

MALIGNANT OVARIAN TUMORS AND PREGNANCY

Stoyan Stoyanov¹, Silviya Mangarova¹, Ivan Todorov¹, Emiliya Kisiova², Maria Magdalena Ignatova³, Koni Ivanova⁴

¹Clinic of Gynecology and Obstetrics – University Hospital “Prof. Dr. Stoyan Kirkovich” – Stara Zagora

²Clinic of Gastroenterology – University Hospital “Prof. Dr. Stoyan Kirkovich” – Stara Zagora

³Clinical oncologic complex – Stara Zagora

⁴Clinic of General and clinical pathology – University Hospital “Prof. Dr. Stoyan Kirkovich” – Stara Zagora

Abstract

The incidence of ovarian tumors during pregnancy is from 1: 300 to 1: 556 pregnant. Of all the ovarian tumors during pregnancy, malignant tumors have a frequency of: 1:15000 to 1: 32000.

Case report: I. K. was admitted to Clinic of Gynecology and Obstetrics of the University Hospital Stara Zagora with a diagnosis of Graviditas m.l. IV. Kysta ovarii dextra. Ultrasound revealed a cyst on the right ovary with an oval shape, smooth inner and outer walls, filled with fluid measuring 111/94 mm. diagnosed as early as 8 weeks of gestation. At 14 gest.week. was hospitalized - right adnexectomy and wedge resection of the left ovary with histological result - serous tumor with low malignant potential.

The second patient N.S. at the age of 25 was admitted with an admission diagnosis of Graviditas ml IV. Kysta ovarii sinistra. Ca 125 values at admission were 432 U / ml. Sonography revealed a single ultrasound homogeneous cyst of the left ovary with a diameter of 75/47 mm at 14 weeks of gestation. From histological examination of the tumor formation - left ovary with a serous tumor with a low degree of malignancy.

The first patient underwent 3 cycles of chemotherapy at - 25, 28 and 31 gestational weeks. At 33 weeks, a spontaneous normal vaginal birth followed. In the second patient, a normal fetus was born after a cesarean section.

The combination of ovarian cancer and existing pregnancy is a rarity that raises many questions in diagnostic and therapeutic terms. Finding the right solution is ambiguous due to the unclear impact of pregnancy on ovarian cancer and borderline variants of ovarian tumors.

Keywords: *pregnancy, serous ovarian tumor, chemotherapy*

Introduction

The incidence of the ovarian tumors during pregnancy varies between 1: 300 to 1: 556 pregnant women. From all ovarian tumors during pregnancy, malignancies have a frequency of 1:15000 to 1:32000 [1]. Most of the patients have no specific symptoms. More often, ovarian tumors are detected antepartally during routine ultrasound screening. Cesarean births, which have been first choice in the recent years, could lead to their accidental detection.

Germ cell tumors are the most commonly diagnosed tumors over the age of 30, and gonadal-stromal tumors are more often common under the age of 30 [2]. Both types of tumors are in the group of epithelial ovarian cancers. There are currently 262 known cases of malignant ovarian tumors and pregnancy in the English literature for the last 30 years, derived from 45 studies / from 01-01.1986 - 31.12.2016 / From them: epithelial tumors – (n=69) and non-epithelial tumors- (n=193) (Germinative cell tumors – (n=145) and sex cord tumors – (n=48)) [3, 4, 5]. Due to their rarity, it is difficult to choose the most appropriate behavior. To clarify each case more precisely, we need to perform some paraclinical and imaging investigations. CT and CAT are dangerous for the fetus during pregnancy and only sonography and MRI can be used [6]. The study of Ca 125 is inaccurate, because pregnancy itself can increase tumor markers in the range of several hundred

(200, 300 E and more). The laboratory levels of Ca 125 above 1000 E are most likely to indicate ovarian cancer. To make the most correct decision we are guided by the following principles [4, 7]:

