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The effects of clinicopathological and imaging findings on recurrence and survival in mammary Paget's disease

Hakan Baysal,[1] Cem Ilgin Erol,[2] Begumhan Baysal,[3] Ibrahim Ali Ozemir,[1] Mehmet Sait Ozsoy,[1] Fatih Buyuker,[1] Gozde Kir,[4] Orhan Alimoglu[1]

[1]Department of General Surgery, Istanbul Medeniyet University, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Istanbul, Turkiye
[2]Department of General Surgery, Erzurum City Hospital, Erzurum, Turkiye
[3]Department of Radiology, Istanbul Medeniyet University, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Istanbul, Turkiye
[4]Department of Pathology, Istanbul Medeniyet University, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Istanbul, Turkiye

ABSTRACT

OBJECTIVE: Mammary Paget's disease (MPD) is a rare presentation type of breast cancer. The aim of this study was to evaluate the clinicopathological and imaging features affecting the invasive component, loco-regional recurrence, prognosis, and survival of MPD.

METHODS: Patients who had undergone surgery due to MPD in a 10-year period were included. Parameters including mammography and magnetic resonance imaging (MRI) findings, tumor stage, molecular subtype, axillary involvement, presence of invasive carcinoma, loco-regional recurrence, overall survival (OS), and disease-free survival (DFS) were recorded and statistically analyzed. P<0.05 was determined as statistically significant.

RESULTS: The study group consisted of 49 women with a mean age of 67.05±14.43 (range: 23–90) years. There was a significant association between the presence of invasive carcinoma and a mass lesion in the MRI (p=0.002). The frequency of sentinel lymph node (SLN) metastasis was significantly higher in patients with multicentric tumors (p=0.029; p<0.05). Locoregional recurrence and distant metastasis were significantly more frequent in patients with axillary involvement (p=0.0336; p<0.05). The mean DFS was 115.02±7.28 months, while the mean OS was 119.29±6.57 months.

CONCLUSION: The presence of a mass lesion on MRI was determined to be significant in recognizing invasive carcinoma in MPD. The rate of SLN metastasis was higher in patients with multicentric tumors than in patients with unifocal tumors. Axillary involvement was associated with impaired DFS.

Keywords: Breast neoplasms; local recurrence; pathology; radiology; survival.

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Mammary Paget's disease (MPD) is characterized by eczematous changes of the nipple-areolar complex (NAC), and there is an underlying ductal carcinoma *in situ* (DCIS) and/or invasive carcinoma in approximately 95% of the patients [1]. It is an uncommon type of breast carcinoma (1–3%), first described by Sir James Paget, who published the findings regarding the relationship between eruption on the nipple and breast carcinoma [2]. The lesions are usually unilateral, and 70–80% of the cases are detected in their post-menopausal period, with

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Correspondence: Hakan BAYSAL, MD. Istanbul Medeniyet Universitesi, Goztepe Prof. Dr. Suleyman Yalcin Sehir Hastanesi, Genel Cerrahi Klingi, Istanbul, Turkiye.
Tel: +90 216 566 40 00 e-mail: hakanbaysal_tr@yahoo.com

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the highest incidence in the seventh decade of life (mean age: 64 years) [3]. The clinical presentation includes symptoms of slow-onset skin changes in the nipple or areola, with or without a palpable mass in the breast [4]. Since MPD is generally treated as a benign dermatologic condition at the beginning, a delay may occur in the diagnosis and treatment. Imaging methods should be used in order to evaluate the NAC, assess the underlying invasive or noninvasive carcinoma, and determine the appropriate treatment plan in patients diagnosed with MPD.

In the setting of clinically and mammographically suspect diagnostic findings, magnetic resonance imaging (MRI) provides high sensitivity for the detection of an invasive carcinoma [5, 6]. MRI of the breast was proven to be effective in the detection of occult breast carcinoma of the NAC associated with MPD, even when there was no clinical suspicion [7, 8]. Multifocality and multicentricity were reported at the rates of 41% and 34% of the cases with MPD, respectively [9]. Ultrasound (USG) and mammography (MMG) are not as specific as MRI in detecting multifocal and/or multicentric diseases as they have some limitations. MRI may be beneficial in the detection of either unifocal lesions not involving the NAC or multifocal/multicentric lesions in the absence of a clinical sign or suspicious MMG findings.

