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Prophylaxis of Ischemic Damage to the Ovaries, Taking Into Account Peculiarities of Blood Supply to the Uterus During Endovascular Treatment of Leiomyomas

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SUMMARY Uterine arteries embolization (UAE) is one of the modern trends in the treatment of uterine bleeding caused by uterine leiomyomas (UL). However, unfavourable results of this method of treatment are observed in 10–15% of cases. This is primarily concerned with the emerging ischemia of ovarian tissue after embolization.

MATERIAL AND METHODS Complex examination and treatment was performed in 48 patients admitted with UL complicated by the development of uterine bleeding. Patients with UL were divided into two groups. In the Group I of patients (n=29) standard embolization was performed, while the patients of the Group II (n=19) with diagnosed interarterial utero-ovarian anastomosis underwent separating technique of UA occlusion using different types of emboli.

RESULTS AND DISCUSSION The features of the uterine blood supply in patients with UL were analyzed from the perspective of the effecacy and safety of endovascular intervention. A methodology of staged EUA was developed, which involved the staged aortography of the infrarenal aorta (for visualization of the ovarian arteries); pelvic arteriography (for evaluating the vascular anatomy of the pelvis and identifying utero-ovarian intearterial anastomoses); selective arteriography followed by UAE first with cylindrical emboli, and then with standard emboli in the form of microspheres. The application of the developed technique did not show dysfunction of the ovaries in both the short and long-term follow-up period up to 18 months in the Group II.

CONCLUSION The separating UA occlusion is a safe and effective way of preventing ischemic damage in the presence of signoficant utero-ovarian inter-arterial anastomoses.

Keywords: uterine leiomyoma, uterine bleeding, uterine artery embolization, utero-ovarian anastomoses, evaluation of treatment results

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UA - uterine arteries
UAE - uterine artery embolization
UL - uterine leiomyoma

INTRODUCTION

Uterine leiomyoma (UL) is the most common female genital tumor, which is diagnosed in 10-52% of patients [1-4]. The leading symptom of the UL is uterine bleeding, and its intensity and character define the severity of the condition of the patient and measures of emergency medical care [5-8]. The basic method of treatment for UL, complicated with uterine bleeding, is surgery (total or subtotal hysterectomy) [9-12]. Patients with this pathology undergo 50% of the performed surgeries in gynecological practice [3, 5, 13]. In recent years, the concept of organ-saving surgery in patients with UL has become generally accepted [14, 15]. In this regard, the improvement of these interventions in patients with UL with the aim of the decrease of the frequency of traditional surgical methods of treatment.

In recent years, an increased interest of interventional radiologists and obstetricians - gynecologists in the use of intravascular methods of treatment in clinical practice has been noted all over the world [16–19]. Due to the development of endovascular techniques, minimally invasive, organ-saving method for the treatment of UL became widely spread - uterine arteries embolization (UAE) [20-22]. Endovascular embolization is one of the most modern trend in the treatment of uterine bleeding, caused by the UAE. Over 200 000 UAEs have already been performed in the world in patients with different gynecological disorders [23, 24].

In the literature the question of UAE reducing the size of the uterus and myoma nodes in patients with UL for implementing reproductive plans is mainly discussed [3, 9, 16, 18]. However, extremely important indication for carrying out an endovascular intervention is the presence of massive uterine bleeding of gynecologic and / or oncologic origin [5, 21]. The main indicator of the effectiveness of endovascular hemostasis is the arrest of uterine bleeding.

UAE has been performed at the N.V. Sklifosovsky Research Institute since 2000. During this time, while providing emergency medical assistance, UAE has been performed more than in 500 women with various gynecological and oncological disorders [21].

Despite the technical progress of mini-invasive interventions, in 10-15% of cases there are poor results of treatment [23]. It is noted, that the emboli in branches uterine artery (UA), supplying the ovary, lead to their failure in 6.6% of patients and are accompanied by the appearance of hypergonadotrophic amenorrhea [25]. It is shown, that non-selective UAE in patients of reproductive age with the aim of treating UL can lead to a pronounced reduction of the function of the ovaries [25]. Thus, it was noted, that the implementation of non-selective EMA leads to a decrease in the concentration of anti-mullerian Hormone 3-fold, inhibin B - more than a 7.5-fold and the appearance of diagnostically significant titers of ovarian antibodies (80.8%) [25]. In many ways, these changes are associated with ischemia of tissue of ovaries after performing UAE. In this regard, for increasing the efficiency and safety of techno ogy of UAE it is advisable to clarify the characteristics of blood supply to the uterus and develop a methodology for eliminating such complications.

