

**IMMUNOLOGICAL DIFFERENCES THREE NEGATIVE AND LUMINAL BREAST
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TOPICALITY

Recent studies have completely changed the idea of the course of malignant diseases, in particular breast cancer (BC). For practical oncology, the addition to the conventional TNM clinical and morphological classification with the concept of four molecular biological subtypes of breast cancer has become important. Genetic classification included a variety of disease options: from luminal A, luminal B to three times negative. A completely new round of research on the biological activity of breast cancer has changed not only the clinical understanding of the process of active metastasis or its long-term latent existence in the body, but also the tactics of treatment based on the results of relapse-free and overall survival. Luminal A and three times negative variants of breast cancer are polar in many ways. Thus, the early luminal A type of breast cancer with a low risk of recurrence is subject to the hormonal system with a presumably intact immunological link of homeostasis at the system level. The standard of treatment for early luminal A breast cancer is reduced to surgery and consistent hormone therapy, since the use of chemotherapy reduces long-term results due to its toxicity, especially in the low-risk group. Three times negative breast cancer is autonomous from hormonal influence and, it is possible, it has high immunogenicity. Such patients continue the treatment for a long time in the form of sequential chemotherapy, up to regimens with compacted doses of cytostatics. The high risk of redivoting this type of breast cancer depends on the effects of growth factors and the microenvironment. With luminal A and a threefold negative type of breast cancer, the relationship between the body and the immune system is different. If in the luminal A subtype of breast cancer, there are fewer violations on the part of the immune system, then in the case of a threefold negative subtype, the violations are more pronounced.

THE AIM OF OUR STUDY

is to compare the systemic parameters of immune homeostasis with the ideas about the course of genetically confirmed luminal A and three times negative subtypes of breast cancer.

MATERIALS AND METHODS

The study was conducted on the basis of RSSPMCOR of the MH RUz from 2012 to 2016. The study included 30 patients with morphologically confirmed breast cancer. The age of patients ranged from 35 to 45 years. The first group consisted of 15 patients with luminal A subtype. And the second group consisted of 15 patients with three times a negative subtype of breast cancer. All patients underwent clinical and laboratory examination, and the state of the immune system was additionally studied using the parameters CD19, CD20, CD4, CD8, NK with the calculation of average values of M/m , statistical significance of t and p . Interpretation of the depth of immunological damage and the toxicity of drug therapy was carried out according to integral criteria for the classification of D. Mail. In accordance with it, selective

immunodeficiency is a decrease in the number of immunoglobulins of various classes or an increase in immunoglobulin M. A common variable immunodeficiency is a decrease in B-lymphocytes below $0.2/10$ in combination with the above. Severe combined immunodeficiency is an additional reduction of T-lymphocyte helper cells lower than $0.5/10$.

RESULTS

The cytokine reaction was estimated by reaction rates for each cytokine (TNF- α , IL-2, IFN- γ) at the time of initiation of cancer therapy and in the dynamics 12 months after the transition to the rehabilitation group. The calculation of cytokine reaction coefficients was carried out according to the formula ($K_p = nCD3 + stim / n CD3 + spont$) in various subpopulations of CD3 + synthesizing TNF- α , IL-2, IFN-spontaneously and stimulated in test systems. The state of hyperactivity is determined by $CR > 100$ Units. Statistical analysis was performed by calculating the average values of M/m , the significant reliability of t and p . and 95% confidence intervals. According to the data obtained in the

immunogram, leukocyte indicators in patients of group 2 are slightly higher than in group 1 (5.1 / 0.07 and 4.43 / 1.56). A similar trend is observed when comparing lymphocytes and granulocytes, as well as in terms of B- and T-lymphocytes. In both studied groups, severe combined immunodeficiency was formed: in one case due to a slowly growing tumor in the body, in the other case due to the chemotherapy. When comparing the mean data, with the luminal A subtype, the frequency of detection of severe combined immunodeficiency is lower than with three times negative. Patients with a threefold negative subtype of breast cancer without chemotherapy are repeated under the scenario of a threefold negative subtype with chemotherapy in comparison with the group with luminal A subtype of breast cancer. Indicators of leukocytes, lymphocytes, granulocytes, as well as all T- and B-lymphocytes with a three-fold negative subtype is higher than with the luminal A subtype. On average, in the luminal A subtype, severe combined immunodeficiency was formed in 68.7% of cases, and in three times negative without chemotherapy, the overall variable immunodeficiency was 66.7%. The exception was NK cells, the number of which with a threefold negative subtype of breast cancer is reduced, which indirectly indicates the beginning of the depletion of reserve capacity and the possible transition of the total variable immunodeficiency to severe. In the group with triply negative breast cancer, it is noted that during chemotherapy, there is a decrease in CD4 + of less than 0.5 / 10 l, which forms a severe immunodeficiency in 77.8%. When comparing cytokine levels in serum in patients of the 1st and 2nd study groups, by the end of the first year of therapy, it was noted that the adjuvant hormonal and chemotherapeutic treatment forms in the body various types of pro-inflammatory responses. In patients with hormone-dependent Luminally A subtype of breast cancer, there is a tendency to the successful involvement of TNF-a, on CD3 +. Typical is the manifestation of normo-reactivity for the Luminal A subtype of breast cancer and the hyperactivity of a threefold negative subtype. In cases of selective metastasis to the liver in patients with Luminale A, the subtype shows an increase in TNF-a in two cases. In one case of selective metastatic lesion of the skin of the chest and lung lymphangitis, a combined activation of the TNF-a and IL-2 system was detected in patients with triple negative breast cancer.

CONCLUSIONS

The patients with luminal A subtype of breast cancer and triple negative subtype after treatment differ in their immunologic parameters. Differences in the system of immunological homeostasis and cytokine reactivity can be the basis for assessing the risks of selective metastasis in breast cancer.

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