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Multidisciplinary Approach in the Treatment of Rare Forms of Ectopic Pregnancy

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Abstract

Multidisciplinary approach in the treatment of rare forms of ectopic pregnancy has been developed, it includes the systemic use of methotrexate, the embolization of uterine arteries and follow-up fetal egg remove. The new method of combination treatment of cervical pregnancy of one-stage use of embolization uterine artery and temporary balloon occlusion of the internal iliac arteries was applied for the first time in Russia. This algorithm helps to preserve the reproductive function of women.

Keywords: Cervical Ectopic Pregnancy; Embolization of Uterine Arteries; Temporary Balloon Occlusion of Internal Iliac Arteries; Argonplasma Coagulation

Introduction

Ectopic pregnancy is one of the main causes of maternal death in the first trimester of pregnancy. Mortality from ectopic pregnancy in Russia in 2015 was 3.6% [1]. Due to the increase in the incidence of ectopic pregnancy and its negative consequences for the reproductive health of women, this problem does not lose its relevance. Today, maternal mortality associated with ectopic pregnancy of various locations is within 1.3-2.2%. In the structure of gynecological diseases, ectopic pregnancy is 9.5%, it also leads to 47% of emergency interventions [2].

In clinical practice, rare forms of ectopic pregnancy are of particular interest, in which diagnosis is significantly difficult, and as a result, timely surgical treatment is delayed [3]. Over the past 15-20 years, clinicians have observed an increase in the frequency of ectopic and, in particular, cervical gestation, including multiple pregnancy.

Cervical pregnancy is a rare form of ectopic pregnancy in which the attachment and development of the ovum occur in the cervical canal. The frequency of its occurrence varies from 1 to 9000-12000 pregnancies and is 0.01-0.0083% [4,5]. Maternal mortality in cervical pregnancy has progressively declined due to improved diagnosis and treatment and has been found to be less than 1%. Today, a true cervical pregnancy is distinguished, when the fetal egg is located in the cervical canal, and cervical-isthmus pregnancy, characterized by the attachment of the fetal egg in the cervical canal and in the isthmus [6]. Changes in the endometrium due to frequent induced abortions, repeated diagnostic curettage

of the uterine mucosa, endometritis, prolonged use of intrauterine contraceptives are the causes of abnormal attachment of the fetal egg during cervical pregnancy. The penetration of the ovum into the cervical canal can be facilitated by submucosal myomatous nodes, cicatricial changes in the internal orifice of uterus caused by previous surgical interventions, as well as isthmic-cervical insufficiency. When the ovum is localized in the cervix, chorionic villi germinate a single-row glandular epithelium and penetrate into the muscle layer of the cervix. Termination of cervical pregnancy occurs as a rupture of the fetus and is accompanied by profuse external bleeding, which is associated with the peculiarities of the blood supply to the cervix from the descending branches of the uterine arteries and the ascending branches of the vaginal arteries, which can directly depart from the internal iliac [6]. For several decades, hysterectomy has been the only method of treating cervical pregnancy [5] (Figure 1).

Figure 1: Removed uterus with disrupted cervical pregnancy.

Currently, numerous foreign publications report various successful methods of cervical pregnancy treatment, either in isolation or in combination, depending on the gestational age and the depth of chorion invasion into the cervix. Drug therapy with methotrexate or methotrexate in combination with folic acid is used in accordance with ASRM guidelines (2006); ACOG (2015); ROAG (2014); RCOG (2016) [7-10]. However, long-term systemic use of cytostatics causes many undesirable effects (stomatitis, toxic hepatitis) and is ineffective in progressive pregnancy with a well-developed chorion [6]. In the Russian Federation, the instructions for the use of methotrexate do not provide for indications and treatment regimens for ectopic pregnancy, and therefore its use off label can only be considered as an alternative to organ removal surgery if it is necessary to preserve reproductive function after the decision of the ethical committee only in gynecological hospitals of medical organizations of the third level, after obtaining informed consent from the patient [15-17].

