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KEY ETIOPATHOGENETIC FEATURES OF FORMATION OF UTERINE MYOMA

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КЛЮЧЕВЫЕ ЭТИОПАТОГЕНЕТИЧЕСКИЕ ОСОБЕННОСТИ ФОРМИРОВАНИЯ МИОМЫ МАТКИ

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Abstract. The steady growth of proliferative diseases from year to year is becoming more and more medical and social importance, which is associated with their clinical manifestations and recurrent course, adversely affect the quality of life and the ability to work of women. Uterine fibroids are the most common benign neoplasm in women of reproductive age. This article discusses the key issues of the etiopathogenesis of uterine fibroids. Uterine fibroids are a monoclonal hormone-sensitive neoplasm and are the most common tumour of the reproductive organs of women. The pathogenesis and developmental mechanisms of uterine fibroids today are complex and not fully understood. Perhaps the underlying theory is the 'clonal expansion of uterine fibroids', it is the clonal expansion that initiates the processes of neoangiogenesis, activated by tumor growth. Although to this day there remain many controversial and unresolved issues.

Аннотация. Неуклонный рост пролиферативных заболеваний из года в год приобретает все большее медико-социальное значение, что сопряжено с их клиническими проявлениями и рецидивирующим течением, негативно сказываются и на качестве жизни, и трудоспособности женщин. Миома матки — наиболее распространенное доброкачественное новообразование у женщин в репродуктивном возрасте. В данной статье рассматриваются ключевые вопросы этиопатогенеза миомы матки. Миома матки представляет собой моноклональное гормоночувствительное новообразование и является самой распространенной опухолью репродуктивных органов женщин. Патогенез и механизмы развития миомы матки на сегодня сложны и не до конца изучены. Пожалуй, основополагающей теорией является «клональная экспансия миомы матки», именно клональная экспансия инициирует процессы неоангиогенеза, активизируемая опухолевым ростом. Хотя и по сегодняшний день остается множество спорных и нерешенных вопросов.

Keywords: uterine fibroids, etiopathogenesis.

Ключевые слова: миома матки, этиопатогенез.

The steady growth of proliferative diseases from year to year is becoming more and more medical and social value [1, p. 1264], which is associated with their clinical manifestations and recurrent course, adversely affect the quality of life and the ability to work of women [2, p. 234]. Today, benign proliferative diseases of the pelvic organs (BPDPO) [3, p. 1452], among them uterine myoma (UM), genital endometriosis (GE) and endometrial hyperplastic processes (EHP), occupy the first place in the overall gynaecological morbidity structure [4, p. 1349]. Moreover, these nosological units continue to be considered as independent and independent diseases with specific mechanisms of development and a characteristic clinical and morphological picture [5, p. 409], which determines the choice of therapeutic and diagnostic tactics, as well as the type of rehabilitation of patients.

Of particular interest is the UM. UM is the most common benign neoplasm in women of reproductive age [6, p. 413]. UM is a monoclonal hormone-sensitive neoplasm and is the most common tumour of the reproductive organs of women [7, p. 350], but it should be noted that there are significant differences in the prevalence of UM. Perhaps the most important reason lies in the fact that different researchers use different methods and diagnostic methods, and each method and method has its own specific level [8, p. 238; 9, p. 375].

Thus, in the course of a study conducted by A. McComaander (2016) in Canada, in 2539 patients in the age groups from 14 to 50 years, the diagnosis of 'UM' was made and verified only in 5.9% of cases, and more than 55% of women who did not the diagnosis 'UM' was made; myomatous nodes were diagnosed by means of ultrasound [10, p. 5], and in the case of using histomorphological methods for studying the material obtained during the hysterectomy, the detectability of UM reaches 68% [11, p. 8740].

In their study, A. McComaander et al. (2016) suggest that the influence of the racial factor on the distribution of UM is associated with: firstly, socio-economic differences and differences in mentality; secondly, with the genetic characteristics of Caucasians and African Americans [12, p. 1370]. The Ministry of Health of the Russian Federation cites data that the share of UM is up to 75% of all gynaecological interventions [13, p. 10], of which almost 1/3 is carried out at reproductive age. The average age of patients undergoing hysterectomy for UM is 38.42 ± 4.14 years. According to Donnez J., around 300,000 surgical interventions for UM have performed annually in the European Union, including about 200,000 total hysterectomies.

