

# Case Report

## A Case of Ovarian Endodermal Sinus Tumor Diagnosed during Pregnancy

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*Pregnancy complicated by endodermal sinus tumor of the ovary is extremely rare. The authors present a case report of a pregnant woman with persistent left adnexal mass and subsequently found to have a primary endodermal sinus tumor of the ovary that was diagnosed at 19 weeks of gestation. After left salpingo-oophorectomy had been performed, the patient chose to terminate the pregnancy before the initiation of combination chemotherapy with bleomycin, etoposide, and cisplatin. The response to chemotherapy was not satisfactory. The patient expired after seven cycles of treatment had been completed because of pulmonary fibrosis and the drug toxicity of bleomycin.*

**Keywords:** *Endodermal sinus tumor, Ovarian cancer, Pregnancy*

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The majority of adnexal masses detected during pregnancy are benign. Functional ovarian cysts from follicles or corpora lutea are the most common adnexal masses found during pregnancy. These are usually resolved by the second trimester. Among persistent adnexal masses diagnosed during pregnancy, dermoids are the most common, followed by benign serous or mucinous cystadenoma. Malignant ovarian neoplasms account for 2%-6% of all persistent adnexal masses diagnosed during pregnancy<sup>(1-4)</sup>. Ovarian cancer in pregnancy has been reported to occur with a frequency ranging from 1 in 18,000 to 1 in 25,000 pregnancies<sup>(5,6)</sup>.

Most of the literature regarding ovarian cancer during pregnancy comprises only case reports. Epithelial ovarian cancer is primarily a disease of older women while germ cell tumors occurring in the reproductive age group lead to overrepresentation in pregnancy. Pregnancy complicated by endodermal sinus tumor of the ovary is extremely rare. Only ten or

more cases have been reported over the last 30 years and there is no established method of treatment. Experience and results need to be shared.

The authors present a case report of a pregnant woman with persistent left adnexal mass and subsequently found to have a primary endodermal sinus tumor of the ovary that was diagnosed at 19 weeks of gestation. After left salpingo-oophorectomy had been performed, the patient chose to terminate the pregnancy before the initiation of combination chemotherapy with bleomycin, etoposide, and cisplatin.

### Case Report

A 27-year-old woman (gravida 1) presented to her physician of antenatal care at a private hospital. Her pregnancy was 8 weeks of gestation at the first visit. Her past medical history was unremarkable. She was on no medication and had no allergies. There was no significant family history. By physical examination, her uterus seemed to be larger than it should have been. Ultrasonography was performed and showed that she had an 8-week and 4-day live intrauterine pregnancy. A solid-cystic mass (8 cm in diameter) posterior to the uterus likely arising from the left ovary was also detected. A diagnosis of intrauterine pregnancy with a corpus luteal cyst of left ovary was made and the patient was

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followed expectantly. At 16 weeks of gestation, a repeated ultrasound confirmed a viable fetus in keeping with gestational age and the complex mass was now 16 cm in diameter. The patient was then referred to another private hospital for surgery. Through a midline incision, left salpingo-oophorectomy was performed at 18 weeks of gestation. Neither ascites nor peritoneal seeding was detected. There was a tumor of the left ovary, measuring 16 cm in diameter, with an intact capsule occupying in the pelvic cavity. The gravid uterus, right fallopian tube, and right ovary were found to be normal. No abnormal lesions were seen in the peritoneal cavity or omentum. Furthermore, there was no enlargement of the pelvic or para-aortic lymph nodes. Unfortunately, the tumor capsule was accidentally ruptured by operative manipulations. Grossly, the tumor consisted of a mixture of cystic and solid areas. The yellowish content was thick and sebum-like. Histological examination revealed an endodermal sinus tumor arising in the dermoid cyst.

The patient was then referred to Siriraj Hospital at 19 weeks gestation for further treatment. On presentation to Siriraj Hospital, ultrasonography showed a live, appropriately grown fetus, which was 19 weeks gestation. All the slides of the patient's left ovary were reviewed by our pathologist. Various patterns of endodermal sinus tumor were found including sheet-like, endodermal sinus, glandular and alveolar patterns. The majority of cells contained vesicular nuclei with moderate nuclear atypia. Schiller-Duval bodies and hyaline droplets were also noted. The tumor cells stained positively for alpha-fetoprotein antibodies. The patient was diagnosed as endodermal sinus tumor of the left ovary, which was categorized at least stage IC according to International Federation of Gynecology and Obstetrics (FIGO) criteria. The natural history, prognosis of disease, available treatment methods, and their possible risks were thoroughly explained and discussed with the patient and her family. At last, they decided to discontinue the pregnancy. The patient was then hospitalized and misoprostol was administered vaginally, followed by continuous infusion of oxytocin. Two days later, the fetus aborted dead without any complication. Computed tomography of the abdomen and pelvis demonstrated an enlarged uterus (extending one-third above pubic symphysis on manual examination). No other abnormalities in the abdomen were detected. Chest x-ray was negative. Examination of serum tumor marker showed that alpha-fetoprotein was 3,402 ng/ml. However, serum LDH and  $\beta$ -hCG were not examined. After the termination of

pregnancy four courses of bleomycin (30 mg iv on days 1,8,15) etoposide (100 mg/m<sup>2</sup> iv on days 1-5), and cisplatin (20 mg/m<sup>2</sup> iv on days 1-5) were given.

