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MOLECULAR BIOLOGICAL AND IMMUNOLOGICAL FEATURES OF BREAST CANCER (LITERARY REVIEW)

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Abstract
Breast cancer is one of the most common forms of malignant neoplasms in the world. The increase in morbidity over the past 10 years amounted to 35.8%, and the number of deaths increased from 13.7 thousand. The ideas about the molecular biological and immunological features of breast cancer are still far from a certain holistic concept and are based, for the most part, on the assessment of a specific receptor complex of cancer cells, interconnected with the degree of differentiation and growth properties of the tumor.

Keywords: Breast cancer, biological characteristics, immunophenotype, immunomorpho logical methods.

Introduction

Breast cancer is one of the most common forms of malignant neoplasms in the world. In all economically developed countries, there is a steady increase in morbidity and mortality from cancer of this localization, and scientific research on this problem is given one of the leading places in cancer science. In Uzbekistan, breast cancer occupies the 1st place in the structure of morbidity and mortality from malignant neoplasms in women. [2,4] The increase in morbidity over the past 10 years amounted to 35.8%, and the number of deaths increased from 13.7 thousand. It is well known that tumors having the same stage according to the TNM classification often differ radically in the aggressiveness of the course of the disease and sensitivity to the

therapy, which is explained by the individual biological characteristics of a particular group of malignant cells (Veronesi U.et al., 1995). Studies on the definition and characterization of these biological features, allowing to adequately assess the rate of tumor growth, the specifics of its "behavior", metastatic potential and features of metastasis, chemoresistance, etc., are widely conducted all over the world. To date, the number of markers detected on human breast cancer cells is quite large. These are receptors of steroid hormones, epidermal growth factor, transferrin, antigens of the main histocompatibility complex of class I and II, expression of Her-2/neu, CD 95, Pgp 170, various genetic disorders and many others. The genes associated with breast cancer BRCA-1 and BRCA-2 were found (Miki Y. et al., 1994; Pisano M et al., 2001), as well as antimetastatic Nm23 genes. Studies of the degree of ploidy and proliferative activity of breast cancer cells have become important. The evaluation of these indicators makes it possible to significantly clarify the prognosis in patients and improve the results of treatment. However, the ideas about the molecular biological and immunological features of breast cancer are still far from a certain holistic concept and are based, for the most part, on the assessment of a specific receptor complex of cancer cells, interconnected with the degree of differentiation and growth properties of the tumor.

At the same time, there is a whole field of immunologically assessed tumor parameters that have not yet been clearly reflected from the standpoint of the need to study them in each patient. This is, firstly, the immunophenotype of the tumor (expression of histocompatibility molecules of classes I and II, adhesion molecules, transferrin receptor, etc.), which has a direct relationship with tumor progression and antitumor immunity.

Secondly, the levels and subpopulations of immunocompetent cells infiltrating breast cancer (this indicator can be useful in assessing the prognosis and in planning various immunotherapeutic measures). And, finally, the importance of immunological methods in assessing the extent of the tumor process, namely, the role of immunohistochemical detection of micrometastases of breast cancer in the lymph nodes and bone marrow of patients.

The condition of the axillary lymph nodes is the most significant prognostic factor in women with operable breast cancer. The study of histological sections using monoclonal antibodies to epithelial antigens makes it possible to increase the frequency of detection of breast cancer metastases in regional lymph nodes. It is known that the correct assessment of the extent of the tumor process at the stage of initial examination is the main point of adequate planning of therapeutic measures,

and the detection of distant metastases radically changes the tactics of treatment of patients.

It has been shown that from 25% to 35% of patients without lesions of regional lymph nodes already have hematogenous micrometastases by the beginning of treatment. The use of modern immunomorphological methods using monoclonal antibodies to epithelial antigens in the study of bone marrow punctate makes it possible to detect even single cancer cells by several million hematopoietic cells, which significantly exceeds the capabilities of a standard cytological and morphological study.