The purpose of this publication is to analyze the characteristics of blood supply of uterus and develop a method for improving the efficiency and safety of uterine bleeding treatment, caused by UL, by the use of separating occlusion of MA and different types of emboli.

MATERIAL AND METHODS

Comprehensive general clinical, gynecological, laboratory, instrumental, angiographic examination and treatment was carried out in 48 patients, admitted to the Department of Acute Gynecological Diseases of N.V. Sklifosovsky Research Institute for UL, complicated by uterine bleeding.

Patients with ULs were divided in two groups. The first (I) group consisted of 29 patients (mean age 42.3 ± 4.25 years); the second (II) group consisted of 19 patients (mean age 44.1 ± 4.47 years). The age of the patients varied from 31 to 49 years [22]. All patients were of reproductive age.

Echographic study with color Doppler was performed by the ultrasonic device LOGIQ P6 (GENERAL ELECTRIC, Korea) using transabdominal (with a frequency of 3.5 MHz) and transvaginal (with a frequency of 6 MHz) sensors.

All patients underwent the complete angiographic examination of the uterine and ovarian arterie with *«GE» Advantx* (USA) and *«Siemens Artis»* (Germany).

When carrying out all endovascular operations for access to the vascular channel femoral artery used. In the majority of patients (45-93.8%) unilateral access was performed, and in 3 (6.2%) patients bilateral access was performed. Catheter *«Roberts»* (*Cook*, USA), with the diameter not exceeding 5*F* (1*F* = 0.33 mm) was used most often, and in cases with bilateral access *Cobra* 5*F* was used.

Upon angiographic examination in 29 patients (60.4%), who formed I group, before UAE only UA were visualized, without significant utero-ovarian anastomoses. In 19 patients (39.6%), which formed II group, utero - ovarian arterio - arterial anastomoses were found. Only after this examination UAE was performed.

UAE results were considered satisfactory with complete arrest of blood flow in the embolized artery. The duration of the procedure ranged from 30 minutes to one hour (the average was 45.0 minutes). There were no complications during UAE in any patient.

The statistical processing of the results of research was performemd with the use of software *«Excel MS Office Professional»* and «*Statistica* 6.0».

RESULTS AND DISCUSSION

The individual characteristics of the blood supply to the uterus in patients with UL can affect the success of the intravascular treatment methods. Therefore, it is advisable to the assess the blood supply to the uterus regarding endovascular intervention.

UA (*a.uterina*) which arises from the internal iliac artery from each side primarily supplies the uterus (Fig. 1). The literature provides a large number of possible options for dividing the internal iliac artery. Most often, it is divided into two sections: anterior and posterior (77%); three sections (14%), four or more (3%) [26].

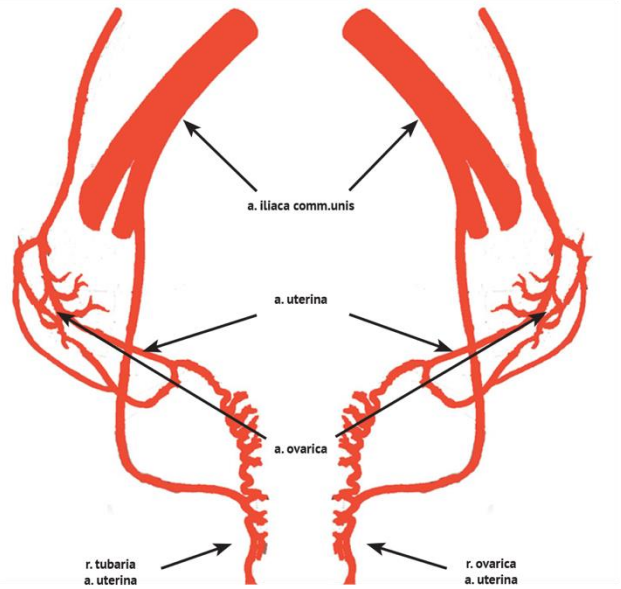

Fig. 1. Arterial blood supply of uterus (scheme)

Several options of origin of UA divergence and large finite branches of the internal iliac artery (superior and inferior gluteal arteries) [27, 28]. The most common case is when UAs are branches of the anterior trunks of internal iliac arteries and have posteriomedial direction. At the same time, UA may originate from internal iliac artery at the site of its separation on the anterior and posterior trunks and further go anteriorly and laterally. [27] In connection with this pre-visualization of the vascular bed with multislice computed tomography and Doppler ultrasound with a three-dimensional reconstruction of vessels is quite justified and allows the time of operation to be reduced, which is spent searching for the necessary arteries and optimal access.

