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Management of a patient diagnosed with ovarian cancer during pregnancy

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Insufficient diagnosis of ovarian tumors during pregnancy and decreased oncological alertness constitute huge problems that can subsequently have an unfavorable outcome for both the pregnant woman and the fetus. The difficulties of diagnosing and treating ovarian cancer during pregnancy were demonstrated on the following clinical case example. In pregnant patient A. at 19–20 weeks of pregnancy, a lesion was found in the area of the right appendages ($100.9 \times 55.4 \times 93.4$ mm, $V = 273$ cm³), with many tissue partitions and parietal tissue inclusions. The growth of the neoplasm was noted (CA-125 884 U/ml) and the pain syndrome occurred in the patient at 23–24 weeks of pregnancy. Magnetic resonance imaging revealed a solid-cystic neoplasm of the right ovary (cystadenoma?) and surgery was performed in November 2019. Based on the results of histological examination, a high-grade serous ovarian cancer was diagnosed without signs of microsatellite instability MSI-H/dMMR (in the right ovary, in the biopsy of the left fallopian tube). The patient received two cycles of polychemotherapy (TC scheme). The treatment was tolerated satisfactorily (CA-125 287.3 U/ml). At a gestational age of 34 6/7 weeks (January 2020), a simultaneous operation was performed, including a lower midline laparotomy, a lower uterine segment caesarean section, extirpation of the uterus with appendages, and an omentectomy. A boy was born (weight 2280 g, height 44 cm) with the Apgar score of 7/7 points, with no complications noticed in the postpartum period. Postoperative histological examination showed metastasis of carcinoma in the left ovary with signs of therapeutic pathomorphosis. The treatment was completed in March 2020 after six cycles of polychemotherapy.

Keywords: ovarian cancer; pregnancy; case report.

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Ведение пациентки с диагнозом рак яичника на фоне беременности

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Недостаточная диагностика опухолей яичника на фоне беременности, низкая онкологическая настороженность составляют пласт проблем, которые впоследствии могут приводить к неблагоприятному исходу и для беременной, и для плода. На примере клинического случая продемонстрированы трудности диагностики и лечения рака яичника при беременности. У повторнобеременной пациентки А. на сроке беременности 19–20 нед. обнаружено объемное образование в области правых придатков ($100,9 \times 55,4 \times 93,4$ мм, $V = 273$ см³) с множеством тканевых перегородок и пристеночными тканевыми включениями. При сроке беременности 23–24 нед. отмечен рост новообразования, появление болевого синдрома (содержание СА-125 — 884 ЕД/мл). Заключение магнитно-резонансной томографии: кистозно-солидное новообразование правого яичника (цистаденома?). Выполнено хирургическое вмешательство (ноябрь 2019 г.). По результатам гистологического исследования диагностирован серозный рак яичника высокой степени злокачественности без признаков микросателлитной нестабильности dMMR/MSI-H (в правом яичнике, в биоптате левой маточной трубы). Назначена полихимиотерапия по схеме паклитаксел + карбоплатин. Проведены два цикла химиотерапии. Пациентка лечение перенесла удовлетворительно (содержание СА-125 — 287,3 ЕД/мл). При сроке беременности 34 6/7 нед. (январь 2020 г.) произведена симультантная операция: нижнесрединная лапаротомия, кесарево сечение в нижнем сегменте матки, экстирпация матки с придатками, оментэктомия. Родился мальчик весом 2280 г, ростом 44 см с оценкой по шкале Апгар 7/7 баллов. Послеродовой период протекал без осложнений. Результат послеоперационного гистологического исследования: метастаз карциномы в левый яичник с признаками лечебного патоморфоза. Лечение закончено в марте 2020 г. после проведения шести циклов полихимиотерапии.

Ключевые слова: рак яичника; беременность; клинический случай.

Как цитировать:

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BACKGROUND

An average of 0.2%–2% of ovarian neoplasms is diagnosed during pregnancy, approximately 1%–6% of which are malignant [1–3]. Diagnostics and treatment of cancer during pregnancy is a complicated problem; however, treatment during pregnancy gives the best potential results for the mother, as well as absence of teratogenic effect on the fetus and its developmental delay [4]. Clinical manifestations of ovarian cancer may be absent during pregnancy. It can be either an accidental finding at ultrasound (US) examination, or manifested clinically during pregnancy and postpartum period.

Ovarian cancer is manifested by pain in the abdomen and lumbar region, constipation, bloating, dysuric manifestations, etc. [5, 6]. These symptoms are nonspecific, as they can occur in a normal course of pregnancy [7]. According to literature, pregnancy has no negative effect on the clinical course of malignant ovarian tumor [8].

