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ECTOPIC PREGNANCY: CLINICAL AND MODERN APPROACHES

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Abstract: Ectopic pregnancy (ectopic pregnancy). It is a pathological pregnancy in which the fetus develops outside the uterine cavity and poses a serious threat to women's reproductive health, accounting for an average of 1-2% of all pregnancies. BTH is an important clinical form of gynecological emergency, which can lead to maternal death and infertility if not detected and treated in time. In this article, the etiology, pathogenesis, clinical course, diagnostic methods and modern treatment approaches of BTH are analyzed on the basis of deep, extensive and modern literature. Also, the article highlights the role of modern ultrasound technologies in early diagnosis and differential diagnosis of BTH, the diagnostic value of ß-hCG monitoring, individual approaches to conservative and surgical treatment, the future fertility prognosis of patients and the risk of recurrence.

Key words: ectopic pregnancy, hCG, transvaginal ultrasound, methotrexate, laparoscopy, salpingostomy, salpingectomy, fertility.

Introduction:Ectopic pregnancy (ectopic pregnancy) is one of the pathological processes encountered in gynecology and obstetrics practice, which seriously threatens maternal mortality and reproductive opportunities. According to global data, BTH accounts for 1.3-2.4% of all pregnancies [10]. The most common location of BTH is the fallopian tubes, accounting for 95-97% of all BTH cases. In the remaining cases, the fetus is located in the ovary (3%), cervix (1%) and abdominal cavity (<1%). Over the past 30 years, the opportunities for early detection and effective treatment of BTH have increased significantly as diagnostic and assisted reproductive technologies have improved [3]. Nevertheless, BTH still accounts for 4-10% of maternal deaths worldwide and is recognized as one of the main gynecological conditions requiring emergency medical care. The development of BTH is caused by many etiological factors: mechanical damage to the fallopian tubes or congenital anomalies, acute and chronic pelvic infections, especially Chlamydia trachomatis and Neisseria gonorrhoeae infections, previous BTH history, fallopian tube surgeries, assisted reproductive technologies (IVF and IUI), smoking, and hormonal imbalances [3]. These factors lead to incorrect implantation of trophoblast cells and the placement of the fetus in the mucous membrane of the fallopian tubes.

Etiology:

Etiological factors leading to the development of ectopic pregnancy (ectopic pregnancy) are complex and multifaceted, they include mechanical, infectious, hormonal and iatrogenic

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factors in the fallopian tubes and the female reproductive system. Mechanical damage to the fallopian tubes and congenital anomalies. The fallopian tubes are the normal transport route for the egg from the ovaries to the uterus. If the tubes are damaged or damaged, the normal migration of the zygote (fertilized egg cell) is disrupted and implantation occurs in the wall of the tube. Congenital abnormalities, such as tubal malformations or dysmotility (movement disorders), increase the risk of BTH. First-degree mechanical damage to the fallopian tubes, such as salpingostomy or salpingectomy performed in a previous ectopic pregnancy, increases the risk of BTH by 10-25%. PID, especially when associated with Chlamydia trachomatis and Neisseria gonorrhoeae infections, can seriously damage the lining and circulation of the fallopian tubes. This, in turn, leads to fibrosis, strictures and adhesions in the wall of the tube, which complicates the normal transport of the zygote. In patients with PID, the risk of developing BTH increases 3-6 times. A previous ectopic pregnancy significantly increases the risk of BTH. According to statistics, the probability of developing BTH again in patients who had BTH before is 10-25%. This is mainly due to a violation of the structure and function of the fallopian tubes as a result of previous pathological implantation. Surgical procedures performed on the fallopian tubes (for example, tubal recanalization, sterilization recovery, salpingoplasty) can disrupt the mechanical condition of the tubes and reduce peristalsis. In addition, assisted reproductive technologies (ART), especially in vitro fertilization (IVF) and intrauterine insemination (IUI), increase the risk of BTH by 2-4 times. After embryo transfer in IVF, there is a possibility of implantation in the fallopian tubes or abdomen as a result of retrograde migration of the embryo. Smoking is considered an independent risk factor for the development of BTH. Smoking reduces the ciliary movement (vibration of microscopic hairs) of the fallopian tubes and disrupts the estrogen/progesterone balance, which causes problems with the movement of the zygote. In women who smoke 1 pack of cigarettes every day, the risk of BTH increases 3-5 times [9]. Hormonal imbalances and contraceptives; An imbalance in the amount of progesterone and estrogen affects the peristalsis of the fallopian tubes and leads to incorrect placement of the implant. For example, the risk of BTH increases slightly with the use of progesterone-only contraceptives or intrauterine devices (IUDs). Also, postcoital contraception (instant contraception) slightly increases the likelihood of developing BTH.