The UA length is about 15 cm, and its diameter is up to 3 mm. It has a tortuous type, passing along the lower edge of the wide ligament of the uterus. The descending section of the UA is isolated, first going along the lateral wall of the pelvis, and then medially along the main ligament of the uterus. Before entering the serous membrane of the uterus UA gives two arteries: the ureteral, which supplies the distal part of the urethra and, cervicovaginal, which supplies the cervix and the upper part of the vagina. The cervicovaginal artery directly departs from the internal iliac artery in 9% of cases [5, 26].

Making a *U* - shaped bend, the UA is directed up the border of the uterus. In the ascending part, collateral arteries depart from the UA: intramural uterine arteries and arteries going to the fundus of the uterus. The distal portion of UA terminates in a broad ligament with two branches : *r.tubaria* going parallel to fallopian tube in its mesentery, and *r. ovarica* [21, 26].

In general, UA deliver about 35–40% of the total blood volume to the uterus [5, 27]. The growth of LM and with hypertrophy of myometrium also lead to the restructuring of the blood supply. With the development of LM, increased blood flow in the uterus is accompanied by a significant dilation of UA, which facilitates identification and selective catheterization. This is one of the conditions for performing UAE.

An important value in the blood supply of uterus belongs to ovarian artery (*a. ovarica*), which originates from the anterior surface of the abdominal aorta, somewhat lower renal arteries origin (at the level of II-III lumbar vertebrae). Its diameter is 0.8-1.0 mm, so often it is not contrasted upon aortography. Arteria ovarica may also begin with common trunk of the aorta (13%), from the renal arteries (10%), but also from the middle adrenal artery (7%) [21, 29].

If LM is present, one of the characteristics of blood supply is an increase in weight of the uterus, which is is accompanied by an increase in the diameter of the uterine and ovarian arteries. The ovarian arteries are especially affected by significant hypertrophy. The degree of hypertrophy, especially in women with large tumor and uterus, significantly exceeds the needs of blood supply [31, 32].

It should be borne in mind that with a significant diameter of the ovarian arteries and the severity of the anastomoses feeding the node, when performing UAE, the risk of iatrogenic damage to the ovaries significantly increases [31].

Approximately in every 10 patient UA are a major source of blood supply to the ovary [5, 17, 27]. An important point is also the detection of large anastomoses between the branches of the uterine and ovarian arteries [20, 25, 29]. Thus, in 10-15% observing their diameter may be sufficient for the development of reflux of embolic particles in the system of ovarian arteries with subsequent lesion of the organ [21, 23]. On the other hand, due to these anastomoses, the perfusion of the uterus and LM nodes can be maintained after performing UAE [9].

In patients with LM, two arterial circuits are detected in the utero-ovarian circulation (Fig. 2) [33]. The main trunk of the UA gives ovarian branch, which directly anastomoses with the ovarian artery - this is the lower circuit of utero-ovarian arterial circulation. The rising branch of UA transforms into the tubal-ovarian branch, which also anastomoses with ovarian artery - this is the upper circuit of the utero-ovarian arterial circulation. Ovarian veins widely anastomose with veins of the broad ligament, fallopian tubes, utero-ovarian ligament, and the veins of the uterus and veins of the suspensory ligament of ovary [22, 23, 33].

