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CLINICAL SIGNIFICANCE OF INFILTRATIVE GROWTH IN BREAST CANCER TUMORS

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ABSTRACT

Even though breast cancer is currently one of the most studied oncological pathologies, the question of the occurrence, characteristics, and prevalence of infiltrating breast cancer remains unclear, as evidenced by the wide dispersion of figures on the frequency of this disease according to various authors - from 2 to 62%. To date, issues related to the diagnosis, selection of adequate treatment, and prediction of the outcome of the disease in infiltrating breast cancer remain particularly complex, considering that in most published studies, a limited number of markers do not allow for full clarification of the biological profile of this type, there is no data on the prognostic significance, and a comprehensive diagnostic algorithm combining morphological and IGC criteria has not been defined.

Key words: Breast cancer, breast tumor growth, infiltrating cancer, immunohistochemistry, invasion.

INTRODUCTION

The relevance of this study is due to the need to develop accurate diagnostic criteria and personalized treatment strategies for infiltrating breast cancer, which will help improve the quality of life and survival of this group of patients. [5,6,9,12] The obtained data will help create new treatment protocols that support an individual approach to this category of patients. In the world, several scientific studies are being conducted in the field of diagnosis and treatment of breast cancer, including the study of the age, morphological, and pathological characteristics of breast cancer patients to identify patterns associated with rare forms of the disease,

conducting immunohistochemical analysis to determine the impact on therapeutic strategies, assessing the type of surgical intervention and its impact on relapses and metastases, and developing algorithms for diagnosis and treatment aimed at patients' characteristics.[1-3,7,10] In our country, to establish the medical system to the world level, as well as reduce the incidence of malignant neoplasms, tasks have been set that allow for the introduction of modern methods of diagnosis and treatment into practice, raising the quality of medical care to a new level, but many aspects such as the molecular genetic profile of the tumor, the biological behavior of the cancer remain unclear.[4,5,8] This leads to ambiguities in the light of which this research is of particular relevance.

The purpose of our research was to develop new criteria for the differential diagnosis of infiltrative breast cancer based on the use of a comprehensive morphological research method with an optimal marker panel to improve the quality of diagnostics and risk assessment for the development of invasive breast cancer.

MATERIAL AND METHODS OF RESEARCH

As a basis for our research, we took the results of a retrospective examination of 128 patients who underwent treatment at republican cancer center from 2020 to 2024 with infiltrating breast cancer. It was determined whether the tumor belonged to infiltrating lobular or ductal cancer. In 118 (88.7%) patients, an infiltrating ductal cancer was diagnosed, and in 10 (6.0%) - infiltrating lobular cancer. Infiltrating ductal cancer, which occurred in 88.7% of cases, was predominantly of the 2nd degree of malignancy and prevailed in all study groups. The studied groups of patients were comparable in terms of the main clinical and morphological parameters. The surgical material underwent morphological examination. The obtained tissue samples were placed in a fixing mixture - neutral formalin.[11] The material was carried out according to the standard method and poured into paraffin. Cuts 5-6 μm thick were stained with hematoxylin and eosin. Morphological studies were conducted using a Carl Zeiss Microimaging light microscope.

RESULTS AND DISCUSSION

To identify differences in the morphological characteristics of the tumor tissue, all parameters were divided into two groups. The first group comprised qualitative nominal indicators, which included the frequency of the main structures of the parenchymal component and the main structures invasion of the tumor node stroma along the periphery. All other descriptive histological parameters were classified into a conditionally quantitative group, the severity of which was

assessed on a point scale. Among the main structures of the parenchymal component of the tumor, we distinguished large and small alveolar structures, trabecular, cribriform, and tubular structures. Trabecular structures (89% of all structures) were most frequently found in the preparations of the IDR variant, while in the IPR variant, they were not detected. Large alveolar structures were detected in ISR and IPR variants of breast cancer (61% and 36%, respectively). The frequency of small alveolar structures increases statistically significantly in the sequence IPR > ISR > IDR. Cribriform structures were found only in the IPR variant of breast cancer, while small acinar structures were observed in the IDR and ISR variants of breast cancer. The average values of the semi-quantitative assessment of microscopic parameters characterizing the inflammatory infiltration of the stromal component were evaluated according to the following features (Table 1).