Pathogenesis:

The pathogenesis of ectopic pregnancy (ectopic pregnancy) is a set of complex biological processes resulting from the disruption of the normal migration of the fertilized egg cell (zygote) through the fallopian tubes[1]. In-depth analysis of the nature of this process is important to fully understand the mechanisms of BTH development and to optimize treatment strategies. In a normal pregnancy, the egg cell released from the ovaries falls into the ampulla of the fallopian tubes, where it is fertilized by spermatozoa. Fertilized egg (zygote) 3-5 days using the ciliary movement of the epithelium of the fallopian tubes and tube peristalsisduring transport to the uterine cavity. But as a result of damage to the tubes, strictures, ciliary dysfunction or hormonal imbalance, this process is disrupted. The zygote is implanted in the ampulla, isthmus or infundibulum of the fallopian tubes. The trophoblast is the outer layer of the zygote, responsible for implantation and placenta formation. As a result of trophoblast invasion (insertion) into the thin and inelastic mucous membrane of the fallopian tube, erosion and destruction of blood vessels occur in the wall of the tube. This, in

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turn, leads to local inflammation, bleeding and thinning of the wall of the tube. Since the wall of the fallopian tube is much thinner and less elastic than the wall of the uterus, the process of trophoblastic growth and implantation causes the wall of the fallopian tube to rupture (rupture) in the short term. Hormonal factors are also involved in the development of BTH [2]. When implantation occurs in the fallopian tube, the secretion of hCG (beta human chorionic gonadotropin) begins. But before reaching the level of ß-hCG concentration observed in intrauterine pregnancy, its growth rate slows down. This prevents normal decidualization (preparation for pregnancy) in the endometrium (uterine lining). In addition, local immune response disorders, cytokines (TNF-α, IL-6) and inflammatory mediators have been found in BTH, which increase inflammation and destruction (destruction) processes in tube tissues[7]. As a result of the destruction of the wall of the tube by the trophoblast, bleeding begins in the tube and into the pelvic cavity. It is clinically manifested in the patient with symptoms of pain in the lower abdomen and vaginal bleeding. If it is not diagnosed at the time of BTH, complete rupture of the tube wall and massive internal bleeding (hemoperitoneum) occur, which poses a serious threat to the patient's life. BTH is usually observed in the ampulla of the fallopian tubes (70-80%). Isthmus (10-15%), infundibulum (5-10%), ovary (<3%), cervix (<1%) and abdominal cavity (<1%)

Clinical course and clinical signs:

The clinical course of ectopic pregnancy (ectopic pregnancy) develops in a diverse and dynamic manner. This pathology is difficult to diagnose due to the lack of specific symptoms in its early stages, non-specific clinical signs and similarities with other gynecological or surgical diseases. In-depth analysis of BTH clinic is important for early diagnosis and prevention of complications. BTH occurs in several clinical forms, and these forms depend on the patient's symptoms, BTH localization and the stage of the process: Progressive (developing) BTH, the fetus develops in the fallopian tubes, trophoblast invasion continues, but the tube has not ruptured. Completing (regressing) BTH stops before the pregnancy develops and resorption of the gestational sac or abortus tubarik (abortion in the tube) occurs. A ruptured (cracked) BTH fallopian tube wall ruptures and blood spills into the pelvic cavity. Pain in the lower abdomen (80-90%): is usually unilateral (left or right) and gradually increases. It is caused by trophoblast invasion, stretching of the tube wall, or inflammation. When the tube ruptures, the pain is sudden and intense, radiating to the pelvis, lower back, or rectum. Vaginal bleeding (60-80%): often dark or brown in color, with a small amount of discharge that does not resemble menstruation. This is the result of the destruction of the decidual layer of the endometrium. Menstrual delay (75%): patient usually 5-8 weeks after last menstrual periodrefers to [8]. These clinical signs indicate the possibility of pregnancy. Fainting, dizziness, tachycardia, arterial hypotension: occurs when BTH ruptures and internal bleeding develops. A drop in blood pressure and tachycardia are symptoms of hypovolemic shock. Pain and peritoneal symptoms on palpation in the pelvic cavity: fluid accumulates in the pelvic cavity as a result of internal bleeding. Pain on palpation in the depth of Douglas and rectal examination reveals a smooth, painful infiltrate on the lower posterior wall [4]. BTH clinical symptoms can be similar to other gynecological and surgical pathologies. Therefore, it is important to differentiate with the following diseases: Spontaneous abortion: abdominal pain and vaginal bleeding are observed, but intrauterine gestation is detected in UTT. Ovarian apoplexy: Sudden onset of abdominal pain and pelvic bleeding, but no signs of

