

High-Grade Serous Carcinoma During Pregnancy: A Case Report and literature review

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ABSTRACT

Introduction: Pregnancy-associated ovarian cancer is a rare condition, with an estimated incidence of 1 in every 15,000–32,000 pregnancies, which leads to low clinical suspicion and delayed diagnosis. Most adnexal masses in pregnancy are benign; however, epithelial tumors, particularly high-grade serous carcinoma, represent the most common and aggressive malignant form.

Clinical Case: We present the case of a 39-year-old woman, parity 2, at term, in whom a right ovarian mass was incidentally identified during a scheduled cesarean section, leading to salpingo-oophorectomy. Subsequent histopathological and immunohistochemical studies were consistent with high-grade serous carcinoma; however, the patient did not undergo oncological follow-up. Six months later, she presented with clinical progression, including ascites, pleural effusion, and a contralateral ovarian mass, confirming advanced stage IV disease with a marked elevation in CA-125. She is currently receiving neoadjuvant chemotherapy with paclitaxel, carboplatin, and bevacizumab.

Discussion: This case illustrates the diagnostic difficulties of ovarian cancer during pregnancy, the limited utility of tumor markers during gestation, and the importance of correctly interpreting ultrasound and intraoperative findings. It also highlights the negative impact of the lack of timely follow-up after an incidental finding, which promotes progression to advanced stages and worsens the prognosis.

Conclusion: Ovarian cancer during pregnancy remains a diagnostic and therapeutic challenge. The detection of adnexal masses during prenatal care or obstetric procedures must be accompanied by histopathological examination and close multidisciplinary follow-up. The documentation of clinical cases helps to increase diagnostic suspicion and improve early detection strategies, with the aim of reducing maternal morbidity and mortality associated with this condition.

KEYWORDS: Ovarian cancer, Pregnancy-associated cancer, adnexal masses, CA-125 antigen, high-grade serous carcinoma

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I. INTRODUCTION

Gestational cancer refers to neoplasms diagnosed during pregnancy or within one year after delivery. Its incidence is estimated at approximately 1 case per 1,000 pregnancies, of which only one-quarter is identified during pregnancy, while about 75% is diagnosed in the postpartum period.¹ Among malignant neoplasms associated with pregnancy, the most common are breast cancer, followed by cervical cancer, hematologic neoplasms, ovarian cancer, colorectal cancer, and melanoma.²

The presence of ovarian adnexal masses during pregnancy is relatively rare, with a reported incidence ranging from 0.15% to 5.7%, and in most cases, these are benign lesions.¹² The malignant transformation of benign ovarian tumors, such as mature cystic teratomas, is an exceptional occurrence. Pregnancy-associated ovarian cancer is a rare condition, with an approximate incidence of 1 in every 15,000 to 32,000 pregnancies. Epithelial tumors constitute the predominant histological type, accounting for more than 65% of cases, of which up to 30% exhibit invasive behavior. Within this group, five main subtypes have been described in pregnant women: high-grade serous (70%), low-grade serous (<5%), endometrioid (10%), clear cell (10%), and mucinous (3%). On the other hand, malignant germ cell tumors account for between 16.5% and 18.5% of cases, with dysgerminoma and yolk sac tumor being the most common. The remainder consists of rare neoplasms, such as sarcomas and ovarian metastases from extragenital primary tumors.¹⁻³

From a diagnostic standpoint, ultrasound is the most commonly used initial tool for detecting incidental ovarian lesions and determining their origin during prenatal care. However, the anatomical and physiological changes characteristic of pregnancy can make it difficult to differentiate between benign and malignant masses. Despite this, ultrasound remains the first-line method, highlighting the importance of the first-trimester ultrasound examination, not only for assessing the pregnancy but also for the early identification of adnexal masses. Non-contrast magnetic resonance imaging is a useful diagnostic alternative for better characterization of ovarian lesions. In contrast, the use of computed tomography should be limited due to the potential risk of early pregnancy loss, fetal malformations, intrauterine growth restriction, increased perinatal mortality, and a higher risk of childhood cancer⁽¹⁻⁴⁾.

