

# CLINICAL CASE

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## CLINICAL CASE OF HETEROTOPIC PREGNANCY AFTER IN VITRO FERTILIZATION

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## КЛИНИЧЕСКИЙ СЛУЧАЙ ГЕТЕРОТОПИЧЕСКОЙ БЕРЕМЕННОСТИ ПОСЛЕ ЭКСТРАКОРПОРАЛЬНОГО ОПЛОДОТВОРЕНИЯ

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Ectopic pregnancy occupies a significant place in the structure of causes of maternal mortality. Timely diagnosis is even more complicated when there is a combination of both uterine and ectopic localization of the ovum. The article describes the clinical observation of heterotopic pregnancy, features of the clinical picture, diagnostic search and treatment strategy. The possibility of preservation of intrauterine pregnancy after surgical removal of a pathologically located second fertilized ovum has been shown. The patient was admitted to the gynecological department with complaints of bleeding from the genital tract against the background of delayed menstruation. An ultrasound examination revealed the presence of dichorionic diamniotic twins, with one fertilized egg localized in the interstitial part of the fallopian tube stump. Surgical removal of the stump with the fertilized egg was performed. The intrauterine pregnancy was preserved. Thus, with timely diagnosis of heterotopic pregnancy and adequate tactics, it is possible to maintain intrauterine pregnancy.

**Keywords.** Heterotopic pregnancy, surgical treatment, prolongation of intrauterine pregnancy, in vitro fertilization.

Приведено клиническое наблюдение сочетания маточной и внематочной беременности после экстракорпорального оплодотворения. Было проведено оперативное удаление культи маточной трубы с беременностью в истмическом отделе с сохранением маточной беременности у пациентки, перенесшей тубэктомия слева по поводу непроходимости маточной трубы при подготовке к программе ВРТ и ту-

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бэктомии справа в связи с последующей трубной беременностью. Показано, что при динамическом наблюдении возможно родоразрешение при доношенном сроке гестации. Используются данные медицинских документов наблюдения пациентки в амбулаторных и стационарных условиях, в том числе результаты лабораторных, инструментальных, гистологических методов исследования. Получено информированное согласие пациентки для публикации результатов наблюдения.

**Ключевые слова.** Гетеротопическая беременность, оперативное лечение, пролонгирование маточной беременности, экстракорпоральное оплодотворение.

## INTRODUCTION

Ectopic pregnancy (EP) continues to be an important issue in obstetrics and gynecology. The etiological factors of abnormal nidation of the fertilized egg are diverse. EP occurs in 1–2 % of total pregnancies and causes up to 10 % of maternal mortality [1; 2]. Risk factors for ectopic pregnancy include inflammatory diseases of the internal genital organs, operations on the fallopian tubes and uterus, hormonal disorders, endometriosis, advanced reproductive age, use of intrauterine contraceptive devices, endocrine diseases, and sexual infantilism [3; 4]. A special place is given to the use of assisted reproductive technologies (ART). [5; 6]. Currently, clinical data is accumulating on the combination of intrauterine and ectopic pregnancy when transferring several embryos in ART programs for patients with a history of tubectomy, i.e., pregnancy develops in the uterine tube stump together with intrauterine pregnancy [7]. The study of risk factors for retrograde embryo migration, in addition to those mentioned, revealed the following: a history of ectopic pregnancy, reconstructive surgery on the fallopian tubes, congenital anomalies of the uterus development, uterine fibroids; the use of gonadotropin-releasing hormone agonists in the ovulation stimulation protocol; ovarian hyperstimulation; intensive progesterone support of the luteal phase; assisted hatching of the embryo,

transfer technique and embryo quality, smoking; patient's age [3; 8; 9].

