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IMMUNOHISTOCHEMICAL STUDY OF INTRATUMORAL LYMPHOCYTES IN BREAST CANCER

***Tillyashaikhov M. N., Shomansurova N. S. and Nishanov D. A.**

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

***Corresponding Author: Tillyashaikhov M. N.**
Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan, Tashkent.

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SUMMARY

The landscape of the subpopulation composition of intratumoral lymphocytes in women with breast cancer was studied. Infiltration of the tumor with T-lymphocytes, as well as a subpopulation of the most significant effector cells of antitumor immunity: mature T-lymphocytes, T-helpers / inductors are shown. The presented results indicate the possibility of a quantitative study of the subpopulation composition of intratumoral breast cancer lymphocytes. These data can be used to develop protocols for immunocorrection in prognostically unfavorable groups. Of course, further research should be carried out taking into account the immunophenotypic characteristics of the tumor, in particular, the receptor molecules that mediate interactions with the cells of the immune system. Understanding and identifying biological markers of tumor growth form the individual molecular phenotype of transformed cells, which characterizes the degree of tumor malignancy, the ability to metastasize, hormonal sensitivity, the effectiveness of chemotherapy, etc. Thus, breast cancer is a genetically heterogeneous disease with various molecular biological and clinical features. Identification of the molecular phenotype of breast carcinomas is an important prognostic factor of the disease and allows personalizing the treatment of patients.

KEYWORDS: Breast tumors, immune chemistry, histology, lymphocytes, immunity, molecular biological markers of oncogenesis, early diagnosis of tumor growth, prognosis of metastasis, oncological risk.

Topicality

It is known that the incidence of breast cancer (BC) is increasing worldwide. Global statistics show that the annual incidence of breast cancer is growing at a faster pace in developing countries than in economically developed countries. Thus, in 2012, 1,670,000 new cases of breast cancer were registered, which amounted to 25% of all cases of malignant tumors. It is the most common form of cancer in women in countries with low and middle economic development than in more developed countries.

In the structure of oncological morbidity, breast cancer ranks first among the female population of Russia and the CIS countries. Its share ranges from 18-22% in Russia, Belarus, Kazakhstan and Kyrgyzstan to 25-33% in Uzbekistan, Azerbaijan and Armenia.[1,2] In 2010, the standardized incidence rates varied: 40-47.3 - in Ukraine, Belarus, Russia, Armenia; 24.6-36.4 - in Azerbaijan, Turkmenistan, Kazakhstan; 16.6-19.4 - in Tajikistan, Uzbekistan.[2]

Specific features of breast cancer are a high growth rate, geographic and territorial unevenness of incidence rates, which is associated with a variety of ethnic, individual socio-demographic and environmental risk factors.[3,4,8] Moreover, it should be noted that breast tumors of various forms, such as fibroadenomas, are common. In this regard, the study of diagnostic and prognostic molecular biological markers in tumor oncogenesis has become an important direction. In the literature, data on the study of the occurrence and development of malignant processes on which the progression of the tumor depends are contradictory. Molecular biological markers of oncogenesis are cancer-specific components of human cells and tissues (nucleic acids, proteins). The study of molecular biological markers of oncogenesis in oncology is carried out in such areas as early diagnosis of tumor growth, prognosis of metastasis, detection of circulating tumor cells, determination of the localization of metastases, assessment of tumor prevalence, detection of factors (risk factors) associated with oncogenesis, and preparation of the clinical prognosis of the tumor. The study of molecular biological markers of oncogenesis in modern oncology is complemented by the identification of genes of susceptibility to oncological diseases for the formation of groups of oncological risk and the solution of the problem of "family cancers", as well as the study of prognostic markers of the effectiveness of anticancer therapy.

Currently, in addition to classical morphological methods, the complex of laboratory studies in oncology includes immunocytochemical and molecular genetic research methods, which has expanded the possibilities of clinical oncology in predicting risk. Thanks to the latest developments in the field of genetics, molecular biology, immunology, biochemistry, as well as the emergence of the latest diagnostic techniques, it has become possible to determine the content of cancer-specific substrates in the studied samples obtained from a patient. Currently, in addition to classical morphological methods, immunocytochemical and molecular genetic research methods have been included in the complex of laboratory studies in oncology, which has expanded the possibilities of clinical oncology in predicting the risk of developing neoplasms, conducting early diagnostics of the oncological process, identifying the localizations of metastases, and determining treatment tactics based on the molecular characteristics of the tumor. for the most favorable prognosis.[5,9,12]

The approaches aimed at identifying the individual pattern of the metabolism of chemotherapeutic drugs are also of scientific interest. In particular, many tumors are characterized by overexpression of the enzyme thymidine phosphorylase. It is in these cases that the appointment of xeloda, a non-toxic precursor of 5-fluorouracil, seems justified. This direction of medicine is still at the initial stages of its development, but there is every reason to believe that molecular approaches to the individualization of anticancer therapy will be further developed in the very near future.[4,9,10,16] The aim of this work was to assess the subpopulation composition of intratumoral lymphocytes in patients with breast tumors.

