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Ovarian cancer diagnosed during pregnancy: clinicopathological characteristics and management

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SUMMARY: **Ovarian cancer diagnosed during pregnancy: clinicopathological characteristics and management.**

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The aim of this study was to discuss the diagnostic and therapeutic dilemmas in cases of pregnant women with adnexal masses, reporting an interesting case with synchronous literature review. The patient, a gravida 2, para 1, 37 year-old woman was diagnosed with a large unilateral adnexal lesion during a scheduled third trimester ultrasound assessment. A large papillary papule with a network of blood vessels showing decreased resistance in blood flow was noticed as well. Surgical intervention revealed ascitic fluid and a large cystic mass arising from the right ovary. Cesarean section and right salpingo-oophorectomy, including the mass, were performed. Frozen section biopsy was positive for malignancy. Total hysterectomy and left salpingo-oophorectomy, total omentectomy, biopsies from the pelvic peritoneum, pelvic/para-aortic lymphadenectomy and appendicectomy followed. Histology showed mucinous ovarian adenocarcinoma Grade I Stage Ic according to FIGO classification. Surgical intervention, in cases of persisting adnexal lesions, is often necessary, even during pregnancy.

KEY WORDS: Ovarian cancer - Pregnancy - Ultrasound - Adnexal mass - Chemotherapy.

Introduction

The diagnosis of an asymptomatic adnexal lesion during pregnancy has become more common after the widespread use of routine ultrasonography (US) (1). It is estimated that approximately 1-4% of pregnant women are diagnosed with an adnexal mass, while about 90% of such lesions revealed during the first trimester will disappear spontaneously (2-4). The most commonly diagnosed, after histological evaluation, adnexal masses during pregnancy are the mature cystic teratomas, the endometrioid cysts and the corpus luteum cysts (1, 5). On the other hand, the risk of malignancy for the adnexal masses diagnosed during pregnancy is only 2-3% (6). Despite this low incidence, ovarian cancer is considered to be the second most frequent gynecological cancer complicating pregnancy (7).

Most patients are clinically asymptomatic and diagnosis is often based on scheduled US examination during prenatal screening. The most common findings associated with a suspicious for malignancy ovarian mass include: the presence of solid components, multiloculated large tumors with increased wall thickness and maximum diameter > 6 cm, gross internal septa, papillary projections, bilateral lesions, decreased resistance in blood flow during Doppler examination or free abnominal - pelvic fluid (8). Additional imaging with magnetic resonance helps in the better definition of the morphological characteristics of the suspicious lesion. On the other hand, computed tomography (CT), although is the most common imaging examination to detect the extension of a suspected ovarian cancer, is avoided during pregnancy due to the negative effects of ionizing radiation at organogenesis.

The management of women diagnosed with asymptomatic adnexal lesions that persist during pregnancy remains controversial (1). The difficulties in the preope-

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rative differential diagnosis and the possibility of malignancy that is not always easily excluded according only to US findings, suggest that surgical intervention and histological examination are often necessary, even during pregnancy.

The aim of this study was to discuss the diagnostic and therapeutic dilemmas in cases of pregnant women with adnexal masses. A case of a pregnant woman whose prenatal ultrasound examination revealed the presence of a large adnexal mass with sonographic characteristics that led to surgical intervention and diagnosis of ovarian cancer is presented with synchronous review of the literature.

Case report

The patient was a gravida 2, para 1, 37 year-old woman, BMI 21.9, non-smoker with history of HPV cervicitis, one first trimesters' surgical abortion and obstetric history of one vaginal delivery three years ago at the 40th week of gestation when a male, healthy, infant with a body weight of 3260 gr. was born. She was presented for scheduled third trimester ultrasound assessment (fetal growth and Doppler examination) at the 32nd week of gestation.

Ultrasound examination showed a fetus with normal growth and normal quantity of amniotic fluid. No fetal anatomic abnormality was detected and Doppler studies of umbilical and middle cerebral arteries were normal. However, a large unilateral adnexal lesion with a maximum diameter of 13.5 cm was detected (Figure 1). The presence of a large papillary papule with a network of blood vessels showing decreased resistance in blood flow was noticed as well, while tumor marker CA-125 was slightly elevated at 74.8 U/ml. The US examination was repeated two weeks later. No changes were observed in the lesion's dimensions; however the levels of CA-125 showed a rapid increase at 641.7 U/ml.