There are rare forms of ectopic pregnancy: multiple, persistent, combination of uterine and extrauterine, which cause additional difficulties in diagnosis [10; 11]. In heterotopic pregnancy, the attachment of the fertilized egg is more often observed in the fallopian tubes (97.7 %), while isthmic localization is less common than others. It is precisely the rarity of pregnancy in the interstitial part of the fallopian tube, the peculiarities of the ultrasound picture that lead to some difficulties in differential diagnosis of uterine and ectopic pregnancies. With this localization, pregnancy develops quite successfully. Its growth is facilitated by good blood supply to this area of the uterus and the development of collaterals during pregnancy.

Of particular interest is the development of an ectopic pregnancy in the stump of the fallopian tube. Usually, tubectomy is performed due to an ectopic pregnancy, as well as the presence of sactosalpinx in preparation for ART programs. At the same time, surgical removal of an extrauterine pregnancy is a necessary condition for treatment. There are cases described in the literature of spontaneous rupture of the uterus along the scar after removal of pregnancy of this localization [12–14]. It is logical to assume a complicated course of preserved uterine pregnancy, the need for high-quality dynamic observation to achieve a positive result.

The aim of the study is to present a clinical case of a combination of intrauterine and ectopic pregnancies with a successful outcome after surgical removal of the fertilized egg located in the interstitial part of the fallopian tube stump in a patient after bilateral tubectomy and pregnancy in an ART program.

### **MATERIALS AND METHODS**

The analysis of the clinical observation of a patient who had a combination of intrauterine and ectopic pregnancy after in vitro fertilization was carried out. Data from medical documents were used: medical records of an inpatient, dispensary card of a pregnant woman, birth history. To diagnose the presence and localization of pregnancy, an ultrasound examination of the pelvic organs was performed upon admission to the gynecological department at 8–9 weeks, determination of  $\beta$ -hCG was carried out. The material removed intraoperatively (fallopian tube stump, elements of the fertilized egg) was sent for histological examination. The excised pieces were fixed in 10 % neutral formalin, after standard processing, paraffin sections were stained with hematoxylin and eosin. Microscopic examination was performed on a Primo Star Carl Zeiss microscope at magnifications  $\times 4$ ,  $\times 10$ . Further studies were carried out as part of monitoring the pregnant woman in an out-patients department.

The patient's informed consent was obtained for publication of the results of observation.

### **CLINICAL CASE**

Patient K., 28-year-old, applied to the gynecology department on June 5 2023

with complaints of bright, spotting bloody discharge from the genital tract and dull pain in the lower abdomen against the background of menstrual delay. A  $\beta$ -hCG test was performed, and a positive result was obtained. An ultrasound examination revealed a dichorionic diamniotic twin pregnancy with one fertilized egg localized in the fallopian tube stump. The patient was hospitalized. Medical history: the patient considers herself ill for two weeks, when dark, spotting, bloody discharge from the genital tract first appeared 6 weeks after the transfer of two embryos under the ART program. The patient has a normosthenic physique, body mass index is  $24.7 \text{ kg/m}^2$ . The general condition is satisfactory. Heart rate is 74 bpm, blood pressure is 109/71 mmHg, body temperature is  $36.2^\circ\text{C}$ . There are no concomitant diseases. The patient experienced menarche at the age of 13, with regular menstruation lasting 7 days every 28 days, which is moderate and painless. She has been sexually active since the age of 15 and has not used protection against pregnancy. The patient is currently married. In 2018, she was examined for primary infertility, due to obstruction of the fallopian tube, laparoscopic tubectomy was performed on the left side. In 2019, the first tubal pregnancy occurred, which ended in laparoscopic tubectomy on the right side. The second pregnancy in 2021 ended in incomplete miscarriage at 7–8 weeks after in vitro fertilization (IVF), complicated by acute endometritis. The current pregnancy is the third one, induced by IVF, transfer of two embryos was performed.

