ejpmr, 2019,6(4), 198-200

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

MODERN DIAGNOSIS AND TREATMENT OF UTERINE SARCOMAS (LITERATURE REVIEW)

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Article Received on 23/01/2019 **Article Revised on 13/02/2019** **Article Accepted on 05/03/2019**

ABSTRACT

Uterine sarcomas (US) are rare malignant tumors of mesenchymal origin. According to statistics, 8 cases of uterine sarcoma are detected annually in the world for 1 million women. The diversity of US, both in morphological structure and clinical features complicates the early and differentiated diagnosis, treatment and prognosis of this pathology. The risk of US after radiation therapy consist by 0,03-0,8%. Uterine fibroids are considered to be an independent risk factor for developing sarcomas in pre - and postmenopausal period. Currently existing methods allow to establish a diagnosis before surgery in only a 1/3 of patients. High malignancy of US, fast progression of the tumor, the tendency to frequent occurrence of local relapses, indicate the need for radical surgery. Timely radiation therapy improves long-term results of treatment.

KEYWORDS: Mesenchymal tumors, leiomyosarcoma, endometrial stromal sarcoma, carcinosarcoma, uterine fibroids, uterine extirpation.

Actual problems. US are infrequent malignant tumors of mesenchymal origin and differ in origin from cancer, which develops from the epithelium. Noteworthy is the fact that all female genitals contain a significant amount of mesenchymal tissue: its proportion to the epithelial is 95:5. With less than 5% of tumors of the genitals are mesenchymal and 95% of epithelial (Zapolska, 2017).

US occur from two tissues: the stroma of the endometrium and muscle tissue. Malignant degeneration of the endometrial stroma may be accompanied by epithelial malignancy (carcinosarcoma), the epithelial component may look benign (adenosarcoma) or absent (endometral stromal uterine sarcoma). Tumors developing as a result of malignant transformation of smooth muscle cells are known as uterine leiomyosarcoma. According to statistics, 8 cases of US are detected annually in the world for 1 million women. In the United States, the incidence of sarcoma is 1 in - 17,1 million women. In Russia, this measure is - 10 cases per 1 million, in St. Petersburg - 7 per 1 million women.[14,15]

The variety of US, both in morphological structure and clinical features complicates the early and differentiated diagnosis, treatment and prognosis of this pathology. In connection with this, we conducted a systematic analysis of the data available in the modern scientific medical literature and devoted to modern aspects of etiology, pathogenesis, diagnosis and treatment of patients with various forms of US. This review is an attempt to summarize the experience of modern medicine in the management of patients with US.

Etiology and pathogenesis in development of sarcomas of the uterus are not clearly established.[1,4,6,14] Some studies have shown the viral origin of this pathology.[8,9,11] In experiments on muscles, the stimulating effect of exogenous estrogens on tumor growth was shown, the severity of which was determined by the duration of their administration.[3,6,8] The age of patients varies from infantile to senile depending on the morphological variant of the tumor. The peak incidence occurs in periods of hormonal changes of the female body as puberty (rhabdomyosarcoma of the uterine body), perimenopausal (leiomyosarcoma body of uterus), postmenopauzalny (carcinosarcomas of the uterine body).[6,7,8,15] Development of leiomyosarcoma of the uterus the fibroid is found in the eligibility period in which most often there has been a rapid growth of fibroids. At this age in a woman's body, neuroendocrine adjustment to happen in the first place the violation of ovarian function. Metabolic estrogen and progesterone accompanied by hyperplasia of ovarian tissue, endometrial hyperplasia, rapid growth of myoma node, etc.[12,13] The pathogenesis of carcinosarcoma of the uterus has a value of hyperestrogenia and chronic anovulation, which are the cause of infertility in women puberty.[11,13,15] The experiments showed a stimulating effect of exogenous estrogen on the growth of uterine

sarcoma (US).[5,6,7] Reproductive disorders of the uterus (primary infertility, lack of delivery, multiple medical abortion) occurs in each quarter of the patients with sarcoma of the uterus. In addition, endocrine-metabolic disorders play a role in the pathogenesis of some histological variants of USdeveloping in the endometrium and myometrium.[5,6,7,15]

Risk factors for US include ionizing radiation (radiation therapy for diseases of the pelvic organs). The risk of developing US after radiation therapy is 0,03-0,8%, the interval between radiation therapy and the appearance of US is from 1,5 to 30 years. These US variants are characterized by an extremely aggressive course and an unfavorable prognosis.[5,6,11,12]

Uterine fibroids are considered to be an independent risk factor for developing sarcomas in pre - and postmenopausal. The combination of uterine myoma with sarcoma occurs in 57.7% of patients with leiomyosarcoma in the fibromatous node, in 59% of patients with leiomyosarcoma and in 23% of patients with endometral stromal sarcoma.[10.15]

Classification of uterine sarcomas. For the first time in 1959, Ober[5,6] proposed the classification of US depending on the type of cells and the source of the tumor. Pure sarcomas are tumors consisting of cells of only one type, and mixed of two or more types. Sarcomas are called homologous tumor composed of cells of tissues are unique to the uterus, heterologous - tissue elements, not connected with the uterus by a common origin. With the accumulation of knowledge about US in 1970, Kempson and Bari[6] proposed a histological classification of US. Modern histological classification of sarcomas of the US developed by a group of GOG (Gynecologic Oncology Group study).[5,6]

Classification of US GOG.