To avoid hysterectomy and preserve fertility, is used the imposition of a circular suture on the cervix, intracervical tamponade with a balloon catheter, the use of double balloon catheters for cervical tamponade [11], hysteroscopic resection of the implantation site of ovum [5,12], selective embolization of the uterine arteries (UAE), ligation of the uterine vessels, internal iliac arteries, temporary balloon occlusion of the common iliac arteries [5]. For the treatment of cervical pregnancy using UAE as the main method, foreign authors proposed the following methods: UAE + cervical tamponade with a Foley balloon catheter + methotrexate injections 1 mg/kg/day, UAE with a gelatin sponge + curettage, UAE with platinum coils + methotrexate injections. In addition, UAE can be used after failed attempts at methotrexate and vascular ligation [13].

Currently, in the Russian Federation, for the treatment of cervical pregnancy, systemic therapy of methotrexate is used alone or in combination with UAE [14], followed by curettage, the imposition of a circular suture on the cervix, as well as ligation of the descending branches of the uterine arteries [6,18].

All of the above initiates the search for new approaches in the diagnosis and treatment of ectopic pregnancies of rare localizations, in particular, cervical and cervical isthmus pregnancies.

Scientific novelty, originality of work

A multidisciplinary approach in the management of patients with rare forms of ectopic pregnancy made it possible to develop and put into practice an algorithm for the treatment of cervical and cervico-isthmus pregnancy, depending on the gestational age, the depth of chorion invasion into the cervix, and the patient's desire

to maintain reproductive function. For the first time in Russia in the F.I. Inozemtsev Moscow Department of Health, a new method of combined treatment of cervical pregnancy with the combined use of uterine artery embolization, temporary balloon occlusion of the internal iliac arteries and argon plasma coagulation of the implantation site of ovum was used, which allowed women to preserve reproductive function. When analyzing foreign publications, there is evidence that in Japan, the authors Jehn-Hsiahn Yang, a Jin-Chung Shih, Kao-Lang Liu, M.D. a method of combined treatment of cervical pregnancy was used, including temporary balloon occlusion of the common iliac arteries and hysteroscopic resection of the ovum, with postoperative intracervical introduction of a balloon catheter.

Based on publications in the domestic literature, none of the hospitals has a similar experience and copyright of the combined treatment of cervical pregnancy using modern X-ray endovascular technologies, which allows a woman to preserve her reproductive function, depending on the gestational age and the depth of chorion invasion into the cervix.

The effectiveness of the proposed therapeutic approaches has been demonstrated in clinical examples.

Clinical Case 1

Patient M., aged 33, was admitted with complaints of nausea, bleeding from the genital tract, pain in the lower abdomen, weight loss of 8 kg. From the anamnesis: Menstrual function is not changed. Childbearing function: 4 pregnancies in total, of which: 2 births (caesarean section in the left uterus in 2010, in 2011), medical abortion - 1. This is the fourth pregnancy, it came on its own. At a gestational age of 4-5 weeks, she turned to a private clinic for medical termination of pregnancy. Conducted medical termination of pregnancy according to the scheme (Mifepristone + Misoprostol) without effect. Nausea and vomiting have been bothering me for a week. Lost 8 kg in weight. According to ultrasound of the pelvic organs: uterine pregnancy 7-8 weeks. Retrochorial hematoma. Trophoblast invasion into the postoperative scar on the uterus after caesarean section? Bicornuate uterus. In the hospital, an ultrasound with color doppler mapping was performed, which diagnosed echo - signs of incomplete duplication of the uterus, progressive cervical-isthmus pregnancy of 7-8 weeks in the left uterus, a scar on the uterus, retrochorial hematoma, signs of invasion of trophoblasts, a postoperative scar (Figure 2).