The aim of this study was to evaluate the effectiveness of clinicopathological and imaging findings on invasive cancer detection, locoregional (LR) recurrence, and survival of MPD.

Highlight key points

- In Paget's disease of the mammary, a mass lesion on MRI was significant in recognizing invasive carcinoma.
- The rate of SLN metastasis was higher in patients with multicentric tumors compared to unifocal tumors.
- Axillary involvement is associated with less DFS.
- HER-2 group had the highest rate of locoregional recurrence.

MATERIALS AND METHODS

Surgically treated patients with MPD between 2011 and 2021 in the Department of General Surgery were investigated retrospectively. This study was approved by the Goztepe Prof. Dr. Suleyman Yalcin City Hospital Clinical Research Ethics Committee (date: July 29, 2020;-number: 2020/0473) and carried out in compliance with the Helsinki Declaration. Written informed consent was obtained from all participants.

All patients underwent physical examinations and routine screening methods in the outpatient clinics of the surgery and dermatology departments. A punch biopsy was performed for the lesions of the NAC, a tru-cut biopsy was performed for breast masses, and a fine needle biopsy was performed in cases with suspicion of clinical and radiological axillary lymph node involvement.

The study was conducted at a single center. Patients between 18 and 90 years of age with a pathology result confirming MPD were included in the study. Patients with distant metastases at the time of diagnosis, having received neoadjuvant chemotherapy (NAC), and having been diagnosed with other system malignancies were excluded.

Data including demographics, clinical and radiological findings, as well as pathological examination results were recorded. The primary tumor-regional lymph node-distant metastasis (TNM) staging system, nipple involvement alone, and association of DCIS and/or invasive carcinoma were used for clinical staging. All radiological MMG and MRI images were interpreted by an experienced consultant breast radiologist who was blind to the final pathology. All patients were operated on in terms of tumor resection and axillary assessment, the results of which were recorded. Pathological examination results, including the histopathological type of the tumor, hormone receptor status, human epidermal growth factor-2 (HER-2) overexpression, and the percentages of the Ki-67 proliferation index, were documented. The radiological findings, tumor subtypes, and Ki-67 scores were evaluated statistically regarding loco-regional recurrence. Pathology results, T stages, and tumor subtypes of the patients were compared regarding axillary involvement. In terms of pathological tumor subtypes, tumors with a profile of ER and/or PR(+)/HER2(-)/Ki67 ≤14% were classified as Luminal A, tumors with a profile of ER and/or PR(+)/HER2(+) or (-)/Ki67 >14% were classified as Luminal B, tumors with a profile of ER(-)/PR(-)/HER2(+) were classified as the HER-2 overexpressed type, and tumors with a profile of ER(-)/PR(-)/HER2(-) were classified as the triple-negative type of breast cancer.

The duration between surgery and recurrence or death was accepted as disease-free survival (DFS). The time period between the date of surgery and death by any cause was defined as overall survival (OS). The presence of distant metastases and mortality rates of the patients were compared. In addition, analyses for DFS and OS were carried out.

Table 1. Distribution of descriptive variables

Age	
Mean±SD	67.05±14.43
Median (Min–Max)	69 (23–90)
	n=49 (%)
Menopausal status	
Premenopausal	24.5
Postmenopausal	75.5
Tumor quadrant	
Single tumor focus	63.3
Multicentric tumor	36.7
T	
Tx	26.5
T1	28.6
T2	28.6
T3	8.2
T4	8.2
N	
No suspicious LN	75.5
Suspicious with USG/PET/MRI	16.3
Proven with biopsy	8.2
ER	
Mean±SD	52.61±45.87
Medyan (Min–Max)	70 (0–100)
ER intensity	
Absent	38.1
Weak	2.4
Moderate	4.8
Strong	54.8
PR	
Mean±SD	29.57±39.41
Median (Min–Max)	1 (0–100)
PR intensity	
Absent	51.2
Moderate	7.3
Strong	41.5
HER-2	
Negative	20.0
Positive	80.0
GRADE	
Grade 1	13.9
Grade 2	52.8
Grade 3	33.3
Ki-67 (n=33)	
Mean±SD	21.73±16.22
Median (Min–Max)	15 (2-60)
Ki-67 (n=33)	
<14%	45.5
>14%	54.5
Luminal A	
Absent	77.6
Present	22.4
Luminal B	
Absent	81.6
Present	18.4
Triple negative	
Absent	98.0
Present	2.0

SD: Standard deviation; Min: Minimum; Max: Maximum; USG: Ultrasound; ER: Estrogen receptor; PR: Progesteron receptor; HER-2: Human epidermal growth factor-2; US: Ultrasonography; PET: Positron emission tomography; MRI: Magnetic resonans imaging.