1. In the case of a unilateral ovarian tumor with good motility and size less than 10 cm (4 inches) and no ascites, ultrasound monitoring until the second trimester of pregnancy is preferred. If the tumor grows during the observation, surgical treatment should be undertaken as soon as possible.
2. When diagnosing an ovarian tumor at the first visit with the following characteristics: standing still in the small pelvis, covering both ovaries, the tumor has septa with increased effect of Collor Doppler or there is freely moving fluid in the small pelvis or abdomen requires urgent surgical treatment.
3. In the presence of an ovarian tumor in one ovary with dimensions over 6 cm with a complex structure or ascites and persists up to 16 g.s., surgery is required.
4. Surgical intervention with low suspicion of malignancy should be performed in 16-18 weeks, when the risk of miscarriage in connection with the corpus luteum is lower and by what time the functional ovarian cysts are resorbed in a large number of cases. After surgery in the first trimester, the risk of miscarriage is about 10%.
5. If ovarian tumors is detected in the third trimester, it is better to wait for fetal maturity if there is a low suspicion of malignancy. The desire for premature birth, in view of faster treatment, has a poor prognosis for the fetus.
6. The principles of surgical treatment are adequate for the type of tumor and its stage of development. They do not depend on the fact that the surgical treatment is during pregnancy or not.
7. In the earliest stages of ovarian cancer, the principles of surgical treatment are unilateral oophorectomy or adnexectomy. This rule applies especially to tumors with borderline malignancy or germ cell tumors. After conservative surgery and subsequent chemotherapy, all patients in the postoperative period have a good prognosis.
8. Invasive epithelial ovarian cancers have the worst prognosis. In them, the surgical treatment consists of a total hysterectomy together with the adnexa, an omentectomy and a multiple lymph node biopsy.
9. There are data on the use of cisplatin and cyclophosphamide or paclitaxel and carboplatin during the second and third trimesters, without significant toxic effects on the fetus and without fetal malformations.

Fortunately, ovarian cancer during pregnancy is detected at an early stage, because pregnant women are under dispensary and sonographic supervision from the earliest stage of pregnancy, before the symptoms of advanced ovarian cancer appear [8]. The prognosis is similar to that outside of pregnancy and depends mainly on the type of tumor and the stage of its development. The hormonal influence of pregnancy can lead to histological changes in serous tumors with low malignant potential and they can be misdiagnosed as invasive carcinomas [9, 10].

First case report

We report a case of patient I. K admitted to Clinic of Gynecology and Obstetrics in University hospital in Stara Zagora with a diagnosis of Graviditas m.l. IV and Kysta ovarii dextra. A routine ultrasound examination revealed a cyst on the right ovary with an oval shape, smooth inner and outer walls, filled with fluid and measuring 111/94 mm (Fig.1). diagnosed early as 8 weeks of gestation. In 14 gestation week the patient was hospitalized and performed conservative surgical treatment – including right adnexectomy and wedge resection of the left ovary with a histological

result from the emergency biopsy - "cyst with borderline malignancy". The final histological result was - "serous tumor with low malignant potential; left ovary - no evidence of malignant process; abdominal punctate - with advanced autolytic changes, and no data for malignant process were found". At the suggestion of the Oncology Committee of the University hospital in Stara Zagora, the histological result was proposed for revision, and after the revision of the slides the histology result was the same. The postoperative period went smoothly and the patient was discharged with preserved pregnancy and with a final diagnosis - Graviditas m.l. IV. There were 3 cycles of chemotherapy in - 25, 28 and 31 gestational weeks. When the patient was in 33 gestation weeks, due to uterine contractions, we performed tocolysis and corticosteroid therapy for prophylactic to increase the fetal lung maturity. Two days later, the patient have spontaneous normal vaginal birth of a fetus weighing 2280g. in good condition followed. There are no complications and malformations of the fetus. The placenta was without change.

Seven days after birth, is done a total hysterectomy, left adnexectomy, omentectomy and the paraaortic lymph nodes dissection. The result from the histological investigation was - "Uterus - proliferative endometrium; ovary - serous papillary cystadenoma; 3. fallopian tube and omentum - acute circulatory disorders. " Cytological analysis of ascites fluid did not show the presence of tumor cells. Postoperatively, 6 courses of chemotherapy with Paclitaxel and Carboplatin were performed.

Second case report

In the second case we report a patient N.S. at 25 years old admitted to the University Hospital in Stara Zagora with an admission diagnosis of Graviditas ml IV and Kysta ovarii sinistra. The laboratory levels of Ca 125 values at the time of the admission were 432 U / ml. Sonography revealed a single-chamber ultrasound homogeneous cyst of the left ovary with a diameter of 75/47 mm and a live fetus with biometric data corresponding to 14 weeks of gestation (Fig.2, 3). A left adnexectomy was performed with a wedge-shaped resection of the right ovary. Regional lymph nodes palpably were not enlarged. From the express histological examination of the tumor formation the result was left ovary with a serous tumor with a low degree of malignancy. From the final histological investigation the same diagnosis was confirmed. From the investigation from the right ovary the histological diagnosis was follicular cysts, fallopian tube - acute circulatory disorders, abdominal point - advanced autolytic and coagulation processes in which there is no evidence of malignant process.

The Oncology Committee of the University Hospital - Stara Zagora recommends radical surgical treatment when the morphological maturity of the fetus is reached. The patient was discharged in clinically healthy with a preserved pregnancy and a definitive diagnosis of Graviditas ml IV with carcinoma ovarii sinistra. At 38 weeks of gestation, a cesarean section was performed, followed by a total hysterectomy along with the right adnexa and a total omentectomy. A male fetus weighing 2550 grams / 47 cm was born in good condition. The postoperative period – was normal. The histological result was: - ovary-follicular cysts; fallopian tube - normal structure; uterus - acute circulatory changes and omentum - with circulatory disorders.