The response to chemotherapy was not satisfactory. The remaining high serum AFP suggested the presence of malignant tumor cells. Although both ultrasonography and CT scan of whole abdomen revealed no disseminations, eight cycles of chemotherapy in total was considered. After seven cycles of treatment had been completed, the serum AFP level decreased to 7.87 ng/ml and LDH was 346 U/L. One month after the last cycle of chemotherapy, the patient had severe dyspnea and was admitted in another private hospital. Pulmonary fibrosis, the toxicity of bleomycin, was diagnosed. She passed away several days later despite the aggressive treatment of steroids and antibiotics.

## Discussion

Endodermal sinus tumor is the second most common malignant germ cell tumor of the ovary and its reported concurrence with pregnancy is extremely rare. There is no established management for the disease. In reviewing the case reports, the authors found that several categories of therapeutic strategies have been carried out. Chemotherapy combined with surgical exploration has been approved to be a standard therapy for non-pregnant women. However, it is still controversial whether the malignancy during pregnancy should undergo chemotherapy since the mother will be put in danger if the treatment is delayed, yet the fetus may be affected by chemotherapy. For these reasons, the management of such cases is individualized for each patient.

Endodermal sinus tumor has also been referred to as yolk sac carcinoma. It is unilateral in almost all cases. Most patients have early-stage disease. Surgical exploration, unilateral salpingo-oophorectomy and a frozen section for diagnosis is usually enough for the treatment of the tumor. Removal of all gross metastases should be done. However, thorough surgical staging is not indicated because all patients need chemotherapy since treatment with surgery alone has an extremely poor prognosis (13% 5-year survival)<sup>(7)</sup>. With the advent of multiagent chemotherapy, there is an 80% survival with early stage disease<sup>(8)</sup>. These tumors are highly responsive to the chemotherapy. Various chemotherapy combinations have been used, however, the regimen of bleomycin, etoposide, and cisplatin (BEP) is favored for its effectiveness and lower rate of long-term sequelae<sup>(9,10)</sup>.

In pregnant women, there is a great concern of potential malformation, growth retardation, and the risk of malignancy in the future offspring. Chemotherapy in those pregnancies complicated with an endodermal sinus tumor is usually disputed, especially after the first trimester.

The presented patient had undergone left salpingo-oophorectomy and was categorized as at least stage IC. She was not re-explored for complete staging. Instead, she was counseled to have chemotherapy (BEP regimen) either with pregnancy, after delivery, or after therapeutic abortion. Chemotherapy in pregnancy is a troublesome problem that many case series and retrospective cohort trials have described. Aviles A et al. reported successful and safe administration of chemotherapy in pregnancy in 43 cases<sup>(11)</sup>. However, it is still prohibited during the first trimester of pregnancy since the high risk for abnormal fetal development<sup>(12)</sup> and high rate of abortion<sup>(13)</sup> were reported in other issues. In spite of that, initiation of chemotherapy in the second trimester has revealed good results, such as in several issues of case reports noting that pregnant women with endodermal sinus tumor delivered a healthy baby after receiving the chemotherapy during the second trimester<sup>(10,12-14)</sup>. Cisplatin has been reported to be used safely in some cases<sup>(15,16)</sup>. However, there are also reports of fetal anomaly in such condition. Furthermore, bleomycin might induce pulmonary toxicity in early childhood and etoposide the new drug may increase acute myeloid leukemia in infancy<sup>(17)</sup>. Therefore, the safety of chemotherapy for the fetus

has not been established. Considering the complication that might happen to the fetus, chemotherapy was postponed until delivery in some case reports. The authors are aware that only six cases were reported to have such treatment during pregnancy<sup>(12,16,18-21)</sup>. Thus three categories of strategies were described; they are (1) receiving chemotherapy during pregnancy (Table 1), (2) receiving chemotherapy after therapeutic abortion<sup>(22,23)</sup> (Table 2 ),(3) receiving chemotherapy after delivery<sup>(24-27)</sup> (Table 2). Management is individualized.

Despite the dilemma of the treatment during pregnancy, drug toxicity of the anticancer drug to the patient herself should also be kept in concern. In the present case, the disease was almost eliminated but the drug complication induced the patient's death. Pulmonary toxicities of bleomycin occur in approximately 10% of treated patient. In approximately 1%, nonspecific pneumonitis induced by bleomycin progresses to pulmonary fibrosis and death. This is usually both dose and age related, being more common in patients over 70 years of age receiving over 400 units total dose. However, it is unpredictable and has been seen occasionally in young patients receiving low doses, such as in this patient.