Table 1. Characteristics of microscopic parameters of infiltrating breast cancer.

(M±G, m)

Parametres	Histologically types of cancer			
	Rare n-28	Ductal infiltrative n-31	Ductal invasive n-69	Total n-128
Total inflammatory infiltration in stroma	0,25±0,44* 0,08	0,61±0,84 0,15	0,99±1,06* 0,13	0,73±0,95 0,08
Round cell infiltration along the periphery of the node	0,68±0,67* 0,13	1,03±1,02 0,18	1,43±0,99* 0,12	1,17±0,98 0,09
Circular cell infiltration of central sites of node	0,18±0,39* 0,07	0,42±0,62** 0,11	0,87±1,06** 0,13	0,61±0,90 0,08

*/**– statistically significant

Solid-alveolar structures in the tumor parenchyma were 2.5 times more common in the mixed type of breast cancer compared to its lobular variant (2.58±0.56 versus 1.04±0.92). (Table 2)

Table 2. Characteristics of necrotic processes in the parenchyma of the breast cancer tumor node depending on its histological variant. (M±G, m)

Parametres	Histologically types of cancer			
	Rare n- 28	Ductal infiltrative n-35	Ductal invasive n-69	Total n-128
Solid-alveolar	1,04±0,92* 0,17	2,58±0,56* 0,10	2,67±0,61 0,07	2,29±0,95 0,08
Necrosis	0,01±0,01* 0,001	0,06±0,25 0,04	0,29±0,60* 0,07	0,17±0,47 0,04

*/**– statistically significant

When analyzing the histological structure of primary tumor nodes, we also evaluated such a parameter as the degree of malignancy of infiltrating ductal carcinoma. (Table 3)

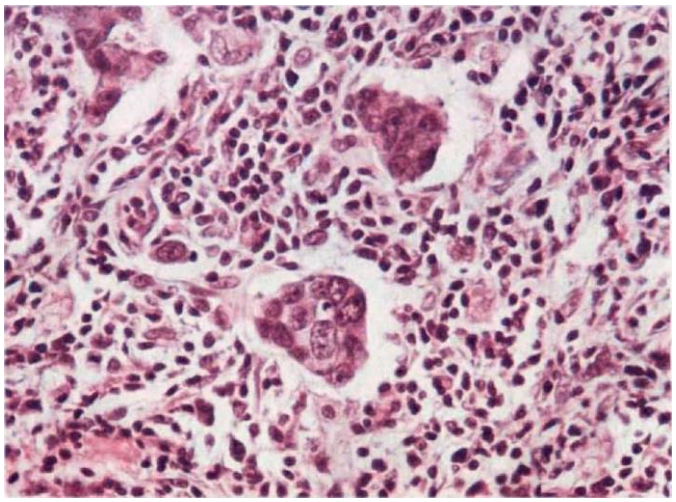
Table 3. Degree of malignancy in patients with infiltrating breast cancer depending on menstrual function

G stage	Menstural status of patients (n, %)		P
	Pre (n-128)	Post (n-166)	
1	15/128 (11,7%)*	4/166 (2,4%)	0,0003
2	105/128 (82,0%)	158/166 (95,2%)	0,0002
3	8/128 (6,3%)	4/166 (2,4%)	0,03
			13,7; p = 0,001

*/**– statistically significant

In the studied group of patients, cases with second-degree malignancy predominated. In the group of patients without preoperative treatment, the 1st and 2nd degrees of malignancy occurred with equal frequency in patients with different menstrual function status (p = 0.20 and p = 0.43, respectively). The third degree of malignancy was observed very rarely. The degree of malignancy was not associated with the size of the primary tumor nodule in either the group of patients with preserved menstrual function or in menopausal patients, regardless of

preoperative treatment. In the primary tumor nodule, the structure of the infiltrative component was analyzed in detail, identifying microalveolar, trabecular, tubular, solid structures, and small groups of tumor cells (Figure 1).