Statistical Analysis

The NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Kaysville, Utah, USA) program was used for statistical analysis. During the evaluation of the study data, descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, and maximum) were used. The conformity of the qualitative data to the normal distribution was evaluated with the Shapiro–Wilk test and graphical investigations. The Mann–Whitney U test was used for the intergroup comparisons of the qualitative variables without normal distribution. The Pearson Chi-square test, Fisher's exact test, and Fisher-Freeman-Halton test were used for the comparison of qualitative data. The statistical significance was evaluated at the level of $p<0.05$.

RESULTS

The study group consisted of 49 women with a mean age of 67.05±14.43 (range: 23–90) years. The clinical and radiological "T" and "N" stages of the patients at the time of diagnosis were evaluated and recorded (Table 1). All patients had undergone USG. In addition, MMG and MRI results could be assessed in 48 and 47 patients, respectively.

Clinical staging of the cases was documented (Table 2). Mastectomy, NAC excision, and breast-conserving

Table 2. Values related to descriptive characteristics

	n=49 (%)
Pathology	
Paget	4.1
DCIS, Paget	26.5
Invasive Paget	69.4
Clinical staging	
Lesion is confined to the epidermis without DCIS	6.1
Associated with DCIS just beneath the nipple	18.4
Associated with extensive DCIS	10.2
Associated with invasive ductal carcinoma	65.3
Surgery performed	
Breast conserving surgery	10.2
NAC excision	16.3
Mastectomy	73.5
Axilla	
Direct axillary dissection	42.9
SLN (+) + axillary dissection	6.1
SLN (-)	51.0
The number of (harvested) lymph nodes	
Median (Min–Max)	10 (0–29)
The number of involved lymph nodes	
Median (Min–Max)	0 (0–29)
Hormonotherapy (HT)	
Yes	71.4
DCIS	4
Invasive	31
No	28.6
Radiotherapy (RT)	
Yes	53.1
Paget	2
DCIS	4
Invasive	20
No	46.9
Chemotherapy (CT)	
Yes	57.1
Invasive	28
No	42.9

DCIS: Ductal carcinoma *in situ;* NAC: Nipple-areolar complex; SLN: Sentinel lymph node; Min: Minimum; Max: Maximum.

surgery (BCS) were performed in 36 (73.5%), 8 (16.3%), and 5 (10.2%) patients, respectively. Axillary dissection was performed in a total of 24 patients (49%), including three patients with a positive SLN. No other intervention was performed in a total of 25 patients with negative SLN biopsy results (51%) (Table 2).

Table 3. Distributions of loco-regional recurrence, distant metastasis, and mortality

	n=49 (%)	Paget	DCIS-Paget	Invasive-Paget
LR recurrence				
Absent	85.7	2	11	29
Present	14.3	0	2	5
Ipsilateral breast	2.0	0	1	0
Thorax wall	4.1	0	1	1
Axilla	8.2	0	0	4
Distant metastasis				
Present	14.3	0	0	7
Absent	85.7			
Mortality	12.2			
Breast cancer	6.1	0	0	3
Other	6.1	0	1	2

DCIS: Ductal carcinoma *in situ*.

LR recurrence was encountered in 7 (14.3%) patients during follow-ups. In addition, distant metastasis was found in 7 (14.3%) patients. Mortality took place in 6 (12.2%) patients, of whom 3 (6.1%) were due to breast carcinoma, 2 (6.1%) to myocardial infarction, and 1 (1.1%) due to Alzheimer's disease (Table 3).

According to the postoperative pathology results, 4.1% (n=2) of the cases were diagnosed with sole Paget's disease, while 26.5% (n=13) had DCIS-Paget's disease, and 69.4% (n=34) of the cases were diagnosed with invasive Paget's disease. The luminal A subtype was found in 22.4% of the patients (n=11), whereas 18.4% (n=9) had the luminal B subtype, and 2% (n=1) had triple-negative cancers according to the molecular subtypes (Table 1).