Magnetic resonance imaging examination revealed an adnexal lesion with papillary papules and maximum diameter of approximately 20 cm. In addition, it showed presence of ascites, without enlarged para-aortic lymph nodes.

Surgical intervention followed at the 36th week of gestation via vertical incision. A large cystic mass (max. diameter 20 cm) arising from the right ovary was found in the abdominal cavity as well as 2 lt. of ascitic fluid. Sample of ascitic fluid was sent for cytological examination. A cesarean section took place and a male, healthy, infant with a body weight of 2530 gr. was born. The right adnexa including the mass were resected and frozen section biopsy was positive for malignancy. Total hysterectomy and left salpingo-oophorectomy, total omentectomy, biopsies from the pelvic peritoneum, pelvic/para-aortic lymphadenectomy and appendicectomy were performed. No macroscopic enlarged lymph nodes or pathology from the organs of the upper abdomen was noticed.

The patient was under close monitoring in the intensive care unit for two days; she recovered well without postoperative complications. The cytological examination of ascetic fluid sample was positive for the presence of malignant cells. Final histological examination showed Grade I mucinous cystadenocarcinoma of the right ovary (Figure 2). The left adnexa, the uterus, the totally 26 removed pelvic/para-aortic lymph nodes, the omentum (40 x 15 cm), the appendix and the biopsies from the pelvic peritoneum were negative for malignant metastatic invasion. The case was classified as Stage Ic ovarian mucinous cystadenocarcinoma and the patient received adjuvant platinum and taxane chemotherapy.

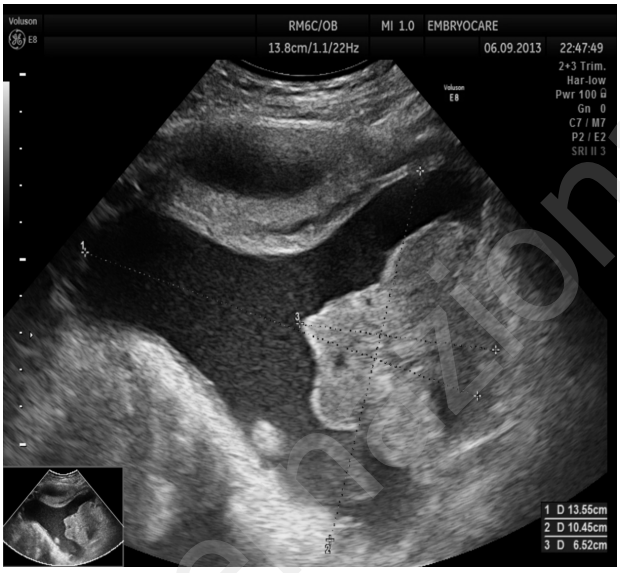

Fig. 1 - Ultrasonographic image of an ovarian cystic lesion (max. diameter 13.5 cm) with a large papillary papule.

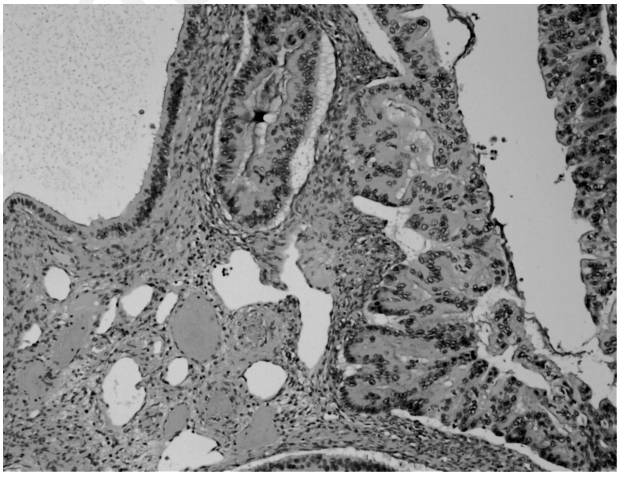

Fig. 2 - Histological section of ovarian mucinous neoplasm showing atypical proliferation and stromal infiltration (H – E, x 120).