At the suggestion of the Oncology Committee the patient was referred to Oncology Centre for adjuvant chemotherapy and medical examination, which she refused. At the moment, she is clinically healthy and annually monitors the values of Ca 125, which are within normal limits.

Conclusion

The incidental finding of an adnexal mass in pregnancy is becoming more common with the increased use of ultrasound [1, 9]. Data from the literature supports a high rate of spontaneous resolution and an extremely low rate of clinically relevant pathology. It is also important to note that no prospective, randomized trials are available to evaluate the various diagnostic and therapeutic options [10, 11, 12]. The combination of ovarian cancer and existing pregnancy is a rarity that raises many questions in diagnostic and therapeutic terms. The diagnosis and management of borderline ovarian tumors during pregnancy are still not standardized, because these tumors are rarely encountered. Finding the right solution is ambiguous due to the unclear impact of pregnancy on ovarian cancer and borderline variants of ovarian tumors.

References:

1. N. Schwartz, I. E. Timor-Tritsch, and E. Wang, "Adnexal masses in pregnancy," *Clinical Obstetrics and Gynecology* 2009;52(4):570–585.
2. J. D. Seidman and R. J. Kurman, "Ovarian serous borderline tumors: a critical review of the literature with emphasis on prognostic indicators," *Human Pathology*, 2000;31(5):539–557.
3. H. Marret, C. Lhommé, F. Lecuru et al., "Guidelines for the management of ovarian cancer during pregnancy," *European Journal of Obstetrics Gynecology and Reproductive Biology*, 2010;149(1):18–21.
4. Matsumoto A, Ito T, Hamaguchi F, Kasuga M, Mikami T, Hino M, Yokoyama R, Yamamura S, Sakata H, Minamiguchi S, Mandai M, Yoshida T. Primary and recurrent serous borderline tumors during pregnancy: a case report and literature review *Int Cancer Conf J.*, 2021;10(3):160-169. doi: 10.1007/s13691-021-00471-5
5. Okumura T, Muronosono E, Tsubuku M, Terao Y, Takeda S, Maruyama M. Anaplastic carcinoma in ovarian seromucinous cystic tumor of borderline malignancy. *J Ovarian Res.* 2018;11(1):77. doi: 10.1186/s13048-018-0449-1.
6. Hanhan HM, Gungorduk K, Ozdemir İA, Gokcu M, Sancı M, Ayaz D, Özeren M. Primary retroperitoneal mucinous cystadenocarcinoma during pregnancy. *Obstet Gynaecol.* 2014;34(6):535-8. doi: 10.3109/01443615.2014.910501.
7. Dayan D, Abu-Abeid S, Klausner JM, Sagie B. Primary Retroperitoneal Mucinous Cystic Neoplasm: Authors' Experience and Review of the Literature. *Am J Clin Oncol.* 2016;39(5):433-40. doi: 10.1097/COC.0000000000000298.
8. Ishioka S, Hayashi T, Endo T, Baba T, Honma H, Saito T. Advanced epithelial ovarian carcinoma during pregnancy. *Int J Clin Oncol.* 2007 Oct;12(5):375-8. doi: 10.1007/s10147-007-0655-0.
9. Valentin L, Ameye L, Franchi D, Guerriero S, Jurkovic D, Savelli L, Fischerova D, Lissoni A, Van Holsbeke C, Fruscio R, Van Huffel S, Testa A, Timmerman D. Risk of malignancy in unilocular cysts: a study of 1148 adnexal masses classified as unilocular cysts at transvaginal ultrasound and review of the literature. *Ultrasound Obstet Gynecol.* 2013 Jan;41(1):80-9. doi: 10.1002/uog.12308.
10. Vidal Urbinati AM, Iacobone AD, Di Pace RC, Pino I, Pittelli MR, Guerrieri ME, Preti EP, Franchi D. Borderline ovarian tumor in pregnancy: can surgery wait? A case series.
11. *Arch Gynecol Obstet.* 2021 May 5. doi: 10.1007/s00404-021-06080-0.
12. Korenaga T.R.K., Tewari K.S. Gynecologic cancer in pregnancy. *Gynecol. Oncol.* 2020;157:799–809. doi: 10.1016/j.ygyno.2020.03.015.

Figure 1: Ultrasound examination revealed a cyst on the right ovary with an oval shape, smooth inner and outer walls, filled with fluid and measuring 111/94 mm.



Figure 2: Sonography revealed a single-chamber ultrasound homogeneous cyst of the left ovary with a diameter of 75/47 mm



Figure 3: Sonography revealed a single-chamber ultrasound homogeneous cyst of the left ovary with a diameter of 75/47 mm