A significant relationship between the presence of a mass lesion and invasive carcinoma was detected according to MRI findings, as the rate of invasive carcinoma was significantly higher in patients with a mass lesion ($p=0.002$; $p<0.01$). However, there was no significant association between the presence of a mass lesion and the pathological N stage, Ki-67 values, disease recurrence status, or LR recurrence rates of the patients ($p>0.05$). In addition, there was a significant relationship between NAC enhancement on MRI and pathological N stage, where lower rates of pathological node positivity were found in patients with positive NAC enhancement ($p=0.038$; $p<0.05$). Neither NAC thickening nor NAC enhancement were associated with the radiological T stage, presence of invasive carcino-

Table 4. Evaluations according to MRI findings (n=47)

	MRI					
	NAC thickening		NAC enhancement		Mass Lesion	
	Absent	Present	Absent	Present	Absent	Present
Pathology						
Paget	0	5.6	0	6.7	9.1	0
Invasive carcinoma	72.7	66.7	70.6	66.7	45.5	88.0
DCIS	27.3	27.8	29.4	26.7	45.5	12.0
p	[b]**1.000**		[b]**0.762**		[b]**0.005****	
Pathological N (+)						
Negative	63.6	52.8	35.3	66.7	68.2	44.0
Positive	36.4	47.2	64.7	33.3	31.8	56.0
p	[b]**0.731**		[aa]**0.038***		[aa]**0.096**	
Ki-67 >%14						
<%14	75.0	37.5	40.0	50.0	25.0	60.0
>%14	25.0	62.5	60.0	50.0	75.0	40.0
p	**0.106**		[b]**0.712**		[aa]**0.055**	
Disease recurrence						
Yes	9.1	27.8	23.5	23.3	22.7	24.0
No	90.9	72.2	76.5	76.7	77.3	76.0
p	[b]**0.416**		[b]**1.000**		[aa]**0.918**	
LR recurrence						
Yes	0	19.4	17.6	13.3	13.6	16.0
No	100	80.6	82.4	86.7	86.4	84.0
p	[b]**0.175**		[b]**0.692**		[b]**1.000**	

aa: Pearson's Chi-squared test; b: Fisher's exact test; DCIS: Ductal carcinoma *in situ*; NAC: Nipple areola complex; LR: Locoregional; *: P<0.05; **: P<0.01.

ma, pathological N stage, Ki-67 values, disease recurrence status, or LR recurrence rates of the patients (p>0.05) (Table 4). MMG findings were not found to be significantly correlated with LR recurrence rates (p>0.05).

Although the number of patients with LR recurrence was higher in the HER-2 group, the difference was not statistically significant. Variables including the rates of the luminal A, luminal B, and triple-negative subtypes, the presence of invasive carcinoma, Ki-67 values, the type of surgery performed, and the T stage of the tumor were not found to pose any significant effects in the development of LR recurrence (p>0.05).

There was a significant difference in the axillary involvement of the patients according to the tumor quadrant groups (p=0.029; p<0.05). The rate of SLN positivity of the patients in the multicentric group was higher than that of the patients in the unifocal tumor group. The luminal A, luminal B, and triple-negative subtypes of the patients did not reveal any significant difference according to the tumor quadrant groups (p>0.05).

There was a significant relationship between the pathological axillary involvement and the radiological T stage of the patients (p=0.002; p<0.01). The axillary involvement rate was also higher in the presence of a radiological mass. There was a statistically significant relationship between axillary involvement and pathology (p=0.001; p<0.01). While the rate of axillary involvement was lower in patients with a pathological diagnosis of DCIS Paget, axillary involvement was determined to be higher in patients with a pathological diagnosis of invasive Paget's disease.

Axillary involvement was determined to be significantly higher in patients with either LR recurrence or distant metastasis (p=0.0336 and p=0.0336, respectively; p<0.05). Axillary involvement was not found to be

Table 5. Comparative data according to axillary involvement (n=49)