Discussion

In agreement with literature data, the patient in this reported case was clinically asymptomatic and diagnosis was based on incidental findings during scheduled prenatal US examination. In another recently published study from our Department, 78.1% of pregnant women were asymptomatic and diagnosis of adnexal lesions was an incidental finding mainly arrived at by chance during ultrasound examination for routine prenatal monitoring, or during a cesarean section for obstetric indications (1). It is true that the early diagnosis of ovarian lesions during pregnancy is achieved thanks to serial ultrasound examinations for prenatal monitoring. This early diagno-

sis probably explains the generally good prognosis for pregnant women diagnosed with ovarian cancer.

Ultrasonography is considered to be the best diagnostic tool in order to reveal adnexal masses in both pregnant and non-pregnant women (9). Several studies suggest that the sonographic characteristics of the adnexal lesions can be sufficient to determine which patients are truly at increased risk for malignancy versus those who can be followed up expectantly (1). With color Doppler examination, a pulsality index below 1.0 in a morphologically suspicious area would suggest malignancy (10). High serum levels of CA-125 are normal finding during the first trimester and then return into normal ranges. This marker is not really useful during pregnancy, but serial measurements remain interesting during the differential diagnosis procedure and postoperative follow-up (11).

In 1963, Munndell suggested that removal of an ovarian mass during pregnancy is indicated for three main reasons: 1. elimination of a potential cause of dystocia, 2. risk of torsion, rupture, or hemorrhage and 3. danger of malignancy (12). On the other hand, other studies support the excision of all persisting adnexal masses into the second and third trimester owing to the risk of malignancy (13). However, the recent study of Leiserowitz et al. showed a low incidence of 2.15% for ovarian cancer among pregnant women with adnexal masses (14). The low incidence of cancer among adnexal lesions during pregnancy in combination with the sufficient results of Doppler in differential diagnosis approach led to the strategy of exploratory laparotomy during pregnancy only for persistent masses with suspicious for malignancy sonographic characteristics.

Remarkable is that our previous study revealed a high incidence of malignancy among pregnant women diagnosed with adnexal masses who were surgically treated (15.6%) (1). In general, the optimal management, in cases of suspicious for cancer ovarian masses during pregnancy, has not yet been established. The treatment aim is to achieve the best oncologic outcome, while preserving the fetus viability (8). Several factors have to be considered as the best strategy in these cases is the individualized management based on the gestational age at diagnosis and the patient's preference. Three main options with both advantages and disadvantages for the mother and the fetus should be discussed. The first is to terminate the pregnancy and perform standard treatment following the recommendations for non-pregnant women. A second approach is to continue pregnancy and delay the surgical investigation until fetal lung maturity is reached. The third scenario is to administer neoadjuvant chemotherapy during pregnancy, until fetal lung maturity is obtained, as platinum / taxanes therapy appears to be safe if it is given after 14 weeks of gestation (8).

Pregnant women with obvious ultrasound findings of simple, small in diameter, ovarian cysts, without vascularization or solid components, could undergo conservative management with routine ultrasonography follow up. In these cases, whenever a cesarean delivery is performed for obstetrical indications, ovarian cystectomy can be performed at that time, avoiding the adverse effect of surgery and anesthesia during the ante partum period to the fetus and the mother.

If there is high suspicion of malignancy or if the patient's clinical condition requires urgent treatment, surgery should not be delayed. Emergency laparoscopy or laparotomy is indicated for complications such as torsion or rupture. A delay in elective surgery is suggested until weeks 16-18 if there is suspicion of low malignancy mass, thus reducing the risk of miscarriage due to hormonal independence of the corpus luteum starting at this gestational age.

Surgical intervention with adequate staging remains the cornerstone of ovarian cancer diagnosis and therapy even during pregnancy. The decision to perform conservative or radical surgery depends on histology, degree of extension, patient's age and desire for fertility preservation.

Conclusions

Adnexal malignancy represent a comorbid disease in pregnancy and examination of the ovaries should be part of pregnancy ultrasound assessment protocols especially in the first trimester. Therapy of ovarian cancer during pregnancy is a challenging clinical condition and patients should be referred to specialized centers. Evidence-based guidelines regarding the therapeutic approach of ovarian cancer during pregnancy are limited and most evidence is based on case reports and retrospective series, since prospective studies or clinical trials do not appear feasible.

Conflict of interest statement. All authors declare that they have no conflict of interest.

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