomycin, and cisplatin for management of grade 3 immature teratoma of the ovary

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Ovarian cancer rarely complicates pregnancy. Usually these malignancies consist of germ cell tumors. Preserving maternal safety along with favorable neonatal outcome is a subject of debate in the management of ovarian cancer during pregnancy. In this report, the authors describe a 25-year-old primigravid woman who was diagnosed to with an ovarian immature teratoma which was diagnosed at 13th weeks of pregnancy during a routine sonography. She underwent oophorectomy at week 21 of her gestation. Then she received three cycles of BEP regimen (bleomycin, etoposide, and cisplatin) during her pregnancy until week 37 of gestation. At 36 weeks she delivered a male baby with mild glandular hypospadias who was otherwise normal. Management of immature teratoma after the first trimester of pregnancy is similar to non-pregnant patients and is safe for both the mother and the fetus.

Key Words: Germ cell tumor, Ovary, Pregnancy, Chemotherapy

INTRODUCTION

Ovarian cancer during pregnancy is a rare event with the incidence of 1:10,000 to 1:50,000.¹ The reported incidence of pregnancy complicated by an immature teratoma is 0.07%.² This tumor is highly malignant and may threaten the life of the mother.³ Treatment of ovarian cancer in a pregnant woman is similar to non-pregnant patients. Treatment methods depends on gestational age, histological type, and tumor grade. Despite adverse effects of operative intervention, the benefits of earlier diagnosis of cancer and its treatment outweigh the risks of avoiding operative intervention during the second trimester. Unilateral salpingo-oophorectomy and surgical staging is the standard care for malignant germ cell tumors in reproductive-aged woman. Adjuvant chemotherapy is required except for stage IA, grade I, immature teratomas and dysgerminomas.

The outcome of pregnancies associated with ovarian malignancies is poor, and treatment should not be delayed in affected patients. There are some reports regarding the successful administration of bleomycin, etoposide, and cisplatin (BEP) chemotherapy during pregnancy for malignant ovarian germ cell tumors.⁴ The patients who received this regimen delivered babies who were developmentally normal and no adverse effects were reported.

Here, we report a case of a pregnant woman with the diagnosis of grade 3 immature teratoma of the ovary to whom the authors administered BEP chemotherapy regimen.

CASE REPORT

A 25-year old primigravid woman presented with an ovarian mass which had been detected during routine obstetric sonographic examination at week 13 of gestation. Her sonography revealed a solid and cystic mass with 76×45 mm dimensions with echogenic areas and septations in favor of a dermoid cyst. The mass showed a growing pattern and her last ultrasound examination showed large right ovarian cyst (130×100 mm) with internal echoes.

She underwent laparotomy at week 21 of gestation in another center. Right oophorectomy and biopsy of the left ovary and omentum had been performed. A diagnosis of immature teratoma was established for the right ovarian mass with normal histology of all other samples. There were no post operation complications. She received three cycles of 20 IU/m² bleomycin, 100 mg/m² per day of etoposide, and 20 mg/m²/day cis-

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platin for five days per week.

Cesarean section was planned for the patient at the 36th week. Two weeks after the end of the third course of chemotherapy, ultrasound examination revealed oligohydramnios (Amniotic Fluid Index equal to 5 cm and the umbilical cord systolic/diastolic (S/D) ratio of 2.59). Estimated fetal weight was in the fifth percentile. After counseling with perinatologist, we decided to terminate the pregnancy. After three doses of colony stimulating factor for leucopenia, she underwent cesarean section and complete staging including partial omentectomy, right salpingectomy, peritoneal biopsy, bilateral lymph node sampling. A male baby with normal appearance with a mild hypospadias was born. The weight of the baby was two kilograms with an Apgar score of 9-10 at 15 minutes. Ultrasound examination of the baby's brain and kidney were normal at his first month of age. Hearing studies and eudiometry of the infant was also normal.

The pathologic examination of the omentum, right salpinx, lymph nodes, and peritoneal samples were normal. Alpha fetoprotein and CA 125 of serum measurements and ultrasound and computed tomography studies of the pelvic and abdominal organs did not show any evidence of tumor recurrence after one year. Her infant was followed up during this period and the last complete medical examination showed normal physical and neurological development after 8 months of birth.

DISCUSSION

Immature teratoma is frequent in young women,¹ and usually present with subacute abdominal pains due to rapid growth of a large, unilateral tumor undergoing capsular distention, hemorrhage or necrosis. In more advanced diseases, ascites may develop and cause abdominal distention.

Persistent adnexal masses are detected in 1 to 2 percent of all pregnancies, and these neoplasms usually are seen during routine obstetric sonographic examination, but occasionally and dramatically, and elevated maternal serum AFP level is the presenting sign of a malignant germ cell tumor.⁵ Immature teratoma associated with pregnancy is very rare and a few cases have been reported, because most women undergo sonography during pregnancy the detection of adnexal masses has increased concomitantly. Management of malignant ovarian germ cell tumors during pregnancy is very important and argumentative. Treatment of malignant germ cell tumors of the ovary during pregnancy should be guided by the time and drug dependent of maternal and fetal prognosis during therapy.⁶

Adverse fetal effects of using bleomycin, etoposide and cisplatin have been reported in two cases. One child exposed to this regimen was born at 28 weeks of gestation with ventriculomegaly secondary to cerebral atrophy.^{4,7} The second was a premature infant born after being treated with bleomycin, etoposide and cisplatin, 7-10 days prior to delivery and developed transient neonatal leucopenia and neutropenia.

This child was also found to have bilateral moderate sensor neural hearing loss at 1 year of age.⁴ In contrast, normal growth and maturation was found in a group of children who had in-uterus exposure to bleomycin.^{8,9}

Few cases have been reported to administer etoposide in addition to other anti-neoplastic agents during the second and third trimesters of pregnancy Han et al.⁴ reported 2 cases with favorable pregnancy outcome after exposure to these chemotherapeutic agents at second and third trimesters of pregnancy, and did not observe any evidence of recurrence of ovarian cancer in the follow up. The infants did not demonstrate any evidence of minor or major anomalies, and showed normal neurological development after a few years.

A child born who was exposed to bleomycin and etoposide between 25 to 28 weeks of gestational age developed ventriculomegaly in utero, and subsequently cerebral atrophy.^{4,7} Of other exposed infants, one had alopecia and hearing loss and three had hematologic abnormalities (e.g. anemia, leucopenia, neutropenia and thrombocytopenia).⁴ These side effects were attributed to etoposide.

Cisplatin has a low trans-placental transfer, so it is possible that the developing embryo is protected from exposure to these agents. The administration of cisplatin at 26 weeks gestation has been associated with neutropenia, hair loss and some hearing impairment in a premature neonate who was delivered 6 days after being exposed.¹⁰

Hypospadias occurs in 1/300 of male newborns. Sexual differentiation and urethral development begins in utero at approximately 8 weeks and is completed by 15 weeks of gestation, and our patient was not exposed to any chemotherapeutic regimen.⁸

In conclusion, adjuvant chemotherapy with BEP regimen for ovarian immature teratomas during pregnancy seems to be safe for both the mother and fetus. However, a definitive conclusion can not be derived yet because of the limited number of cases currently available in the literature.

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