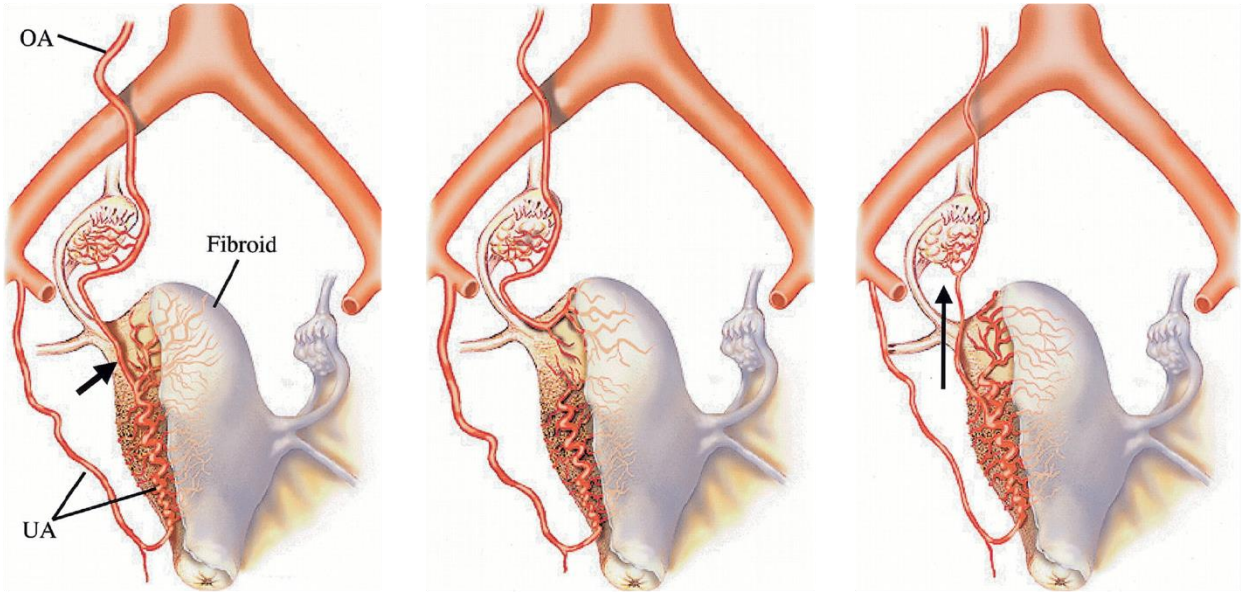

Fig. 2. Types of utero-ovarian artery anastomoses (M.K. Razavi, K.A. Wolanske, G.L. Hwang et al., 2002)

The vascular network of the ovary is also diverse and controversial - in fact, the ovary can be compared with the cavernous body with a huge amount of arteriolo-venular anastomoses and shunts. Features of the utero - ovarian circulation are determined by two main factors [31]. The first is the value of pressure in the main vessels of the circuit (uterine and ovarian arteries), the second is the quantity of volumetric flow in these arteries. If in arterioles of ovarian branches of UA and ovarian artery the pressure is the same, then the blood, passed in the ovary tissue ovary through tubo-ovarian arterioles, will go to the upper arterial circuit and get into the uterus. The content of gonadal hormones in the portions of blood, taken from a tubo-ovarian arterioles, exceeds their content in the ulnar vein 2-8-fold. [32]

Detected differences in concentration of gonadal hormones in various vascular circuits are evidence of the existence of the reverse-flow "transfer" of hormones of the veins of the ovary to the arterial vascular circuits and ovary, and fallopian tube, that provides delivery of high concentrations of hormone to some areas of internal genitalia [31].

Due to the long spasm of UA and activation of blood flow through ovarian artery, blood enriched with hormones can fall into the uterus through two (upper and lower) arterial circuits [32]. The mechanism of "transfer" works in the following manner. The arterial system of the ovary and efferent arterial vessels of the uterus, located in its ligamentous apparatus, are enveloped in venous plexuses and lymphatic vessels. Furthermore, vessels, supplying the uterus and ovary, are surrounded with edematous fiber, containing small cystic lacunae. That is, efferent and afferent blood vessels are very close to each other, and to the interstitial fluid. If the circulation is impaired significantly and the outflow is abnormally high (typical for LM), liquid from its venous bed containing very high concentrations of sex steroids may leak, which, in its turn, can accumulate in the extracellular fluid.

Due to LM hyperplasia of vessels, circulation and outflow from the uterus are observed, which creates the possibility of local abnormally high level of hormones and stimulates the growth of the tumor. Preliminary analysis of the diagnostic angiogram allows you to identify the characteristics of blood supply to the LM and choose the best method of treatment for this pathology.

We had developed a technique of staged UAE, which implied preliminary aortografy of infrarenal aorta - to determine the ovarian arteries; pelvic arteriography - for assessing the vessels of the pelvis and visualization of utero - ovarian anastomoses. Only after this study selective arteriography and embolization of UA were performed.

Before the start of endovascular occlusion it is extremely important to determine the type of utero-ovarian anastomoses and evaluate the risk of ischemic damage to the ovaries or inadvertent reflux of embolic particles from UL - through the utero - ovarian anastomoses - to the abdominal aorta. The presence of such anastomoses is indicated by the reflux of a radiopaque contrast agent into the ovarian arteries. In the presence of dilated ovarian arteries and the significant network of arterial anastomoses between the uterine and ovarian arteries endovascular occlusion od UA should begin with the administration of cylindrical emboli through the catheter (diameter 500-700 microns, length up to 10 mm) up to the termination of reflux of radiopaque agent from UA to ovarian arteries. Cylindrical emboli are not able to overcome the utero - ovarian anastomoses and occlude only UA. In this manner, performance of the methods of UAE is the nature of the occlusion, separating uterine and ovarian arteries. After that, one should switch to the introduction of standard emboli in the form of microspheres with a diameter of 500–700 μm until the symptom of contrast “retention” appears in the lumen of the initial sections of the UA.

