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Research Article

CLINICAL CHANGES IN ECTOPIC PREGNANCY OBSERVED IN WOMEN

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ABSTRACT

Ectopic pregnancy is the most common pathology in gynecologic practice, leading to the reduction and loss of reproductive function. Diagnosis of ectopic pregnancy in cases of its occurrence interrupts and intra-abdominal bleeding does not provide significant difficulties. Of interest is the search for ectopic gestational sac located in rare forms of ectopic pregnancy. Although progress has been made in the diagnosis and treatment of ectopic pregnancy is not possible to achieve reduction of complications associated with it.

KEYWORDS

Ectopic pregnancy, risk factors, diagnostics, treatment.

INTRODUCTION

Ectopic pregnancy occupies one of the leading places in the structure of maternal mortality: it is in the first place as the cause of intra-abdominal bleeding and in second place in the structure of acute gynecological diseases. An ectopic pregnancy was first described in the 17th century, but the diagnosis was made only after the death of the patient. The case of intravital diagnosis of an ectopic pregnancy was recorded in 1812. Until 1870, only 500 cases of ectopic pregnancy were described in the world literature, and the treatment methods used did not give a positive result. In 2018, the maternal mortality rate from an ectopic pregnancy in Russia amounted to 0.26 per 100,000 live births, and in Uzbekistan - 0.29 [3, 14]. The purpose of this review article is to provide obstetrician-gynecologists with the most complete information

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about the problems associated with an ectopic pregnancy and how to solve them. An ectopic pregnancy is one of the common causes leading to infertility. Ectopic pregnancy does not belong to the considered reproductive losses, however, to date, it continues to remain one of the main problems of reproductive medicine related to the subsequent fertility of a woman. After an ectopic pregnancy, many develop adhesions in the pelvis, in 60-80% of patients - infertility, in 20-30% of patients - repeated ectopic pregnancy [8].

In recent years, there has been a tendency to increase the frequency of ectopic pregnancy. One of the main factors in the occurrence of an ectopic pregnancy is inflammatory diseases of the female genital organs, which in the etiology of an ectopic pregnancy make up 42-80% [2, 24]. Particularly noteworthy are sexually transmitted infections, and this is especially true for chlamydial salpingitis, which occurs in 50-60% of patients with ectopic pregnancy. Inflammatory diseases of the internal genital organs lead to impaired patency, damage to the neuromuscular apparatus of the fallopian tube and neuroendocrine disorders, which contributes to the occurrence of an ectopic pregnancy. An equally important risk factor for ectopic pregnancy is abortion, almost every second woman has a history of it [8, 21]. The frequency of ectopic pregnancy with the use of intrauterine contraceptives (IC) reaches 3-4%, which is almost 20 times more than in the general population. While taking oral contraceptives containing progestogens, the frequency of ectopic pregnancy rises to 2 per 100 women / years, which is apparently caused by the inhibitory effect of progestogens on the uterine mucosa and a slowdown in the contractile activity of the fallopian tubes against the background of preserved ovulation [6, 15].

Against the background of taking ovulation inducers, the frequency of an ectopic pregnancy increases to 10%, and with the development of ovarian hyperstimulation syndrome, the risk of ectopic pregnancy increases three times in comparison with the general population. Previous surgical interventions on the tubes are also a risk factor for the development of an ectopic pregnancy. Reconstructive plastic surgery is often accompanied by a violation of the anatomy. This explains the very high (up to 25%) frequency of ectopic pregnancy after such operations. Operations that are accompanied by a high risk of tubal pregnancy are salpingostomy, neosalpingostomy, fimbrioplasty, ovariosalpingolysis, and tube anastomosis [19, 4].

The presence of tumors or tumor-like formations of the uterus and appendages, endometriosis of the uterus and appendages, genital infantilism, the onset of pregnancy in late reproductive age, smoking 1.5-3.5 times increases the risk of an ectopic pregnancy. Sometimes an ectopic pregnancy occurs in women

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with perfectly normal fallopian tubes that do not have known risk factors. Thus, the factors contributing to the occurrence of an ectopic pregnancy are diverse, but they are often found in combination. The most common form of ectopic pregnancy is tubal (96.5-98.5%). The location of the ovum in the fallopian tube, according to the United States and Russia, is presented as follows: interstitial department - 2-3% and 2-3%, respectively; isthmic - 11-12% and 10-40%; ampullar - 80% and 30-60%; fimbrial - 4-5% and 5-10% [1, 22].