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Microalveolar structures were clusters of tumor cells, either round or slightly irregular in shape, resembling a rounded form. The morphological structure of cells forming this type of structure varied from small with moderately pronounced cytoplasm and rounded nuclei to large with hyperchromatic, irregularly shaped nuclei and moderate cytoplasm. Trabecular structures were either short, formed by a single row of small, sufficiently monomorphic cells, or wide, consisting of 2-3 rows of medium-sized cells with moderately pronounced cytoplasm, with rounded normochromic or hyperchromic nuclei. Tubular structures were formed by a single row of sufficiently monomorphic cells with normochromic rounded nuclei. Solid structures varied in size and consisted of either small cells with moderately pronounced cytoplasm and monomorphic nuclei or large cells with abundant cytoplasm and polymorphic nuclei. Cell groups were either individual cells or clusters of 1-4 cells, variable in their morphological structure. Most often, the infiltrative component had a mixed structure. In the group without preoperative treatment, the frequency of microalveolar structures was not related to the state of menstrual function ($\chi 2 = 0.7$; $p = 0.41$), while in the group of patients with neoadjuvant chemotherapy (NACT), microalveolar structures in the infiltrative component were more often detected in menopausal patients. The representation of microalveolar structures in the infiltrative component was determined using a three-point system, where 1 point indicated cases with microalveolar structures up to 10%, 2 points - >10% - <75% of microalveolar structures, 3 points > 75%. In the group without preoperative treatment, the severity of microalveolar structures in the infiltrative component, as well as their presence, did not depend on the state

of menstrual function ($\chi 2 = 5.5$; $p = 0.14$). In patients with NACT, a greater number of microalveolar structures in the infiltrative component were identified in the group of menopausal patients. Trabecular, tubular, and solid structures were found equally frequently in patients with different menstrual function states, both in the group without NACT and in the group with NACT (respectively: trabecular $\chi 2 = 0.07$; $p = 0.78$ and $\chi 2 = 0.3$; $p = 0.59$; tubular $\chi 2 = 2.4$; $p = 0.12$ and $\chi 2 = 0.64$; $p = 0.42$; solid $\chi 2 = 0.7$; $p = 0.38$ and $\chi 2 = 1.7$; $p = 0.20$).

In patients without preoperative chemotherapy, groups of cells in the infiltrative component were found with approximately the same frequency in both women with preserved menstrual function and menopausal patients ($\chi 2 = 0.04$; $p = 0.83$). In the group of patients with NACT, cases of the presence of cell groups in the infiltrative component were more often observed in patients with preserved menstrual function. To exclude NACT's influence on the morphological structure of the neoplasm, we conducted a study of the infiltrative component of the tumor in the group of patients without preoperative treatment.

Conclusion. The invasive ductal carcinoma (IDC) variant of breast cancer, based on its microscopic picture, is characterized by a statistically significantly higher degree of malignancy, mitotic activity of tumor cells, severity of inflammatory infiltration of the stromal component, and the presence of cribriform structures and necrotic processes in the parenchyma. The invasive lobular carcinoma (ILC) variant of breast cancer, unlike the IDC variant, is characterized by the severity of stromal hyalinosis and infiltration of adipose tissue, the predominance of trabecular structures in the parenchyma, and the presence of "dark" cells. Summarizing the obtained results, we can conclude that in the ductal variant of breast cancer, microscopic signs of 1-4 clusters are expressed, and in the lobular variant, signs of 5-6 clusters are expressed.

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