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FEATURES OF THE IMMUNE MICROENVIRONMENT IN VARIOUS MOLECULAR BIOLOGICAL SUBTYPES OF BREAST CANCER

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Abstract

This article is devoted to the peculiarities of the immune microenvironment of a tumor in various molecular biological subtypes of breast cancer.To study the immune microenvironment, we conducted an IHC study of CD4, CD8, CD20 markers. Our study showed the presence of strong relationships between the molecular biological subtypes of breast cancer and the immune microenvironment of the tumor, which may indicate its potential role as a predictive and prognostic factor in breast cancer. Given these data, it can be assumed that this relationship creates a modern view of more effective treatment with a favorable prognosis and increases survival among patients with breast cancer.

Keywords: *microenvironment, lymphocytes, breast cancer*

Introduction

Breast cancer is the most common malignant neoplasm among women worldwide. In recent decades, there has been a trend of increasing incidence and mortality in both developed and developing countries (Li J.J., Tsang J.Y., Tse G.M. 2022; Toss M.S. et al. 2020). The course of breast cancer depends on many factors such as histologic and molecular biologic characteristics. Nevertheless, more and more studies have recently focused on the influence of tumor microenvironment on the course, response to treatment and prognosis of breast cancer (Giannoudis A. et al. 2022; Mir M.A. 2022; Russo M., Nastasi C. 2020).

Purpose of the study: To determine the relationship between immunohistochemical features of tumor cells and their cellular microenvironment in breast cancer.

Materials and methods

The study included 102 breast cancer patients who were under dispensary observation at the Tashkent city branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology. In order to study the immune microenvironment, we conducted an IHC study of CD4, CD8, CD20 markers. A posteriori comparisons were performed using Pearson's chi-square criterion with Hill's correction. The strength of associ-

ation between categorical indicators was assessed using Cramer's V, whose values were interpreted according to the recommendations of Rea & Parker (2014).

Differences were considered statistically significant at $p < 0.05$.

Results

We analyzed CD4 status depending on the molecular-biological subtype.

According to the obtained data, when comparing CD4 status depending on the molecular biological subtype, we found statistically significant differences ($p < 0.001$) (Pearson's Chi-square method used).

The association between molecular biological subtype and CD4 status was strong (Cramer's V = 0.86). We analyzed the type of tumor infiltration by CD4 lymphocytes depending on the molecular biological subtype.

Figure 1. *Analysis of CD4 status according to molecular biological subtype*

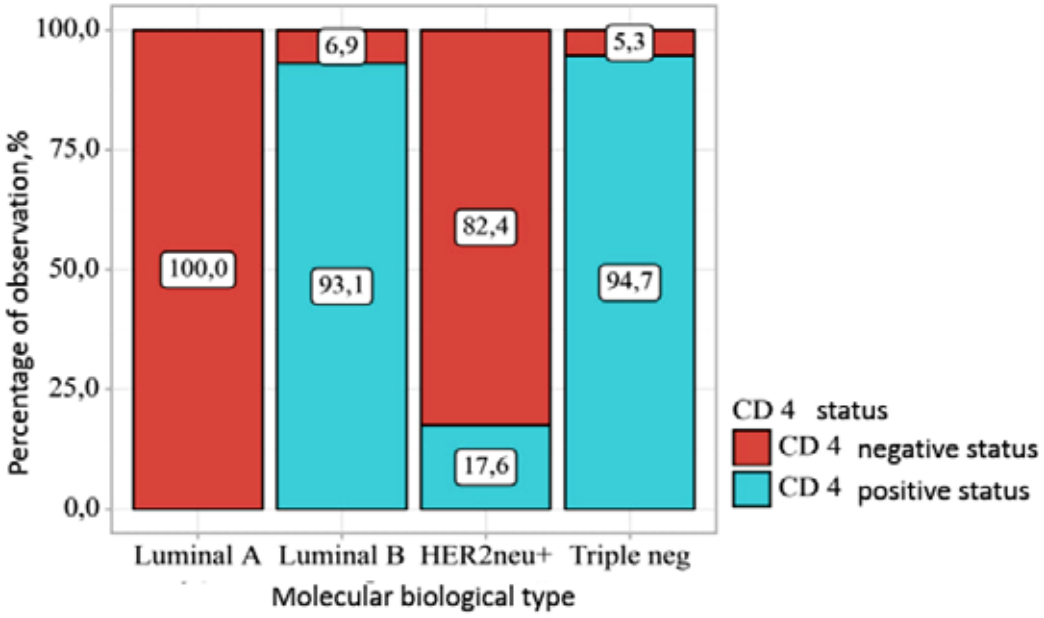

Table 1. *Analysis of the type of tumor infiltration by CD4 lymphocytes depending on the molecular biological subtype*

