The management of ovarian cancer in pregnancy: a rare case report

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INTRODUCTION

In Indonesia, ovarian cancer is the third leading cause of cancer-related death in women. 43 Indonesian women died of ovarian cancer at the Dr. Soetomo General Academic Hospital in Surabaya, Indonesia, between 2014 and 2017. Ovarian cancer is the eighth most common malignancy and the seventh leading cause of cancer-related death in women, with a morbidity incidence of 6.1 per 100,000 women and a mortality rate of 4.3 per 100,000.1

Ovarian tumors are found in approximately 1 in 1000 pregnancies. During pregnancy, the reported incidence of adnexal tumors ranges from 0.15 to 5.7%. Ovarian cancer is the sixth most common malignancy detected during pregnancy, following breast, thyroid, cervical, and Hodgkin lymphoma. One study, however, discovered that ovarian cancer ranked sixth in the Asian population.1,3 As a result, ovarian cancer affects 1 in 12,500-25,000 pregnancies on average. Few ovarian tumors are cancerous, with the vast majority being benign or borderline. It is unusual for benign ovarian tumors, such as dermoid cysts, to progress to malignancy. In the literature on this subject, just four cases have been published.4-6

Cancer care during pregnancy is complicated by the simultaneous management of three distinct yet interdependent entities: the mother, the fetus, and the disease.4-8 Despite the relatively low prevalence of epithelial ovarian cancer in women of reproductive age, around 25–50 percent of ovarian cancers identified during pregnancy involve epithelial cell types. Even though epithelial cancer is the most prevalent outside pregnancy and accounts for nearly 90 percent of all ovarian cancers, germ cell tumors are the most prevalent during pregnancy. Pregnancy is characterized by several physiological changes, including an increase in endogenous sex and growth hormones, which may have unpredictable effects on the clinical progression of cancer.6,7,9 The 5-year survival rate for ovarian cancers that cause pregnancy complications is expected to be between 72% and 90%. Because of early disease identification, most ovarian cancers detected during pregnancy have a positive prognosis.6,9 Ovarian cancer has a terrible prognosis, with just a 35% 10-year survival rate, but adolescents and young adults have up to an 85% 10-year survival rate.6

While the evidence regarding the efficacy of surgery and adjuvant chemotherapy is clear, the appropriate treatment protocol for ovarian cancer during pregnancy, especially the timing of initiating intervention, has not yet been established due to the paucity of cases and is generally tailored to the patient’s circumstances. In this report, we aimed to present our experience in managing a rare case of ovarian cancer in pregnancy.

CASE REPORT

A 24-year-old pregnant lady (G2P0A1, 24 weeks gestational age, [GA]) was brought to our hospital after a routine prenatal ultrasound revealed a 15x18 cm left adnexal tumor. We discovered the complex adnexal mass, which was approximately 20x13.3x16 cm in size, in the left ovary, producing severe bilateral hydrenephrosis on magnetic resonance imaging (MRI). The laboratory tests performed were within normal limits except for higher serum lactate dehydrogenase levels. At 34 weeks GA, the pregnancy was terminated via cesarean section. The baby (female, 1,600 g) was born alive with no congenital defects and an Apgar score of 3-5-7. Following that, a unilateral salpingo-oophorectomy was performed. Pathology indicated a high-grade serous carcinoma of the left ovary with positive ascites fluid but no evidence of metastases to the pelvic lymph nodes, omentum, or peritoneum (stage IC). We had planned to treat the woman with a paclitaxel-carboplatin combination, but she declined because she preferred to breastfeed her infant. She had no abdominal issues at 15 months and was still breastfeeding the baby.

Conclusion: Pregnancy-related epithelial ovarian cancer is uncommon but is a possibility. Clinical findings, diagnostic, and treatment strategies are still quite similar to non-pregnant patients, except for the timing of chemotherapy initiation. Further research is needed to provide evidence regarding these mother-infant dyads’ survival and health outcomes.
case of a pregnant patient with ovarian cancer and review the related literature.