The result of pelvic ultrasound examination on June 5 2023 was the following: two

fetal eggs were detected in the uterine cavity. The first fetal egg was 38 mm in diameter. The embryo was visualized, its length was 22 mm, which corresponded to a gestational age of 8 weeks and 6 days. The heart beat was positive. The yolk sac was visualized with a diameter of 3.9 mm. The predominant localization of the villous chorion was on the posterior wall, closer to the fundus of the uterus. The structure of the chorion had not changed. The second fetal egg, 21 mm in diameter, was visualized in the stump of the fallopian tube on the right side. The embryo was visualized, its length was 20 mm, corresponding to a gestational age of 8 weeks and 4 days. The heart beat was also positive. The yolk sac had a diameter of 4.1 mm. There were no peculiarities in the right and left ovaries. The conclusion indicated an 8–9 week pregnancy with dichorionic diamniotic twins and an ectopic pregnancy on the right. On June 6 2023, a telemedicine consultation was held with the National Medical Research Center for Obstetrics, Gynecology and Perinatology named after academician V.I.Kulakov, Ministry of Health of the Russian Federation. Given the presence of tubal pregnancy, it was recommended to perform a tubectomy while preserving uterine pregnancy.

The surgery on June 8 2023 revealed that the uterus was up to 9 weeks of gestation of soft consistency. There was a rounded thin-walled formation measuring 6x7 cm in the area of the uterine tube stump. The left fallopian tube wasn't visualized as it had been removed. The ovaries weren't visually changed. A section was made in the thin part of the right uterine tube stump formation. An embryo 4 cm long and chorionic tissue were removed from the cavity. The uterine tube stump was removed.

The abdominal cavity was dried. Napkins and instruments were checked. The abdominal cavity was closed tightly. A cosmetic suture was applied to the skin. An aseptic bandage was placed. Blood loss was 50 ml.

Gross specimen included embryo, chorion, uterine tube tissue. Pregnancy was confirmed histologically. On the 7th day after the operation, the patient was discharged in satisfactory condition under observation of the gynecologist in an outpatients department. The following discharge recommendations were given: to appear at the antenatal clinic on June 16 2023; to treat the postoperative wound for a month; to wear a bandage for up to three months; to avoid physical exertion; to avoid heat treatments for two months; to abstain from sexual intercourse for two months; to consult a gynecologist at the patient's medical facility with the results of histology.

Further dynamic observation was carried out on an outpatient basis in accordance with the clinical protocol "Normal pregnancy". Ultrasound examination was performed at 12 weeks, fetal heart rate was 155 beats per minute, crown-rump length was 56 mm, nuchal translucency thickness was 1.7 mm. The nasal bone was visualized. Dopplerometry of the tricuspid valve was normal. Dopplerometry of the venous duct was 1.05. Fetal dimensions corresponded to the gestational age. The results of maternal serum biochemistry were the following: free  $\beta$ -hCG subunit 68.28 IU/L (1.327 MoM); PAPP-A: 6.115 IU/L (1.458 MoM).

"The calculated risks were as follows: trisomy 2 – 1 in 5,621, trisomy 18 – 1 in 13,134, trisomy 13 – less than 1 in 20,000, preeclampsia before 37 weeks of pregnancy – 1 in 1,856, fetal growth restriction before

37 weeks – 1 in 395, spontaneous delivery before 34 weeks – 1 in 1,659. Considering the anamnestic data, cervical measurement was performed at 16 weeks of gestation, the length of the closed part of the cervical canal was 39 mm. Further repeated examinations with an interval of two weeks did not reveal shortening of the cervix until 24 weeks.