Tumor markers are also considered in the diagnostic approach; however, their interpretation should be approached with caution because some exhibit physiological elevations during pregnancy, particularly CA-125 and β hCG, especially in the first trimester. However, there are other markers that are minimally affected by pregnancy and may prove more useful, such as carbohydrate antigen 19-9 (CA 19-9), carcinoembryonic antigen (CEA), and antiMüllerian hormone (AMH). In addition, elevated levels of inhibin B, lactate dehydrogenase (LDH), and human epididymal protein 4 (HE4) may aid in diagnosis and

monitoring.²⁻⁴

The management of ovarian cancer during pregnancy includes surgery, chemotherapy, and radiation therapy. Surgery is indicated when the adnexal mass exceeds 10 cm in diameter, persists beyond the first trimester, or contains solid or mixed components. The period considered safest for surgery is the beginning of the second trimester, between 16 and 20 weeks of gestation. Regarding chemotherapy, the treatment of epithelial ovarian cancer in pregnant patients is based on regimens with paclitaxel or docetaxel in combination with carboplatin or cisplatin. Germ cell tumors and ovarian stromal tumors can be treated with paclitaxel and carboplatin as first-line therapy, or with alternative regimens such as bleomycin, vinblastine, and cisplatin (BVP) or cisplatin, etoposide, and bleomycin (PEB) as second-line therapy. It is recommended to initiate chemotherapy starting in the second trimester, due to the increased risk of congenital malformations when administered in the first trimester, and to discontinue it before week 35 to allow for adequate maternal and fetal hematologic recovery. Finally, radiation therapy is not indicated during pregnancy for the treatment of gynecologic neoplasms, except in extreme situations where fetal viability is not possible.²⁻⁴

II. CLINICAL CASE

We present the case of a 39-year-old woman, with two previous pregnancies and one cesarean section, and a history of type 2 diabetes mellitus diagnosed during the first trimester of pregnancy. She was 38.3 weeks pregnant, as confirmed by ultrasound. It is important to note that she had undergone a first-trimester ultrasound (at 13.5 weeks), which reported a normally progressing pregnancy with no abnormalities in the adnexa, including the fallopian tubes and ovaries.

The patient was admitted as scheduled for a cesarean section and bilateral tubal occlusion, as she was at term with a history of a previous cesarean section as well as associated comorbidity, in this case type 2 diabetes; The planned procedure was performed on March 14, 2025; however, during the surgical procedure, a mass attached to the right ovary was identified, measuring approximately 5 × 6 cm, with chocolate-colored contents (Figure 1). In light of this finding, the surgical plan was modified, and a Kerr-type cesarean section, a left Kroenner-type fimbriectomy, a right salpingo-oophorectomy, and ligation of the uterine arteries were performed. The postoperative course was favorable, and the patient was discharged 48 hours later with an appointment for follow-up at the obstetrics outpatient clinic and pending histopathological results; however, no further follow-up by the patient was documented.



Figure 1: Intraoperative findings of the ovarian tumor; note the irregularity of its surface.

Six months later, the patient returned due to progressive enlargement of the abdominal circumference, accompanied by abdominal pain, gastric fullness, and loss of appetite, for which she was admitted to the hospital on November 13, 2025, for evaluation. A pelvic ultrasound was performed on November 14, 2025, which revealed abundant free fluid in all peritoneal spaces, resulting in a floating uterus. The uterus measured $76 \times 40 \times 58$ mm, with regular borders, a homogeneous myometrium, and a linear central endometrium 4 mm thick. Attached to the right adnexa and displaced toward the midline, a rounded image was identified, with regular margins and mixed composition, containing solid and cystic areas; the solid component showed central vascularity on microvascular color Doppler, measuring $13 \times 10 \times 14$ cm, classified as ORADS 4.

