

CLINICAL-DIAGNOSTIC ASSESSMENT OF PATIENTS WITH OVARIAN CANCER**Kamyshov S. V.***

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ABSTRACT

The aim of the study was to assess the clinical and diagnostic characteristics of patients with ovarian cancer who were recommended to accompany immunopharmacotherapy. According to the ultrasound examination, a tumor of more than 10 cm was detected in 143 (54.8%) patients and up to 10 cm in 118 (45.2%) patients. One-sided lesion was observed in 113 (43.3%) of them and bilateral - in 148 (56.7%) patients. The abdominal dissemination was absent in 107 (41.0%) patients, it had insignificant sizes - in 91 (34.9) and up to 2 cm - in 63 (24.1%) patients. The presence of ascitic fluid in the abdominal cavity was absent in 145 (55.6%) patients, up to 2 liters were determined in 65 (24.9%) and more than 2 liters in 51 (19.5%) patients. Tumor cells in ascites or flushing of the abdominal cavity were found in 73 (62.9%) patients and absent in 43 (37.1%) of 116 patients with ascites. When the EIPHT methods were assigned to patients with OC, the results of clinico-diagnostic studies were taken into account in the greatest extent. Anamnestic data, the presence of specific antitumor or nontraditional types of treatment before admission to hospital, histological type of tumor, macroscopic form of growth and the extent of its prevalence were taken into account. As is customary, EIPHT methods were designed, first of all, to reduce toxic manifestations after chemotherapy and radiation therapy, as well as to improve the overall condition after extensive surgery in patients with oncogynecological diseases.

KEYWORDS: ovarian cancer, polychemotherapy, immunotherapy, 5-year survival, morphological features of the tumor.

INTRODUCTION

Annually, cancer affects 12 million people worldwide, and the number of cancer cases in the world has increased by twenty percent over the past decade.^[4,8,11,13]

In recent years, progress has been made in the study of immunology and immunotherapy of cancer, including ovarian cancer (OC). The data have been obtained that malignant tumors develop on the basis of pronounced disorders of the immune system that arise already in premalignant diseases, are determined by the prevalence of the tumor process and are aggravated by the applied therapeutic effect (surgery, radiation, chemotherapy, hormone therapy). These data and information on a more favorable course of the disease with preserved immunity induce many researchers to further study the state of the immune system and develop on this basis more effective treatment regimens including immunotherapy.^[9,10]

OC continues to be the fourth leading cause of cancer death among women and continues to be the most fatal of gynecological tumors. The recurrence rate of patients with ovarian cancer is approximately 75%, which is equivalent to approximately 2500 patients per year. In this group of patients with relapses, many patients have a life expectancy of 2 to 3 years, so that ovarian cancer can

be classified as a "chronic disease". The incidence of ovarian cancer in Russia is 16.4, and the mortality rate is 8.2 per 100 000 female population. In this case, the 5-year survival rate is 30% without taking into account the stage. Such disappointing results of treatment are explained by the fact that 75% of patients with ovarian cancer enter the oncological institution with the III-IV stages of the process.^[12,13] In the structure of oncogynecological diseases in 2015 in Uzbekistan, the OC was ranked 10th in the overall oncological morbidity structure with a frequency of 2.3 cases per 100,000.^[4,6,8]

Modern chemotherapy, provided that it is carried out adequately, allows the remission of the disease to be achieved in about 75% of OC patients, including 40% of complete regressions, but it is well known that about 50% of patients at different times (on average 16-18 months) experience relapses. Therapy of relapses is the most controversial section of oncogynecology. More or less clearly, it is possible to formulate only strategic tasks common to the vast majority of oncological patients with disseminated disease: relapse therapy is palliative, and, with this in mind, its main objectives are to prolong life and improve its quality by reducing or, if

possible, complete elimination of symptoms due to tumor growth.^[2,5,9]

Currently, the most effective in the tactics of managing patients with OC is a comprehensive approach, which includes surgical intervention, chemotherapy, and sometimes radiation treatment. However, even complex treatment does not always prolong the life of patients. In patients with malignant neoplasms, there is a decrease in immunity, especially the cellular part of the immune system, which is the most important in the mechanisms of protecting the body from tumor growth. Moreover, the initial immunosuppression is intensified both at the stage of surgical intervention and during the chemotherapy.^[5,6,9,11]

The lack of tangible progress in the treatment of ovarian cancer over the years explains the desire of scientists to improve the first-line chemotherapy regimen, and the emergence of a large number of new antineoplastic agents leads to the search for the most effective combination.^[5,9]

The methods of treatment of patients with OC are still not unified, numerous. At the same time, the surgical method of treatment has received general recognition. The optimal volume of surgical treatment for malignant tumors of the ovaries is extirpation (supravaginal amputation) of the uterus with appendages, resection of the large omentum, and also the most complete removal of the visualized tumor nodes (individual metastases). In the case of the impossibility of performing a radical operation in patients with advanced ovarian cancer, removal of individual tumor nodes is justified.^[6,10]