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pregnancy. Acute appendicitis: pain in the right lower abdomen, but menstruation is late and ß-hCG is not positive. Endometriosis: chronic pelvic pain and dysmenorrhea, but no pregnancy. BTH symptoms are vague and slow at first. Symptoms worsen over time as the trophoblastic growth and implantation process increases. When the tube ruptures, the clinical picture suddenly worsens: sharp pain, unconsciousness, pale skin, tachycardia and hypotension develop. This condition is life-threatening and requires immediate surgical intervention. Palpation of the abdominal wall reveals unilateral pain and stiffness. Pelvic palpation may indicate a painful lateral mass or painful free fluid. On bimanual examination, the uterus is smaller than normal and soft, but with a painful mass on the side. A painful infiltrate or fluid may be detected in the depth of Douglas.

Diagnostics:

Reliable and early detection of ectopic pregnancy (ectopic pregnancy) is the most important step in clinical practice. Since the symptoms of BTH can be ambiguous and can be confused with other pathologies, a modern and integrated approach is used in diagnosis. The combination of clinical, laboratory and instrumental methods in diagnostics ensures high accuracy and sensitivity. ß-hCG (beta human chorionic gonadotropin) monitoring: β-hCG is the main marker to confirm pregnancy[5]. In a normal intrauterine pregnancy, the level of ß-hCG doubles every 48 hours. In BTH, this growth slows down or remains stable. If ß-hCG is >1500-2000 mIU/mL and transvaginal ultrasound does not show an intrauterine fetus, the probability of BTH is high. If the hCG level rises <66% in a 48-hour period, there is a risk of ectopic pregnancy. Serum Progesterone Levels: Progesterone levels help assess whether a pregnancy is viable. <5 ng/mL is less likely to have a viable pregnancy and more likely to be BTH or abnormal intrauterine pregnancy. > 20 ng/mL is a high probability of viable intrauterine pregnancy. Hemoglobin and hematocrit levels: If there is internal bleeding when a BTH ruptures, the hemoglobin and hematocrit will decrease. Transvaginal ultrasound (TVUS): is the main and sensitive method of BTH diagnosis. Endometrial pseudosac: A false fetal sac of fluid is seen in the endometrium. External Gestational Sac: A sac that is abnormally located in the fallopian tube or elsewhere. "Bagel sign" and "Ring of fire": Doppler mode reveals a hyperechoic ring around the gestational sac and high blood flow. Free fluid in the pelvic cavity:It may be a sign of internal bleeding. Laparoscopy: If the laboratory and instrumental results do not allow making a clear diagnosis or the patient develops hemodynamic instability, laparoscopy is used. Visually, ectopic pregnancy is detected and, if necessary, surgical treatment is carried out at the same time. Culdocentesis (puncture from the depth of Douglas): Used to determine the presence of free blood in the pelvic cavity. If bloody fluid is detected, the possibility of BTH rupture is confirmed. If the patient presents with late menstruation and abdominal pain: β-hCG >1500-2000 mIU/mL → TVUS is performed. If intrauterine fetus is not visible → high probability of BTH β-hCG <1500 mIU/mL after 48 hours ß-hCG is re-measured. Growth <66% → BTH likely → TVUS recommended. In case of spontaneous abortion, a gestational sac and, if necessary, chorionic villi are detected in the endometrium. In ovarian apoplexy, TVUS shows a follicular cyst or a bleeding cyst, and ß-hCG is negative.