Subsequently, the study was supplemented with plain and contrast-enhanced computed tomography of the chest and abdomen, which revealed a 30% right pleural effusion and an anteverted uterus with a homogeneous appearance and no lesions. The right ovary measured 2×2 cm, with no contrast uptake; while the left ovary was found to be enlarged, with well-defined lobulated margins and solid poles, which compressed and displaced adjacent structures, with contrast uptake. The findings were consistent with stage II left ovarian carcinoma, associated with right pleural effusion and ascites. The histopathological and immunohistochemical studies obtained during the surgery performed in March were reviewed, reporting the following:

Histopathology (March 26, 2025): sample of the right ovary and fallopian tube showing a poorly differentiated neoplasm (Figures 2a and b), with extensive areas of necrosis and hemorrhage, measuring 4.6×4.0 cm; fallopian tube with remnants of Walthard's cysts and mesothelial cysts, which is why immunohistochemistry was requested.

Immunohistochemistry (April 7, 2025): p53 positive, PAX8 negative, CK7 positive, estrogen receptors negative, concluding a p53(+)/CK7(+) immunophenotype, consistent with high-grade serous carcinoma with p53 overexpression (Figure 2c).

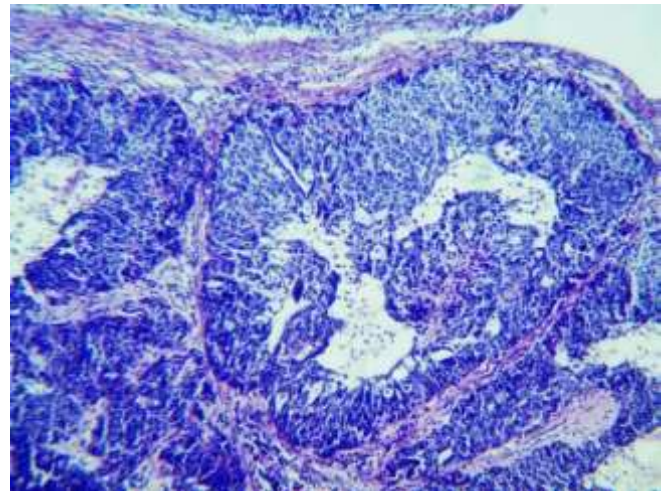


Figure 2a: Poorly differentiated neoplasm with a solid architectural pattern and areas of transitional appearance.

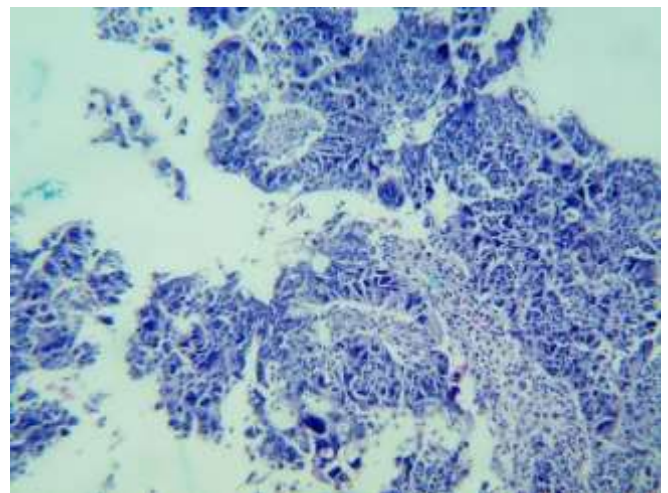


Figure 2b. Marked nuclear pleomorphism with formation of multinucleated giant cells.

