ejpmr, 2018,5(6), 393-396

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

CLINICAL-DIAGNOSTIC ASSESSMENT OF PATIENTS WITH UTERINE CERVICAL CANCER

Kamyshov S. V.*

Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan.

***Corresponding Author: Kamyshov S. V.**
Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan.

Article Received on 29/03/2018 **Article Revised on 19/04/2018** **Article Accepted on 09/05/2018**

ABSTRACT

The aim of the study was to assess the clinical and diagnostic characteristics of patients with cervical cancer, who were recommended to accompany immunopharmacotherapy. Consequently, in the majority - 44.4% of patients were diagnosed with the IIIB stage of the disease. In most cases, 52.2% of the patients examined had a tumor volume ranging from 10 to 15 cm.[3] The initial tumor in most patients ie. in 61.2% it was not possible to determine with the help of clinical and instrumental methods. In the majority of 44.0% of patients with cervical cancer, the tumor spread to the upper third of the vagina. When appointing EIPHT methods, patients with cervical cancer were treated with anamnestic data, the presence of specific antitumor or nontraditional types of treatment before admission to hospital, as well as the histological type of tumor, the macroscopic form of growth and the extent of its prevalence.

KEYWORDS: Cervical cancer, clinical and morphological features, degree of differentiation.

INTRODUCTION

Increased attention to the problem of growth of oncological morbidity is one of the characteristic features of the modern healthcare system of all developed countries. This is due, above all, to a steady trend of increasing malignant neoplasm among the population, which has reached fairly high rates and will increase in the foreseeable future.

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.[1,5,7,9] The reasons for this prevalence of cancer are several. First, in the XX century there was an epidemiological transition.

Its essence is the replacement of mass infectious and parasitic diseases, resulting in the emergence of chronic and so-called degenerative diseases, which include, in the first place, diseases of the cardiovascular system and cancer. Secondly, due to the fact that the modern type of population with a high birth rate has replaced the "traditional" type of reproduction, with the birth rate and premature mortality from traditional causes declining in all developed countries, the number of elderly and senile people has increased among the population, among which oncological morbidity is the highest. Thirdly, diagnostics and the account of oncological diseases have improved. Finally, there is a true increase in the prevalence of tumors, which is a consequence of the fundamental restructuring of the environment as a result of the scientific and technological revolution.

Residents of highly developed countries, especially urban ones, are constantly exposed to various carcinogenic factors. All this occurs against a background of constant stressful situations, which, as is known, are accompanied by depression of the body's immune system.[5,8] In recent years, progress has been made in the study of immunology and immunotherapy of cancer, including cancer of the cervix. Data have been obtained that malignant tumors develop on the basis of pronounced disorders of the immune system that arise even with precancerous 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 regimens with the inclusion of immunotherapy methods.[10,12,14,18]

Currently, cervical cancer (C C) occupies one of the leading places in the structure of female cancer morbidity and mortality in developing countries and is an important medical and social problem in all economically developed countries.[4,7,9,12] This form of

cancer accounts for about 10% of all reported cancer cases in the world.[13,16,17,18] Despite some successes in the diagnosis and treatment of cancer in the female genital area, CC occupies one of the leading positions. Cervical cancer is ranked fifth among all malignant tumors and the second among tumors of reproductive organs in women.[17,18]

In the structure of oncogynecologic diseases in 2015 in Uzbekistan, CC ranked 3rd in the overall oncological morbidity structure with a frequency of 4.7 cases per 100,000.[5,6,8,10] In recent years, there has been an increase in the incidence and "rejuvenation" of the age of the sick.[5,9,10,13] In 2008, according to the Globocan system, 529,800 new cases of CC were registered in the world, 275,100 women died from disease progression.[16,17] The age peak of the incidence of CC falls on the age of 45-55 years, although there is a rapid increase in the frequency of CC among women younger than 30 years. To date, radiation therapy (RT) and surgical methods for treating locally advanced forms of CC are the most effective and are considered standard. The use of high doses of RT leads to tissue damage and impaired pelvic organs, which in turn limits the increase in the radiation dose.[11,14,15,18] 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 CC, who were recommended to accompany immunopharmacotherapy.

MATERIALS AND METHOD

The study included 268 patients with cervical cancer (CC) $T_{2-3}N_{0-1}M_0$ stages (II-III clinical stages) who underwent treatment in oncogynecology and chemotherapy departments of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan from 2005 to 2014. All patients underwent clinico-laboratory blood tests, including a general blood test, urine, biochemical and immunological studies, and instrumental studies. Cervical cancer patients underwent combined therapy in adjuvant or neoadjuvant mode, including polychemotherapy with a cisplatin regimen of 75 mg / m^2 + cyclophosphamide 1000 mg / m^2 for 1 day for 4-6 courses 1 time every 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 ± 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.