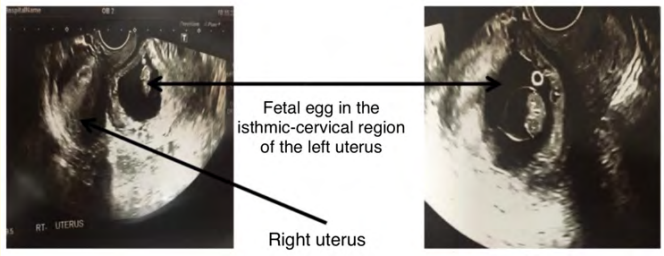

Figure 2: Progressive isthmic-cervical pregnancy 8-9 weeks in the left uterus.

Given the weight loss of 8 kg, nausea, periodic vomiting, it was decided to refuse the taking of methotrexate due to the large number of side effects. Due to the high risk of bleeding, it is recommended to perform UAE (Figure 3) followed by evacuation of the fetal egg under laparoscopy control in order to control trophoblast invasion into the postoperative scar (Figure 4).

Arteriography revealed contrasting of the arterial network of the fetal egg, anastomosis of the arcuate branches of the left and right uterine arteries, determined the diameter of the blood supplying arteries and priority blood supply. Angiograms visualize the priority blood supply from the left uterine artery, which is associated with the localization of the fetal egg in the isthmic-cervical region of the left uterus. On the contralateral side, selective UAE was performed with Embosphere microspheres 700-900 microns (MeritMedical). On control angiograms, the uterine arteries are visualized only in the proximal segments, the intrauterine arterial network is not contrasted (Figure 2).

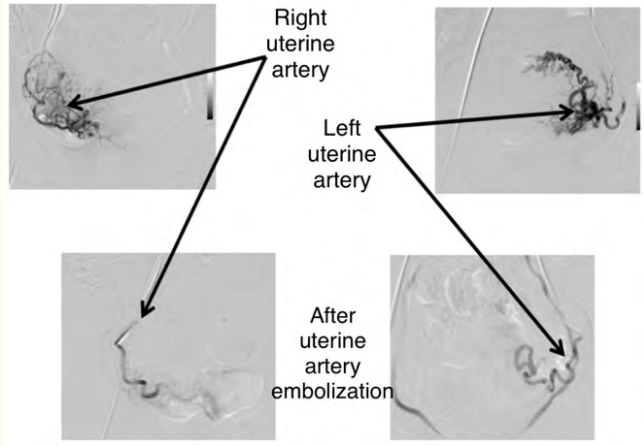

Figure 3: Embolization of the left and right uterine arteries.

After UAE in a deployed operating room under the control of laparoscopy, the fetal egg was evacuated from the isthmic-cervical region of the left uterus. Laparoscopic control was performed to assess the depth of chorion invasion into the postoperative scar. If trophoblast invasion was detected, an additional excision of the scar and metroplasty would be performed, which was not required in our case.

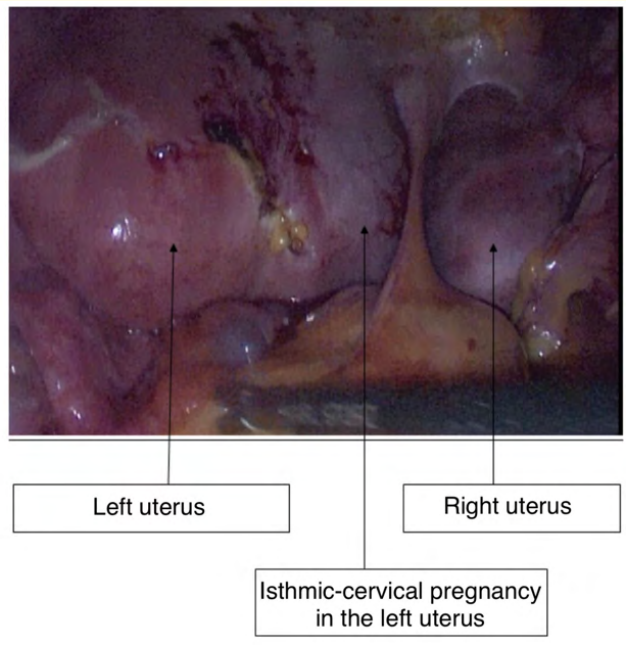

Figure 4: Laparoscopic picture after UAE.