Until 34 weeks, the patient received micronized progesterone 200 mg per day vaginally. Then, at 19 weeks of pregnancy, a second screening ultrasound examination was performed. There was one fetus in the uterine cavity in cephalic presentation, according to fetometry data, it corresponded to 19 weeks of gestation. The placenta was on the back wall of the uterus, closer to the fundus, its thickness was 22 mm, maturity degree was 0. The amount of amniotic fluid was normal. The umbilical cord had three vessels, central attachment to the placenta. The length of the closed part of the cervical canal was 38 mm, the internal os was closed. Dynamic monitoring showed no pathology. Dopplerometry of blood flow velocity in the “mother – placenta – fetus” system revealed no abnormalities. Similar studies at 32–34 weeks also indicated the normal development of pregnancy, absence of fetal malformations and signs of placental insufficiency. Cardiotocography was regularly performed from 32 weeks of pregnancy every two weeks and also indicated a satisfactory condition of the fetus. At 38–39 weeks of gestation, the patient was hospitalized in an obstetric hospital for delivery. The condition was satisfactory. Abdominal circumference was 98 cm, height of uterine fundus was 37 cm, head presentation of the fetus. Pelvic dimensions were 24–27–29–18.5 cm, which corresponded to a generally

uniformly narrowed pelvis of the 1st degree of narrowing according to the classification of A.F. Palmov. Solovyov index was 1.5. Estimated fetal weight was 3580 g according to ultrasound examination results. The main factor determining the delivery tactics was surgical intervention in the first trimester of pregnancy in the amount of removal of the isthmic portion of the fallopian tube, combined with anatomically narrow pelvis and reproductive history of the woman. It was collectively decided to proceed with a planned operative delivery by caesarean section. A male fetus weighing 3,510 g and 52 cm long was delivered, Apgar score was 8/8 points. A scar was noted in the area of the right uterine corner during the surgery, without penetration into the uterine cavity. The blood loss amounted to 680 ml.

## RESULTS AND DISCUSSION

Both domestic and foreign literature emphasize the increasing incidence of rare forms of ectopic pregnancy. Combinations of uterine and ectopic pregnancies occur on average once in 30,000 pregnancies. More often than not, abnormal attachment of the fertilized egg occurs in different parts of the fallopian tube. When the location of the fertilized egg is in the intramural or isthmic portion of the tube, the ultrasound picture may mimic a uterine pregnancy. Literature data show that even indications of voluntary sterilization or tubectomy do not exclude the development of an ectopic pregnancy in the future [5; 7]. Special attention should be paid to the patients who have undergone removal of the fallopian tubes and transfer of several embryos in ART programs [8; 9]. It is these women who are at high risk of

heterotopic pregnancy. A concerning point is the localization of the fertilized egg in one of the corners of the uterus detected by ultrasound. The appearance of complaints about pain in the lower abdomen and spotting, bloody discharge from the genital tract should prompt a differential diagnosis between threatened miscarriage and heterotopic pregnancy. The uniqueness of the described case lies in the fact that an ectopic pregnancy developed in the isthmic part of the uterine tube stump up to 8–9 weeks.

Thus, women with a history of surgery on the fallopian tubes, including tubectomy, are at risk of developing heterotopic pregnancy. These factors play a significant role in the retrograde migration of the fetal egg. Ultrasound examination greatly facilitates determining the localization of the fetal egg and conducting differential diagnosis between uterine and ectopic (isthmic) pregnancy. Timely removal of an abnormally localized fetal egg increases the likelihood of carrying a uterine pregnancy to term. At the same time, a complicated course of pregnancy is expected, primarily miscarriage and premature birth. When planning observation in an out-patients department conditions, it is necessary:

- 1) to perform cervical measurement at 16–24 weeks;

- 2) in special cases, to provide progesterone support;

- 3) to carry out delivery in accordance with the obstetric situation and the extent of surgical intervention performed during this pregnancy.

## CONCLUSIONS

In the presented clinical case, risk factors for ectopic pregnancy were a history of

ectopic pregnancy, operations on the fallopian tubes (bilateral tubectomy), and in vitro fertilization.

Early diagnosis of this pathology using ultrasound examination allowed timely removal of the ectopic fetal egg with further carrying a uterine pregnancy to term and delivery at full-term pregnancy.

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Naumova V.Ya., Semyonova M.V., Mukhametgalimova A.R. – research concept and design.

Naumova V.Ya., Semyonova M.V., Mukhametgalimova A.R. – data collection and processing.

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