Material and research methods. The study was conducted among women with breast tumors, who underwent a biopsy of tumor tissue or surgery during a comprehensive examination to verify the diagnosis. The diagnosis of breast cancer in all cases was confirmed morphologically. Immunohistochemical studies were carried out with test systems from "Dako", (Denmark) to verify the expression of CD - clusters. in tumor tissue samples. So, we studied the surgical and biopsy material in 30 women with a Carcinoma diagnosis in situ.

Systems used: CD3 (membrane staining) SP7 Thermo Scientific 1: 150 10 mmol Tris, 1 mm EDTA (pH 6.0); CD4 (membrane staining) IF 6 DCS 1:40 10 mM Tris, 1 mM EDTA (pH 9.0); CD8 (membrane and cytoplasmic staining C8 / 1448 DAKO RTU 10 mmol Tris, 1 mM EDTA (pH 9.0); CD95 (membrane staining of endothelial cells) QBEnd-10 DAKO 1: 150 10 mmol Tris, 1 mM EDTA (pH 9, 0) The intensity of reactions localized in the cytoplasm and on cell membranes was assessed semi-quantitatively on a scale from 0 to 3 points, taking into account the severity of the reaction and its localization: 0 - no reaction; 1 - weak; 2 - moderate; 3 - strong reaction.

Statistical processing of the material was carried out using Excel 2010, Statistica 6.0. The assessment of the reliability of the differences was carried out according to the Student's criteria based on the indicators t and p. A p-value <0.05 was considered statistically significant.

Obtained research results. A study of subpopulations of intratumoral lymphocytes isolated from tumor material in patients with breast cancer was carried out. The predominant type of lymphocytes in the tumor tissue were mature T cells (CD3 +) - 82.4%, then there were CD4 + T - lymphocytes - 47.8%. T-cytotoxic (CD8 +) lymphocytes - 38.4%. The proportion of CD8 + / CD4 + cells was high.

The subpopulation composition of intratumoral lymphocytes in patients with breast cancer is of great clinical importance. With operable cancer, based on these data, it is possible to identify groups of patients with a favorable and unfavorable prognosis.[7,8,10,13,15] The data obtained can be used to plan and carry out therapeutic interventions such as immunotherapy and / or chemotherapy in patients with a poor prognosis. So, in the work of Subbotina it was shown that the immunohistochemical analysis of the material makes it possible to characterize the subpopulation composition of intratumoral lymphocytes. Immunohistochemical assessment allows to assess the levels of intratumoral lymphocytes quantitatively, which is accurate when assessing the dynamics of changes during the treatment.

As shown above, mature T cells (CD3 +) prevailed in the material of breast cancer patients, followed by CD4 - T cells.

These data confirm the results of previous studies regarding the dominant role of the T-lymphocytic link of immunity in the infiltration of breast cancer tissue.[6,13] It was shown quantitative confirmation that among tumor-infiltrating lymphocytes, CD4 cells predominate over cytotoxic CD8 + lymphocytes. It is known that the predominance of CD4 cells is a factor of unfavorable prognosis,[5,6] it can be considered justified to consider the possibility of developing methods for increasing the levels of CD8 lymphocytes and the CD8 / CD4 ratio in tumor tissue of breast cancer patients. This issue should be considered individually, taking into account the peculiarities of the subpopulation composition of lymphocytes in breast cancer tissue.

The analysis of apoptosis of T - lymphocytes - CD95 +, capable of suppressing the immune response to tumor antigens, is of great importance in studies of antitumor immunity. Of greatest interest are breast cancer cases, which, based on the subpopulation composition of intratumoral lymphocytes, can be regarded as prognostically unfavorable. Thus, in the literature there are similar observations with minimal tumor infiltration by lymphocytes and a low content of T-cytotoxic (CD8 +) cells.

Thus, we have assessed the landscape of the subpopulation composition of intratumoral lymphocytes in women with breast cancer. Thus, we have studied tumor infiltration with T-lymphocytes, and a subpopulation of the most significant effector cells of antitumor immunity: mature T-lymphocytes, T-helpers / inductors. The presented results indicate the possibility of a quantitative study of the subpopulation composition of intratumoral BC lymphocytes. These data can be used to develop protocols for immunocorrection in prognostically unfavorable groups. Of course, further research should be carried out taking into account the immunophenotypic characteristics of the tumor, in particular, the receptor molecules that mediate interactions with the cells of the immune system.

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