For the first time in a study by J. Palmer et al. from 1958 to 2007, 41 cases of ovarian cancer during pregnancy were described using a combined method of treatment (surgery and chemotherapy) [7]. Surgery and chemotherapy are performed after week 16 of pregnancy (complete organogenesis of the fetus) if a woman wishes to maintain her pregnancy. Chemotherapy must be completed three weeks before the expected date of delivery due to predictable hematological complications [9].

Long-term follow-up of children whose mothers received chemotherapy during pregnancy showed no signs of increased risk of congenital abnormalities or mental retardation [4]. Despite some complexity, according to international recommendations, cancer treatment during pregnancy should be performed according to generally accepted principles. Thus, cancer treatment is possible during pregnancy without threat for the mother and the fetus.

DESCRIPTION OF THE CASE

Patient A. is a 34-year-old, multigravida, with a history of term delivery by cesarean section in 2012, without complications.

A US scan of the pelvic organs was performed before planning for pregnancy, which revealed no pathology. Heredity was aggravated due to ovarian cancer in her maternal grandmother.

The patient was registered in the antenatal clinic with this pregnancy at a term of 14/15 weeks, was examined regularly by the obstetrician-gynecologist, and had no complaints.

The initial screening was performed upon registration; the US of the pelvic organs revealed no pathological changes.

When performing repeated US at gestational age of 19/20 weeks, a space-occupying lesion was found in the area of the right appendages measuring $100.9 \times 55.4 \times 93.4$ mm, $V = 273$ cm³, with many tissue partitions and parietal tissue inclusions. The patient was consulted by a gynecologist-oncologist, who recommended to determine the level of CA-125 and control US to assess the neoplasm growth dynamics.

The patient was monitored by an obstetrician-gynecologist, and a second examination was performed at a term of 23/24 weeks of gestation, of which results showed neoplasm growth in the right appendages, with CA-125 level of 884 U/ml. The patient complained of pain in the lower right abdomen.

The patient was hospitalized for surgical treatment at the D.O. Ott Research Institute of Obstetrics, Gynecology, and Reproductology with a diagnosis of 24/25 weeks of pregnancy; malignant neoplasm of the right ovary and pain syndrome.

Magnetic resonance imaging (MRI) of the pelvic organs revealed a multi-chamber solid neoplasm of the right ovary with a size of $130 \times 90 \times 80$ mm. In the upper pole of the neoplasm, a cyst was found with multiple thin septa measuring 90×70 mm; in the lower pole, a thick-walled cyst was noted with protein content, iso-intensive on T1-WI with a soft tissue component protruding into the cyst cavity up to 12 mm thick, characterized by a hyperintense signal on diffusion-weighted imaging and hypointense on apparent diffusion coefficient. In the central sections of the neoplasm between the large cysts described, multiple cysts of different sizes ranging from 10 to 25 mm in diameter were detected; a pathological soft tissue component was determined in the cysts cavity and between cysts. The left ovary is usually located, with the size of 30×20 mm and homogeneous in structure.

Conclusion of MRI indicated a solid-cystic neoplasm of the right ovary (cystadenoma) (Fig. 1).

Results of fibrogastroduodenoscopy revealed cardiac insufficiency and erythematous gastropathy.

A US scan of the abdominal organs was performed, which revealed no pathological neoplasms.

Surgical intervention was performed (November 2019) in the form of diagnostic laparoscopy, conversion laparotomy, adnexectomy on the right, and biopsy of the left fallopian tube, greater omentum, and peritoneum of the right lateral canal (Fig. 2).

Based on histological examination results, a high-grade serous ovarian cancer was diagnosed without signs of microsatellite instability deficient mismatch repair/high-frequency microsatellite instability (in the right ovary, in the biopsy sample of the left fallopian tube).

The level of CA-125 tumor marker decreased from 884 to 357 U/ml after the surgery.

