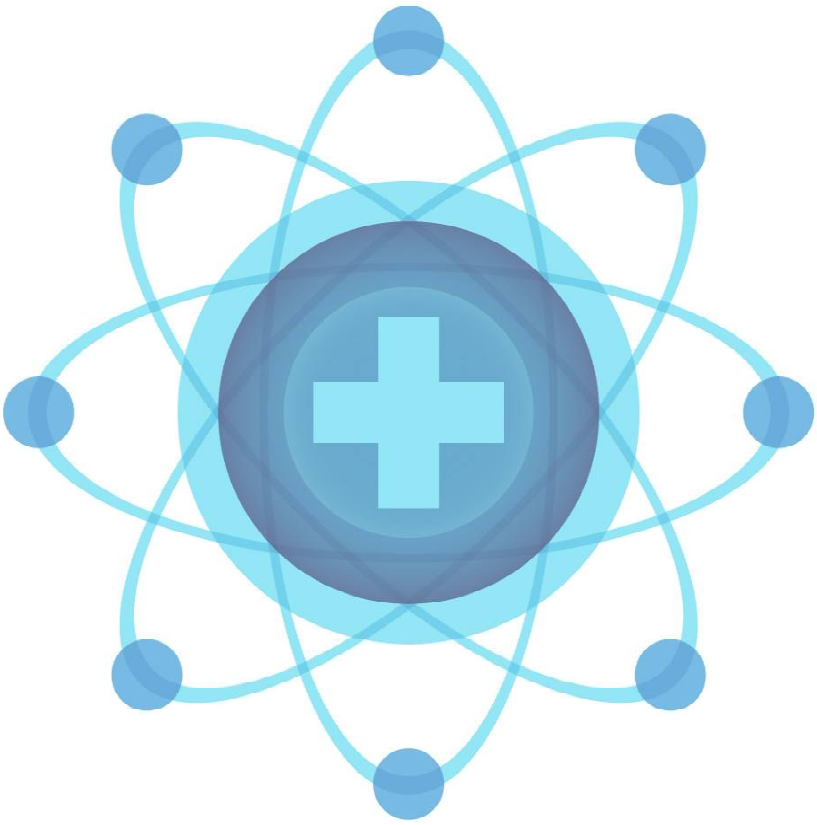

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CONTENT

FEATURES OF IMMUNOBIOLOGICAL HETEROGENEITY IN PATIENTS WITH OSTEOSARCOMA

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Abstract

The aim of the research was to study the characteristics of immune changes in patients with osteosarcoma before starting therapy. The presence of an immunodeficiency state in patients with osteosarcoma, which was expressed in deep T - cellular immunodeficiency and activation of the humoral immunity, was established, which allows early immunological diagnosis of the progressive course of the malignant process. It is planned to further study the cytokine status, which plays an important role in the formation, development and progression of osteosarcoma. Consequently, our results will help practitioners in understanding the molecular-immunological behavior in osteosarcoma, which will make it possible to establish the immunopathogenetic features of the course of the disease, its severity and prognosis, to differentiate periods of exacerbation and remission, which will also make it possible to assess the effectiveness of drug therapy. The immunoreactivity of patients with osteosarcoma is characterized by an increase in the total number of leukocytes, which is a sign of inflammation, CD8 + cytotoxic T lymphocytes, CD16 + lymphocytes, CD20 + lymphocytes and CD38 + lymphocytes, small and large CICs against the background of suppression of CD3 + lymphocytes, CD4 + and IRI. The pronounced indicators of suppression of immunity and the progression of the disease were IRI and CIC. On the part of humoral immunity factors, the increased serum values of IgG and IgA turned out to be of paramount importance. An imbalance of T-lymphocyte subpopulations was also revealed. There is a decrease in the immunoregulatory index from 0.4 to 1.1 (normally from 1.5 to 2.0), which is an indicator of an unfavorable course of the disease and immune response.

Key words: osteosarcoma, immunity, cellular parameters of immunity, humoral parameters of immunity, heterogeneity of immunity, oncology.