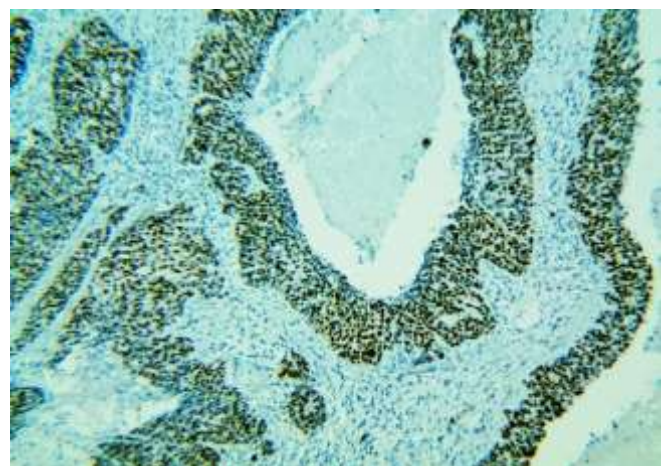


Figure 2c. Positive, diffuse, nuclear immunostaining for p53 in the malignant neoplastic cells.

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Laboratory tests and tumor markers showed the following results:

March 13, 2025: Hb 10.8 g/dL, Hct 31%, platelets 177,000/ μ L, white blood cells 9,100/ μ L, glucose 105 mg/dL, creatinine 0.4 mg/dL, AST 16 U/L, ALT 10 U/L, DHL 199 U/L, PT 11.2 s, aPTT 28 s.

November 14, 2025: CA-125 834 U/mL, CA 19-9 14 U/mL.

November 23, 2025: Hb 14.7 g/dL, Hct 44%, platelets 261,000/ μ L, white blood cells 9,500/ μ L, glucose 203 mg/dL, creatinine 0.6 mg/dL, AST 32 U/L, ALT 36 U/L, BT 1.3 mg/dL, BI 1.2 mg/dL, BD 0.1 mg/dL, DHL 211 U/L, Na 138 mEq/L, K 3.8 mEq/L, Cl 101 mEq/L.

November 28, 2025: Hb 10 g/dL, Hct 30%, platelets 325,000/ μ L, white blood cells 7,700/ μ L, glucose 112 mg/dL, creatinine 0.6 mg/dL, AST 44 U/L, ALT 32 U/L, CA-125 1,390 U/mL.

In conclusion, the patient has been diagnosed with stage IV high-grade carcinoma of the right ovary and a left ovarian mass, which warrants treatment with neoadjuvant chemotherapy consisting of paclitaxel/carboplatin + bevacizumab; the patient is currently receiving her first cycle.

III. DISCUSSION

Pregnancy-associated ovarian cancer is a rare condition, with an estimated incidence of between 1 in 15,000 and 1 in 32,000 pregnancies, which leads to a low level of clinical suspicion and hinders timely diagnosis ^(5,6). The case described in this text illustrates the diagnostic and therapeutic challenges of this condition, as well as the clinical consequences of an incidental diagnosis without adequate oncological follow-up.

The literature indicates that most adnexal masses detected during pregnancy are benign; however, approximately 1–6% are malignant neoplasms ⁷. Among these, epithelial tumors account for more than 65% of cases, with high-grade serous carcinoma being the most common and aggressive subtype ^{5,8}. This histological type is characterized by rapid growth, early peritoneal dissemination, and a high recurrence rate, which is consistent with the clinical course observed in this patient, who developed ascites, pleural effusion, and tumor progression a few months after delivery.

A relevant aspect of the case is that the first-trimester ultrasound showed no adnexal abnormalities. This is consistent with reports indicating that high-grade serous carcinomas may not be detectable in early stages, as they lack obvious precursor lesions and can develop or progress rapidly during pregnancy ^(8,9). Furthermore, physiological changes during pregnancy can hinder the accurate ultrasound characterization of ovarian masses, increasing the risk of diagnostic underestimation ⁷.