RESULTS AND DISCUSSION

When assigning methods of extracorporeal immunotherapy to patients with cervical cancer, we tried to take into account the results of clinical and diagnostic studies to the greatest extent. Analysis of the anamnestic data of patients with cervical cancer showed that the majority - 196 (73.1%) of patients in the period from the first visit to the gynecologist for complaints before the diagnosis of cervical cancer, conservative anti-inflammatory therapy was conducted. 33 (12.3%) patients were treated independently by unconventional methods, and 16 (4.9%) performed electrocoagulation without histological examination. Specific antitumor treatment before admission to the hospital most of the patients did not receive. A small proportion of patients with cervical cancer underwent specific antitumor treatment. For example, 15 (5.6%) patients previously had DTGT (SOD 40-50 Gy) without any special effect and 8 (3.0%) to patients - SLT (DTGT + brachytherapy). Of these, 3 managed to achieve partial regression of the tumor, and 5 patients - stabilization of the tumor process with some subsequent improvement in symptoms (Table 1).

Table 1: The distribution of cervical cancer patients on previously conducted types of treatment.

Type of treatment	Immunotherapy group (IT)						Total, n=268	
	1 EIPHT, n = 83		2 EIPHT + PPh, n = 67		3 without IT, n=118			
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Treatment in the period from the first treatment until the establishment of cervical cancer								
Anti-inflammatory	63	75,9	54	80,6	79	66,9	196	73,1
Unconventional	11	13,3	6	9,0	16	13,6	33	12,3
Electrocoagulation	3	3,6	3	4,5	10	8,5	16	4,9
Previous treatment for cervical cancer								
DTGT (SOD 40-50 Gy)	5	6,0	2	3,0	8	6,8	15	5,6
DTGT (SOD 50 Gy) + brachytherapy (SOD 50 Gy)	1	1,2	2	3,0	5	4,2	8	3,0

Morphological analysis of surgical material and biopsy results in patients with CC showed that the majority of 255 patients (95.1%) had histologically diagnosed squamous cell CC, and 13 (4.9%) had clear cell adenocarcinoma.

Table 2: Morphological characteristics of cervical cancer.

Type of cancer	Immunotherapy group (IT)						Total, n=268	
	1 EIPHT, n = 83		2 EIPHT + PPh, n = 67		3 without IT, n=118			
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Histological structure of cancer								
Planocellular	78	94,0	65	97,0	112	94,9	255	95,1
Clear cell	5	6,0	2	3,0	6	5,1	13	4,9
Type of squamous cell carcinoma								
non-squamous	44	53,0	41	61,2	62	52,5	147	54,9
squamous	39	47,0	26	38,8	56	47,5	121	45,1
The degree of differentiation								
low differentiated	39	47,0	36	53,7	63	53,4	138	51,5
Moderately differentiated	15	18,1	12	17,9	19	16,1	46	17,2
Highly differentiated	29	34,9	19	28,4	36	30,5	84	31,3

Morphologically, 147 (54.9%) patients had non-coronary squamous cell carcinoma and 121 (45.1%) had squamous squamous cell carcinoma. In terms of tumor differentiation degree, 138 (51.5%) patients had a low-grade cancer, 46 (17.2%) had moderately differentiated cancer, and 84 (31.3%) had a highly differentiated cervical cancer.

With the help of clinical and instrumental research methods, a macroscopic form of tumor growth and the prevalence of the tumor process were determined in all patients with CC.

Table 3: Clinical characteristics of cervical cancer.

Prevalence rate	Immunotherapy group (IT)						Total, n=268	
	1 EIPHT, n = 83		2 EIPHT + PPh, n = 67		3 without IT, n=118			
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Stage								
IIA	15	18,1	12	17,9	23	19,5	50	18,7
IIB	17	20,5	15	22,4	24	20,3	56	20,9
IIIA	14	16,9	10	14,9	19	16,1	43	16,0
IIIB	37	44,6	30	44,8	52	44,1	119	44,4
Tumor volume, cm^3.								
to 10	10	12,0	11	16,4	16	13,6	37	13,8
from 10 to 15	45	54,2	33	49,3	62	52,5	140	52,2
from 15 to 20	28	33,7	23	34,3	40	33,9	91	34,0

The prevalence of the tumor on the walls of the vagina								
Limited to the cervix	22	26,5	16	23,9	25	21,2	63	23,5
to the upper third	38	45,8	30	44,8	50	42,4	118	44,0
to the middle third	16	19,3	12	17,9	19	16,1	47	17,5
to the lower third	7	8,4	9	13,4	24	20,3	40	14,9

Thus, in the majority - 119 (44.4%) patients were diagnosed with the IIIB stage of the disease. In most cases, in 140 (52.2%) of the examined patients, the tumor volume in the range from 10 to 15 cm^3 was detected. The initial tumor in most patients - in 164 (61.2%) with the help of clinical and instrumental methods could not be determined. The majority - in 118 (44.0%) patients the tumor spread to the upper third of the vagina.