	Patients with axillary involvement		
	Absent	Present	p
Radiological T stage			[aa]0.003**
No mass	12 (92.3)	1 (7.7)	
Mass	15 (44.4)	21 (55.6)	
Pathology			[a]0.001**
Paget	2 (100)	0 (0)	
DCIS Paget	12 (92.3)	1 (7.7)	
Invasive Paget	13 (38.2)	21 (61.8)	
Luminal A			[b]0.169
Absent	24 (63.2)	14 (36.8)	
Present	4 (36.4)	7 (63.68)	
Luminal B			[b]0.470
Absent	24 (60.0)	16 (40.0)	
Present	4 (44.4)	5 (55.6)	
Triple (-)			[b]1.000
Absent	27 (56.3)	21 (43.8)	
Present	1 (100)	0 (0)	
LR recurrence			[b]0.033*
Yes	1 (14.3)	6 (85.7)	
No	27 (64.3)	15 (35.7)	
HER-2			[a]0.637
Negative	5 (83.3)	1 (16.7)	
Positive	16 (66.7)	8 (33.3)	
Distant metastasis			[b]0.033*
Yes	1 (14.3)	6 (85.7)	
No	27 (64.3)	15 (35.7)	
Mortality			[b]0.381
Absent	26 (60.5)	17 (39.5)	
Present	2 (33.3)	4 (66.7)	

a: Fisher-Freeman-Halton test; aa: Pearson Chi-squared test; b: Fisher's exact test; *: P<0.05; **: P<0.01.

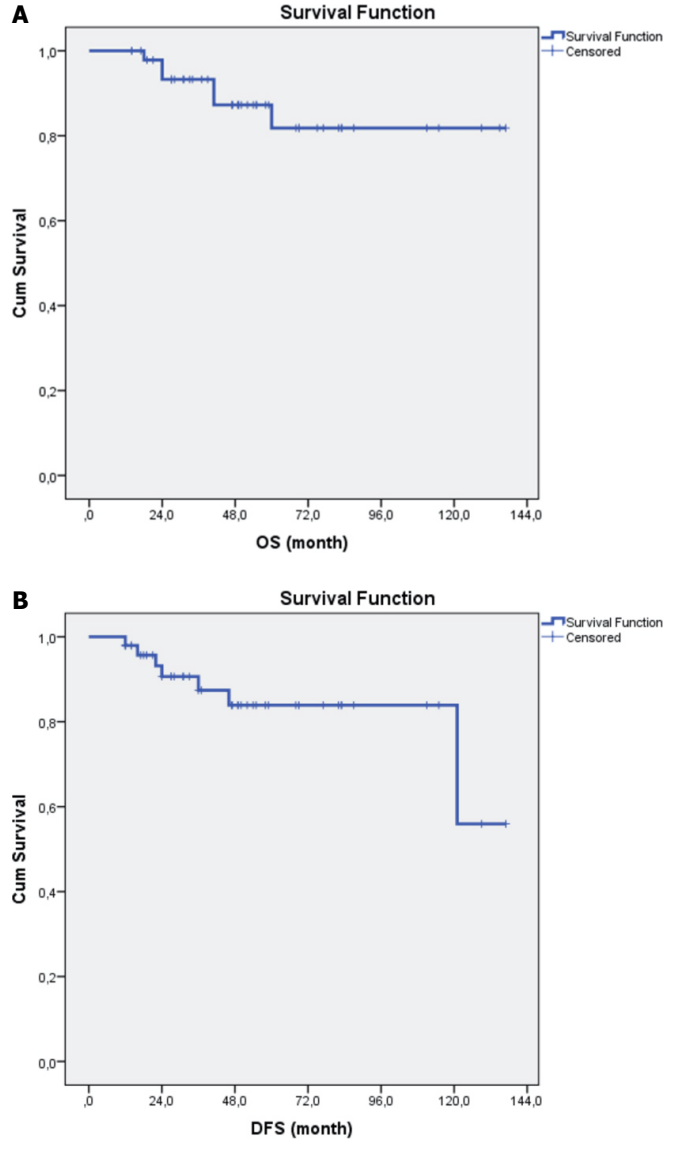

Figure 1. **(A)** Overall survival. **(B)** Disease-free survival.

associated with other variables, including the luminal A, luminal B, and triple negative subtypes, HER-2 positivity, and mortality rates of the patients (p>0.05) (Table 5).

Mortality took place in six (12.25%) patients among the total study group of 49 patients who had undergone breast surgery. The mean OS was calculated as 119.29±6.57 months, with a median of 83 months. The last death was observed in the 134th postoperative month and the cumulative survival rate in this month was 81.87% with a standard deviation of 7.2% (Fig. 1A).

Among the 13 patients with DCIS, only one (7.69%) patient died, and the OS in this subgroup of patients was 125.7±8.85 months. Among the 34 patients with invasive carcinoma, 5 (14.71%) deaths were observed, and the mean OS in this subgroup was 113.3±10.1 months. It was observed that 27 (87.1%) patients with a single tumor focus were alive as 4 (%) deaths were encountered, whereas 16 (88.9%) patients with multicentric tumors were alive as 2 (%) deaths took place.

