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Organ-Preserving Approach in Treatment of Uterine Leiomyoma

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Keywords: leiomyoma; symptoms; conservative treatment; organ-preserving surgeries

Abstract.

Uterine leiomyoma is one of the most common benign hyperproliferative diseases of the female reproductive organs. According to the literature, its prevalence among women of reproductive age is estimated to be approximately 20–40%. Moreover, it is diagnosed more often (up to 75-85%) when carrying out morphological investigations of macro specimens after hysterectomy. In recent years the proportion of young patients with this pathology has increased. For a long period of time radical hysterectomy has been the most common method used to treat the disease. During the past decades the possibilities of organ-preserving treatment of the disease expanded due to the achievements of modern pharmaceutical industry and implementation of new technologies. As a result, surgical interventions themselves changed and the proportion of surgeries such as conservative myomectomy, uterine artery embolization, hysteroscopic resection of submucous fibroid increased. The data on surgical interventions allowed us to eradicate the symptoms of uterine leiomyoma preserving fertility in many patients, however, the risk of tumor recurrence and growth is still present. The recurrence rate after organ-preserving surgeries remains high and, according to the results of various studies, accounts for 2-50% of cases. Considering the above-mentioned data prevention of tumor recurrence is of great relevance. Based on the results of diagnostic program including endocrinologic, immunological and morphological investigations there was found that in women with isolated uterine leiomyoma dyshormonal disease, inflammatory processes of the genital organs, chronic endometritis, pathology of the receptor apparatus of uterine tissues occur more often; hyperprolactinemia, relative or absolute hyperestrogenemia and increased production of antibodies are more often diagnosed in women with uterine leiomyoma and co-existent dyshormonal pathology of the mammary and thyroid gland. According to the literature, in isolated uterine leiomyoma therapy aimed at correcting local factors including anti-inflammatory therapy, local hormone therapy or uterine artery embolization is recommended. In comorbidity correction of systemic metabolic disorders, namely anti-stress therapy, systemic hormone therapy, immune system correction, treatment of co-existent somatic pathology which may include local use of hormones and organ-preserving surgical interventions should be performed first of all. Thus, modern medicine has in its arsenal various organ-preserving, conservative, surgical including minimally invasive methods of treatment implementation of which allows us to improve quality of life in such patients as well as to enhance fertility and reproductive health of women.

Problem statement and analysis of the recent research

Uterine leiomyoma is one of the most common benign hyperproliferative diseases of the female reproductive organs. According to the literature, its prevalence among women of reproductive age is estimated to be approximately 20–40%. Moreover, it is diagnosed more often (up to 75-85%) when carrying out morphological investigations of macro specimens after hysterectomy [1, 4, 5]. Uterine leiomyoma is the most common benign tumor of the female genital tract leading to infertility in 20-45% of cases and surgery including the removal of an organ in 50-70% of cases and, accordingly, it is the main cause of a performance decrement among modern women and the deterioration in the quality of life. Symptoms of leiomyoma such as uterine hemorrhage, anemia, pain, symptoms of compression of adjacent organs result in significantly reduced physical health of a woman and deterioration of her emotional state as well as often lead to female infertility and pathological course of pregnancy [2]. In recent decades the ratio of symptomatic course of leiomyoma has increased according to different authors from 60% by 75% [1-5]. In recent years the proportion of young patients with this pathology has increased. According to Tatarchuk TF, et al. during a 10 years' follow-up of women being treated in clinical hospitals of Kyiv the proportion of patients at the age of 31-40 years increased significantly while the proportion of young patients under 30 years of age increased by almost 4 times [9-11].

The objective of the research was to analyze the available literature on the assessment of this problem as well as to search for new approaches to its solution. The progress of fundamental sciences achieved over the past decades allowed us to advance in studying the etiology and pathogenesis of uterine fibroid. However, the leading mechanisms of its development remain uncertain and debatable. Leiomyoma often develops together with dyshormonal pathology of the mammary and thyroid gland, obesity and hepatobiliary disorders [1, 9, 11, 12]. In co-occurrence of the pathology of the mammary gland uterine leiomyoma usually develops secondary to chronic stress in patients with a hereditary predisposition to proliferative diseases and positive anamnesis for recent allergic events. It is accompanied by thyroid dysfunction, high body mass index, pathology of the liver and cardiovascular system while isolated leiomyoma is more often observed secondary to chronic inflammatory genital diseases and vaginal dysbiosis, miscarriage, prolonged use of intrauterine contraceptive devices as well as postabortal and postpartum complications [1, 11, 14]. It should also be noted that isolated leiomyoma is characterized by a slow asymptomatic growth sometimes reaching a large size and symptoms of compression of adjacent organs while in comorbidity it is often accompanied by rapid growth and pronounced clinical manifestations including menometrorrhagia and pain syndrome deteriorating the quality of life in a woman even if its size is small [5, 14, 15].

