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# ROLE OF LOCAL IMMUNE SYSTEM IN BREAST CANCER

**Abstract**

**Objective:** to study the correlation between the expression of tumor microenvironment receptors and molecular biological subtypes of breast cancer, as well as their effect on prognosis.

**Keywords:** breast cancer, tumor, microenvironment.

**Introduction**

It is obvious that tumor cells do not function independently, but in close interaction with the microenvironment consisting of many cells and structural complexes. Currently, the crucial role of the tumor microenvironment in its progression and drug resistance has become apparent. ME consists of many non-tumor cells, such as endotheliocytes, pericytes, fibroblasts, enzymes, hormones, extracellular matrix, etc. immunological ME consists of cells and soluble mediators.

**Materials and methods**

To improve the diagnosis and treatment of breast cancer by studying the tumor microenvironment, its impact on the course and prognosis, we analyzed a group of 457 breast cancer patients.

1491 histological preparations belonging to 457 breast cancer patients were examined.

We studied the following immune cell phenotypes: $CD3^+$ $CD4^+$, $CD8^+$, PD-L1, EGFR, CK5/6, SMA, and E cadherin.

The process of immunohistochemical staining included: making a cut from a tissue matrix 4 microns thick, its dewaxing and rehydration, unmasking the antigen, immunohistochemical staining, dehydration and stabilization with a filling medium, inspection and evaluation of the obtained glasses.

The immunohistochemical study was conducted according to this method on the basis of the diagnostic clinic Mediofarm LLC "PREMIUM DIAGNOSTICS". Immunohistochemical examination (IHC) of the surgical material was performed on serial paraffin sections in the laboratory of LLC "Premium Diagnostics" at 618A Uygur Street, Uchtepa district, Tashkent; license No. 1260–00 series A No. 005951. The drug has a registration certificate No. Tv/X 00058/03/15, registration date 13.03. 2015 with the registration certificate period 13.03.2020: manufacturer Dako Denmark A/S, Dania Dakoproduktionsvej 42, DK-2600 Glostrup Denmark.

**Results**

First, to get a general idea of the MO tumor phenotype, we present general indicators of the presence of certain markers depending on the stage of breast cancer (Table 1).

Table 1.– Distribution of patients depending on the presence of markers depending on the stage of breast cancer

| Markers | Breast cancer stage | | | |
|---|---|---|---|---|
| *1* | *2* | *3* | *4* | *5* |
| CD3+ n=162 | 30(32.6%) | 65(34.2%) | 41(32.5%) | 27(55.1%) |
| CD4+ n=120 | 23(25%) | 46(24.2%) | 33(26.2%) | 18(36.7%) |

| *1* | *2* | *3* | *4* | *5* |
|---|---|---|---|---|
| CD8+ n=180 | 34(36.9%) | 78(41.1%) | 49(38.9%) | 19(38.8%) |
| PD-1 n=202 | 41(44.6%) | 83(43.7%) | 55(43.7%) | 23(46.9%) |
| PD-L1 n=125 | 25(27.2%) | 51(26.8%) | 35(27.8%) | 14(28.6%) |
| EGFR n=119 | 21(22.8%) | 48(25.6%) | 33(26.2%) | 17(34.7%) |
| CK5/6 n=101 | 20(21.7%) | 41(21.6%) | 27(21.4%) | 13(26.5%) |
| SMA | | | | |
| **Total** | 92(20.1%) | 190(41.6%) | 126(27.6%) | 49(10.7%) |

Tumor markers have a weak correlation with the stage of the tumor process, which indicates an independent potential of the tumor that does not depend on the stage of the process. Most of the indicators had a slight difference depending on the stage, only the $CD3^+$, $CD4^+$, EGFR and CK5/6 indicators at the fourth stage of the tumor process had a slight difference from the other stages ($\chi^2 = 3.84$, $p < 0.05$). The increase in these indicators is most likely associated with macrophage infiltration and severe hypoxia, which could play a stimulating role in these indicators. In the first, second and third stages of the tumor process, these indicators did not have a significant difference, depending on the size or expansion of the tumor.

Thus, the expression of the above markers does not depend on the stage of the process, but is an indicator of the biological activity and potential of the tumor.

Table 2. – Distribution of patients depending on the presence of markers depending on the morphological structure of breast cancer

| **Markers** | **Morphological structure of breast cancer** | | | |
|---|---|---|---|---|
| | **1** | **2** | **3** | **4** |
| CD3+ n=162 | 22(24.2%) | 92(40.2%) | 30(31.25%) | 18(43.9%) |
| CD4+ n=120 | 18(19.8%) | 65(28.4%) | 23(23.9%) | 14(34.1%) |
| CD8+ n=180 | 21(23.1%) | 103(44.9%) | 37(38.5%) | 19(46.3%) |
| PD-1 n=202 | 49(53.8%) | 93(40.6%) | 45(46.9%) | 15(36.6%) |
| PD-L1 n=125 | 34(37.4%) | 53(23.1%) | 30(31.3%) | 8(19.5%) |
| EGFR n=119 | 35(38.5%) | 51(22.3%) | 24(25%) | 9(21.9%) |
| CK5/6 n=101 | 24(26.4%) | 49(21.4%) | 24(25%) | 4(9.8%) |
| α – SMA n=39 | 25(27.5%) | 8(3.5%) | 6(6.3%) | – |
| **Total patients** | 91(19.9%) | 229(50.1%) | 96(21.1%) | 41(8.9%) |

*Note: 1-lobular cancer, 2-ductal cancer, 3-lobular ductal cancer, 4-other forms of breast cancer*

$CD3^+$, $CD4^+$, and $CD8^+$ were more likely to show high levels in mixed forms and ductal, which correlated with a favorable tumor course and the best therapeutic response of neoadjuvant cancer therapy ($\chi^2 = 6.04$, $p < 0.001$).