CONCLUSION

At the appointment of EIPHT methods, patients with CC were considered to the greatest extent the results of clinical diagnostic studies. 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.

REFERENCES

1. Box B.A., Russell C.A. Breast Cancer in «Manual of clinical Oncology» ed. Casciano D.A., 2004; 233–257.
2. Cheever M.A. Twelve immunotherapy drugs that could cure cancers // Immunol Rev., 2008; 222: 357–368.
3. Cheung N.V. Chapter 32: Therapeutic antibodies and immunologic conjugates. In: Niederhuber J.E., Armitage J.O., Doroshow J.H., Kastan M.B., Tepper J.E., eds. Abeloff's Clinical Oncology. 5th ed. Philadelphia, Pa: Elsevier, 2014.
4. Coosemans A., Baert T., Vergote I. A view on dendritic cell immunotherapy in ovarian cancer: how far have we come? // Facts Views Vis Obgyn, 2015; 7(1): 73-78.
5. Curtsinger J.M., Gerner M.Y., Lins D.C., Mescher M.F. Signal 3 Availability Limits the CD8 T Cell Response to a Solid Tumor // J. Immunol, 2007; 178: 6752-6760.
6. Drerup J.M., Liu Y., Padron A.S., Murthy K., Hurez V., Zhang B., Curiel T.J. Immunotherapy for ovarian cancer // Curr. Treat. Options. Oncol, 2015; 16(1): 317.
7. Ebbehoj E., Langkjer S. Comparison between different parameters of cell viability. In vitro studies in a human cervix cancer cell line // Journal of Experimental & Clinical Cancer Researches, 1995; 14(1): 95-101.
8. Eskander R.N., Tewari K.S. Immunotherapy: an evolving paradigm in the treatment of advanced cervical cancer // Clinical Therapeutics, 2015; 37(1): 20–38.
9. Geiger T.L. Monogamy and polygamy in T-cell receptor (TCR) chain association // Blood, 2007; 109: 5-6.
10. Ito F., Chang A.E. Cancer immunotherapy. Current status and future directions // Surgical Oncology Clinics of North America, 2013; 22(4): 765–783.
11. Kasimir-Bauer S, Oberhoff C, Schindler AE. A summary of two clinical studies on tumour cell dissemination in primary and metastatic breast cancer: methods, prognostic significance and implication for alternative treatment protocols (Review) // Int. J. Oncol, 2002; 20(5): 1027-1034.
12. Menderes G., Black J., Schwab C.L., Santin A.D. Immunotherapy and targeted therapy for cervical cancer: an update // Expert Rev. Anticancer Ther, 2016; 16(1): 83-98.
13. Paradkar P.H., Joshi J.V., Mertia P.N., Agashe S.V., Vaidya R.A. Role of cytokines in genesis, progression and prognosis of cervical cancer // Asian Pac. J. Cancer Prev., 2014; 15(9): 3851-3864.
14. Pardoll D. Chapter 6: Cancer immunology. In: Niederhuber J.E., Armitage J.O., Doroshow J.H., Kastan M.B., Tepper J.E., eds. Abeloff's Clinical Oncology. 5th ed. Philadelphia, Pa: Elsevier, 2014.
15. Siegel R.L., Miller K.D., Jemal A. Cancer statistics, CA // Cancer Journal for Clinicians, 2015; 65(1): 5–29.
16. Su M., Huang C.X., Dai A.P. Immune Checkpoint Inhibitors: Therapeutic Tools for Breast Cancer // Asian Pac. J. Cancer Prev., 2016; 17(3): 905-910.
17. Zsiros E., Tanyi J., Balint K., Kandalaft L.E. Immunotherapy for ovarian cancer: recent advances and perspectives // Curr. Opin. Oncol, 2014; 26(5): 492-500.
18. Zsiros E., Tsuji T., Odunsi K. Adoptive T-cell therapy is a promising salvage approach for advanced or recurrent metastatic cervical cancer // J. Clin. Oncol, 2015; 33(14): 1521-1522.