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NAVIGATING DISTANCE METASTASES IN MULTIFOCAL BREAST CANCER

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ABSTRACT

Purpose of the study: to analyze the process of tumor metastasis in patients with multifocal breast cancer (BC). Material and method: a retrospective analysis of data from 133 patients treated at the Republican Specialized Scientific and Practical Center of Oncology and Radiology and its branches during the period 2018-2023. Results: Conclusion: for patients with multifocal characteristics, the frequency of tumor involvement in regional lymph nodes is higher; however, there is practically no difference compared to unifocal tumors in terms of metastasis to distant organs.

Key words: multifocal, breast cancer, metastasis.

INTRODUCTION

The clinical significance of multifocal and multicenter breast cancer (MBC) is increasingly recognized because of its association with unwanted results and processing complexities. Neri et al. pointed out that the choice of surgical intervention in multifocal cases considerably influences survival rates, demonstrating a need for tailor -made approaches [16]. Likewise, Ataseven et al. Assessed how multifocal diseases are correlated with locoregional and distant metastases, indicating that these patients may experience lower overall survival, in particular post-nineadjuvant [1].

Characteristically, multifocal and multicenter cancers often have greater biological heterogeneity, which complicates treatment. Li et al. discussed how this heterogeneity can affect the response models to systemic therapy, revealing that separate molecular profiles may require different treatment strategies [13]. In addition, it has been shown that the impact of the total size of lesions in multifocal cancers is correlated with survival results, which suggests that a precise tumor characterization is essential for prognosis [2, 3, 8, 14].

The challenges in the management of multifocal breast cancer include problems related to local recurrence and remote metastases. Kanumuri et al. noted that these results are significantly worse compared to unifocal cases, which implies that multifocality serves as a prognostic factor [9]. The effectiveness of variable surgical techniques is still under study, certain studies defending more aggressive approaches in cases of multifocality to improve local control [5, 11, 15].

Despite progress, treatment methods remain imperfect and often hampered by the aggressive nature of multifocal diseases [4-9, 10, 12, 21]. As Zhang et al. Points out, multifocal tumors have a more significant clinical challenge, requiring a continuous evaluation of therapeutic strategies to optimize patient results [22]. Thus, the exploration of innovative approaches, including personalized medicine and targeted therapies, is justified to treat the multifaceted implications of multifocal breast cancer [16-20].

Aim of the study to analyze the metastatic characteristics of tumors in multicentric multifocal cancer.

MATERIAL AND METHODS OF RESEARCH

This study retrospectively analyzed the data of 133 patients treated at the Republican Specialized Scientific and Practical Center of Oncology and Radiology and its branches from 2018 to 2023. When tumors were detected in different quadrants of the breast, it was considered multifocal; when 2 or more tumors were detected in a single quadrant, it was considered multicentric. Clinical pathological data, including patient age, menopausal status, tumor size, number, lymph node status, and metastasis to distant organs, were obtained from medical records.Statistical data analysis was performed using the DataTab online program. Descriptive statistics and the chi-square test were used.

RESULTS AND DISCUSSION

The analysis of hematogenous metastasis frequency in relation to regional lymph node status and the presence of local tumor recurrences yielded very

interesting results. It was found that lymph node involvement with metastases increases the likelihood of distant metastases, which was evident in both patients with and without tumor recurrence (Table 1).

Dependence of hematogenous metastasis frequency in breast cancer patients on regional lymph node status and the presence of local recurrences

Lymph nodes	Distant metastases n (%)			
metatsases				
	No		Yes	
	M_0	M_1	M_0	M_1
Yes (N_0)	197/224	27/224	24/35	11/35
	(88%)	(12%)	(68,5%)	(31,5%)
No (N+)	177/ 247	70/247	16/41	25/41
	(71,6%)	(28,4%)	(39,1%)	(60,9%)
	x ² =19,0;p=0,000013		$x^2 = 6$.6; p=0,01

The obtained data confirm that the presence of initial metastases in regional lymph nodes during surgical intervention is a crucial indicator signifying a high risk of hematogenous dissemination. We investigated the correlation between the occurrence of distant metastases and the number of affected lymph nodes, taking into account the presence of disease recurrence. A clear correlation was observed only in patients without disease recurrence and manifested as a higher frequency of metastasis with an increasing number of lymph nodes affected by metastases (Table 2).

Table 2

Dependence of MTS on affected lymph nodes					
Number of metastatic nodes		Residive n(%	()	·	
1 - 3	104/135	31/135	5/13	8/13	
	(59,1%)	(22,9%)	(38,4%)	(61,6%)	
4 - 9	48/67	19/67	3/12	9/12	
	(72%)	(28%)	(25%)	(75%)	
10 ≤	15/30	15/30	3/9	6/9	
	(830%)	(50%)	(33,3%)	(67,7%)	
	X ² =8,9; p=0,01		X ² =0,52; p=0,7		

However, the percentage of lymph nodes with metastases, calculated from the total number of removed regional lymph nodes, proved to be associated with the appearance of distant metastases, both in patients without disease recurrence and in cases where they occurred (Table 1). As shown in the table, the development of distant metastases occurred when a greater number of regional lymph nodes were involved in the process.

Table 3

Dependence of hematogenous metastasis on the percentage of lymph node
metastasis and the presence of disease recurrence

Distant metastases	Residive of metastases		
	No	Yes	
No (Mo)	34,1±26,3	37,6±23,03	
Yes (M1)	51,7±31,6	56,1±32,4	
	P=17,02; p=0,000052	P=3,9; p=0,05	

As mentioned above, in cases where patients developed local recurrences and hematogenous metastases, we evaluated the timing of their detection. It was interesting to analyze how the status of regional lymph nodes influenced the detection time of these forms of breast cancer progression. It was found that there is a correlation between these features. In cases with metastases to the axillary lymph nodes, recurrences and hematogenous metastases were mostly detected synchronously (Table 4).

Table 4

Distribution of patients with local recurrences and distant metastases in regional lymph nodes according to the time and status of their detection

Lymph node	Regionar and distant metastases n (%)		
metastases	Synchron	Metachron	
N ₀	2/18(11%)	9/18(50%)	
N ₁₋₄	16/18(89%)	9/18(50%)	
		X ² =6,4; p=0,01	

Thus, the conducted study demonstrated that regional spread of the tumor in breast cancer increases the frequency of distant metastases, independent of disease recurrence. The most crucial indicator is the percentage of lymph nodes affected by the tumor. A more aggressive course of the disease, characterized by local relapses and synchronous development of hematogenous metastases, is most frequently observed in breast cancer patients with regional nodal involvement. In breast cancer, true primary multiple tumors and intra-organ metastases - multifocality occur with approximately the same frequency. Analysis of the morphological structure of clinically detected tumor nodes did not reveal any significant features associated with similarities or differences in the histological structure of multiple growth foci. An important prognostic parameter, such as the number of lymph nodes involved in the tumor process, was also high in multifocal growth, where it did not depend on the receptor status of the primary tumor, as in patients with unicentric breast cancer.

CONCLUSION

The obtained results indicate that for patients with multifocal tumor growth, identified during clinical and instrumental examination, the frequency of tumor involvement in regional lymph nodes significantly increases when two or more quadrants of the breast are affected. It was established that there is no clear correlation between the morphological structure of the tumor and the frequency of regional metastases in multifocal breast cancer growth.

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