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FEATURES OF THE COURSE OF ENDOMETRIAL CANCER (CLINIC, TREATMENT, PROGNOSIS)

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RESUME

Endometrial cancer ranks sixth in the structure of cancer incidence in women, being an important public health problem in almost all countries. In the structure of the incidence of malignant neoplasms in women, endometrial cancer occupies the sixth place, accounting for 5.3% of all tumors. Survival of patients with endometrial cancer with metastases is dependent on the stage, depth of tumor invasion and treated with the use of neoadjuvant chemotherapy and subsequent radical surgery: so indicators five-year relapse-free and overall survival was 79.6 percent and 87.5%, respectively in patients with endometrial cancer stages IB2 – IIIB, which is about 20% higher than among patients who underwent only radiation combined terapiya.

KEYWORDS- *Endometrial cancer, chemotherapy, treatment, malignancy.*

RELEVANCE OF THE PROBLEM

Endometrial cancer ranks sixth in the structure of cancer incidence in women, being an important public health problem in almost all countries. In the structure of the incidence of malignant neoplasms in women, endometrial cancer occupies the sixth place, accounting for 5.3% of all tumors. In 2018, 569,847 patients with this disease were identified worldwide, which accounted for 3.2% of the total number of diagnosed malignant tumors. 311,365women died from SEM [1; 3; 8].

According to leading oncogynecologists, at the present stage, there are two multidirectional strategies for solving the problem of cervical cancer. The first of them involves the introduction, promotion and improvement of methods for active detection of patients with precancerous conditions and early stages of SEM, the second, no less important, is associated with improving the effectiveness of treatment of patients with locally advanced forms of this disease.

At the present stage of development of the healthcare system, there are a number of obstacles, both organizational and economic, that hinder the further dissemination and promotion of this method [10]. Despite the fact that cytological screening has been used for several decades, recently there has been an increase in the number of newly identified patients with locally advanced forms of SEM.

The improvement of the technical base and the use of new aggressive radiation therapy regimens have significantly improved the results of treatment of patients with locally advanced SEM. An increase in the life expectancy of patients led to an increase in the frequency радиоиндуцированных первично множественных of radioinduced primary multiple metachronousнныхmalignant tumors [5; 7; 8]. This is due to the fact that during radiation exposure, a

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woman's body is exposed to a certain carcinogenic effect, which in the future may lead to the development of new malignant tumors or leukemia. The frequency of primary multiple malignancies that develop after radiationtherapy is 5-26% [7; 8].

The dissatisfaction of oncogynecologists with the results of combined radiation therapy in locally advanced SEM has led to the fact that over the past few decades, the effectiveness of chemotherapy has been actively studied, the introduction of which marked the opening of a new era in the treatmentof such patients [9; 10]. Some authors have shown that the use of cytostatics reduces the size of the neoplasm, which increases the effectiveness of radiation therapy. In addition, due to the systemic distribution of drugs, it is possible to eliminate lymphogenic and hematogenic micrometastases [9; 10]. Despite the success achieved in the treatment of patients with locally advanced SEM, the relapse rate remains high, reaching 35%, and side effects associatedwith radiation remain [7; 9;1-0]. Currently, the five-year survival rate for IB2 stage of the disease isabout 80%, IIB-65%, III-40% [8; 10].

Materials and methods of research. Distribution of the studied patients by stage endometrial cancer is shown in tables 1 and 2. In all groups, patients with stage IIB of the disease prevailed, IB2 and IIIB stages were slightly less common. In general, among the studied patients, PEM the ratio of patients with different stages was approximately the same.

Table 1
Distribution by stages of the main group of patients

Stage endometrial cancer	Number of patients		Metastases in Pelvic metastases	
	N	%	n	%
IB2	13	25	2	3.8
IIB	21	40.3	6	11.5
IIIB	18	34.6	3	5.7
Total	52	100	11	21.1

Table 2
Distribution by stages of patients in the comparison group

Stage endometrial cancer	Number of patients	
	n	%
IB2	12	26,1
IIB	21	45,6
IIIB	13	28,3
Total	46,100. 0	

The youngest patient included in the study was 26 years old, and the oldest was 67 years old. In the main group of patients, the average age was 42.1±10.5 years. 16 patients (7.7%) were younger than 30 years, 22 (10.5%) were older than 60 years. The age distribution of patients in all groups studied was approximately the same (Table 3).