The five-year results of one surgical intervention in OC, despite the continuing improvement of surgical technique, do not exceed 40% (for all stages of epithelial malignant tumors of the ovaries). In general, unsatisfactory long-term results of treatment are due to the fact that in the majority of cases in the III-IV stage of the disease it is technically impossible to perform the operation in a radical volume, and it is necessary to limit ourselves to the removal of the main tumor masses. But even at the first stage of the disease, the five-year survival rate for surgical treatment alone does not exceed 50-60%.^[8,9,10,12] In recent years there has been an increase in the incidence and "rejuvenation" of the age of the sick.^[5,8]

The incidence rate worldwide varies from 10 to 40 per 100,000 female population, with almost half of the patients dying within the first year due to late diagnosis of the disease.^[3,5,6,9] These differences are due to the organization and quality of medical care in a particular region (primarily the development of screening programs), sexual traditions, and, according to the latest data, depend on the type of HPV infection.^[6,9,11,12]

Traditional methods of treatment of oncogynecological diseases, among which the main, along with surgical ones, are chemotherapy, alone or in combination with radiotherapy and radiotherapy, are often not effective enough. In addition, all these effects themselves cause immunosuppression, which results in the suppression of bone marrow hematopoiesis and infectious complications, as well as the development of intestinal dysbiosis. As a result, the immune system, possibly already weakened by the development of the tumor, is subjected to yet another, additional stroke, suppressing its activity. It follows that a successful cure for a tumor may depend on a balance between the antitumor efficacy of chemotherapeutic complexes and the immune system's potential, sufficient (or insufficient) to cope with the remaining number of tumor cells after treatment.

The aim of the study was to assess the clinical and diagnostic characteristics of patients with ovarian cancer who were recommended to accompany immunopharmacotherapy.

MATERIALS AND METHODS

The study included 261 patients with ovarian cancer (OC) of T₂₋₃N₀₋₁M₀ stages (II-III clinical stages) who underwent treatment in oncogynecology and chemotherapy departments of Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan from 2006 to 2015. Patient groups were studied: patients with OC who received immunotherapy in the form of extracorporeal immunopharmacotherapy (EIPHT); patients with ovarian cancer who received immunotherapy in the form of extracorporeal immunopharmacotherapy and plasmapheresis (EIPHT + PPh); patients with ovarian cancer without immunotherapy (IT). All patients underwent clinico-laboratory blood tests, including a general blood test, urine, biochemical and immunological studies, and instrumental studies. Combined therapy in adjuvant or neoadjuvant regimen was carried out in patients with OC, including polychemotherapy with the cisplatin regimen of 75 mg / m² + cyclophosphamide 1000 mg / m² for 1 day for 4-6 courses 1 time in 3 weeks and surgical treatment in the volume of a radical operation. Chemotherapy was performed in both adjuvant and neoadjuvant regimens. EIPHT and EIPHT + PPh in patients with OC using immunomodulator - azoxime bromide (polyoxidonium, Russia). EIPHT was performed to reduce toxic effects after chemotherapy and radiotherapy. EIPHT was performed by exfusion of 500-1000 ml of autoblood in sterile containers "Gemakon" or "Terumo" and its centrifugation at 3000 rpm for 30 minutes. 50-80 ml of the supernatant of the blood plasma were removed. Then the obtained leukotrombomass and erythrocytic mass were incubated with an immunotropic drug in a total dose of 30 mg at 37°C for 60-100 min, with the subsequent return of the conjugate to the circulatory system of the patients. Immunotherapy was performed in the hospital, when patients were admitted

to chemotherapy and radiation therapy. In total, patients received 2 EIPHT sessions at the beginning of admission to hospital and before discharge from the hospital.

During the statistical analysis of the data presented in the work, the results of the research were entered into databases prepared in Microsoft Excel XP. Numerical (continuous) values were presented as mean arithmetic mean values and mean error ($M \pm m$). A comparison of the quantitative traits was carried out with the help of the Student's test, for continuous variables - the paired Student test. As a boundary comparative criterion for the statistical significance of reliability, $p < 0.05$ was assumed.

The results obtained and their discussion. When assigning methods of extracorporeal immunotherapy to patients with ovarian cancer, they tried to take into account the results of clinical and diagnostic studies to the greatest extent.

The analysis of the anamnestic data of patients with ovarian cancer made it possible to establish that conservative anti-inflammatory therapy was carried out during the period from the first visit to the gynecologist about complaints before the diagnosis of OC, most of them 215 (82.4%) patients (Table 1).

Table 1: Distribution of patients with ovarian cancer on previously conducted types of treatment.

Type of treatment	immunotherapy group (IT)						Total, n= 261	
	4		5		6th			
	EIPHT, n= 78		EIPHT + PPh, n= 73		withoutIT, n= 110			
	Abs.	%	Abs.	%	Abs.	%		
Treatment in the period from the first treatment to the establishment of OC								
Anti-inflammatory	63	80.8	60	82.2	92	83.6	215	82.4
Unconventional	11	14.1	9	12.3	13	11.8	33	12.6
Hormonal therapy	4	5.1	4	5.5	5	4,5	13	5.0

Specific antitumor treatment before admission to hospital patients with OC did not receive. 33 (12.6%) patients were treated independently by unconventional methods, and 13 (5.0%) had hormonal therapy for nodular goiter and ovarian cysts.