About 5% of ectopic pregnancies have a rare localization: simultaneously in both tubes, in the interstitial part of the tube, ovary, closed rudimentary horn, cervix, between the leaves of the broad ligament, abdominal cavity, scar area after cesarean section, transitional form, combination of uterine and ectopic pregnancy. Information on the prevalence of rare forms of ectopic pregnancy is limited and presented as follows: ovarian - 1: 7000 births, in a closed rudimentary horn - 1: 100000 births, cervical - 1: 8000 - 18000 births, abdominal - 1: 3000-10000 births [1, 18] . One of the rarest forms of ectopic pregnancy is simultaneous bilateral tube pregnancy - 5 cases per 1 million studies of surgical material. Rare forms of ectopic pregnancy are often not taken into account by practitioners, are diagnosed late and cause high maternal morbidity and mortality.

Interstitial pregnancy accounts for 2% of ectopic pregnancies. Patients with interstitial tubal pregnancy in most cases go to the doctor later than with ampullar or isthmic. The pregnancy rate in the uterine angle increases to 27% in patients with a history of salpingoectomy, IVF, and embryo transfer. Interstitial tubal pregnancy is associated with most of the deaths caused by ectopic pregnancy in general, since it is often complicated by a rupture of the uterus.

Ovarian pregnancy is one of the rarest ectopic pregnancy options: of 200 ectopic pregnancies, one is truly ovarian. In recent years, an increase in its frequency has been noted, which is associated with some types of intrauterine and oral hormonal contraception.

Pregnancy in a closed rudimentary horn occurs due to the transperitoneal migration of a fertilized egg or sperm. Anatomically, this pregnancy can be attributed to the uterine one, however, due to the fact that in most cases the rudimentary horn has no message with the vagina, clinically such a pregnancy proceeds as an ectopic one. The development of pregnancy in a closed rudimentary horn leads to its rupture early due to a significant defect in the structure of the endometrium and severe hypoplasia of the myometrium.

Cervical pregnancy is quite rare, but it is very dangerous. The risk of cervical pregnancy is increased by a previous abortion or cesarean section, Asherman's syndrome, the mother taking diethylstilbestrol, uterine fibroids and IVF during pregnancy. In this case, the

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ovum is implanted in the cylindrical epithelium of the cervical canal. The trophoblast villi penetrate deep into the muscle membrane of the neck, which leads to the destruction of its tissues and blood vessels, and ends with massive bleeding. With an intraligamentary ectopic pregnancy, the fetal egg develops between the leaves of the wide ligament of the uterus, where it enters a second time after a rupture of the tube wall towards the mesentery of the fallopian tube. Abdominal pregnancy, both primary and secondary, is extremely rare, in about 1.4% of cases of ectopic pregnancy. Abdominal pregnancy is usually the result of secondary implantation: tubal miscarriage, rupture of the uterus, rupture of the elementary horn of the uterus, rupture of the ovary. A fetal egg can attach to various organs of the abdominal cavity. Very rarely, abdominal pregnancy reaches a long time. As a rule, it ends with rupture of the capsule of the fetus in the early stages, heavy bleeding and peritoneal shock. The clinical manifestations of abdominal pregnancy are diverse, depending on the location and gestational age. The prognosis for mother and fetus during abdominal pregnancy is very serious. Maternal mortality, usually from massive blood loss, reaches 20%, and perinatal - 40-95%. Congenital malformations and deformities are observed in 21.4% of the fetuses. Some cases of abdominal pregnancy are described, with a manifesting picture of an acute abdomen and hemorrhagic shock.