Table 3
Age distribution of the studied patients.

Age group	Number of patients			
	Main group =52		Comparison group =46	
	n	%	n	%
Up to 30	3	5,7	2	4,3
30-39	10	19,2	10	21,7
40-49	25	48,1	22	47,8
50-59	13	25	12	26,1
60 and more	than 6	11.5	5	10.8
Total	52	100.0	46	100.0

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As can be seen from Table 3, the largest number of patients were in the age range of 30-39 years (55 women-56.1%), 40-49 years (22 patients, 22.4%) and 50-59 years (15 patients, 15.3%). There were 72 patients in the reproductive period (73,4%), 26 (26,5%) the patients were inthe firstand postmenopausalstages . Among the comparison group patients, the average age was 43.7±11.2 years. 5 patients (5.1%) were younger than 30 years, 11 patients (11.2%) were older than 60 years. Patients in the age range 30-49 years prevailed (67 women – 68.3%).

We did not observe primary multiple synchronous malignant neoplasms.

Table 4
Concomitant somatic diseases in operated patients

Concomitant diseases	Main group n=52		Comparison group n=46	
	abs	%	**abs**	**%**
CHD Hypertension	13	25	11	23.9
Bronchial asthma	2	3.8	0	0
GI, chronic cholecystitis	3	5.7	5	10.8
Gastric ulcer and 12-P. K.	1	1,9	2	4,3
Chronic pyelonephritis	18	34,6	12	26,1
Concomitant gynecological diseases				
Uterine fibroids	8	15.3	5	10.8
Ovarian tumor	3	5,7	4	8,6

Thus, in the groups of patients who underwent radical surgery after neoadjuvant chemotherapy, there were no significant differences in the age composition of patients, as well as in the stages of SEM.

The most frequent clinical manifestation of the disease in patients of all the studied groups was abnormal vaginal discharge, which was observed in 68 patients (69.3%), and in 19 (19.3%) cases, the discharge was abundant and had the character of periodically recurring bleeding. 26 patients (26.5%) had pain in the lower abdomen, 29 (29.6%) had menstrual irregularities, and 21 (21.5%) had serous or purulent vaginal discharge. 57 patients (58.1%) had no complaints at the time of treatment. 75 patients had a history of cervical erosion, 37 (37.6%) women had no regular visits to the gynecologist.

MRI revealed the presence of a tumor focus in all the SEM patients studied (Fig. 1). MRI images of the pelvis of a patient with SEM stage IB2 show a soft tissue formation located in the anterior lip of the cervix (Fig. 2.6 A, B), with a pronounced restriction of diffusion (Fig. 2.6 C, D), without signs of spreading tothe parameters . Neoplasms were characterized by irregular shape and indistinct uneven contours.

CONCLUSION

In all groups, patients with stage IIB of the disease prevailed, IB2 and IIIB stages were slightly less common. In general, among the studied patients, PEM the ratio of patients with different stages was approximately the same.

The youngest patient included in the study was 26 years old, and the oldest was 67 years old. In the main group of patients, the average age was 42.1±10.5 years. 16 patients (7.7%) were younger than 30 years, 22 (10.5%) were older than 60 years.

Themajority of patients were aged 30-39 years (55 women-56.1%), 40-49 years (22 patients, 22.4%) and 50-59 years (15 patients, 15.3%). There were 72 patients in the reproductive period (73,4%), 26 (26,5%) the patients were peri-and postmenopausal. Among the comparison group patients, the average age was 43.7±11.2 years. 5 patients (5.1%) were younger than 30 years, 11 patients (11.2%) were older than 60 years. Patients in the age range 30-49 years prevailed (67 women – 68.3%).

The most frequent clinical manifestation of the disease in patients of all the studied groups was abnormal vaginal discharge, which was observed in 68 patients (69.3%), and in 19 (19.3%) cases, the discharge was abundant and had the character of periodically recurring bleeding. 26 patients (26.5%) had pain in the lower abdomen, 29 (29.6%) had menstrual irregularities, and 21 (21.5%) had serous or purulent vaginal discharge. 57 patients (58.1%) had no complaints at the time of treatment. 75 patients had a history of cervical erosion, 37 (37.6%) women had no regular visits to the gynecologist.