While recurrence was not determined in 42 (85.71%) surgically treated cases, 7 (14.29%) recurrences were detected. The mean DFS was calculated as 115.02±7.28 months, with a median of 68.5 months. The last recurrence was observed in the 121st month, where the cumulative DFS rate in this month was 55.9%, with a standard deviation of 2.32% (Fig. 1B).

DISCUSSION

Since there is generally an underlying DCIS, invasive carcinoma, or a combination of these in MPD, it is necessary to get some tests performed to determine the possible malignancy and to be able to evaluate the optimal treatment plan in all patients with clinically suspected or biopsy-proven MPD [10]. Due to the possibility of multricentricity in patients reported to have non-invasive carcinoma or Paget's disease, it is important to evaluate the entire breast when a subareolar tumor is found on physical examination [11]. MMG can detect the underlying disease in 50–71% of patients [5]. However, MMG findings, including the NAC, may not always be pathognomonic for MPD. In addition, the extent of the disease may be underestimated by MMG in up to 43% of cases [9]. While invasive disease is determined in 90–94% of patients presenting with a palpable mass, patients without a clinical mass have rather noninvasive disease, and 60–68% of them have DCIS alone [12]. Also in our series, invasive carcinoma was determined in 20 (95%) of 21 patients with a clinically palpable mass. DCIS was detected in 13 (50%) of 26 patients without a clinically palpable mass. Since MMG has some limitations in the evaluation of patients with Paget's disease, MRI should be performed to facilitate further surgical treatment planning [5]. MRI can distinguish the abnormal nipple and tumors confined to the retroareolar tissue from the tumors including the NAC. Even though it is not suspected clinically, MRI can show nipple involvement [13, 14]. In cases of MPD, the underlying carcinoma may not take place just under the NAC; it can take place at a distant site without a clear connection. MRI may be beneficial in determining distant, multifocal, or multicentric lesions when there is no clinical sign or a suspicious mammographic finding. In our series, 18 (36%) patients had multicentric lesions. However, asymmetrical abnormal enlargement of the nipple or the NAC is not always pathognomonic for MPD because this finding can be seen in other conditions such as the elongation of the nipple adenoma or breast neoplasms toward the nipple [15]. From another point of view, false-positive results were also reported on breast MRIs performed in order to evaluate the NAC in cases assessed for MPD [16].

Moon et al. [17] demonstrated NAC enhancement in all lesions with MPD as either partial or complete enhancement. While NAC enhancement and an increase in NAC thickness were significantly correlated with malignant invasion of the NAC, the authors found that maximum tumor size, tumor multiplicity, or pattern of the malignant mass were not correlated with malignant NAC invasion. It was reported that there was no significant correlation between malignant NAC involvement and the pattern of the malignant mass.

In our study, we compared the thickening and contrast enhancement of the NAC, the presence of a mass lesion on MRI with radiological T stage, pathology results, pathological node positivity, Ki-67>14 scores, and the findings of LR recurrence. There was a significant relationship between the presence of a mass lesion and the radiological T stage ($p<0.01$). The rate of invasive carcinoma was higher in cases with a mass lesion as well ($p<0.01$). However, the pathological node positivity rate with positive NAC enhancement was low ($p<0.05$). We determined no significant correlation of the NAC thickness and enhancement with T stage, presence of invasive carcinoma, or LR recurrence rates in our study group ($p>0.05$). A surgical approach was the preferred treatment option for MPD cases. Commonly used treatment methods for MPD include simple mastectomy, modified radical mastectomy, breast-conserving surgery (BCS), and NAC excision, depending on whether Paget's disease of the breast is associated with ductal carcinoma or not, the histological type of ductal carcinoma, and the axillary lymph node status. DCIS is higher in cases without ductal carcinoma, while axillary lymph node metastasis is rare in these patients. Therefore, SLN biopsy or axillary lymph node dissection is recommended in the management of axillary lymph nodes according to the extent of lymph node involvement [18, 19]. We performed mastectomies on 36 patients (73.5%), NAC excision, and BCS on 13 patients (26.5%). Our axillary lymph node management was as follows: axillary dissection (3 cases with a positive SLN biopsy) was performed in a total of 24 patients (49%), while the axilla was preserved due to negative SLN biopsies in 25 patients (51%).