Blood loss during the evacuation of the egg from the isthmic-cervical region of the left uterus was 70.0 ml. On the 4th day the patient was discharged from the hospital in a satisfactory condition.

Due to an adequate approach and properly performed treatment using minimally invasive videoendoscopic and X-ray endosurgical technologies, the patient's reproductive function was preserved.

Clinical example 2

Pregnant R., aged 29, was admitted to the gynecological department with a diagnosis of cervical pregnancy 9-10 weeks. From the anamnesis: menstrual function is not changed. Childbearing function: total pregnancies 5 (given), of which: childbirth: 2 (2012, 2014). medical abortions: 2 - surgical in 2013, 2016 This pregnancy is the fifth, came on its own. She is not registered in the antenatal clinic. Cervical pregnancy was diagnosed by ultrasound on an outpatient basis.

On bimanual examination, the vaginal part of the cervix is shortened to 2.5 cm, barrel-shaped, cyanotic, the external orifice is located eccentrically, its edges are sharply thinned. The shortened part of the cervix passes into the amniotic sac, soft formation, in size corresponding to the gestational age. Above the amniotic sac and somewhat to the side of it, the body of the uterus is palpable - dense, slightly larger than normal. B- hCG -15,000 IU.

In ultrasound with color doppler mapping, the uterus is 64x49x62 mm in size, the structure of the myometrium is not changed. M-echo 5 mm. A fetal egg was localized in the cervix of the uterus below the internal orifice, the size of the embryo corresponded to 9-10 weeks, the heartbeat was recorded, a high vascularization of the peritrophoblastic region was noted. The depth of chorion invasion into the myometrial cervix was 8 mm. The thickness of the cervix in the area of chorion invasion is 2 mm (Figure 5).

Figure 5: Progressive cervical pregnancy 9-10 weeks.

Given the gestational age of progressive cervical pregnancy of 9-10 weeks, the depth of chorion invasion of 8 mm into the cervix wall, the patient's interest in further reproductive function, and the high risk of massive bleeding, it was decided to conduct a combined treatment with the combined use of uterine artery embolization and temporary balloon occlusion of the internal iliac arteries.

At the first stage, systemic therapy of methotrexate was performed, according to clinical recommendations, at a dose of 50

mg/m^2 based on the conclusion of the medical commission and the signing of the patient's voluntary informed consent.

Then produced selective embolization of uterine arteries. Arteriography revealed that the uterine arteries were hypertrophied and pathologically altered. For the embolization of uterine arteries, particles of 700-900 microns were used. On the control angiograms, the uterine arteries are visualized only in the proximal segments, the intrauterine arterial network is not contrasted (Figure 6), but the vessels of the ovum were contrasted due to the ascending branches of the vaginal arteries extending from the internal iliac (Figure 7).

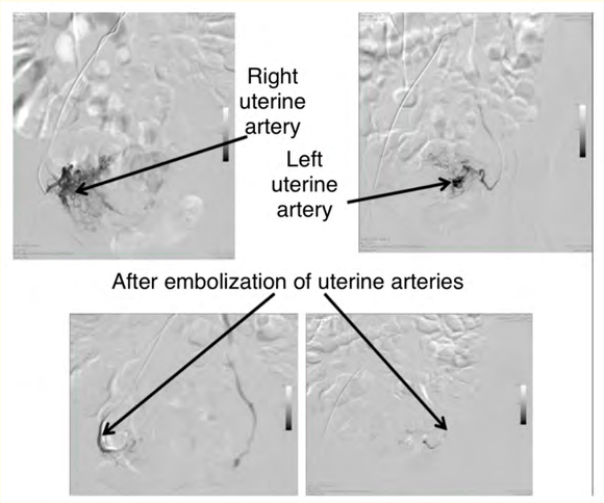

Figure 6: Embolization of the left and right uterine arteries.