MRI revealed the presence of a tumor focus in all the patients with SEM studied. The tumor volume parameters determined by MRI data in stage IB2 were from 3.0 to 73.3 cm3, on average-36.6±17.0 cm3, IIB – from 32.2 to 103.1 cm3, on

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average-64.9±19.9 cm3, IIIB - from 32.2 to 145.1cm3, on average-72.3±23.6cm3.

It was found that in most patients with SEM (82.4%) of stage IB2, the volume of neoplasms did not exceed 50cm3. In total, 6 patients (6.1%) without parametric fiber infiltration had a tumor size above 50cm3.

Pathomorphological examination revealed that the histotype of tumors in all cases corresponded to squamous cell carcinoma. Immunohistochemical study allowed to determine the expression of markers p16, Ki-67, p53, p63, CEA, Ki-67 (Figs. 2.8, 2.9). The immunophenotype of squamous cell carcinoma was indicated by positive expression of p16 and p63, negative expression of CEA, and a high proliferative index (Ki-67 in all cases, more than 50%).

Patients in the main group underwent complex treatment, including neoadjuvant chemotherapy followed by radical surgery and / or chemoradiotherapy. Depending on the method of neoadjuvant chemotherapy, three subgroups were identified.

Subgroup 1: 26 patients who received drug treatment using two courses of intravenous infusion of cytostatics.

Subgroup 2: 17 patients who underwent one course of neoadjuvant chemotherapy with a combination of intravenous irentgenangiosurgical intra-arterial administration of chemotherapy drugs in combination with embolization of the tumor arteries.

Subgroup 3: 9 patients who underwent 2 courses of chemotherapy, the first of which consisted of a systemic infusion of cytostatics, the second-a combination of intravenous and X-ray angiosurgical intra-arterial administration of chemotherapy drugs in combination with embolization of the tumor arteries.

Patients of the first subgroup underwent two courses of chemotherapy. Cytostatics were administered sequentially for one day. Against the background of standard premedication, including dexamethasone 20 mg intramuscularly for 12 and 6 hours, an H1-histamine receptor blocker (diphenhydramine) intravenously for 30 minutes, an H2-histamine receptor blocker (kvamatel, zantak) 30 minutes before the introduction of cytostatics, paclitaxel was administered intravenously at a dose of 175 mg/m2. Then, after hydration with 0.9% NaCl solution at a dose of 400 ml, carboplatin (AUC6) was administered intravenously. The dosage was calculated using the Calvert formula: AUC x (CC + 25), where CC is the creatinine clearance.

A second course of chemotherapy was performed according to a similar scheme after 21 days.

The second subgroup consisted of female patients, most of whom had different intensity of spotting from the genital tract. After hemostatic and corrective measures, they underwent one course of chemotherapy according to the following scheme: the first day – intravenous infusion of paclitaxel at a dosage of 175mg/m2 and carboplatin at a dosage of 1/2 AUC 6 against the background of standard premedication and the use of antiemetics. The second day – intra-arterial administration of carboplatin at a dosage of 1/2 AUC 6 in combination with uterine artery embolization.

CONCLUSIONS

1. The highest incidence of endometrial cancer was found in the age group of 30-39 years with the largest number of patients in the reproductive period.
2. The use of neoadjuvant chemotherapy in patients with SEM stages IB2 – IIIB allowed to achieve complete tumor regression in 5.7% of cases, partial-in 83.3%. Radical operations were performed in 91.9% of cases.
3. Limiting theие riskа of adverse prognostic factors with careful dynamic monitoring of the tumor process is one of the main conditions for using multicomponent treatment of patients with SEM. The technological basis for monitoring is the integration of MRI and ultrasound into diagnostic standards.
4. Patients with endometrial cancer with detected metastases should be treated with special (chemo, chemoradiotherapy with subsequent radical operations), as this leads to an improvement in the results (in our study by more than 20%) and an increase in the life expectancy of these patients.
5. Survival of patients with endometrial cancer with metastases is dependent on the stage, depth of tumor invasion and treated with the use of neoadjuvant chemotherapy and subsequent radical surgery: so indicators five-year relapse-free and overall survival was 79.6 percent and 87.5%, respectively in patients with endometrial cancer stages IB2 – IIIB, which is about 20% higher than among patients who underwent only radiation combined terapiya.

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