Based on the results of diagnostic program including endocrinologic, immunological and morphological investigations there was found that in women with isolated uterine leiomyoma dyshormonal disease, inflammatory processes of the genital organs, chronic endometritis, pathology of the receptor apparatus of uterine tissues occur more often; hyperprolactinemia, relative or absolute hyperestrogenemia and increased production of antibodies are more often diagnosed in women with uterine leiomyoma and co-existent dyshormonal pathology of the mammary and thyroid gland. According to the literature, in isolated uterine leiomyoma therapy aimed at correcting local factors including anti-inflammatory therapy, local hormone therapy or uterine artery embolization is recommended. In comorbidity correction of systemic metabolic disorders, namely anti-stress therapy, systemic hormone therapy, immune system correction, treatment of co-existent somatic pathology which may include local use of hormones and organ-preserving surgical interventions should be performed first of all [1-4, 5, 12].

However, despite the considerable progress in the study of the morphology and pathogenesis of uterine leiomyoma as well as the achievements of modern pharmaceutical industry and the development of new technologies it should be noted that surgical method of

treatment of this pathology (hysterectomy and myomectomy) remains the leading one. Surgeries for the removal of uterine leiomyoma account for 80% of planned surgical interventions while in 90% of cases hysterectomy is performed in women of reproductive age [4, 15]. However, this surgical intervention results in irreversible infertility [4, 15]. At the same time, the increase in the proportion of young women with this gynaecological disorder and their desire to preserve vaginal function and the uterus are quite significant and according to various authors constitute 42%-65% [5]. The analysis of the structure of motivation to preserve the uterus made and published by several authors allowed us to detect the increase in the proportion of older women that is obviously due to social activity of a modern woman, her conscious postponement of fertility to a more mature age. On the other hand, the introduction of modern reproductive technologies expands the age limits of fertility in a woman and creates the possibilities of carrying a pregnancy and delivering babies even during perimenopause [11, 12, 14].

The data mentioned above justify the need for wider introduction of organ-preserving methods in treatment of uterine leiomyoma as well as the search for individual approaches to the management of this category of patients. The selection of methods of treating uterine leiomyoma is known to depend on the size of the tumor, clinical symptoms and localization of the lymph nodes, age of the patient, her reproductive plans and to a greater extent, somatic pathology associated with tumor formation. There is no doubt that the main purpose of organ-preserving conservative treatment of uterine leiomyoma is not only to eradicate its symptoms and to restore reproductive function, but also to achieve stable hemostasis and to prevent uterine and endometrial cancer. In pathogenetic treatment of uterine leiomyoma non-hormonal medications and hormone therapy aiming at inhibiting growth of tumor cells as well as at preventing the development of complications are used. Considering the results of fundamental studies and mechanisms of developing leiomyoma there were introduced anti-stress therapy and immune-modulating therapy as well as anti-inflammatory, antioxidant, angioprotecive, antiplatelet therapies, vitamins, lymphatic drugs [1, 3, 5, 12].

Hormone therapy is one of the most common approaches to treatment of hyperproliferation of the uterus and its use is based on the concept of hormone-dependence of cancer creating absolute or relative hypoestrogenemia. However, the use of progestogens and oral contraceptives is mainly aimed at eradicating symptoms of menometrorrhagia; it does not significantly affect the size of myomatous nodules and results in a range of side effects. Prolonged use of progestogens requires careful monitoring of hemostasis and lipid profile [13, 14, 17].