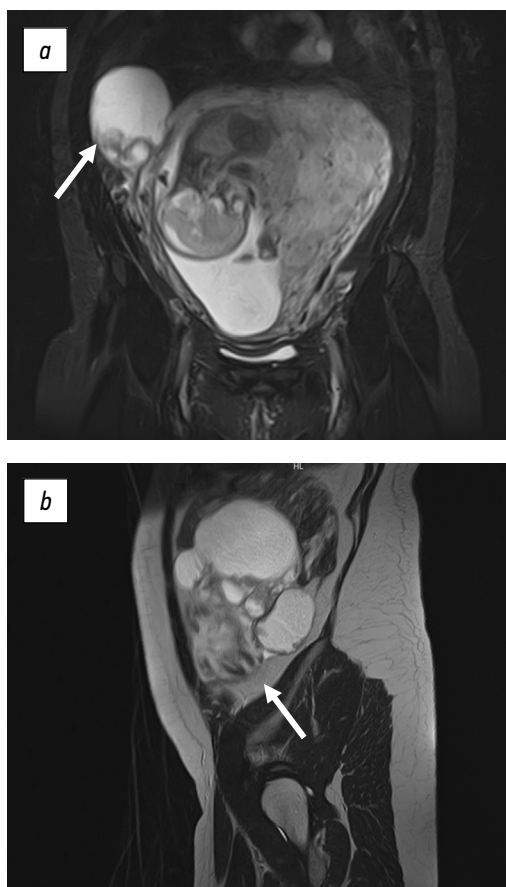


Fig. 1. Magnetic resonance imaging. T2-WI in coronal (a) and sagittal (b) planes showing a cystic-solid formation of the right ovary (arrow)



Fig. 2. Gross specimen: right appendages, omentum biopsy sample

For further treatment, the patient was referred to the V.A. Almazov National Medical Research Center of the Ministry of Health of the Russian Federation (obstetric and gynecological hospital level IIIB).

A case conference was held, further management approach for the patient was discussed, and provisional diagnosis of malignant neoplasm of the ovary, stage IIa (T2aNxM0G3) was made; condition after laparotomy,

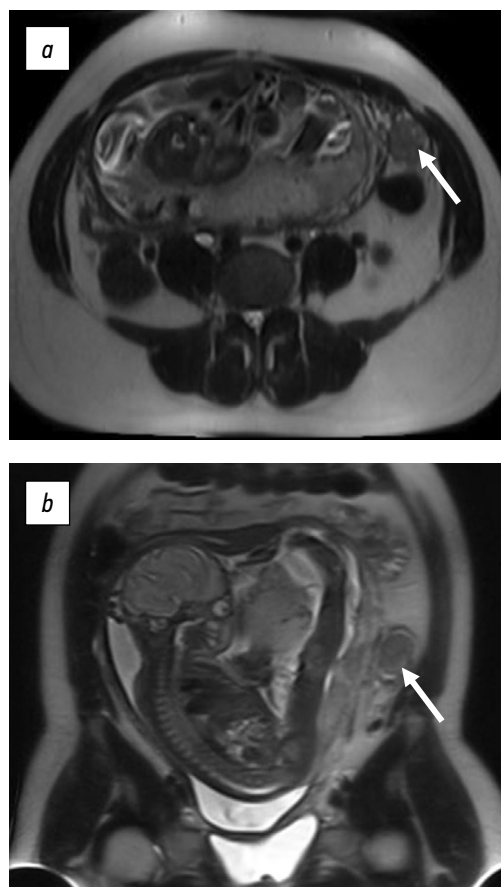


Fig. 3. Magnetic resonance tomograms, weighted by T2, in the axial (a) and coronal (b) planes, showed a solid neoplasm of the left ovary, 19 × 14 × 12 mm in size

adnexectomy on the right, and biopsy of the greater omentum and left fallopian tube, was made.

A conversation was held with the patient and relatives (in agreement with her); the nature of the disease, course characteristics, risks of progression, and risks of various treatment options for the health of the patient and the fetus were explained in detail. Taking into account the histological structure of the tumor, process prevalence, patient's desire to maintain the pregnancy, and polychemotherapy (PCT) was prescribed according to the scheme (paclitaxel + carboplatin), as well as repeated MRI examination of the pelvic organs and abdominal cavity, and control of the CA-125 level. One-stage surgical delivery was performed in a radical volume. The combination therapy (after delivery) of up to six PCT cycles was continued.

Before the initiation of PCT, MRI studies of the pelvic and abdominal organs were performed

Conclusion indicated pregnancy at week 27; solid neoplasm of the left ovary (39 × 25 × 29 mm); MR presentation without signs of metastatic lesions of the abdominal organs.

Two PCT cycles were performed according to the standard scheme with 175 mg/m² of paclitaxel, and AUC-6 of carboplatin. The treatment was satisfactory, with CA-125 level of 287.3 U/mL.

According to dopplerometry results at a gestational age of 33 2/7 weeks, an increase in circulatory disorders in the mother–placenta–fetus system from degree IA to degree II was recorded. A repeated MRI study of the pelvic organs was performed, which revealed partial regression of the tumor (Fig. 3).