The intraoperative finding of an ovarian mass with chocolate-colored contents suggests a lesion initially interpreted as benign, which has been previously described in the literature. Several authors note that macroscopic appearance is

insufficient to rule out malignancy; therefore, any suspicious adnexal mass detected during pregnancy or intraoperatively during a cesarean section should undergo definitive histopathological examination and close follow-up ^{2,6}. In this case, although a salpingo-oophorectomy was performed and a subsequent histopathological diagnosis was obtained, the lack of follow-up contributed to therapeutic delay and disease progression.

With regard to tumor markers, CA-125 has limitations during pregnancy due to its physiological elevation, particularly in the first trimester; however, it regains its diagnostic and prognostic value in the postpartum period ^{1,7}. In this patient, the markedly elevated CA-125 levels at follow-up were consistent with advanced disease, as has been described in high-grade serous carcinomas in stages III and IV ⁷.

From an imaging perspective, ultrasound is the initial method of choice for evaluating adnexal masses during pregnancy; however, gadolinium-free magnetic resonance imaging is considered a safe and effective complementary tool for characterizing complex lesions ^{3,8}. Computed tomography, although it should be avoided during pregnancy, is essential in the postpartum period for staging, as was the case here, allowing for the identification of pleural involvement and abdominal dissemination consistent with advanced disease ⁴. The current management with neoadjuvant chemotherapy based on paclitaxel and carboplatin, combined with bevacizumab, is consistent with international recommendations for advanced epithelial ovarian cancer ⁹. Several studies have demonstrated that this regimen improves the tumor response rate and facilitates optimal subsequent cytoreductive surgery, with a positive impact on overall survival ^{9,10}. The use of bevacizumab is contraindicated during pregnancy, but its administration outside of pregnancy, as in this patient, is widely supported in advanced stages.

Finally, this case highlights the importance of a multidisciplinary approach and timely follow-up of incidental findings during obstetric procedures. The detection of an ovarian mass during a cesarean section represents a key opportunity for early diagnosis; however, without continuity of care, the potential benefit may be lost, with significant consequences for maternal prognosis ^(2,6).

IV. CONCLUSION

The association between ovarian tumors and pregnancy has a low incidence and prevalence, which has limited the literature on the subject regarding their relationship; it is worth noting that epithelial carcinoma is the most common and, as it is a rare condition with low clinical suspicion, only 25% are diagnosed during pregnancy; the remaining patients are diagnosed in the postpartum period, which is significant because this not only delays diagnosis but also treatment for patients affected by this pathological condition. Therefore, ovarian tumors can currently be considered a significant health problem impacting morbidity and mortality among the

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female population worldwide, as they often present asymptotically or with minimal clinical manifestations. At this point, adequate prenatal care is essential, given that first-trimester ultrasound should not only be used for fetal purposes—such as confirming pregnancy viability, determining the number of fetuses, or detecting major fetal malformations, as mentioned by the ISUOG—but also to assess maternal health, for example, the condition of the ovaries, fallopian tubes, and uterus, in order to facilitate maternal and fetal antenatal care and thereby ensure better health outcomes for both the mother and the newborn. It is worth noting that despite significant scientific advances, the diagnosis of ovarian cancer during pregnancy remains a major challenge; This is due to the physiological changes that occur during pregnancy, which in turn alter the interpretation of imaging studies and thereby make it difficult to accurately determine whether an ovarian tumor is malignant or benign; however, we can rely on other imaging studies, such as magnetic resonance imaging (MRI).

On the other hand, regarding tumor markers, these are often affected during pregnancy, with a significant increase in CA 125 as well as hCG, mainly in the first trimester; others, such as ACE and CA 19-9, among others, tend not to be affected by the state of pregnancy.

Finally, given the difficulty of diagnosis and the impact on a pregnant patient, timely treatment is crucial. It is important to raise awareness that this condition can occur during pregnancy, making it highly relevant to document cases such as the one described here. This will help increase diagnostic suspicion and reduce maternal morbidity and mortality rates associated with ovarian cancer in pregnant women.

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