High rates of co-occurrence of uterine leiomyoma and somatic pathology (hypertensive disease, diabetes mellitus, obesity, hepatobiliary disorders) require the prevention of systemic effects of gestagens by means of their local application using the levonorgestrel-releasing intrauterine system. The use of the levonorgestrel-releasing intrauterine system is effective in eradicating clinical symptoms of leiomyoma and preventing co-existent endometrial hyperplasia being not associated with systemic side effects (headache, mastalgia, acne). However, its application does not provide any evidence of decreased size of fibromatous nodules and the uterus in general and has several contraindications (submucous node, endometrial polyposis) [2]. Based on the hypothesis suggesting that leiomyomas are progesterone-dependent tumors and, accordingly, they increase in size when using progestogens, as presented in the literature, significant reduction in uterine size by 26.5% was observed when using antiprogesterone drugs (mifepristone) for 3 months [2].

Based on the currently existing literature data on stimulating effect of estrogens and progesterone on myomatous nodules the most pathogenetically justified method of hormone treatment of leiomyoma includes, without a doubt, drugs inhibiting the synthesis of sex steroids. Nowadays one of the most common methods to reduce the synthesis of ovarian sex steroids is medically induced menopause by means of gonadotropin-releasing hormone (GnRH) analogs. This

group of drugs inhibits the synthesis of estrogens and progesterone blocking the production of gonadotropic hormones of the pituitary gland under conditions of controlled hypohormonemia. Estrogen and progesterone deficiencies lead to the reduction in uterine blood flow, tumor size and symptom severity. In addition, GnRHs inhibit the activity of certain growth factors (insulin-like growth factor 1, epidermal growth factor in particular) and cell proliferation as well as reduce the sensitivity of tumor to estrogens. This group of drugs is also highly effective in eradicating symptoms of fibroid in terms of stopping bleeding, reducing symptoms and signs of pain syndrome as well as reducing the size of nodules. However, the use of these preparations is limited by a significant number of estrogen deficient conditions including vegetative-vascular and psychopathological manifestations and in prolonged use – by metabolic disorders of bone tissue trophism. Considering all the above-mentioned data this group of drugs may be recommended to use as an independent method in conservative therapy for leiomyoma among female patients during perimenopause as well as a complex or combined preoperative preparation [1, 5, 7, 8].

In recent years, some cases regarding the use of antigonadotropins which inhibite the secretion of FSH and LH blocking ovarian steroidogenesis (danazol and synthetic steroidal hormone – gestrinone) with the aim of creation of hypoendocrine profile have been reported in the literature. However, wide introduction of these drugs is limited by their androgenic effects.

Thus, the possibilities of organ-preserving treatment of the disease expanded significantly due to the achievements of modern pharmaceutical industry and implementation of new technologies. As a result, surgical interventions themselves changed and the proportion of surgeries such as conservative myomectomy, uterine artery embolization, hysteroscopic resection of submucous fibroid increased. With the development of laparoscopic surgery laparoscopic technique for the myolysis of uterine fibroids (myoma coagulation) was developed in Germany. Laparoscopic myolysis and laser photocoagulation under ultrasound guidance is used primarily to treat small nodules [15]. New possibilities of organ-preserving therapy appeared due to the introduction of minimally invasive techniques in practice. Among them bilateral endovascular uterine artery embolization is one of the most promising methods [16]. The data on surgical interventions allowed us to eradicate the symptoms of uterine leiomyoma preserving fertility in many patients, however, the risk of tumor recurrence and growth is still present. The recurrence rate after organ-preserving surgeries remains high and, according to the results of various studies, accounts for 2-50% of cases [5]. In addition, though the methods of organ-preserving surgery improved they are still surgical interventions with some disadvantages and complications.

Conclusions

Thus, modern medicine has in its arsenal various organ-preserving, conservative, surgical including minimally invasive methods of treatment implementation of which allows us to improve quality of life in such patients as well as to enhance fertility and reproductive health of women. The optimization of the algorithms for organ-preserving treatment of uterine leiomyoma opens up new horizons in terms of the preservation of reproductive potential being of great medical, social and economic importance. Considering a high prevalence, diametrically opposed interpretations of the mechanism of tumor development, the absence of unified approaches to diagnosis and differentiated organ-preserving treatment of leiomyoma further study of the etiology and pathogenesis as well as the development of the system of providing medical and preventive care for women with this pathology are promising.

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