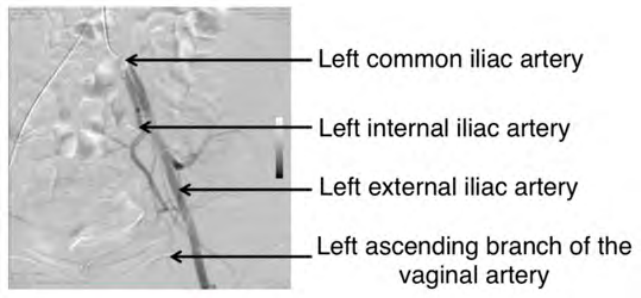

Figure 7: Contrast after embolization of uterine arteries.

Given this situation, a temporary balloon occlusion of the internal iliac arteries was performed.

The left and right internal iliac arteries (IIA) were catheterized selectively contralaterally from the femoral access using hydrophilic guide wire 0.035 inches. Subtraction angiography was performed. Balloon catheters 7.0×40 mm were inserted into the internal iliac arteries and positioned immediately below the bifurcation of the common iliac artery, the balloons were inflated at a pressure of 6 atm. During the control angiography, the internal iliac arteries are not contrasted, the vessels of the fetal egg are not contrasted, the blood flow through the common and external iliac arteries is preserved (Figure 8).

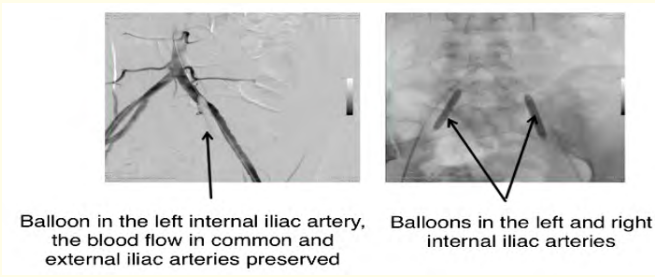

Figure 8: Temporary balloon occlusion of the internal iliac arteries.

Under the conditions of an expanded operating room, the fetal egg was evacuated with a vacuum excholeator under ultrasound control. After evacuation of the ovum, argon plasma ablation of the implantation site was performed, taking into account the depth of chorion invasion and active blood supply to this area, the thickness of the cervix 2 mm, the penetrating ability of the argon plasma torch from 0.5 to 3 mm, this method of coagulation is the most acceptable in this situation [19]. Then the balloon catheters were deflated, bleeding from the implantation site was not observed, after which they were removed. The total blood loss was 100.0 ml, the occlusion of the internal iliac arteries was 20 minutes. In the postoperative period, the patient underwent antibacterial anti-inflammatory therapy, dynamic ultrasound control and β-hCG (human chorionic gonadotropin) (Figure 9). In dynamics, β -hCG progressively decreased (Figure 10).

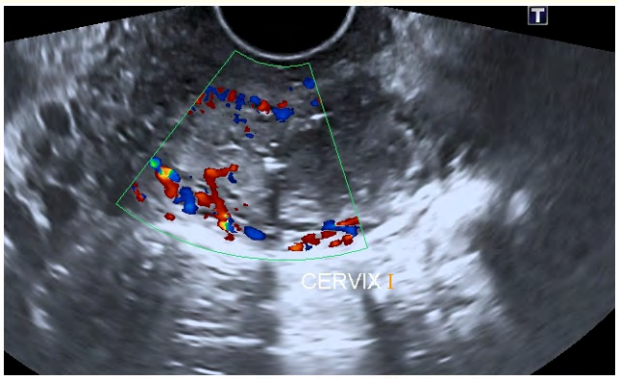

Figure 9: The implantation site of the fetal egg in the cervix on the 7th day after Operations.