Thus, clinical and clinical experimental work in the field of studying the immunophenotype of the primary tumor, local immune status, immunodetection of micrometastases in regional lymph nodes and bone marrow can provide opportunities for improving the diagnosis and differential diagnosis of breast cancer, for more accurate prediction of its course and for the development of immunotherapy methods, which is undoubtedly an urgent task of modern clinical oncology and is important from both theoretical and practical points of view. In the structure of oncological diseases of the female population in Russia, as in most developed countries of the world, breast cancer (breast cancer) occupies the first place and tends to steadily increase, and women are ill at the most working age. In Russia in 2007, its share was 20%. 1 million new cases of breast cancer are registered in the world according to the World Health Organization. It is impossible not to note the increase in mortality from breast cancer. In Moscow and St. Petersburg, the 5-year survival rate is 59.6-59.3%. According to various institutions, about 35% of newly identified patients have stage Sh-1. Distant metastases occur in 50% of breast cancer patients, the median survival rate of patients with metastatic breast cancer is 24-36 months and only 15% live for more than 5 years [12].

Recent studies have shown that the growth of most malignant tumors is accompanied by significant violations of various parts of the body's immune response. Studies conducted in cancer patients indicate a decrease in the number of natural killers, T-helpers, functional activity of T-lymphocytes, an increase in T-suppressors and their functional activity.

It has been established that a decrease in the level of T-cell infiltration of the tumor has a certain connection with regional metastasis or the presence of micrometastases [16,5,7,18,23,55]. The size of the tumor is not correlated with the levels of lymphocytic infiltration of the tumor. It has been proved that an increase in the number of intratumoral T-killers is a factor of favorable prognosis in breast cancer patients, mainly without regional metastasis [4,12,24,33,57,64]. Moreover, the infiltration of the tumor by CY8+ lymphocytes is of the greatest importance. The relationship

between the degree of prevalence of the tumor process and the level of SB8+ lymphocytes has been established. An increase in the level of infiltration of C08+ cells is observed more often in patients who do not have metastases to regional lymph nodes, and a decrease in their number is more typical for late stages of breast cancer. When using neoadjuvant chemotherapy in breast cancer patients, the levels of tumor infiltration by T cells vary in different directions. An increase in their level in comparison with the initial values was noted more often than a decrease. This tells us about the effectiveness of chemotherapeutic treatment, but indirectly refutes that chemotherapy initially affects the lymphoid system, including the intratumoral. The dynamics of subpopulations of intratumoral lymphocytes has a certain prognostic value [27]. The greatest interest in the subpopulations of intratumoral lymphocytes is represented by C025-positive cells. They are one of the indicators of antitumor effect. Thus, in the presence of CA 25+ cells in the tumor, when using chemotherapeutic treatment, the antitumor effect increases significantly, and in the absence of the effectiveness of the treatment was 5 times lower. The dynamics of C025+ cells depend on the treatment regimen: when using the same treatment regimen, the level of effector cells SB8+ and SB25+ in some cases increases or remains at the same level. When using a different scheme, we can observe the opposite effect. As for B-cell infiltration, there were no correlations [13].

The work of the University of California (USA) proved that the infiltration of breast cancer tumor tissue by cytotoxic lymphocytes (SB8+) is a factor in a favorable prognosis, and pronounced infiltration of SB4+ by lymphocytes and macrophages, on the contrary, worsens the prognosis [8,9,15]. The prognostic role of the subpopulation composition of intratumoral lymphocytes in breast cancer is also quite well known.

In univariate analysis, the dominant prognostic role belongs to SB8+ lymphocytes [1]. In the absence of pronounced infiltration of breast cancer by SE8+ cells, C04+ lymphocytes contribute to tumor invasion and the development of distant metastases of breast cancer by influencing the prothumoral activity of tumor-associated macrophages [3,6,7]. The combination of these data suggested that three cell types - SB4+ and SB8+ lymphocytes, as well as SB68+ macrophages - may play a major role in the prognosis of breast cancer. Based on these data, a three-marker immune signature was proposed for a more accurate assessment of the prognosis in breast cancer patients [3,5,60]. The immune profile of SV8H1&B is characteristic of primary breast cancer, which, even in cases of surgical treatment only, is characterized by high rates of overall and relapse-free survival. On the contrary, immune responses correspond to a group of patients at risk of developing distant metastases and reduced survival. [1,2,22,57]

Thus, to date, prognostically favorable immunological parameters of the composition of intratumoral lymphocytes in breast cancer are clear. An urgent task is to find ways of immunotherapeutic effects on the subpopulation composition of intratumoral lymphocytes in order to correct it and improve the prognosis in patients. Our work is dedicated to solving this urgent problem.

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