Topicality. Osteosarcoma is referred to as the most aggressive human tumor disease, which is mainly due to the tendency of these neoplasms to early hematogenous dissemination [1,4,7,8,11]. Despite the success achieved in recent years in the treatment of these diseases, a number of aspects related to the biological characteristics of osteosarcoma remain poorly understood [4,8,9,14,25]. One of the directions, the study of which can influence the results of treatment, is the study of the characteristics of immune behavior and heterogeneity in this category of patients.

In recent years, a number of new techniques have been actively introduced into clinical practice to assess the immunity of patients, in particular, the study of the phenotype of peripheral blood lymphocytes using monoclonal antibodies to their differentiating antigens [6,10,17,21,26]. At the same time, information on the state of immunity in patients with osteosarcoma was obtained using insufficiently informative research methods on a small clinical material [4,7,13,17]. The currently available information does not allow to fully describe the changes in immunity characteristic of these diseases on an equal footing of the populations and subpopulations of blood lymphocytes. We studied the immunological changes occurring against the background of combined treatment, and the true changes in osteosarcoma, especially immune

Material and research methods. Research had been carried out at the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan since 2005. There were 221 patients with verified osteosarcoma under observation. The control group consisted of 48 healthy individuals of the same age and sex. The diagnostic program included generally accepted measures, such as an objective examination, anamnesis, X-ray examination of the affected bone, X-ray examination of the chest organs, ultrasound of the tumor zone and surrounding tissues, regional lymph nodes, abdominal organs and retroperitoneal space, in order to identify distant metastases, cytological examination of the primary tumor and obligatory histological examination of biopsy and postoperative material with an assessment of the degree of therapeutic pathomorphosis. Analysis of the distribution of the examined patients by sex: men - 133 (60.1%), women - 88 (39.8%). With the distribution of patients by age in our studies, it turned out that osteosarcoma was more common in the group of patients from 18 to 35 years old (45.3%) with the incidence of the disease among men 28.9 ± 3.0% (64) and women 16.3 ± 2.4% (36). The average age in the general group was 23.78 ± 1.52 years for women and 21.24 ± 0.80 years for men. The prevalence of the process was assessed according to the International TNM classification (classification of the International Union Against Cancer, 2007). In accordance with this, in the studies, patients were distributed taking into account the stage of the disease: in 187 (84.6 ± 3.2%) patients, stage T2N0M0 was determined, in 26 (11.8 ± 1.7%) - T2N0Ml, T1N0M0 - in 8 (3.6 ± 0.8%). According to the clinical classification, the patients were also divided into stages: IB - 8 (3.6 ± 1.2%), IIA - 12 (5.4 ± 1.5%), IIB - 125 (56.5 ± 3.3%), III - 62 (28.0 ± 3.0%), IVA - 11 (4.9 ± 1.4%), IVB - 3 (1.3 ± 0.7%).

Immunological studies included the study of cellular and humoral parameters of the immune system of patients with osteosarcoma before treatment. Immunological studies were carried out at the Institute of Immunology of the Academy of Sciences of the Republic of Uzbekistan, in the laboratory of immunocytokines. Determination of cellular immunity (CD3 +, CD4 +, CD8 +, CD16 +, CD20 +), as well as identification of activation markers of lymphocytes (CD38 + and CD95 +) was carried out using monoclonal antibodies, Sorbent, Moscow. The humoral link of immunity was assessed in the serum of peripheral blood by the ELISA method. For clarity of the results obtained, all the studied parameters of the state of the immune system of patients were converted into percentages in relation to 100% for the norm. The reliability of the differences revealed in the analysis of quantitative features was assessed using the Student-Fisher test. Methods of variational parametric and nonparametric statistics with M, σ, m, relative values (frequency,%) were used, the statistical significance of the obtained measurements when comparing the mean values was determined by the Student's test (t) with the calculation of the error probability (P) when checking the normal distribution (by kurtosis criterion) and equality of general variances (F - Fisher's criterion). The level of significance $p < 0.05$ was taken as statistically significant changes.