Modern treatment approaches:

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The main goal in the treatment of ectopic pregnancy (ectopic pregnancy) is to save the patient's life, restore reproductive health to the maximum and reduce complications. The choice of treatment is determined by taking into account the general condition of the patient, the location of BTH, the level of β-hCG, the size of the gestational sac and the patient's birth plans. Three main approaches are used in modern clinical practice: observation (expectant management), drug treatment and surgical intervention[6]. If the patient's condition is stable, symptoms are minimal, and BTH is not developing, conservative observation is recommended. In this way, the body eliminates BTH by itself. Indications: β-hCG <200 mIU/mL and declining, gestational sac <2 cm. The patient is asymptomatic and hemodynamically stable. Procedure: Monitoring of ß-hCG level every 48-72 hours. If any symptom worsens or an increase in ß-hCG is detected, medical or surgical treatment is performed.

Medical treatment:

Methotrexate (MTX) is an antifolate drug that inhibits proliferation of trophoblast cells and causes resorption of gestational tissue.-Indications: β-hCG <5000 mIU/mL, Gestational sac <3.5-4 cm, No embryonic heartbeat. The patient's symptoms are minimal and hemodynamically stable. Administration regimens: Single dose regimen: 50 mg/m² MTX administered intramuscularly (IM). ß -hCG level is determined on the 4th and 7th days, if β-hCG decreases by more than 15%, monitoring is continued, if the decrease is insufficient, an additional dose of MTX is given. Multiple regimen: MTX 1 mg/kg IM orally, used in combination with leucovorin (folate antagonist). Success rate: ~85-90% (in properly selected patients). Complications: Abdominal pain, nausea, increased liver enzymes. Hemodynamic instability, BTH rupture, or if the above conservative methods fail, surgical treatment is performed. Indications: BTH rupture and internal bleeding. Hemodynamically unstable. Medical treatment failure. ß -hCG >5000 mIU/mL and/or gestational sac >4 s Methods: Laparoscopic salpingostomy: Open the fallopian tube, remove the BTH, save the tube. Best for restoring reproductive health. Laparoscopic salpingectomy: Complete removal of the fallopian tube (if the tube is severely damaged or BTH is repeated). Laparotomy:It is used in excessive bleeding and hemodynamic instability. After surgery: it is necessary to monitor the level of β-hCG until it completely decreases. In recent years, minimally invasive approaches have been developed, such as ultrasound-guided aspiration of chorionic villi and injection of MTX or calcium chloride into the chorionic villi or gestational sac. These methods are used especially for cervical or interstitial BTH.

Prognosis and risk of recurrence:

Regardless of the treatment method, 50-80% of patients have a chance to have a healthy birth in the next pregnancy. However, there is a 10-25% risk of BTH recurrence. ~10% of patients develop infertility, especially if both fallopian tubes are affected. Correct and timely treatment of BTH improves maternal health, preserves reproductive potential and reduces maternal mortality.

Summary:

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Ectopic pregnancy (ectopic pregnancy) is a pathology that seriously threatens reproductive health, and its early diagnosis and individual treatment approach are important. The development of BTH can be caused by various factors, including damage to the fallopian tubes, infections, previous pregnancies, surgical operations, and reproductive technologies. Clinical indications are variable and can be confused with other pathologies, so diagnosis should have high sensitivity. Three main approaches are used in the treatment of BTH: observation (expectant management), drug treatment (methotrexate) and surgical intervention. Each patient's condition, ß-hCG level, gestational sac size and birth plans are taken into account. Modern treatment methods are effective in maintaining the health of patients and preventing complications, helping to restore the reproductive potential to the maximum. Although BTH is a serious pathology that increases the risk of maternal mortality and infertility, its early diagnosis and modern treatment strategies improve maternal health and preserve reproductive opportunities. In recent years, the prognosis for BTH has improved significantly as a result of improvements in diagnostic and treatment approaches.

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