THE ROLE OF ENDOMETRIOSIS IN THE FEMALE REPRODUCTIVE SYSTEM.

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The work examines the female disease endometriosis, its symptoms, drug treatment and surgical intervention. Endometriosis is a chronic progressive estrogen-dependent disease, characterized by high prevalence, especially among women with pelvic pain (40-80%) and infertility (25-80%). The choice of methods for treating endometriosis is wide, but there is no single approach and it is determined individually, taking into account the goal (treatment of pelvic pain or infertility).

Key words: Endometriosis, infertility, pathology, endometrium, drug therapy, contraceptives, hormones, menstruation.

Endometriosis is a tumor pathological process in which benign tissue growth occurs outside the uterine cavity, similar in morphological and functional properties to the endometrium. In the structure of gynecological diseases, endometriosis is in third place, following inflammatory diseases of the uterine appendages and myoma. The prevalence of endometriosis in the general population reaches 10% [7].

The prevalence of endometriosis is high among women with infertility, ranging from 25 to 70%, and among women with pelvic pain, from 40% to 80%, according to variousauthors[11,14].

Women with endometriosis often report chronic pelvic pain, although its nature and severity vary and do not correlate with the stage of the disease based on the results of laparoscopy. This pain can manifest itself in the form of dysmenorrhea (cyclic pain associated with menstruation), dyspareunia (pain during or after sexual intercourse), and pelvic or abdominal pain, and significantly reduces the woman's overall quality of life.

The main problem for women suffering from endometriosis is the risk of recurrence. The recurrence rate of endometriosis symptoms ranges from 21.5% after 2 years to 50% after 5 years after surgical treatment [7] .

Traditionally, two different conditions are distinguished: internal endometriosis (adenomyosis), characterized by the presence of endometrial glands and stroma in the myometrium, and external, when endometrioid heterotopias are located in the pelvis or in organs located at a fairly large distance from the primary focus (for example, in the lungs). Pelvic endometriosis is divided into 3 clinical forms:

1) implants on the surface (superficial endometriosis);

2) ovarian cysts limited by ectopic endometrium (endometriomas);

3) nodules of endometrial tissue mixed with cells of adipose and connective tissue, located deep under the peritoneum (deep endometriosis).

Intestinal endometriosis is characterized by the formation of endometrioid foci infiltrating at least the proper lamina of the muscular layer of the intestine,

What causes pain and various disorders of the gastrointestinal tract (diarrhea, constipation, bloating, mucus discharge with feces,

rectal bleeding) and symptoms mimicking irritable bowel syndrome [12].

When endometrioid nodes infiltrate the wall of the colon or rectum, causing stenosis of the lumen, symptoms of partial intestinal obstruction may be present. Endometrioid foci are removed by resection; in this case, surgical intervention, which significantly alleviates pain and improves quality of life, Clinical manifestations of endometriosis depend on the localization of the process, the degree of damage to the genitals and adjacent organs, and individual pain threshold. Painless (asymptomatic) forms of endometriosis occur even with severe infiltrative damage, but this is always the exception. The "calling card" of endometriosis is symptoms directly related to menstruation and most pronounced during this period: dysmenorrhea (mainly algomenorrhea) - 82.7-83.4%; pain syndrome of varying severity - 48.3-50%; dyspareunia - 33.4-34.5%. Bleeding in endometriosis is also predominantly cyclical — hyper-, polymenorrhea is usually observed, prolonged perimenstrual bloody discharge and anemia are also characteristic. Dysuria (urination disorders) and dyschezia (painful and/or difficult defecation) are observed with infiltrative lesions of adjacent organs (bladder and/or ureters and intestines, respectively). The literature describes the "four dys" syndrome (dysmenorrhea, dyspareunia, dysuria, dyschezia), observed during menstruation in patients with endometriosis. Infertility is one of the most significant and distressing symptoms of endometriosis, its frequency is 35-40%. Thus, the fertility rate (the ratio of the number of births to the number of women of reproductive age) in healthy women is 0.15–0.20, while in patients with endometriosis it is 0.02–0.1, i.e. it is an order of magnitude lower [1].

Although several pathogenetic hypotheses have been proposed, the exact pathogenesis of endometriosis remains unclear. At the same time, it is clear that endometriosis develops as a result of dissemination of the endometrium into ectopic areas with subsequent formation of ectopic endometrial complexes. It is assumed that the presence of these ectopic foci leads to the development of symptoms associated with the disease. Ectopic tissue of endometrial origin consists of glandular epithelium and stroma and is characterized by a predominance of benign characteristics combined with features (invasion and neoangiogenesis) that make it similar to malignant neoplasms. Many theories have been proposed to explain the causes of endometriosis depending on the factors that cause its development: retrograde menstruation, genetic

predisposition, peritoneal cell metaplasia, and impaired immune control. Sampson's theory is the most popular and

The generally accepted theory of the origin of endometriosis: it is assumed that endometrioid implants arise as a result of retrograde menstrual reflux of endometrial tissue into the abdominal cavity through the fallopian tubes, which is confirmed by the detection of endometrial fragments. The spontaneous development of endometriosis only in humans and primates supports the assumption that only menstruating species may be affected by this disease. At the same time, retrograde menstruation is probably a very common phenomenon, but endometriosis develops only in some women, which indirectly indicates the role of other factors in its development (immunological, genetic, disruption of the biochemical composition of the environment in the abdominal cavity).