Diagnosis of abdominal pregnancy is very difficult. A classic finding with ultrasound scan is the absence of echoes of the myometrium between the maternal bladder and the fetus, poor visualization of the placenta. To confirm the diagnosis, CT and MRI can be useful to distinguish between the anatomical structures, the place of attachment of the placenta and the vascular connections involved. Differential diagnosis of abdominal pregnancy includes miscarriage, intrauterine fetal death, placental abruption, acute abdomen during pregnancy, uterine fibroids with intrauterine pregnancy.

Late abdominal pregnancy with a live fetus requires immediate surgical intervention. The attitude of doctors to the separation of the placenta remains controversial. Its separation during surgery may be accompanied by damage to neighboring organs, bleeding. Complications with an abandoned placenta: bleeding, infections, bowel obstruction, preeclampsia, failure to breastfeed due to placental hormones. It is extremely rare (1: 30000) that a combination of uterine and ectopic pregnancy (heterotopic pregnancy) is observed when there is a normally developing uterine in combination with tube pregnancy in the uterine cavity. In recent years, due to the use of assisted reproductive technologies in the treatment of infertility (stimulation of ovulation), the frequency of heterotopic pregnancy has increased to 1: 100 pregnancies.

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In recent years, with the increasing prevalence of delivery by cesarean section, a new form of ectopic pregnancy has appeared - in the area of the uterine scar. Kanat-Pektas M. and co-authors. (??) presented a systematic review of clinical trials of women with ectopic pregnancy in the scar area after cesarean section. A thorough search of electronic databases showed that between January 1978 and April 2014, 274 articles were published. The methods of treatment and restoration of fertility in this form of ectopic pregnancy are considered. The most commonly used methods were systemic administration of methotrexate, embolization of the uterine artery, dilation and curettage, hysterotomy and hysteroscopy. According to the review, hysteroscopy and laparoscopic hysterotomy are safe and effective surgical methods. Uterine embolization should be reserved for cases of massive bleeding or if arteriovenous malformation is suspected. Systemic administration of methotrexate, dilatation, and curettage are not recommended as first-line treatment. These procedures are associated with a high risk of complications and hysterectomy.

Some researchers propose to distinguish the so-called transitional forms of tubal pregnancy, in which the fetal egg is simultaneously located in neighboring sections of the tube or in adjacent organs of the abdominal cavity: tubal abdominal, tubal-ovarian, fimbrial, etc.

In general, the diagnosis of an ectopic pregnancy is quite difficult. This is due to a variety of clinical manifestations - from minor pain in the lower abdomen with scanty spotting from the genital tract to hemorrhagic shock. Abdominal pain is observed in 95% of cases of ectopic pregnancy. Delayed menstruation from several days to several weeks occurs in 90% of cases. Bloody discharge from the genital tract occurs in 50-80% of cases. Soreness of the uterine appendages during bimanual examination is a constant symptom, which is often combined with soreness of the cervix when it is displaced. An increase in the uterus is observed in 25% of cases of an ectopic pregnancy. The size of the uterus is usually less than the expected gestational age.

Of great importance for the diagnosis of ectopic pregnancy are additional research methods: ultrasound scan, determination of the level of the HCG subunit in the blood, as well as laparoscopy. Transvaginal ultrasound scanning has a high resolution. A progressive uterine pregnancy can be diagnosed already from 1.5-3 weeks, while the diameter of the fetal egg is 4 mm. The cardiac activity of the embryo is determined after a 3.5-week gestation period. The transvaginal ultrasound technique allows you to visualize the fetal egg about 1 week earlier than with the transabdominal technique. Color Doppler Mapping (CDM) allows you to visualize increased vascularization in the area of ectopic trophoblast. This

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increases the diagnostic sensitivity during ectopic pregnancy from 71 to 87% compared with transvaginal ultrasound.

Son elastography is a new promising method in the early diagnosis of ectopic pregnancy. It made it possible in 100% of cases to accurately diagnose an ectopic pregnancy with a moderate increase in the level of HCG, when the visualization of the fetal egg using standard imaging modes was still not available.

Of great importance in the diagnosis of ectopic pregnancy is the identification of the level of human chorionic gonadotropin, which is determined starting from the 7-8th day after fertilization. HCG is different in carbohydrate and amino acid composition, therefore, quantitative determination of it increases specificity and significantly increases the accuracy of diagnosis. The rate of increase in HCG levels in the blood helps to differentiate between normal and ectopic or non-developing pregnancy. In normal pregnancy, the HCG content in the blood doubles every 2 days.

