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THE IMPORTANCE OF TUMOR GROWTH TYPES IN MAMMARY CANCER

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Abstract

Breast cancer (BR) is the most common form of malignant neoplasms among women worldwide, and its prevalence is constantly growing. With the development of modern radiation imaging technologies, such as magnetic resonance imaging (MRI), it plays a key role in preoperative diagnostics, which allows for the identification of multifocal and multicentric forms of breast cancer and a more accurate and timely assessment of their prevalence (Buzenkova A. V., Tashireva L. A., Zavyalova M. V., Perelmuter V. M., 2022). Modern diagnostic methods allow for the determination of these parameters with high accuracy, however, existing prognostic models often do not sufficiently accurately account for their complex effect, which limits the possibilities of individualization of treatment and optimization of treatment strategies. Breast cancer is the most common form of malignant tumors among women worldwide, and its prevalence is constantly growing (Kakhkharov A.Zh., 2023). Modern technologies, such as magnetic resonance imaging (MRI), play an important role in preoperative diagnostics, which allows for the identification of multiple tumor foci and a more accurate and timely assessment of their spread (Grishina K. A., Muzaffarova T. A., Khailenko V. A., Karpuhin A. V. 2016; Demidov S. M., Demidov D. A., Sazonov S. V., Churakova E. I. 2018). Multifocal (MF) and multicentric (MC) breast cancer are forms of the disease in which the presence of two or more tumor foci is noted. In MF, all foci are located in one quadrant of the mammary gland, while in MS, they are distributed into different quadrants (Alimkhodzhaeva L. T., 2011; Kakhkharov A.Zh., 2023). However, in the scientific literature, there is often no clear definition of the term “quadrant,” which creates difficulties in standardizing approaches and research methodology (Alimkhodzhaeva L. T., 2011).
Keywords: *Breast cancer, multifocal and multicentric forms, tumor, unifocal tumor*

Material and methods

The study included 100 patients diagnosed with breast cancer from 2011 to 2022 based at the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology and its Tashkent city branch.

Analysis of tumor size depending on the type of tumor growth – unifocal, multifocal, and multicentric – revealed a number of significant and significant differences, which is confirmed by a high level of statistical significance (p=0.002). According to the data

obtained, the average size of the unifocal tumor was 12.39 units, the interquartile range was from 9.04 to 14.98, which indicates a relatively small length and mass of the tumor node. In multifocal tumors, the average volume reached 20.16, while the interquartile range ranged from 13.32 to 25.29, indicating a more massive and branched nature of the lesions characterizing these forms. Similarly, multicentric tumors show a large size – on average 18.69 and an interquartile range from 11.92 to 26.63. Statistical analysis using the nonparametric Kruskal-Wallis criterion confirmed that the differences between the groups were statistically significant ($p<0.05$), which indicates the presence of high reliability in various durations of tumor processes depending on their morphological variant. Theoretically, this data may be associated with modern ideas about the pathogenesis and morphology of breast tumors, where multifocal and multicentric forms are a more pronounced manifestation of heterogeneity of hereditary or molecular genetic anomalies, leading to extensive proliferation of tumor clones. Such a large volume is associated with the presence of several foci, which can have different biological activity, degree of differentiation, and metastasis potential. According to the literature, larger tumors are also associated with high invasiveness, the probability of regional and long-term spread, as well as a poor prognosis for the patient. These factors require increased attention in clinical practice, since the presence of extensive tumors requires more extensive surgical intervention, possibly combined therapy methods, as well as increased control in the postoperative period. Importantly, an increase in the size of the tumor node at the diagnostic stage serves as a predictor of already possible complications, more severe clinical manifestations, as well as a high risk of recurrence and development of the disease. In this regard, systematic accounting of volume as an important prognostic factor contributes to a more accurate assessment of the severity of the disease, planning treatment tactics, and predicting the outcome in certain groups of patients. In general, the data confirm the need to include tumor size analysis in standard protocols for the diagnosis and treatment of breast cancer to increase the effectiveness of the individual approach and improve clinical outcomes.

Research results

Analysis of tumor characteristics depending on the type of growth of breast cancer, including unifocal, multifocal, and multicentric variants, revealed many statistically significant differences, indicating different morphological and molecular heterogeneity of these forms of the disease. In particular, the most pronounced correlation was revealed with the number of tumor nodes: in unifocal tumors, mainly one node is observed, while in multifocal and multicentric forms, the presence of two or more tumor formations is more often noted, which is confirmed by the statistical indicator $p<0.001$. This indicates the high prevalence and complexity of the morphological picture in multifocal and multicentric tumors, which requires special attention when choosing stages of diagnosis and treatment tactics. Also, an important result of the analysis was the high frequency of infiltrating tubular carcinoma in multifocal and multicentric tumors ($p =0.002$), which indicates the aggressiveness and high potential for invasive growth of these forms. As for the degree of differentiation of weakly differentiated tumors, such as GIII, despite their statistical significance, the differences turned out to be less pronounced and did not reach a strict level of $p<0.05$, which indicates the need for further research. At the same time, such parameters as ER status, PR, HER2, molecular subtypes (luminal A, luminal B HER2-negative, HER2-positive, three times negative) did not show statistically significant differences between growth types ($p>0.05$). This indicates the high heterogeneity of clinical and molecular characteristics in various growth forms, which complicates their identical association with morphological species. It should also be noted that the T, N, and M indicators of tumor progression, as well as the molecular profile, such as the degree of ER, PR, and HER2 positivity, do not differ statistically significantly depending on the growth type ($p>0.05$). This indicates that the localization and prevalence of tumor foci generally do not depend on the morphological variant of growth and should be assessed independently. These results to-

gether indicate that it is the prevalence and morphological structure of the tumor nodes and their histological type that are the main features associated with the tumor growth type, which can be important for prognostic assessment and determination of the most effective treatment methods. The obtained data emphasize the complexity of the pathogenetic mechanisms of breast cancer and indicate the need for a comprehensive analysis of all clinical, pathological, and molecular parameters to form an individual approach to the treatment and prognosis of the disease. See Table 1.