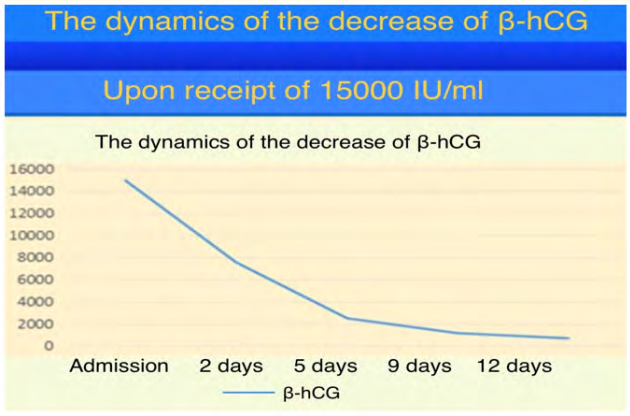

Figure 10: The dynamics of the decrease in β-hCG.

On the 7th day, the patient was discharged from the gynecological hospital in a satisfactory condition.

Combined treatment of cervical pregnancy with systemic therapy of methotrexate, combined with the use of uterine artery embolization and temporary balloon occlusion of the internal iliac arteries, followed by evacuation of the fetal egg from the cervix and additional coagulation of the implantation site with an argon plasma, reduced the risk of bleeding and preserved reproductive function in a young woman (Figure 11).

A year later, this patient was admitted to the gynecological hospital with a progressive uterine pregnancy (Figure 12), which

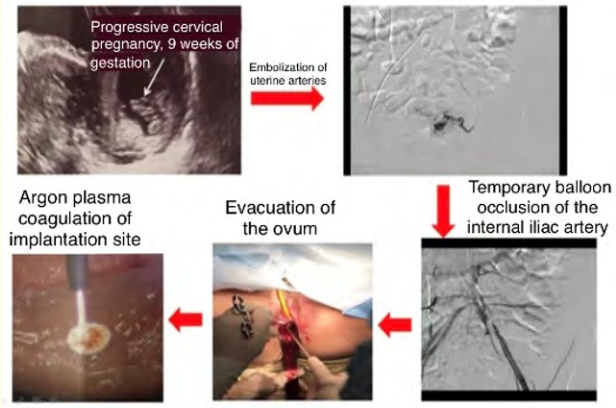

Figure 11: Combined treatment of cervical pregnancy.

confirms the effectiveness of the proposed method and the correctness of the chosen algorithm for managing this particular patient.

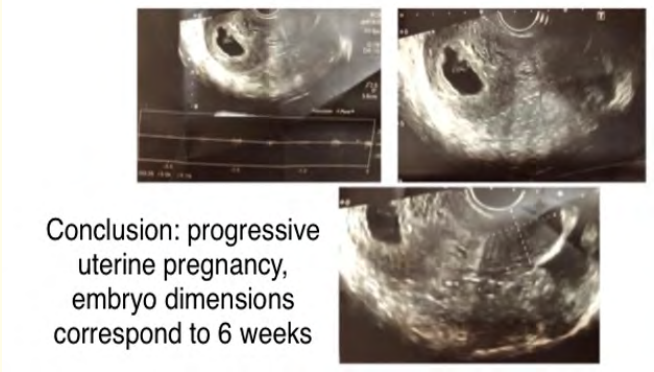

Figure 12: Progressive uterine pregnancy. Embryo sizes correspond to 6 weeks.

Discussions

With the close cooperation of the departments of the multidisciplinary hospital of the State Budgetary Institution of Health, City Clinical Hospital after F.I. Inozemtseva, Moscow Department of Health and the Department of Obstetrics and Gynecology of the Medical Faculty of the Russian National Research Medical University after N.I. Pirogov treated from 2015 to 2017 5 patients with cervical isthmus pregnancy and 2 patients with cervical pregnancy.