Currently, the possibility of radioimmunological testing of HCG in blood serum makes it possible to establish a diagnosis of ectopic pregnancy in 98.8% of cases. If by immunological tests the amount of HCG is detected at about 1 IU / ml, then radioimmunological testing reveals significantly lower amounts of HCG - 1 mIU / ml. The advantages of the radioimmunological method for determining HCG are its high sensitivity and specificity, the absence of cross-reactions with other hormones and proteins that are identical in structure, and the ability to accurately determine the daily amount of secreted hormone. A type of radioimmunological control is the immunoradiometric method - the determination of antigen using labeled antibodies, which allows the detection of HCG in serum a week before the expected menstruation. Laparoscopy is the most accurate, reliable and informative method for detecting an ectopic pregnancy, and in almost 100% of cases it allows you to establish the correct diagnosis, and in many cases to carry out surgical treatment. Laparoscopy also has known disadvantages. Usually, if a patient is suspected of having an ectopic pregnancy, laparoscopy should be performed at the final stage, when the use of other, less invasive research methods does not allow the doctor to establish an accurate diagnosis [21, 26].

Puncture of the abdominal cavity through the posterior arch retains its relevance and significance, allows you to diagnose an interrupted and interrupted ectopic pregnancy in various conditions and in the absence of the possibility of using ultrasound. The advantages of culdocentesis are the speed and relative safety of the procedure. The disadvantages include soreness and frequent dubious results. Curettage of the uterine cavity in order to diagnose an ectopic pregnancy is undesirable.

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At the present stage, there are several different approaches to the treatment of tubal pregnancy: surgical, drug and expectant management of patients. A common method for treating ectopic pregnancy is the surgical method. Over the past two decades, minimally invasive surgery techniques have been used predominantly. Laparoscopic access in the treatment of patients with ectopic pregnancy worldwide has in most cases become the method of choice. Laparoscopy has undeniable advantages over laparotomy: a small incision, a shorter duration of the operation, an insignificant frequency of complications, the possibility of implementing organ-preserving principles, shortening the patient's hospital stay, and early physical and social rehabilitation. Dynamic laparoscopy is especially indicated in cases of suspected chorionic persistence: visual monitoring of the fallopian tube, its reorganization, and, according to indications, local administration of methotrexate, however, there have recently been opponents of methotraxate administration [24].

With laparoscopy, both radical (salpingoectomy) and conservative plastic surgery are performed. Organ preserving operations on the fallopian tube are possible in the form of salpingotomy followed by suturing of the wall of the fallopian tube after removal of the ovum or salpingostomy, when the incision of the wall of the fallopian tube is not sutured after removal of the ovum and the wound heals by secondary intention. After any of these techniques for treating an ectopic pregnancy, the fallopian tube can maintain its normal function.

The nature of plastic surgery depends on the location of the fetal egg. When localized in the fimbrial region, the fetal egg is extruded (rather traumatic manipulation) or aspirated using an aquapurator. When the fetal egg is localized in the tube ampule, salpingotomy is also more often performed. With isthmic localization of the ovum, salpingotomy or resection of the tube segment with the ovum with anastomosis is applied end-to-end. With interstitial localization of the ovum, laparotomy and salpingoectomy with excision of the tubular angle of the uterus are advisable. With this localization, it is usually not possible to use laparoscopic access.

The necessary conditions for laparoscopic operations are a satisfactory condition of the patient and stable hemodynamics. An absolute contraindication for laparoscopy in ectopic pregnancy is hemorrhagic shock of the 3-4th degree, which most often occurs with blood loss exceeding 1500 ml. Relative contraindications are: unstable hemodynamics (hemorrhagic shock of 1-2 degree) with blood loss not exceeding 1500 ml; interstitial localization of the ovum; the location of the ovum in the extra uterine horn; rupture of the wall of the fallopian tube. General contraindications for laparoscopy: obesity, severe adhesions, cardiovascular and pulmonary failure.