Table 1. *Analysis of tumor features depending on the type of tumor growth*

Indicators	Classes	Growth type			p.
		Unifocal growth	multifocal growth	multicentric growth	
T	T1	12 (27.3)	2 (6.7)	8 (30.8)	0.395
	T2	23 (52.3)	21 (70.0)	13 (50.0)	
	T3	2 (4,5)	1 (3,3)	1 (3.8)	
	T4	7 (15.9)	6 (20.0)	4 (15.4)	
N	No.	20 (45.5)	12 (40.0)	12 (46.2)	0.172
	N1	18 (40.9)	12 (40.0)	10 (38.5)	
	N2	1 (2.3)	4 (13.3)	1 (3.8)	
	N3	1 (2.3)	2 (6.7)	3 (11.5)	
	Nx	4 (9.1)	0 (0.0)	0 (0.0)	
M	M0	39 (88.6)	26 (86.7)	22 (84.6)	0.888
	M1	5 (11.4)	4 (13.3)	4 (15.4)	
number of tumor nodes	Derivative 2	44 (100.0)	0 (0.0)	0 (0.0)	< 0.001* $p_{\text{unifocal growth – multifocal growth}} < 0.001$
	Derivative 3	0 (0.0)	25 (83.3)	23 (88.5)	
	4 derivatives	0 (0.0)	4 (13.3)	3 (11.5)	
	1 derivative	0 (0.0)	1 (3,3)	0 (0.0)	
Histological variant	infiltrating breast cancer	42 (95.5)	24 (80.0)	16 (61.5)	0.002* $p_{\text{unifocal growth – multicentric growth}} < 0.001$
	infiltrating lobar cancer	2 (4,5)	6 (20.0)	10 (38.5)	
Degree of differentiation	GI	14 (31.8)	10 (33.3)	5 (19.2)	0.265
	GII	24 (54.5)	15 (50.0)	20 (76.9)	
	GIII	6 (13.6)	5 (16.7)	1 (3.8)	
EAR	ER positive state	27 (61.4)	17 (56.7)	17 (65.4)	0.799
	ER negative state	17 (38.6)	13 (43.3)	9 (34.6)	
PR	PR is positive	25 (56.8)	16 (53.3)	16 (61.5)	0.825
	Negative PR	19 (43.2)	14 (46.7)	10 (38.5)	
HER 2 neu	HER 2 neu positive condition	10 (22.7)	8 (26.7)	8 (30.8)	0.756
	HER 2 neu negative condition	34 (77.3)	22 (73.3)	18 (69.2)	

Indicators	Classes	Growth type			p.
		Unifocal growth	multifocal growth	multicentric growth	
Molecular types	Luminal type A	10 (22.7)	4 (13.3)	7 (26.9)	
	Luminal type B, HER2 neu negative	10 (22.7)	3 (10.0)	1 (3.8)	
	Luminal type B, HER2 neu positive	8 (18.2)	12 (40.0)	10 (38.5)	0.159
	HER2 neu positive	2 (4,5)	3 (10.0)	3 (11.5)	
	Triple negative type	14 (31.8)	8 (26.7)	5 (19.2)	

** – the difference in indicators is statistically significant (p< 0.05)*

This indicates the high prevalence and complexity of the morphological picture in multifocal and multicentric tumors, which requires special attention in the stages of diagnosis and the choice of treatment tactics. Also, an important result of the analysis was the high frequency of infiltrating tubular carcinoma in multifocal and multicentric tumors (p=0.002), which indicates the aggressiveness and high potential for invasive growth of these forms. As for the degree of differentiation of weakly differentiated tumors, such as GIII, despite their statistical significance, the differences turned out to be less pronounced and did not reach a strict level of p<0.05, which indicates the need for further research. At the same time, such parameters as ER status, PR, HER2, molecular subtypes (luminal A, luminal B HER2-negative, HER2-positive, three times negative) did not show statistically significant differences between growth types (p>0.05). This indicates the high heterogeneity of clinical and molecular characteristics in various growth forms, which complicates their identical association with morphological species. It should also be noted that the T, N, and M indicators of tumor progression, as well as the molecular profile, such as the degree of ER, PR, and HER2 positivity, do not differ statistically significantly depending on the growth type (p>0.05). This indicates that the localization and prevalence of tumor foci generally do not depend on the morphological variant of growth and should be assessed independently. These results together indicate that it is the prevalence and morphological structure of the tumor nodes and their histological type that are the main features associated with the tumor growth type, which can be important for prognostic assessment and determination of the most effective treatment methods. The obtained data emphasize the complexity of the pathogenetic mechanisms of breast cancer and indicate the need for a comprehensive analysis of all clinical, pathological, and molecular parameters to form an individual approach to the treatment and prognosis of the disease.

Conclusion

Analysis shows that the morphological type of growth is closely related to prognostic signs, the degree of metastasis, and the probability of recurrence, which emphasizes the importance of taking these indicators into account for predicting outcomes and individualizing treatment strategies. The obtained data indicate the need for deep integration of morphological and molecular characteristics into multifactorial prediction assessment systems, which will allow increasing the accuracy of determining treatment tactics and increasing the survival rate of patients through a more individualized approach. In the future, such studies should help to identify the molecular mechanisms of highly heterogeneous tumors and develop new targeted therapeutic methods, which will open up new prospects for breast treatment.

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