Indicator	Categories	Molecular biological subtype				χ2	df
		Luminal subtype A	Luminal subtype B	HER2 neu positive subtype	Triple negative subtype		
Type of tumor infiltration by CD4 lymphocytes	No lymphocyte infiltration of the tumor	18 (100.0)	2 (6.9)	14 (82.4)	2 (5.3)		
	Intratumoral infiltration with lymphocytes	0 (0.0)	18 (62.1)	3 (17.6)	28 (73.7)	76.526	6
	Intrastromal infiltration with lymphocytes	0 (0.0)	9 (31.0)	0 (0.0)	8 (21.1)		

< 0.001; pLuminal subtype A – Luminal subtype B < 0.001, pLuminal subtype A – Triple negative subtype < 0.001; pLuminal subtype B – HER2 neu positive subtype < 0.001, pHER2 neu positive subtype – Triple negative subtype < 0.001; * – differences are statistically significant (p < 0.05)*

According to the presented table, when comparing the type of tumor infiltration by CD4 lymphocytes depending on the molecular-biological subtype, we found statistically significant differences ($p < 0.001$) (Pearson's Chi-square method used).

The correlation between molecular biological subtype and the type of tumor infiltration by CD4 lymphocytes was relatively strong (Cramer's V = 0.61).

We analyzed CD8 status depending on the molecular-biological subtype.

According to the presented table, when analyzing CD8 status according to molecular biological subtype, significant differences ($p < 0.001$) were found (method used: Pearson's Chi-square).

Figure 2. *Analysis of CD8 status according to molecular biological subtype*

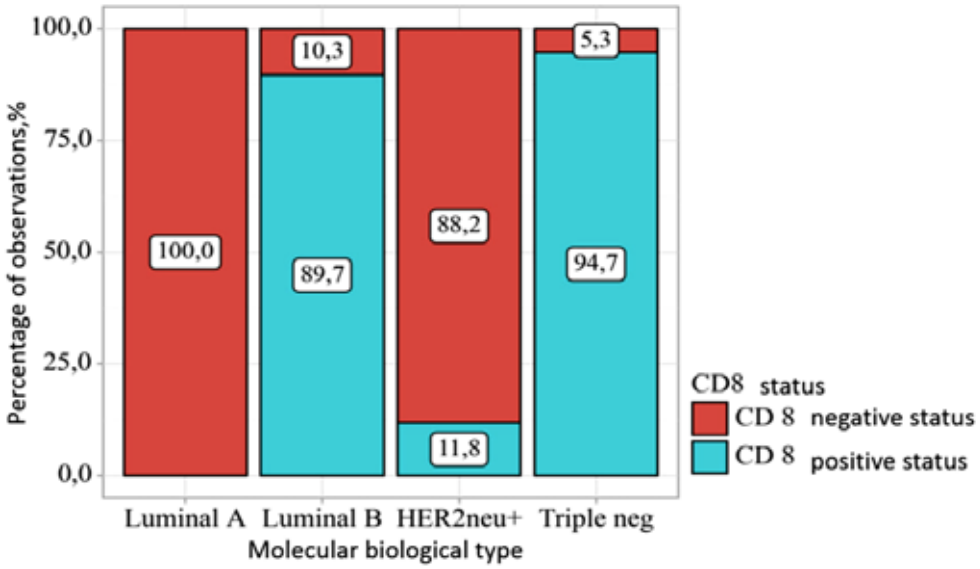

Table 2. *Analysis of the type of tumor infiltration by CD8 lymphocytes depending on the molecular biological subtype*

Indicator	Categories	Molecular biological subtype				χ2	df
		Luminal subtype A	Luminal subtype B	HER2 neu positive subtype	Triple negative subtype		
Type of tumor infiltration by CD8 lymphocytes	No CD8 lymphocyte infiltration of the tumor	18 (100.0)	3 (10.3)	15 (88.2)	2 (5.3)	79.526	6
	Intratumoral infiltration with CD8 lymphocytes	0 (0.0)	14 (48.3)	2 (11.8)	27 (71.1)		
	Intrastromal infiltration with CD8 lymphocytes	0 (0.0)	12 (41.4)	0 (0.0)	9 (23.7)		

< 0.001; pLuminal subtype A – Luminal subtype B < 0.001, pLuminal subtype A – Triple negative subtype < 0.001; pLuminal subtype B – HER2 neu positive subtype < 0.001, pHER2 neu positive subtype – Triple negative subtype < 0.001; * – differences are statistically significant (p < 0.05)*

The association between molecular biological subtype and CD8 status was strong (Cramer's V = 0.86).

We analyzed the type of tumor infiltration by CD8 lymphocytes depending on the molecular-biological subtype.