The case conference had discussion regarding the patient in order to determine further therapeutic approach. Taking into account the presence of fetal growth retardation syndrome and incident disorders of fetal-uterine blood flow, it was decided to refuse PCT cycle 3 due to the high risk of perinatal complications. In addition, performing preterm delivery by cesarean section with a single-step surgery in a radical volume (extirpation of the uterus and left appendages, omentectomy) and subsequent continuation of PCT was decided. In the early postpartum period, suppression of lactation is indicated due to the need to continue PCT, which is incompatible with breastfeeding.

At a term of 34 6/7 weeks (January 2020), a simultaneous surgery was performed, including lower midline incision, cesarean section in the lower segment of the uterus, extirpation of the uterus with appendages, and omentectomy.

A boy was born weighing 2280 g, with height of 44 cm, and an Apgar score of 7/7 points. The postpartum period was uneventful.

In the postpartum period, lactation was suppressed. The result of postoperative histological examination showed metastasis of carcinoma in the left ovary with signs of therapeutic pathomorphosis. Lymph nodes examination showed no signs of tumor process.

Final diagnosis was the premature second delivery at a term of 34 6/7 weeks; scar on the uterus after cesarean section in 2012; malignant neoplasm of the ovary, stage IIA, T2aN0M0G3R0, condition after laparotomy, adnexectomy on the right at a term of 24/25 weeks, two cycles of PCT according to the paclitaxel + carboplatin scheme, lower midline incision, cesarean section in the uterus lower segment, extirpation of the uterus with appendages, and omentectomy.

The patient was discharged in satisfactory condition with the child on day 14 of the postoperative period.

The examination revealed a mutation in the *BRCA1* gene, and therefore it is necessary to conduct a case conference with a medical geneticist to determine a selective screening program in scope of additional regular breast examination using MRI and mammography annually or performing preventive surgeries.

The treatment was completed in March 2020 after six cycles of PCT. The patient is monitored by an oncologist-gynecologist, and the last examination was in September 2020, which revealed disease remission. The child was healthy.

DISCUSSION

Oncological alertness, a multidisciplinary approach to the treatment of patients with cancer during pregnancy and joint patient treatment by an obstetrician-gynecologist and a gynecologist-oncologist enabled the determination of timely management approach for pregnant woman and reduce the risk of potential complications in the mother and the fetus. An important aspect is the time and mode of delivery since unreasonable preterm delivery can lead to predictable negative consequences for the fetus. In accordance with the main recommendations of the European Society of Medical Oncologists and the European Society of Gynecological Oncologists, it is necessary to treat pregnant women with an established diagnosis of malignant tumor in the same way as non-pregnant women, without delay, and the combination of cancer and pregnancy is not an indication for early delivery or termination of pregnancy. Prenatal exposure to a malignant neoplastic process, in combination with or without treatment, does not impair cognitive functions, state of the cardiovascular system, and general development of children [10]. This clinical case demonstrates main problems in the management of patients who are pregnant with established ovarian cancer. Absence of pathognomonic signs of the disease and low oncological alertness of the doctor led to a late diagnosis establishment and delayed start of therapy.

After the ovarian cancer diagnosis establishment, the patient was managed in full accordance with the international clinical guidelines. Management errors included the fact that the ovaries were not described in the initial US scan during pregnancy, which determines the need to introduce a point on the size and structure of the ovaries into the US protocol in the first trimester. After the detection of a large ovarian tumor during the repeated US screening (19/20 weeks) and a high level of CA-125 tumor marker, active treatment was started, and surgical intervention was performed immediately. In this case, the surgery was performed only at a term of 25 weeks, and stage II ovarian cancer was established. The prescription of chemotherapy for the treatment and prolongation of pregnancy is in accordance with the clinical guidelines of the European Society for Medical Oncology and the European Society of Gynecological Oncology. The treatment was performed in the Perinatal Center with the participation of a gynecologist-oncologist, obstetrician-gynecologist, neonatologist, and anesthesiologist. During the use of chemotherapy, the tumor of the second ovary regressed according to MRI data. Due to the approach selected, the pregnancy was prolonged to week 34 6/7.

The preterm delivery was determined by concerns about possible deterioration of the fetus during the course

of PCT. Nevertheless, preterm delivery and simultaneous implementation of a radical surgery provided a favorable outcome for the mother and fetus.

CONCLUSIONS

Management of patients with cancer during pregnancy should be multidisciplinary. The joint treatment of female patients by an obstetrician-gynecologist and a gynecologist-oncologist enables the determination of timely management

approach and timing and method of delivery, as well as reduce the risk of potential complications in the mother and the fetus.

ADDITIONAL INFORMATION

Patient consent. The patient voluntarily signed an informed consent for the publication of personal medical information in anonymized form in the Journal of Obstetrics and Gynecological Diseases.

Conflict of interest. Authors declare no conflict of interest.

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