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MULTIFOCAL/MULTICENTRIC BREAST CANCER: HISTOLOGICAL STRUCTURE OF TUMOR

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ABSTRACT

Aim: This study aims to analyze the histological and molecular biological characteristics of large and small tumors in multifocal and multicentric breast cancer (BC) patients. **Materials and methods:** Data from 133 patients treated at the Republican Specialized Oncology and Radiology Scientific Practical Center and its branches between 2018 and 2023 were retrospectively analyzed. **Results:** Results revealed no significant statistical difference in the age of patients among the groups ($p = 0.324$). However, significant differences were observed in lymph node involvement ($p = 0.001$), histological grade ($p = 0.02$), histological type ($p = 0.03$), and type of surgery ($p = 0.001$). The study showed that multifocal and multicentric tumors are biologically more aggressive than unifocal tumors, with a higher tendency to metastasize and poorer prognosis. **Conclusion:** The results of the study confirmed that the characteristics of multifocal breast cancer can be a necessary criterion for predicting the outcome of the disease.

Key words: multifocal, multisentric, breast cancer, histological examination, immunohistochemistry.

INTRODUCTION

Breast cancer [BC] is explained by the uncontrolled division and proliferation of cells in the milk ducts or lobes. [1,5,6] In the case of clinical diagnosis of breast cancer, the presence of multiple tumor nodes is detected during mammography or ultrasound examinations in the preoperative period. Multifocal (MF) and multicentric (MS) tumor nodes are characterized by the location of several nodes in one quadrant of the mammary gland and in different quadrants, respectively. [1]

Today, there are insufficient criteria for the standard definition and differential diagnosis of multifocal tumors. The incidence of multifocal tumors is 9-75%.[2,3]

The tumour-nodular-metastasis (TNM) classification is used to describe multifocal tumours.[4] Because tumour size (T) is an important predictor of lymph node damage[N]. It is generally recommended to report the histological level, pathological type, and other pathological features of the largest tumour in MF/MS breast cancer.[2,3,7] In these guidelines, it is assumed that the prognosis depends mainly on the largest tumour, without considering the overall characteristics of the tumour and the heterogeneity of the various lesions. To predict multifocal tumors, of course, there is a lack of scientific research on the analysis of not only the largest, but also small nodules. Therefore, in our research work, we also studied the histological structure of small nodules.

Purpose of the study: analysis of the specific histological and molecular biological characteristics of large and small tumor nodes in multifocal and multicentrically located multifocal cancer.

MATERIALS AND METHODS

This study retrospectively analyzed the materials of 133 patients treated at the Republican Specialized Scientific and Practical Center of Oncology and Radiology and its branches in 2018-2023. When a tumor was detected in different quadrants of the breast, it was assumed to be multifocal; when 2 or more tumors were detected in one quadrant, it was assumed to be multicentric.

Sorting of patients. Among the patients diagnosed with tumors of other organs and metastases of stage IV of breast cancer, we did not accept them for research. Clinically and pathologically confirmed patients with MF and MS were taken. Unifocal (UF) tumors were divided into the following groups: 68 (51.12%), MF-17 (12.8%), MS-48 (36.1%).

Data collection. Clinical pathological data, i.e., patient age, menopausal status, tumor size, number, lymph node status, histological type, lymphovascular invasion, pathological type, surgical intervention, immunohistochemical parameters (including estrogen receptors [ER], progesterone receptors [PR], human epidermal growth factor receptors [HER-2], Ki-67), fluorescence in situ hybridization (FISH) and molecular subtypes (luminal subtype) were obtained from electronic medical data, medical histories, or pathological data.

When assessing the size of the tumor, large nodes are represented as Tmax, and the second node as Tmin. In the case of detection of heterogeneity in the tumor nodes, hormonal and epidermal growth factor receptors were studied through IGH. Proliferative activity in the tumor nodes was determined by studying the Ki-67 protein.

Statistical analysis. Statistical data processing was performed using the DataTab online program. Descriptive statistics, t-test, chi square (x2) statistical tests were used.

RESULT

The average age of the women taken for the study was 48.8±9.6. Of the 133 patients, 89 (66.91%) were in the premenopausal period, 44 (33.1%) were in the postmenopausal period. Other characteristics of the breast cancer tumor are presented in Table 1.

Table 1

Comparative analysis of the histological characteristics of the tumor formation in multifocal and unifocal breast cancer

	MF	**MC**	**MF/MC**	**UF**	**p (MF-MS UF ga nisbatan)**
Number of patients n	17	48	65	68	
Age *n(%)* **50≥ n(%)** **50<**	 12(70.6) 5(29.4)	 26(54.1) 22(45.9)	 38(56.71) 27(41.53)	 38(55.8) 30(44.12)	0.324
T_{max} *n(%)* **T_1** **T_2** **T_3**	 7(41.12) 9(52.9) 1(5.88)	 7(14.6) 36(75) 5(10.41)	 14(21.53) 45(69.2) 6(9.2)	 27(39.7) 39(57.4) 2(2.94)	0.523
Tumor size (M±SD)	23.9±3.12	26.1±1.3	24.22±2.41	23.4±2.8	0.062
T_{min} *n(%)* **T_1** **T_2** **T_3**	 3(17.6) 10(58.8) 4(23.5)	 0 32(66.6) 16(33.3)	 3(4.61) 42(64.6) 20(30.7)	 - 	 -
O'sma hajmi (M±SD)	19.5±1.7	15.4±2.1	17.5±1.7	18.4±3.4	0.002
Lyph node status					