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However, there are reports of the successful use of laparoscopic surgery with significant blood loss, rupture of the tube, interstitial and "old" tube pregnancy.

Laparotomy is used to treat those patients who have hemodynamic disturbances, as well as localization of the fetal egg in the region of the rudimentary uterine horn. Laparotomy access is preferred for surgeons who do not own laparoscopy in patients where laparoscopic access is obviously difficult: with severe obesity, the presence of a significant amount of blood in the abdominal cavity, with a pronounced adhesive process in the abdominal cavity.

For drug treatment, the most commonly used anticancer drug is methotrexate, which is a structural analogue of folic acid. Methotrexate prevents the transition of folic acid into its active form. This leads to disruption of the synthesis of amino acids, which are necessary for the formation of DNA in the embryo. In 1982, Tapaka first reported the successful treatment of interstitial pregnancy with methotrexate in a 19-year-old woman. The patient was diagnosed with laparotomy, the abdominal wall is tightly sewn, and methotrexate was given parenterally. According to the results of hysterosalpingography performed after treatment, both pipes were passable. Methods of administration of methotrexate are different: systemic administration orally and parenterally; local administration with laparoscopy, under ultrasound control or transcervical; combined introduction (a combination of systemic and local methods). The dosage of methotrexate is individual.

In recent years, a relatively new method has come into clinical practice - endovascular uterine artery embolization (UAE). According to some researchers, UAE, devoid of a number of serious limitations of surgical and conservative treatment, may become the method of choice in patients with cervical pregnancy. A method for the combined treatment of cervical pregnancy was proposed, consisting of superselective embolization of the uterine arteries in combination with the intra-arterial administration of methotrexate and the use of mifepristone (600 mg) orally. This method allowed to preserve the reproductive function of women.

The technique of operation during abdominal pregnancy depends on the location of the fetal egg. Usually, the operation is reduced to the removal of the fetal egg and subsequent hemostasis. Implantation of a fetal egg in the abdominal cavity (in the omentum, intestine, parietal or visceral peritoneum) is rare, but if this happens, pregnancy can be terminated. In such cases, with laparotomy, the main technical difficulties are in the separation of the placenta. In most cases, it is better not to touch the placenta, especially in the second or third trimester of pregnancy, hoping for its spontaneous resolution. To accelerate and enhance this process, methotrexate can be administered.

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Treatment for ovarian pregnancy involves removal of the fetal egg or wedge-shaped resection of the ovary and maintaining the maximum amount of healthy ovarian tissue. Ovariectomy is rarely required. Treatment of pregnancy in a rudimentary horn consists in the removal of a rudimentary horn with an adjacent fallopian tube. With intraligamentary localization of pregnancy, the peritoneum of the broad ligament above the hematoma is first dissected, which is removed together with the fetal egg, then salpingoectomy is performed.

Ectopic pregnancy increases the risk of re-ectopic pregnancy and future fertility problems. According to one study, the incidence of pregnancy after conservative or surgical treatment of ectopic pregnancy was 80%, and the average time until conception was 9-12 months, and fertility after expectant management and surgical treatment is the same. Ectopic pregnancy increases the risk of developing a similar condition in the future by 7-13 times. This means that in 50-80% the next pregnancy will be uterine and in 10- 25% - ectopic. All patients with ectopic pregnancy should be informed of the increased risk of its occurrence in the future.

The high probability of repeated ectopic nidation of the fetal egg after organ-preserving operations for tubal pregnancy dictates the need to improve methods of organ-saving treatment and postoperative rehabilitation, as well as a delayed study of the condition of the fallopian tubes after organ-preserving treatment to highlight a group of patients at high risk for repeated ectopic pregnancy.

CONCLUSION

This article provides an overview of the types of ectopic pregnancy, risk factors and current aspects of treatment, namely:

- information on an ectopic pregnancy, frequency of occurrence, risk factors that contribute to the development of this pathology, and classification of this pathology;
- describes modern methods of diagnosis and treatment of this pathology, possible complications during surgery and the postoperative period.

This review article will be useful to obstetricians, gynecologists working in gynecological clinics

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