In all 48 patients with LM a comprehensive angiographic examination of ovarian and uterine arteries was performed, which included plain angiography of infrarenal part and bifurcation of the aorta, iliac vessels.

The angiographic examination in 29 patients of I group before UEA visualized only UA without prominent utero - ovarian anastomoses. In 19 patients of II group prominent utero - ovarian and arterio - arterial anastomoses were revealed. It should be noted, that in the II group with identified utero – ovarian and arterio - arterial anastomoses in 11 patients (57.9% of all identified anastomoses) anastomoses of I type were detected (Fig. 3). After this study UEA was performed.

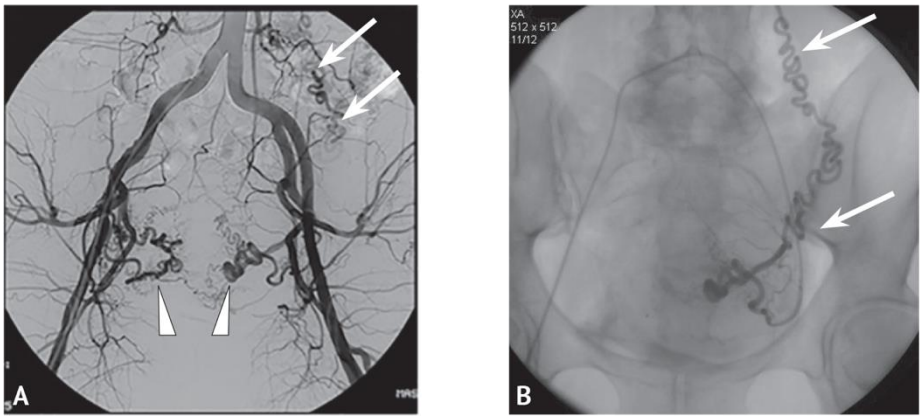

Fig. 3. Angiograms of a female patient D. with uterine leiomyoma: A — aortogram; the dilated and convoluted uterine arteries (conical arrows) and the dilated and tortuous ovarian artery (standard arrows) are visualized; B — selective arteriogram; through arterio-arterial anastomoses of type I, the dilated and tortuous left ovarian artery retrogradely contrasts (standard arrows)

Patients of I group (29 cases) underwent standard UEA using spherical microemboli *PVA*, size 500-700 microns (*Cook*, USA), spherical hydrogel emboli "Emboks" (Plastis - M, Russia) and microspheres *"Embosphere"* (*Merit Medical*, USA) with a size of of 500-700 microns. In three observations, reflux of the contrast agent in the distal parts of the ovarian arteries appeared by the end of endovascular occlusion of UA. At this, the UAE procedure was terminated.

In patients of II group (19 cases) due to detection of utero - ovarian anastomoses cylindrical emboli "Emboks" with the length 10 mm and diameter 500-700 microns (Plastis - M, Russia) were used in order to prevent occlusion of ovarian arteries during UAE. These emboli occluded only the UA and were unable to overcome the utero - ovarian inter-arterial anastomoses. For occlusion each UA required from 20 to 40 emboli. UAE was finished with standard emboli in the form of microspheres.

At first glance, the development of amenorrhea in the postembolization period may seem paradoxal in 3 patients (10.3%) of group I, in whom prominent utero - ovarian anastomoses were not diagnosed. However, the appearance of reflux of the contrast agent at the final stage of the standard UAE, noted in these patients, confirmed the presence of these anastomoses. The opening of these anastomoses occurred already after occlusion of the main branches of UA, supplying the LM, that, probably, and has led to ischemia tissue of ovaries. At the same time, patients of the II group, who underwent separating UAE, had no impaired function of the ovaries. In the period of outpatient monitoring to 18 months none of these patients had observed the development of artificial amenorrhea.

CONCLUSION

The results conducted studies suggest that, the developed method of separating occlusion of uterine arteries is effective and safe in regard to the prevention of ischemic damage to the ovaries with identified prominent utero - ovarian arterial anastomoses. For separating occlusion of uterine arteries it is advisable to carry out this procedure, first using cylindrical emboli " Emboks" (Plastis - M, Russia), and then standard emboli in the form of microspheres. The use of this technique has not been accompanied by intraoperative complications, and in the long-term period of observation to 18 months no impaired function of the ovaries had been observed.

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