n(%)					
Positive	9(52.9)	32(66.6)	41(63.07)	32(47.07)	0.001
negative	8(47.1)	16(33.3)	24(36.9)	36(52.94)	
G grade *n(%)*					0.02
I	2(11.8)	4(8.33)	6(9.2)	6(8.82)	
II	3(17.6)	8(16.66)	11(16.9)	21(30.8)	
III	12(70.5)	36(75)	48(73.8)	41(60.3)	
Histological types					0.03
n(%)	17(100)	41(85.4)	58(89.2)	61(89.7)	
Ductal lobular	0(0)	1(2.08)	1(1.53)	0(0)	
Other	0(0)	6(12.5)	6(9.2)	7(10.29)	
Surgical treatment					0.001
n(%)	10(58.8)	41(85.4)	51(78.4)	53(77.9)	
Mastectomy	7(41.2)	7(14.6)	14(21.5)	15(22.05)	
Organ saved					

The results show that there is no statistically significant difference between the age of patients with multifocal and monofocal breast cancer (p-0.34). That is, the patient's age did not affect the tumor's growth characteristics. Although there are differences between the main tumor size groups T1, T2, T3, they are not statistically significant (p-0.523). The difference in lymph node involvement in multifocal and monofocal breast cancer is very significant (p-0.001). Statistically significant results were also obtained on the histological level of the tumor (p-0.02), histological type (p-0.03), and the performed surgical approach (p-0.001). This analysis shows the significance of each factor, taking into account such factors as the characteristics of the patients' tumors, lymph node damage, histological level and type, and type of operation. In the presence of statistically significant differences (p-values less than 0.05), this can affect the patient's treatment process or prognosis.

Conclusions of the IGH study for multifocal tumor MF and MS The results of the study on ER, PR status, Her2/neu expression, and Ki-67 protein are presented in the table below.

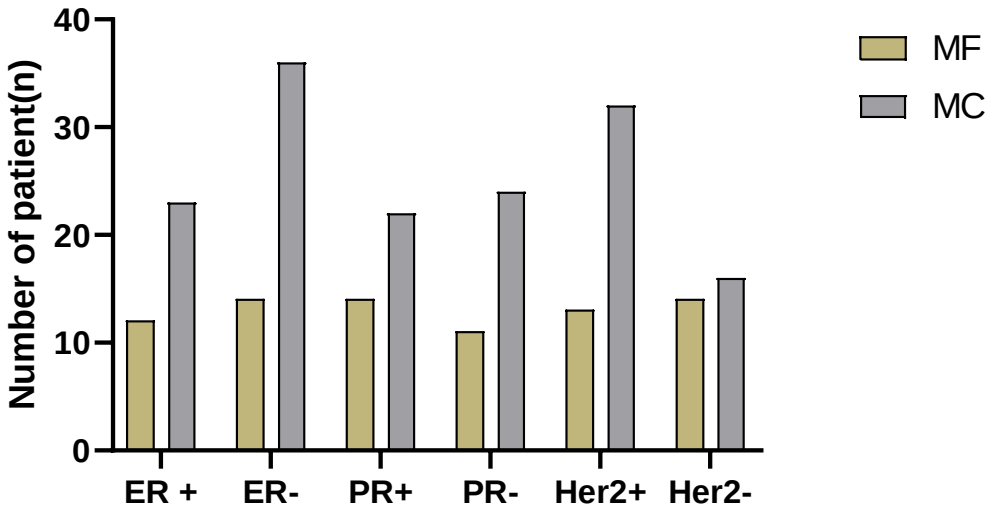

Figure 1. Receptor status in breast tumors MF and MC

ER+ was noted in 12 cases (70.6%) in the MF group, and ER+ in 23 cases (47.9%) in the MS group. It can be seen that ER+ patients prevailed in the MF group (p-0.01). This value makes the difference between ER+ and ER-patients statistically significant. Therefore, the presence of ER+ and ER- can be significant in the development of cancer - multifocal.

In the MF group, PR+ was positive in 14 (82.35%) patients, and in the MS group, PR+ was positive in 22 (45.8%) patients (p-0.062). The difference between PR+ and PR-patients is statistically insignificant, i.e., the influence of the PR receptor status on the multifocal development of the tumor is insignificant. The results for Her2/neu expression were statistically significant (p-0.019). This indicates that the epidermal growth factor plays an important role in the multifocal nature of cancer. In the MF group, 10 patients (58.8%) had Ki-67 ≥30, and in the MS group, 39 patients (81.25%) had Ki-67 <30. There is a significant difference between patients with a high Ki-67 index, which indicates the aggressiveness of the tumor (p-0.03).

CONCLUSION

Our study supports the hypothesis that MF/MS cancers are biologically more aggressive than monofocal tumors. This type of cancer has a high tendency to metastasize and predicts the unfavorable outcome of the disease.

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