The distribution of postoperative pathology results was as follows: 2 (4.1%) patients with Paget's disease alone, 13 (26.5%) patients with DCIS-Paget, and 34 (69.4%) patients with invasive Paget's disease. Axillary involvement was detected in one (7.7%) patient with DCIS and in 21 (61.8%) patients with invasive carcinoma. A significant relationship was found between axillary involvement and the radiological T stage ($p<0.01$). While the statistically significant relationship between axillary involvement and pathology was low in patients with DCIS, the rate was found to be significantly higher in patients with invasive carcinoma ($p<0.01$). There was a significant difference among the tumor quadrant groups in terms of axillary

involvement ($p<0.05$). The rate of SLN metastasis in patients in the multicentric tumor group was determined to be higher than the rate of SLN metastasis in patients in the group with a unifocal tumor.

While the HER-2 positivity rate of MPD was higher than that of breast carcinoma without Paget's disease, the ER and PR positivity rates of MPD were lower than that of breast carcinoma without Paget's disease [20–22]. In our study, while the ER and PR positivity rates of MPD were lower, the positivity of patients who had HER-2 investigations was determined to be higher.

Overall and DFS periods in MPD can be prolonged with selected comprehensive care. Local treatment for early breast carcinomas will help lower the probability of LR recurrence and distant metastasis and thus prolong survival. However, invasive recurrences were reported to occur following surgery in some studies [23, 24].

Dalberg et al. [4] concluded that the type of surgery had no impact on DFS in their patients followed up for 25 years. Two risk factors determined by the authors for recurrence or death were concomitant invasive carcinoma and the presence of a palpable mass.

In the present study, the mean DFS of our 49 patients was 115.02+7.28 months, with a median of 68.5 months. We determined LR recurrence in 7 patients. When we investigated the tumor subtypes of these patients, six of them were positive for HER-2 overexpression ($p>0.05$). We consider that this issue may be due to our limited sample size. Axillary involvement was significantly more frequent in patients with LR recurrence ($p<0.05$). Although there are few studies in the literature showing the relationship between axillary involvement and LR recurrence in MPD, Han et al. [22] stated that axillary involvement negatively affected DFS. We did not determine any significant correlation between tumor subtypes, Ki-67 scores, and the presence of invasive carcinoma with LR recurrence.

Axillary involvement was also significantly correlated with the development of distant metastasis ($p<0.05$). Song et al. [19] reported the onset time of LR recurrence to be an average of 51 months and the time for the development of distant metastasis to be an average of 62 months. In our study, we determined these periods to be earlier at 39.4 and 42 months, respectively. Kar et al. [25] found the OS for patients with MPD to be 58±9.5 months (95% CI: 39.2–76.7). While 43 of our patients (87.8%) were alive, six of them died during follow-ups. Three of these six patients died due to breast carcinoma, two of them due to myocardial infarction, and one died due to Alzheimer's disease. The mean OS was 119.29±6.57 months, with a median of 83 months.

The limitations of this study may be considered as its relatively small sample size despite MPD being a rare entity, its retrospective design, and the lack of managing all patients with standardized imaging protocols. Another limitation of the study was having the patients received radiotherapy in different centers and the lack of standardization of hormone therapy and chemotherapy regimens during the postoperative long-term follow-up period. A distinctive characteristic of the study is the comparison of MRI findings and loco-regional recurrences of the patients one by one with different tumor pathologies and subtypes. In addition, this is a study in which pathology types and quadrant involvements are compared one by one to be able to evaluate axillary management in MPD. The management of LR recurrence and the favorable impact of this management on survival can be determined with prospective studies that will be conducted with larger sample sizes.

Conclusions

Since MPD is a rare disorder, some uncertainties remain about the treatment and patient management. In our study, the presence of a mass on an MRI was found to be significant in terms of recognizing invasive carcinoma. HER-2 positivity was determined to be the most significant among all groups regarding LR recurrence. Axillary involvement was significantly more frequent in patients who further developed LR recurrence and distant metastasis. Currently, while the necessity of the SLN biopsy procedure in MPD and breast carcinomas are discussed, SLN positivity was found to be significantly higher in patients with multicentric MPD.

Ethics Committee Approval: The Goztepe Prof. Dr. Suleyman Yalcin City Hospital Clinical Research Ethics Committee granted approval for this study (date: 29.09.2020, number: 2020/0473).

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