1. Non-epithelial tumors

A. Endometral stromal tumors.
I. Stromal nodule.
II. Stromal sarcoma of low grade.
III. Stromal sarcoma of high degree.
B. Smooth muscle tumor with uncertain malignant potential.
C. Leiomyosarcoma
I. Epithelioid
II. Myxoid
D. Mixed endometral stromal and smooth muscle tumor
E. Low-grade (undifferentiated) endometral sarcoma.
F. Other soft tissue tumors
I. Homologous
II. Heterologous.
II. Mixed epithelial-non-epithelial tumors

A. Adenosarcoma.
I. Homologous
II. Heterologous.
III. With excessive stromal growth.
B. Carcinosarcoma (malignant mixed mesodermal tumor, or malignant mixed Muller tumor)
I. Homologous
II. Heterologous.

The clinical profile of US is characterized mainly by two symptoms - bleeding from the genital tract of different duration and «rapid» growth of the uterus.[5,6,11,12,13] The reason of bleeding in leiomyosarcoma and endometrial stromal sarcoma is hyperplastic or atrophic endometrium the uterine body, and in patients with carcinosarcoma of the uterus - vessels of the decaying tumor. In addition, weakness, weight loss, prolonged subfebrile or hectic temperature, anemia unrelated to uterine bleeding suggests that uterine sarcoma with complications (tumor germination into the surrounding tissues, metastases to the lungs, liver, bones, brain head).[6,11,12]

Diagnosis US. Methods suitable for early diagnosis of US, not yet. Currently existing methods allow to establish the diagnosis of sarcoma before surgery in only one third of patients.[6,7,9,11,14]

Clinical methods of research (gynecological and physical examination) allow to make only a tentative diagnosis. Ultrasound examination of the pelvic organs is a routine method of research in Oncology. Ultrasound allows us to determine the location, size and structure of the tumor, as well as the ability to assess the state of neighboring organs and regional lymph nodes. Cytological examination of smears, aspirate from the uterine cavity, punctate of tumor nodes is insufficiently sensitive and specific.[5,6,7,9,11] Diagnostic separate curettage of the uterine cavity is currently the only method of diagnosing US before surgery. But the information content of the tissue in different histologic variants of US, so when carcinosarcoma it is - 79,8%, while endometrial is only - 56,8%.[9,11,12,13]

Over recent years, diagnosis of US is used immunohistochemical analysis, allowing us to carry out differential diagnosis of as among the many variants of sarcomas, and between benign (fibroids, fibromyoma) and malignant tumors, and intermediate forms (proliferating fibrolipoma) mesenchymal tumors. Markers of mesenchymal differentiation include desmin, smooth muscle actin, vimentin, type IV collagen and cytokeratins. The study of oncogenes proteins (p53, Bax, Bcl-2, Her2/neu, FasL, Ki67, VEGF, Fltl, Flkl, EGFR, TP) involved in apoptosis, proliferation and neoangiogenesis can provide valuable information on the biological behavior of the tumor and pathogenesis to researchers.[6,7,8,9] Immunohistochemical method is important in the morphological diagnosis of uterine endometrial, most of which (96,6%) are characterized by the expression of vimentin.[9] Today, according to the literature, knowledge of the prognostic characteristics of US is considered to be the key to understanding the development of the disease, which is extremely

important for the assessment of individual prognosis and probability response to therapy.

Treatment. In the clinical course and outcomes of treatment patients with US, not only the histological type of tumor is important, but also the localization, tumor size, depth of invasion, the degree of malignancy and differentiation, the number of mitoses and the presence of tumor necrosis. The methods used in the treatment of US should be not only radical, but also adequate to the biological properties of the tumor, which are individual for each clinical situation. The modern method of treatment of patients with US is primarily a surgical method, in the tactics of which there are a number of controversial issues, for example, the volume of surgery - extended extirpation of the uterus with appendages with lymph node dissection of the pelvic paraaortic lymph nodes (omentectomy), or organ-preserving surgery in reproductive age.[6,9,10,]

According to some authors in recent years have the following types of transactions: when leiomiosarcoma in the reproductive age – laparotomy, extirpation of uterus without appendages, and in postmenopausal period - with appendages.[6,9,10] Based on data the high frequency of regional lymphogenic metastasis (24,1%), the operation of choice for patients with low-grade endometrial tissue should be extended uterine extirpation with appendages, and in undifferentiated US it is advisable to perform the removal of a large omentum, the probability of metastasis in which exists in every 1/3 patient.[9.10] In widespread tumor processes, surgery is also performed, the purpose of which is to clarify the stage of the disease and remove the large masse of the tumor.[1,5,6,9,10]

The expansion of surgical interventions on regional lymphatic collectors in the form of systemic lymphadenectomy, regardless of the intraoperative visual assessment of the pelvic lymph nodes, as well as the removal of the greater omentum, is a reflection of our views on the surgical treatment of endometrial stromal sarcomas. This is especially important due to the fact that there are still no alternative treatments comparable in efficiency with surgery. In addition, the introduction of advanced surgery in the standard of treatment will serve as the basis for a correct comparison of the effectiveness of the three treatments. The results obtained and further accumulation of clinical experience through joint studies of various clinics will only contribute to the adequacy of treatment and increase the life expectancy of patients.

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