CASE PRESENTATION

A 24-year-old woman with a second pregnancy (gravida 2) and a history of miscarriage was referred to Dr. Soetomo Hospital's Obstetrics Outpatient Clinic due to an asymptomatic solid cystic adnexal mass with a diameter of 15x18 cm in the left adnexa discovered in the routine ultrasound report at 24 weeks GA. Color Doppler imaging revealed enhanced vascularity in the cysts. There were just minor ascites, and the peritoneum and liver were normal. There was no history of endometrial, ovarian, colorectal, or breast cancer in the patient's family.

On magnetic resonance imaging (MRI), we found that the complex adnexal mass, about ±20x13.3x16 cm in size, was located in the left ovary, causing severe hydronephrosis of the right and left kidneys. In contrast, the uterine and right ovary showed no abnormalities (Figure 1). However, the laboratory tests performed were within normal range except for elevated serum levels of lactate dehydrogenase. The result of the biological markers were normal cancer antigen 125 (CA-125), normal carcinoembryonic antigen (CEA), and elevated alpha-fetoprotein (AFP) with absolute values of 14.4 U/mL (reference range: <35 IU/mL), 0.37 ng/mL (reference range: <5 ng/mL), and 162 ng/mL (reference range: <15 g/mL), respectively.

Multidisciplinary counseling was used: the patient and family were informed about surgical operations at 34 weeks the possibility of laparotomy results, maternal and fetal risks, and the possibility of chemotherapy treatment after delivery. The pregnancy went smoothly: many obstetric ultrasounds confirmed normal fetal growth and development. Fetal lung maturation was conducted before surgery. At 34 weeks, a cesarean section was performed. The baby (female, 1,600 g) was born alive, with no congenital defects and an Apgar score of 3-5-7. At the moment of birth, the placenta appeared normal. Exploration revealed a 30 cm left ovarian mass with a tumor developing across the capsule (Figure 2).

A unilateral salpingo-oophorectomy and a frozen portion were performed for pathology evaluation. A serous carcinoma of the left ovary was discovered in a frozen section. Then we performed an omentectomy, ascitic fluid paracentesis, bilateral pelvic lymph node dissection, and several peritoneal biopsies. Histopathology assessment of the left ovarian mass, omentum, and lymph nodes showed: 1) malignant tumors infiltrated fibrous connective tissue stroma of the ovary until growing over the capsule with many mitoses, consistent with high-grade serous ovarian carcinoma in the left ovary; 2) the ascitic fluid result is positive for malignancy (adenocarcinoma); and, 3) there was no sign of metastasis on a bilateral pelvic lymph node, omentum, and peritoneum. The patient was therefore diagnosed with ovarian cancer IC due to confirmed malignant cell in ascitic fluid (T1c3 or International Federation of Gynecology and Obstetrics (FIGO) stage IC3) with no sign of local (N0) and far metastasis (M0).
The postpartum check-up went smoothly. The follow-up ultrasound and chest radiograph revealed no evidence of relapse or metastasis. We scheduled paclitaxel-carboplatin chemotherapy for this patient's postpartum treatment. However, the patient declined since she preferred to breastfeed the infant. She currently has no abdominal-related issues 15 months after surgery. She continues to breastfeed and has no concerns about her infant's health or development.

**DISCUSSION**

A tiny number of pregnant women are identified with adnexal masses by routine obstetrical ultrasounds, primarily in the first trimester. The great majority of these masses are harmless pregnancy-related masses that will disintegrate on their own within the first 16 weeks of pregnancy. However, in this case, the tumor was discovered in the second trimester and grew in size during pregnancy. In this section, we will go over the diagnostic and intervention difficulties that can arise when dealing with a persistent adnexal tumor suspected of being neoplastic throughout pregnancy.

An MRI of an adnexal mass is very useful for discriminating between bone and muscular tissue, as in leiomyomas, endometriomas, and complicated masses with solid components. When ultrasonography is equivocal, when masses are too large to be thoroughly assessed with ultrasound, or when there is a significant risk of malignancy, an MRI can assist in establishing an accurate diagnosis. However, the risk of gadolinium-contrast becoming poisonous in amniotic fluid due to dissociation of the ion from the chelating molecule limits its use during pregnancy to instances when the advantages to the mother outweigh the risks to the fetus. As a result, in this investigation, we did not use contrast MRI to lessen the danger to the fetus.