The pathogenesis and mechanisms of UM development are complex and not fully understood. Three key mechanisms for the development of uterine fibroids are distinguished: involving the hypothalamic–pituitary system in the pathological process; with severe impaired ovarian function; with predominant changes in the function of the uterus.

UM is considered a hormone-dependent myometrium tumour. More often, fibroids occur at reproductive age and regress after menopause, when the level of sex hormones rapidly decreases. Perhaps the fundamental theory is the 'clonal expansion of UM', it is the clonal expansion that initiates the processes of neoangiogenesis, activated by tumor growth. For intensive tumor growth, a well-developed vascular network is necessary, but at the same time, the activation of neoangiogenesis contributes to the adaptation and regeneration of tissues due to damage. Angiogenic factors together with cytokines activate the proliferation of endotheliocytes. The tumor has a randomly organized vascular network, which has excessive vascular permeability. Numerous

studies have shown that the implementation of hormonal activity is carried out through a system of complex-specific local growth factors, which, in turn, control the growth and differentiation of cells.

The formation of myoma nodes begins at the stage of embryogenesis. Low-differentiated cells are affected by various factors even at the stage of intrauterine development, in which the growth initiation begins under the influence of estrogen and progesterone. Differentiation of the progenitor cell may also be due to the presence of neoplastic transformation of the physiological myometrium. MM in its morphogenesis can undergo 3 stages of tissue metabolism: the first is due to the presence and formation of the active growth zone, with active cellular metabolism; In the second stage, an intensive progressive growth of a neoplasm is observed, with no obvious signs of differentiation, the third stage fully combines the signs of the 2nd stage with the additional presence of cell differentiation and maturation of the pool of cells.

It is known for certain that UM has a monoclonal origin, according to experts, it is the pool of monoclonal cells that actually initiates neoplastic processes in the myometrium, but most of the mechanisms are not fully understood [11, p. 8741]. Trigger factors that are involved in the further formation and development of tumor neoplasms include genetic mutations, as well as the influence of sex hormones in a consolidated complex with biochemical processes in the extracellular matrix myomas [4, p. 1348]. The primary cell, from which atypical cells begin to form, is the mesenchymal cell (MK) or smooth muscle cell (SMC) of the myometrium. Many researchers cite evidence that during cytogenetic studies, chromosomal abnormalities (aberrations, deletions, chromosomal rearrangements with a change in loci) are repeatedly found. The locus 12q of the XV chromosome is most often affected, it is also called the locus of aberrant multilevel tumor growth, and according to the research conducted by Wise L. A. [10, p. 6] is very significant in the development of UM. Thanks to a group of researchers led by Wise LA, a gene was identified — HMGA₂ (formerly HMGIC), which is directly related to the development of tumor mechanisms, and it is this gene that provides cell proliferation, as well as the HMGA₁ gene (formerly HMGIIY), which provides tissue architectonics. Myoma nodes have high-estrogen and progesterone receptors. So A. McComaander et al. (2016) share the view on the correlation between the occurrence and development of UM with hormonal status (UM does not occur at puberty in girls and extremely rarely in menopausal and postmenopausal women). In menopause, UM regresses, but morphological studies prove that UM persists, only decreasing in size. However, most experts are similar in the opinion that the exact functional role of estrogen and progesterone in the mechanisms of UM development remains extremely paradoxical. The well-known fact that UM is much less common in women with more than 2 genera in history. Progesterone, which has an amphoteric effect on UM (estradiol and progesterone are involved in the development of uterine fibroids, using opposite paths), is also believed to play a significant role in the occurrence of uterine fibroids. According to the literature, cited above, the most significant risk factors for UM development are: overweight, postponed inflammatory diseases of the pelvic organs, frequent intrauterine interventions. In these works, it is noted that combinations of dyshormonal diseases of endometomyometry and stromal tissue (components of the extracellular complex) are not accidental, as evidenced by the peculiarities of premorbid background, the similarity of clinical manifestations, as well as the pathogenetic features of uterine fibroids, genital endometriosis and endometrial hyperplastic processes caused by identity risk factors for their development.

In conclusion of this review, I would like to note that there is no single reason for the emergence and development of UM. Many different factors are involved in this process, which explains its frequent distribution and heterogeneity of the tumor itself while taking into account morphohistochemical features, location, number of nodes and the nature of their growth, as well as

clinical manifestations. High medical and social significance requires further detailed study of the aetiology, pathogenesis and methods for its timely diagnosis and treatment of UM.

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