Patients admitted to the gynecological department were examined in accordance with the order of the Ministry of Health of Russia dated November 12, 2012 No. 572n "On approval of the procedure for providing medical care in the field of obstetrics and gynecology (with the exception of the use of assisted reproductive technologies)" and clinical recommendations (treatment protocol) "Ectopic pregnancy" from 2017. When establishing the diagnosis of cervical-isthmus or cervical pregnancy, according to the algorithm developed and put into practice, this pathology was treated (Figure 13).

In the treatment of cervical isthmus and cervical pregnancy, the choice of management tactics was based primarily on the women's desire to maintain reproductive function [6]. At the first stage, systemic taking of methotrexate (50 mg/m^2) was carried out according to the scheme (without the introduction of leucovorin), followed by embolization of the uterine arteries and delayed evacuation of the ovum [4]. In the presence of contraindications to the taking of the drug, they proceeded immediately to UAE and subsequent vacuum aspiration of the fetal egg. If there is a suspicion of chorion invasion into the postoperative scar on the uterus after a caesarean section in cervical-isthmus pregnancy, the fetal egg was evacuated under laparoscopic control, with confirmation of germination, excision of the scar followed by metroplasty.

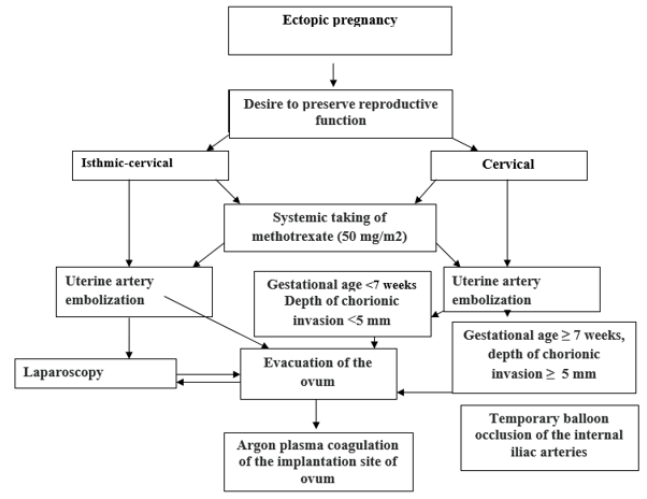

Figure 13: Algorithm for managing patients with cervical isthmus and cervical pregnancy.

The tactics of managing patients with cervical pregnancy depended on the gestational age, the depth of chorion invasion into the myometrium of the cervix, and blood supply characteristics. The choice of the gestation period and the depth of chorion invasion was based on the morphogenesis of the implantation site: the first wave of trophoblast invasion starts from the 4th week, lasts up to the 8th week of gestation and includes the most important processes of autochthonous angiogenesis in the stroma of mesenchymal villi (from the 20th-21st day) and intensive cytotrophoblast invasion into stroma of the cervix, characterized by gestational restructuring of the arteries and the beginning of the formation of uteroplacental blood flow. In cervical pregnancy for a period of 7 weeks of gestation and a depth of chorion invasion into the cervical myometrium of more than 5 mm, with continued blood supply to the fetal egg from the ascending branches of the vaginal arteries, temporary balloon occlusion of the internal iliac arteries was performed, followed by evacuation of the fetal egg and argon plasma coagulation of its implantation site.

Conclusions

The given clinical examples indicate the expansion of the possibilities of using UAE in isthmic-cervical pregnancy in an isolated form with subsequent evacuation of the ovum, or in combination with systemic therapy of methotrexate and delayed vacuum aspiration, and in the combined treatment of cervical pregnancy in combination with temporary balloon occlusion of the internal iliac arteries.

A developed and properly selected individual algorithm for managing each patient with moderate forms of ectopic pregnancy (cervical and isthmic-cervical localization) allows adequate treatment and preservation of reproductive function.

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