We performed many biomarker tests to investigate the probability of causation. The antigenic determinant CA-125 is expressed in ovarian epithelial tumors, but it is physiologically raised during pregnancy; increased CA-125 is detected between 30 and 40 days of gestation, with a peak between 35 and 60 days of gestation and a reduction by the end of the first trimester. However, only 50% of early-stage tumors in pregnant patients with stage I ovarian cancer have a CA-125 score larger than thirty international units. Alpha-fetoprotein (AFP), lactate dehydrogenase (LDH), and human chorionic gonadotropin (hCG) are all altered during pregnancy, reducing their therapeutic value. We discovered normal CA-125 and high LDH levels in this investigation, while the final pathology result was epithelial ovarian cancer.

Adnexal tumor malignancy incidence in pregnancy ranges from 1% to 6%, making ovarian cancer the fifth most common kind of tumor in pregnancy. Even though epithelial cancer is the most common outside of pregnancy, accounting for almost 90% of all ovarian malignancies, it is less common than germ cell tumors, the most common gynecologic malignancy during pregnancy. Extra-uterine high-grade serous carcinoma (HGSC) is one of the primary causes of cancer death in women, accounting for the majority of the morbidity and mortality associated with ovarian carcinoma outside of pregnancy. The median overall survival for patients with high-grade tumors was 40.7 months in a study of 16 thousand eight hundred fifty-four patients with HGSC (95.7%) and 755 patients with low-grade serous ovarian cancer (4.3%), while it was 90.8 months for women with low-grade tumors. The patient in our study was diagnosed with high-grade serous ovarian cancer, which is uncommon during pregnancy.

Aside from diagnostic difficulties, there is also a treatment dilemma due to a lack of evidence and established protocol. Pharmacological research suggests that weekly paclitaxel and 3-weekly paclitaxel have a low fetal toxicity profile during the second and third trimesters of pregnancy. Although platinum-based drugs have been linked to significant placental transfer, cisplatin poses a dose-dependent risk of ototoxicity in infants exposed during pregnancy. Early chemotherapeutic medication exposure has been linked to fetal malformation rates ranging from 14 to 19 percent. Exposure during the second and third trimesters, on the other hand, resulted in deformity rates comparable to healthy pregnant women (up to 6%).

While prognosis and quality of life should be prioritized, chemotherapy during the second trimester appeared to be safer than chemotherapy during the first or third trimesters and had been used in similar circumstances. However, the hazards of this operation must be recognized.

Another issue to consider before starting chemotherapy is breastfeeding during the postpartum period. While paclitaxel and carboplatin amounts in breast milk decreased after 72-316 hours, there is no reliable data on newborn safety.

Chemotherapy has long been accepted as a medical cause to discontinue nursing. However, after consulting with the multidisciplinary cancer care team, the patient made an informed decision to postpone the adjuvant chemotherapy in order to reduce the danger to the infant during pregnancy and breastfeeding. A large multicenter study is needed to give further evidence about the survival and outcomes of mother-infant dyads with ovarian cancer. This case report demonstrates limitations in generalizing the study's validity and an absence of demonstrating a cause-and-effect relationship. It is also worth noting that there is no comparison group. This study advises using a case-series methodology to determine the unique characteristics of individual individuals in this rare case.

**CONCLUSIONS**

Ovarian high-grade serous carcinoma in pregnancy is uncommon, and little is known about it. The goal of treating ovarian cancer during pregnancy is to achieve the best oncologic outcome while preserving the viability of the fetus. In conclusion, the findings of this case suggest that somewhat delayed treatment on a patient with high-grade serous cancer of the ovary may be considered to limit the danger to the fetus. More study is needed to provide knowledge about these mother-infant dyads' survival and health outcomes.

**AUTHOR CONTRIBUTION**

All authors have contributed to this research process, including conception and design, analysis and interpretation of...
the data, article drafting, critical revision of the article for important intellectual content, and final approval.

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**CONFLICT OF INTEREST**

There are no conflicts of interest to declare.

**ETHICAL CONSIDERATION**

A subject voluntarily consented to the study’s publication, understanding that the patient’s identity would remain private. ICMJE (International Committee of Medical Journal Editors) ethics approval has been obtained.

**REFERENCES**