Results of the research

The study of the state of the immune system in osteosarcoma undergoes certain difficulties, which are expressed in the instability of the course of the oncological process, in the presence of various forms and morphological variants of the disease. In connection with the above, the study of the immune system of patients with osteosarcoma has not only scientific, but also practical importance for assessing the state of the immune system and predicting the disease.

It is known that the leading role in the antitumor defense of the organism is given to the cellular link of immunity, where T-lymphocytes play a key role. The expression of T-cell markers of lymphocytes was determined by the relative number of CD3 + T-lymphocytes, CD4 + T-helpers / inducers and CD8 + T-cytotoxic lymphocytes, as well as by the value of the CD4 + / CD8 + ratio (immunoregulatory index - IRI).

It was found that the phenotypic markers of T-lymphocytes include CD3 +, CD4 +, CD8 + receptors. It has been shown that the triggering and regulation of the effectiveness of the immune

response is largely determined by the specific antigen of T-lymphocytes. It is known that the degree of surface expression of CD3 + receptors on the membrane of T-lymphocytes reflects its transmissive function and makes it possible to identify the total number of T-lymphocytes [4,5,8,14,16,24,27].

Analysis of the T - cellular link of immunity showed that the state of the immune system of patients with osteosarcoma is manifested by an imbalance of cellular and humoral parameters of immunity.

At the same time, the immune system of patients with osteosarcoma is characterized by an increase in the total number of leukocytes, which is a sign of inflammation against the background of suppression of the total number of lymphocytes, CD3 + T-lymphocytes, CD4 + T-lymphocytes, IRI against the background of an increase in CD8 + T-lymphocytes, CD16 + T-lymphocytes , CD20 + B-lymphocytes, CD38 + T- and B-lymphocytes and CD95 + marker of apoptosis, as well as an increase in CIC of small and large values. The results obtained characterize the state of immunoreactivity of patients with osteosarcoma, and can serve as diagnostic and prognostic criteria for monitoring during therapy. Thus, the most informative were the changes at the level of subpopulations of activation markers.

As for the humoral factors of immunity, it should be noted that in patients with osteosarcoma, there is a significant increase in the concentration of IgG and IgA against the background of a decrease in the serum concentration of IgM.

Thus, for the first time in Uzbekistan, an attempt was made to conduct a study of immunity at the level of populations and subpopulations of lymphocytes depending on osteosarcoma. The studies were carried out in comparison with the indicators of the control group.

Thus, the features of the immune status of patients with osteosarcoma in comparison with healthy individuals have been established. The signs of osteosarcoma were revealed, the characteristic variability of which is reflected in the picture of immunological parameters. Changes in populations and subpopulations of lymphocytes that occur before the start of specific therapy have been studied. The immunological parameters characteristic of osteosarcoma were determined.

An immunodeficiency state was revealed in patients with osteosarcoma, which was expressed in deep T - cellular immunodeficiency and activation of the humoral link of immunity, which allows for early immunological diagnosis of the progressive course of the malignant process. It is planned to further study the cytokine status, which plays an important role in the formation, development and progression of osteosarcoma. Consequently, our results will help practitioners in understanding the molecular-immunological behavior in osteosarcoma, which will make it possible to establish the immunopathogenetic features of the course of the disease, its severity and prognosis, to differentiate periods of exacerbation and remission, which will also make it possible to assess the effectiveness of drug therapy.

Thus, the analysis revealed that the immunoreactivity of patients with osteosarcoma is characterized by an increase in the total number of leukocytes, which is a sign of inflammation, CD8 + cytotoxic T lymphocytes, CD16 + lymphocytes, CD20 + lymphocytes and CD38 + lymphocytes, CIC of small and large values against the background of suppression of CD3 + lymphocytes , CD4 + lymphocytes and IRI. The pronounced indicators of suppression of immunity and the progression of the disease were IRI and CIC. On the part of humoral immunity factors, the increased serum values of IgG and IgA turned out to be of paramount importance. An imbalance of T-lymphocyte subpopulations was also revealed. There is a decrease in the immunoregulatory index from 0.4 to 1.1 (normally from 1.5 to 2.0), which is an indicator of an unfavorable course of the disease and immune response.

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