PD-L1 was expressed in breast cancer, which correlated with the presence of lymphocyte infiltration, younger age, high malignancy, lack of ER, overexpression of HER2, clinical subtypes of TNBC, as well as basal-like and HER2-rich molecular subtypes ($\chi^2 = 7.51$, $p < 0.001$).

EGFR was more often expressed in the lobular and ductal lobular forms of breast cancer, which indicated an unfavorable course of these tumors, a worse response to treatment, and early metastasis ($\chi^2 = 5.98$ $p < 0.001$).

– SMA, being a marker of myofibroblasts in invasive breast cancer, was an unfavorable factor regardless of the tumor subtype. Expression ranged up to 27.5% and averaged 8.5%. It is a predictor of regional and long-term metastasis ($\chi^2 = 6.71$, $p < < 0.001$).

Table 3.– Distribution of patients depending on the presence of markers depending on the breast cancer subtype

| Markers | Subtypes of tumors | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| $CD3^+$ n=162 | 80(52.3%) | 43(40.2%) | 17(26.6%) | 22(16.5%) |
| $CD4^+$ n=120 | 63(41.2%) | 38(35.5%) | 9(14.1%) | 10(7.5%) |
| $CD8^+$ n=180 | 95(62.1%) | 53(49.5%) | 17(26.6%) | 15(11.3%) |
| PD-1 n=202 | 46(30%) | 41(38.3%) | 33(51.6%) | 82(61.7%) |
| PD-L1 n=125 | 27(17.7%) | 24(22.4%) | 21(32.8%) | 53(39.8%) |
| EGFR n=119 | 9(5.9%) | 14(13.1%) | 25(39.1%) | 71(53.4%) |
| CK5/6 n=101 | 5(3.3) | 11(10.3) | 18(28.1%) | 67(50.4%) |
| α – SMA n=39 | – | 1(0.9%) | 9(14.1%) | 28(21.1%) |
| **Total** | 153 | 107 | 64 | 133 |

*Note: 1-subtype: luminal A, 2-subtype: luminal B, 3-subtype: Her-2 neu positive, 4-subtype: triple negative*

As we can see from the data provided in the table, in luminal type A breast cancer, $CD3^+$ was found in 52.3%, $CD4^+$ in 41.2% and $CD8^+$ in 62.1%, while in triple-negative breast cancer, these indicators were 16.5%, 7.5% and 11.3%, respectively. Given the fact that triple-negative cancer has a poor prognosis, these markers are highly reliable prognostic factors. A higher expression of these parameters in breast cancer is a convincing sign of a more favorable course of this pathology ($\chi^2 = 4.58$, $p < 0.01$).

In contrast, PD-1, PD-L 1, EGFR, and CK 5/6 in luminal tumors were lower than triple-negative values. In luminal type A, PD–1 = 30%, PD-L 1–17.7%, EGFR – 5.9%, and CK 5/6–3.3%, whereas in triple-negative cancers, these indicators were 61.7%, 39.8%, and 53.4%, respectively.

a-SMA in luminal type A was absent, in luminal type B it was only 0.9%, in Her-2 neu it was positive 14.1%, and in triple-negative 21.1%, which once again, based on highly reliable statistical data, proves that this factor is not favorable as a prognostic predictor.

**Conclusion**

Data analysis showed that there is a strong correlation between the expression of the above markers and molecular biological subtypes of breast cancer.

## References:


1. Choi S. D., Atakhanova N. E., Shayusupov N. R., Iskhakov D. M., Kakhkharov A. Zh. Clinical-morphological and molecular-genetic factors of breast cancer relapse prognosis // Surgery of Uzbekistan.– Tashkent,– No. 2. 2018.– P. 43–47.
2. Tillyashaykhov M. N. [Organization of the oncological service of Uzbekistan at the present stage and prospects for further development].– No. 1. 2017.– P. 5–7.
3. Hu W., Li X., Zhang C., Yang Y., Jiang J., Wu C. Tumor-associated macrophages in cancers // Clin Transl Oncol. 2015.– P. 1–8.
4. Marsh T., Pietras K., McAllister S. S. Fibroblasts as architects of cancer pathogenesis // Biochim Biophys Acta.– Vol. 1832.– № 7. 2013.– P. 1070–1078.
5. Vangangelt K., van Pelt G., Engels C., et al. Prognostic value of tumor-stroma ratio combined with the immune status of tumors in invasive breast carcinoma // Breast Cancer Res Treat.– Vol. 168. 2017.– № 3.– P. 601–612.