The therapeutic strategies for malignant tumors in the second trimester of pregnancy are still a divisive problem. Delaying of postoperative chemotherapy may increase the recurrent rate of the disease; on the other hand, use of chemotherapy during pregnancy is definitely a danger to the fetus. Histology, clinical stage of the tumor, as well as the desires of the

**Table 1.** Case reports of endodermal sinus tumor complicated pregnancy treated with chemotherapy during pregnancy

Reference	Gestational age at diagnosis	Stage	Therapy during pregnancy	Gestational age at delivery	Therapy after delivery	Outcome of mother	Outcome of fetus
Malone 1986 <sup>(12)</sup>	25	IC	RSO, PVBx3	32	PVBx3	12 months NED	Healthy
Kim 1989 <sup>(18)</sup>	18	IC	LSO, PVBx6	37	PVBx2	33 months NED	Healthy
Metz 1989 <sup>(19)</sup>	13	I	LSO, VB/Dox/Cyx5	37	VB/Dox/Cyx7	12 months NED	Healthy
Elit 2002 <sup>(20)</sup>	23	II	LSO, BEPx3	28	BEPx4	16 months NED	Ventriculomegaly
Han 2005 <sup>(21)</sup>	18	IC	RSO+omentectomy, BEPx5	40	BEPx6	6 years NED	Healthy
Robova 2007 <sup>(16)</sup>	22	IC	LSO+omentectomy, Px4	35	TAH+RSO+PLN+PALN, BEPx3	28 months NED	Healthy

*Note.* RSO, right salpingo-oophorectomy; LSO, left salpingo-oophorectomy; BSO, bilateral salpingo-oophorectomy; TAH, total abdominal hysterectomy; PLN, pelvic lymphadenectomy; BEP, bleomycin, etoposide, cisplatin; PVB, cisplatin, vinblastine, bleomycin; VB, vinblastine; Dox, doxorubicin; Cy, cyclophosphamide; P, cisplatin; NED, no evidence of disease

**Table 2.** Case reports of endodermal sinus tumor complicated pregnancy treated with chemotherapy after therapeutic abortion or delivery

Reference	Gestational age at diagnosis	Stage	Therapy during pregnancy	Gestational age at delivery	Therapy after delivery	Outcome of mother	Outcome of fetus
Ito 1984 <sup>(22)</sup>	9	I	Termination	-	TAH+LSO+ PLN, MMCx6	-	-
Farahmad 1991 <sup>(23)</sup>	17	I	Termination	-	TAH+BSO+ PLN, PVBx6	27 months NED	-
Present case	17	IC	LSO+Termination	-	BEPx6	death	-
Van der Zee 1991 <sup>(24)</sup>	18	I	LSO	33	BEPx4	24 months NED	Healthy
Rajendran 1999 <sup>(25)</sup>	19	IA	RSO	31	BEPx4	12 months NED	Healthy
Shimizu 2002 <sup>(26)</sup>	19	IC	RSO	36	BEPx3	27 months NED	Healthy
Aoki 2005 <sup>(27)</sup>	17	IC	RSO	35	BEPx7	Recurrence at gestation age 34 weeks	Healthy

*Note.* LSO, left salpingo-oophorectomy; RSO, right salpingo-oophorectomy; BSO, bilateral salpingo-oophorectomy; TAH, total abdominal hysterectomy; PLN, pelvic lymphadenectomy; BEP, bleomycin, etoposide, cisplatin; PVB, cisplatin, vinblastine, bleomycin; MMC, mitomycin C; NED, no evidence of disease

patient and her family to maintain the pregnancy should be carefully considered before management is performed.

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### มะเร็งรังไข่ชนิด endodermal sinus tumor ที่ตรวจพบขณะการตั้งครรภ์

อิสริรินทร์ ธนบุญยวัฒน์, มงคล เบญจามิบาล

การตั้งครรภ์ที่พบร่วมกับมะเร็งรังไข่ชนิด endodermal sinus tumor เป็นภาวะที่พบบได้น้อยมาก ผู้ศึกษา รายงานผู้ป่วยตั้งครรภ์รายหนึ่งซึ่งพบก่อนที่ปีกมดลูกข้างซ้ายซึ่งต่อมาได้รับการผ่าตัดขณะที่มีอายุครรภ์ 19 สัปดาห์ และได้รับการวินิจฉัยว่าเป็นมะเร็งรังไข่ชนิด endodermal sinus tumor หลังจากได้รับการผ่าตัดเอาปีกมดลูก ข้างซ้ายออก ผู้ป่วยได้ขอเลือกที่จะยุติการตั้งครรภ์ก่อนที่จะเริ่มต้นการรักษาด้วยยาเคมีบำบัดโดยให้สูตรรวม ซึ่งประกอบด้วย bleomycin, etoposide และ cisplatin อย่างไรก็ตาม ผู้ป่วยมีการตอบสนองต่อการรักษาที่ไม่ดี หลังจากได้รับยาเคมีบำบัดทั้งสิ้น 7 รอบ ผู้ป่วยก็เสียชีวิตจากพังผืดในปอดซึ่งเป็นผลข้างเคียงจากยา bleomycin