In addition, an alternative theory of embryonic rudiments suggests that endometriosis may develop from Müller cells scattered in the peritoneal cavity, which, under the influence of certain biochemical stimuli, may become activated and form endometrial tissue. Another hypothesis, which also helps explain the extraperitoneal localization of the disease, suggests that the origin of endometrioid lesions may be associated with metaplasia of peritoneal cells and differentiation of mesothelial cells into endometrial cells. It has finally been suggested that blood and lymphatic vessels may play a role in the dissemination of endometrial cells over long distances. The human endometrium contains a small population of cells with functional properties of stem cells with the corresponding markers and functional characteristics, which has led to an assumption about their role in the pathogenesis of endometriosis.

Endometrial stem cells undergo cyclic monthly regeneration under physiological conditions after menstruation. These cells are presumably responsible for the proliferation and cyclic regeneration of endometrial tissue after menstruation. Endometriosis is the only disease in which the benign proliferative process affects the unchanged tissue of adjacent organs. Characteristic features of endometriosis are the ability to infiltrative growth, the absence of a pronounced capsule around the endometrioid focus (except for endometrioid cysts), the possibility of metastasis to distant organs.

The severity of the disease, the ambiguity of tactical approaches and the lack of pathogenetic treatment methods predetermined the interest of many domestic and world researchers in a comprehensive study of this disease, however, despite numerous studies, the results remain unsatisfactory: 35-50% of patients with endometriosis suffer from pain or infertility, relapses are observed in almost half (40-45%) of patients during the first 5 years after surgical treatment. The main tactical provisions that can improve the results of endometriosis treatment are the following: Timely diagnosis. It is

extremely important for both the prognosis of the disease and, especially, for the restoration of impaired fertility, where the time factor and age play a decisive role.

According to the data presented by the World Endometriosis Research Foundation (WERF), diagnosis of the disease is delayed by an average of 7 years, and in some cases — up to 30 years. During this "lost time", reproductive problems are not resolved, in addition, in 10% of cases, widespread forms with extragenital localization of endometrioid foci are formed, in 0.65% of patients, endometrioid cancer is diagnosed. It must be recognized that in modern conditions, with the availability of highly informative additional research methods (ultrasound, MRI), this is unacceptable. It is advisable to examine patients with endometriosis in the following volume and sequence: standard general clinical and gynecological, including rectovaginal examination; extended colposcopy, oncocytological examination; ultrasound of the pelvis and kidneys (in the presence of retrocervical endometriosis); tumor marker testing (CA-125 for ovarian endometriosis, CEA, MCA for retrocervical endometriosis); rectoscopy or colonoscopy with biopsy for retrocervical endometriosis; cystoscopy with biopsy for infiltrates behind the bladder tissue or symptoms of cyclic hematuria; CT or MRI for widespread forms of endometriosis and, finally, laparoscopy. And although at present "endometrioid disease" is considered a surgical disease, and such indications for surgical treatment in patients with endometriosis as the presence of prolonged bleeding leading to anemia, severe pain syndrome in the absence of effect from conservative therapy or the impossibility of its implementation, infertility, the presence of endometrioid cysts (diameter 4 cm or more), the presence of widespread, infiltrative forms of endometriosis are not discussed, the question is still relevant: is it advisable to laparoscopically confirm the diagnosis of endometriosis? Undoubtedly, any surgical intervention is accompanied by the risk of surgical (including personal and technical), anesthetic, infectious, thromboembolic and other complications.

It is worth listening to the opinion of the President of the WES (World Endometriosis Society) R. Vercellini that "the general belief that preliminary laparoscopy should always be performed to accurately diagnose the disease should be challenged, since non-surgical diagnosis of endometriosis has demonstrated its high reliability." Pragmatic, i.e. an individual approach - development of an optimal diagnostic and therapeutic individual program. The goal of treatment should be determined by the main problems of the patient (elimination of pain and / or bleeding, restoration of fertility or simply improving the quality of life). Exclusion of oncopathology, both directly related to the long-term existence of the process (although malignant transformation of endometrioma is quite rare), and oncopathology of another genesis. "Masks" of endometriosis with various localizations of implants are often not only benign diseases, such as uterine myoma, chronic salpingo-oophoritis, benign