According to the presented table, when analyzing the type of tumor infiltration by CD8 lymphocytes depending on the molecular-biological subtype, we found statistically significant differences ($p < 0.001$) (method used: Pearson's Chi-square).

The correlation between molecular-biological subtype and the type of tumor infiltration by CD8 lymphocytes was relatively strong (Cramer's V = 0.62).

According to the findings, when CD20 status was compared according to molecular biological subtype, significant differences ($p < 0.001$) were found (method used: Pearson's Chi-square).

The association between molecular biological subtype and CD20 status was strong (Cramer's V = 0.78).

We analyzed the type of tumor infiltration by CD20 lymphocytes depending on the molecular-biological subtype.

Figure 3. *Analysis of CD20 status according to molecular biological subtype*

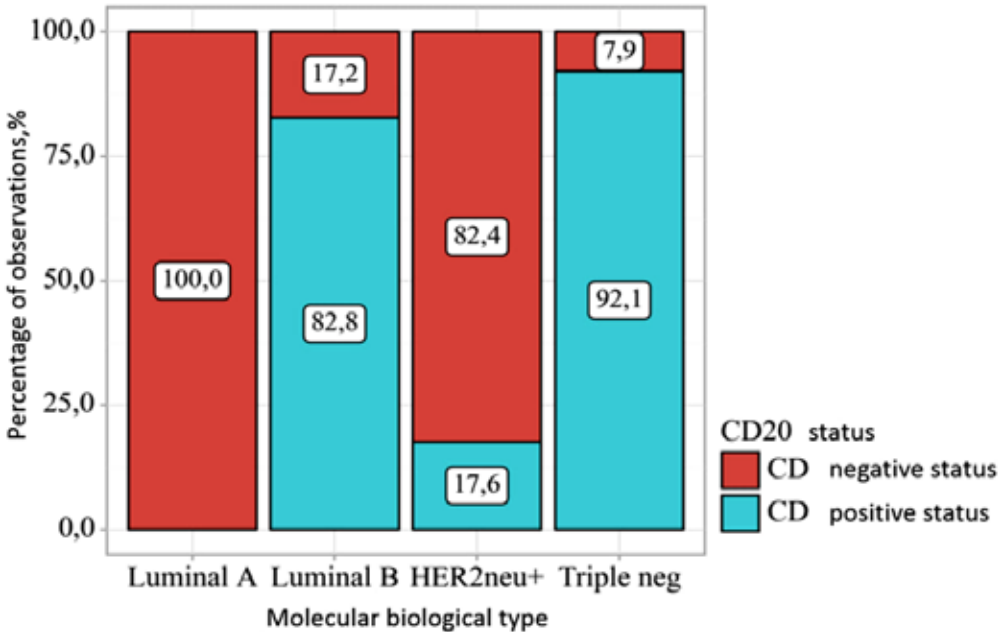

Table 3. *Analysis of the type of tumor infiltration by CD20 lymphocytes depending on the molecular biological subtype*

Indicator	Categories	Molecular biological subtype				χ2	df
		Luminal subtype A	Luminal subtype B	HER2 neu positive subtype	Triple negative subtype		
Type of tumor infiltration by CD20 lymphocytes	No CD20 lymphocyte infiltration of the tumor	18 (100.0)	5 (17.2)	15 (88.2)	1 (2.7)	72.353	6
	Intrastromal tumor infiltration by CD20 lymphocytes	0 (0.0)	19 (65.5)	2 (11.8)	27 (73.0)		

Indicator	Categories	Molecular biological subtype				χ2	df
		Luminal subtype A	Luminal subtype B	HER2 neu positive subtype	Triple negative subtype		
	Intratumoral tumor infiltration by CD20 lymphocytes	0 (0.0)	5 (17.2)	0 (0.0)	9 (24.3)		

< 0.001; pLuminal subtype A – Luminal subtype B < 0.001, pLuminal subtype A – Triple negative subtype < 0.001; pLuminal subtype B – HER2 neu positive subtype < 0.001, pHER2 neu positive subtype – Triple negative subtype < 0.001; * – differences are statistically significant (p < 0.05)*

According to the table below, when analyzing the type of tumor infiltration by CD20 lymphocytes depending on the molecular biological subtype, statistically significant differences (p < 0.001) were found (method used: Pearson's Chi-square).

The association between molecular biological subtype and type of tumor infiltration by CD20 lymphocytes was relatively strong (Cramer's V = 0.6).

Conclusion

Our study showed strong correlations between molecular biological subtypes of breast cancer and the immune tumor microenvironment, which may suggest its potential role as a predictive and prognostic factor in breast cancer. Considering these data, we can assume that this relationship creates a modern view of more effective treatment with a favorable prognosis and increases survival among patients with cancer.

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