Analysis of histological preparations in patients with ovarian cancer showed that in the majority of 222 (85.1%) of the examined patients, cystadenocarcinoma was diagnosed, in 39 (14.9%) patients other forms of OC were seen (Table 2).

Table 2: Morphological characteristics of ovarian cancer.

Type of cancer	immunotherapy group (IT)						Total, n = 261	
	4		5		6th			
	EIPHT, n = 78		EIPHT + PPh, n= 73		without IT, n = 110			
	Abs.	%	Abs.	%	Abs.	%		
Histological structure of cancer								
Cystadenocarcinoma	68	87.2	60	82.2	94	85.5	222	85.1
Other forms	10	12.8	13	17.8	16	14.5	39	14.9
Type of cystadenocarcinoma								
Serous	41	52.6	42	57.5	64	58.2	147	56.3
Endometrioid	16	20.5	15	20.5	19	17.3	50	19.2
Mucinous	10	12.8	8	11.0	10	9.1	28	10.7
Clear cell	6	7.7	7	9.6	7th	6.4	20	7.7
Mixed	5	6.4	1	1.4	10	9.1	16	6.1
Degree of differentiation								
Low-differentiated	18	23.1	22	30.1	32	29.1	72	27.6
Moderately differentiated	36	46.2	36	49.3	57	51.8	129	49.4
Highly differentiated	24	30.8	15	20.5	21	19.1	60	23.0

147 (56.3%) patients had serous cystadenocarcinoma, 50 (19.2%) had endometrioid cystadenocarcinoma, 28 (10.7%) had mucinous cystadenocarcinoma, and 20 (7.7%) had clear-cell cystadenocarcinoma and 16 (6.1%) patients with mixed-type cystadenocarcinoma. 72 (27.6%) patients had a low-grade cancer, 129 (49.4%)

had a moderately differentiated cancer, and 60 (23.0%) had a highly differentiated cancer.

In the case of OC, in the majority - in 107 (41.0%) of the examined patients the III C stage of the disease was diagnosed (Table 3).

Table 3: Clinical characteristic of ovarian cancer.

Prevalence rate	immunotherapy group (IT)						Total, n= 261	
	4		5		6			
	EIPHT, n = 78		EIPHT + PPh,n= 73		Without IT, n= 110		Abs.	%
	Abs.	%	Abs.	%	Abs.	%		
Stage								
II A	11	12.8	8	11.0	13	11.8	32	11.9
IIB	10	16.7	13	17.8	16	14.5	39	14.9
IIC	6	9.0	6	8.2	8	7.3	20	7.7
IIIA	10	14.1	10	13.7	15	13.6	35	13.4
IIIB	9	10.3	8	11.0	11	10.0	28	10.7
IIIC	32	41.0	28	38.4	47	42.7	107	41.0
Tumor size according to ultrasound								
up to 10 cm	37	47.4	32	43.8	49	44.5	118	45.2
more than 10 cm	41	52.6	41	56.2	61	55.5	143	54.8
Side of defeat								
Unilateral defeat	34	43.6	30	41.1	49	44.5	113	43.3
Two-sided defeat	44	56.4	43	58.9	61	55.5	148	56.7
Dissemination in peritoneum								
No	30	38.5	32	43.8	45	40.9	107	41.0
bulging	26	33.3	26th	35.6	39	35.5	91	34.9
up to 2 cm	22	28.2	15	20.5	26	23.6	63	24.1
Ascites								
No	41	52.6	42	57.5	62	56.4	145	55.6
up to 2 l	21	26.9	17th	23.3	27	24.5	65	24.9
more than 2 l	16	20.5	14	19.2	21	19.1	51	19.5
Tumor cells in ascites of the abdominal cavity, n= 116								
there is	21	63.6	22	71.0	30	57.7	73	62.9
No	12	36.4	9	29.0	22	42.3	43	37.1

According to the ultrasound examination, a tumor of more than 10 cm was detected in 143 (54.8%) patients and up to 10 cm in 118 (45.2%) patients. One-sided lesion was observed in 113 (43.3%) of them and bilateral - in 148 (56.7%) patients. The abdominal dissemination was absent in 107 (41.0%) patients, it had insignificant sizes - in 91 (34.9) and up to 2 cm - in 63 (24.1%) patients. The presence of ascitic fluid in the abdominal cavity was absent in 145 (55.6%) patients, up to 2 liters were determined in 65 (24.9%) and more than 2 liters in 51 (19.5%) patients. Tumor cells in ascites or flushing of the abdominal cavity were found in 73 (62.9%) patients and absent in 43 (37.1%) of 116 patients with ascites.

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