ovarian tumors, coccygodynia, proctitis and paraproctitis, irritable bowel syndrome, hemorrhoids, chronic spastic colitis, adhesive intestinal obstruction, hemorrhagic cystitis, but also malignant tumors of the ovaries and intestines (in particular, Schnitzler's metastasis). Evaluation of the need for surgical intervention and selection of the optimal surgical component of endometriosis treatment. High qualification of the surgeon. Endometriosis is a serious disease, and the success of treatment is largely determined by the experience of the surgeon. Laparoscopy should be performed only by a doctor who can, if necessary, carry out adequate surgical treatment in full (laparoscopy is initially unacceptable only for diagnostic purposes). Relapses and repeated operations on the ovaries lead to a loss of the time interval for restoring fertility and a decrease in the ovarian reserve. The high recurrence rate of infiltrative forms of endometriosis is due not only to the difficulties in determining the true boundaries of the lesion, but also to the conscious refusal of an insufficiently experienced surgeon to take a radical approach to removing the infiltrate located near vital organs, which inevitably leads to repeated traumatic surgeries, which, due to the localization of the process (intestines, bladder, ureters, main vessels and cellular spaces of the small pelvis), can be accompanied by severe intra- and postoperative complications. Ideal therapy should meet the following requirements: pain relief, regression of endometrioid lesions even in severe forms of the disease and preservation of fertility. Ideally, the patient should be provided with the opportunity to choose a drug from the standpoint of effectiveness/cost.

The tactics of management should be differentiated depending on the severity of the disease, the patient's age and her reproductive goals, and the earlier surgical removal or destruction of the most significant foci of endometriosis is performed, the better the treatment results. Modern methods of drug therapy of endometriosis do not lead to a cure, but have a positive effect on the restoration of the generative function, prevent the occurrence of common forms of the disease, and play an important role in the prevention of relapses of the disease. The basis for the prevention of severe and combined forms is early diagnosis of mild and moderate forms of endometriosis and active combined tactics (laparoscopic surgery and drug therapy). Access - in the absence of pronounced adhesions, damage to the intestine and urinary system - laparoscopic is preferable. The best effect is achieved when performing operations with subsequent administration of adjuvant therapy. In patients of reproductive age, even in the presence of widespread forms of endometriosis, reconstructive plastic surgery should be performed and radical surgery should be resorted to only in cases where all other possibilities of both surgical and drug treatment have been exhausted.

Combined oral contraceptives (COCs). They have been used for over 50 years. The positive aspects are: low cost, the possibility of long-term and repeated use, as well as the contraceptive effect, which is important for young and sexually active women.

COCs have long and firmly occupied a certain "niche" in the treatment of endometriosis, namely, the relief of dysmenorrhea and, above all, algomenorrhea (efficiency - 60-95%). For treatment, drugs containing dienogest as a gestagenic component are used (dienogest - 2 mg, ethinyl estradiol - 0.03 mg). The method of application is discussed, but many prefer to prescribe the drug in a continuous mode, which ensures the absence of a menstrual-like reaction. According to P. Vercellini et al., COCs after endometrioma removal reduce the risk of relapse or extend the duration of the post-relapse period. However, recently there has been evidence that COCs do not adequately relieve pain and dyspareunia, and their use for dysmenorrhea correlates with surgically confirmed endometriosis in subsequent years, and in the case of prescribing these drugs for severe primary dysmenorrhea - with deep invasive forms of endometriosis. The presence of an estrogen component in COCs for the treatment of endometriosis - an undoubtedly estrogen-dependent disease - is also discussed, which draws attention to other medications, the effectiveness of which is supported by evidence. Progestogens. The levonorgestrel-releasing intrauterine system Mirena contains 52 mg of levonorgestrel with a daily release of 20 mcg of the drug directly into the endometrium. Levonorgestrel is a synthetic gestagen from the group of 19-norsteroids - one of the most potent progestins with maximum biological activity and pronounced antiestrogenic, antigonadotropic action, weak androgenic action. High concentrations of levonorgestrel in the endometrium contribute to a decrease in the sensitivity of its estrogen and progesterone receptors, exerting a strong antiproliferative effect [2,3].

For patients with stage 3–4 endometriosis and pronounced adhesions, surgical treatment should be performed in level 3 hospitals (hospitals providing specialized, including high-tech, medical care to women, developing new methods for diagnosing and treating gynecological pathology). In diagnosed nodular forms of adenomyosis against the background of abnormal uterine bleeding, surgical treatment will also be the optimal method of choice of therapy [5,6,10].

Conclusion.

To date, many aspects of the etiology and pathogenesis of endometriosis have not been sufficiently studied, and active research work is being carried out. Methods of surgical and conservative treatment are being developed and improved. Practicing doctors, understanding the impossibility of a complete cure for the disease, have concentrated their efforts on developing new methods of drug therapy and improving surgical treatment methods. Thus, researchers and doctors are working intensively in various areas, the results of which will improve the quality of medical care for patients with endometriosis.

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