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Clinicopathological Analysis of 117 Female Patients Diagnosed with Pure Mucinous Breast Cancer

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ABSTRACT

Background: Pure mucinous breast carcinoma (PMBC), a rare subtype defined by >90% extracellular mucin, generally has a favorable prognosis. This study investigated the clinicopathological parameters of PMBC to better understand its tumor biology and clinical outcomes.

Methods: In this descriptive study, we analyzed the clinicopathological parameters of 117 female patients diagnosed with PMBC.

Results: The mean patient age was 53.1 years; 54.7% were postmenopausal. Most tumors were pT2 (53.4%), with metastatic lymph nodes in 27.7% of patients. The lung and bone were the most common sites of distant metastasis. Common treatments included surgery, endocrine therapy (89.7%), and radiotherapy (60%). Higher Ki-67 levels were associated with chemotherapy use (P=.005). Tumors were predominantly estrogen receptor–positive (90.5%), progesterone receptor–positive (79.3%), and HER2-negative (89%). Molecular subtyping, though limited by missing data, identified most tumors as luminal A or B.

Conclusion: PMBC is a rare cancer of older women, typically presenting as hormone receptor-positive, HER2-negative tumors with low rates of nodal metastasis. Despite its indolent nature, metastasis to the lung and bone can occur. Surgical resection followed by endocrine and radiation therapy remains the standard approach. The role of multigene assays in guiding systemic therapy for PMBC requires further investigation.

INTRODUCTION

Mucinous breast cancer (MBC) is a rare entity that accounts for 1% to 4% of all breast cancers.[1] MBC is characterized by the presence of extracellular mucin and is classified by mucin content. MBC is classified as mixed mucinous breast carcinoma when the mucin content is more than 10% but less than 90%, and pure mucinous breast carcinoma (PMBC) is diagnosed when extracellular mucin comprises more than 90% of the tumor.[2] MBC can be further classified as type A (paucicellular) vs type B (hypercellular) based on neuroendocrine features.[3]

PMBC is usually diagnosed in older peri- or postmenopausal women, and imaging findings can be nondiagnostic. Mammography identifies PMBC as a well-circumscribed lesion that is isoechoic to the fat tissue of the breast on ultrasonography; these results can be misinterpreted and may cause a delay in diagnosis.[4,5] However, in contrast to other solid tumors, a delay in the diagnosis of PMBC may not cause adverse outcomes.[6] On magnetic resonance imaging, PMBC has a very specific, gradually

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enhancing contrast pattern with a very high signal intensity on T2-weighted images.[7] By definition, PMBC is a cluster of tumor cells with a low to intermediate nuclear grade suspended in pools of mucin where the mucin content is greater than 90%.[10]

Molecular aberrations seen in estrogen receptor (ER)-positive, progesterone receptor (PR)-positive, human epidermal growth factor receptor 2 (HER2)-negative invasive ductal carcinoma of the breast, such as 1q gains and 16q losses, are not typically seen in MBC.[11,12] PMBC is usually associated with hormone receptor positivity (ER and PR) and HER2 negativity, and lymph node involvement is uncommon.[8,9] PMBC has a favorable prognosis, with the most significant prognostic predictor being nodal status.[10,13] A more recent variant of PMBC with micropapillary features has been recognized, which reveals more aggressive behavior with higher rates of lymph node metastasis and lower overall and recurrence-free survival rates.[14,15]

The most common treatment strategy for MBC is surgical resection, followed by adjuvant hormonal therapy for hormone receptor–positive tumors.[16] In HER2-positive tumors, combined chemotherapy and anti-HER2 therapies have been associated with a low risk of recurrence.[17]Additionally, the Ki-67 proliferation marker may further help in the decision to undergo chemotherapy.[18,19] Multiple multigene assays analyzing tumor genomic profiles or molecular biomarkers have also been designed to assess prognosis and guide systemic therapy choices in ER-positive/HER2-negative early-stage breast cancer, including the Oncotype DX (21-gene recurrence score), MammaPrint (70-gene signature), and PAM50; however, data on the application of these tests in PMBC and MBC remain scarce.[20-22]

This study aims to analyze the clinicopathological characteristics of PMBC in a Turkish cohort and explore correlations with treatment and outcomes.

METHODS

This descriptive study identified female patients diagnosed with PMBC from the MKA Breast Cancer Clinic Database of more than 8000 patients with breast cancer. This study was approved by the Ethics Committee of Ankara City Hospital #1, Ankara, Turkey (ethics code E1-23-3571), and complies with the Declaration of Helsinki.

One hundred seventeen female patients with breast cancer who were diagnosed with PMBC were identified from this database, and their corresponding molecular characteristics, including ER, PR, and HER2 tumor status as per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines, were collected. Age at diagnosis, location of the involved breast, tumor size, pathological TNM stage, treatment modalities, status of distant metastasis, and recurrence were also included. Clinical electronic medical records, pathology reports, and progress notes were reviewed to gather patient demographic information and longitudinal follow-up data.

A histoscore (H-score) was applied for immunohistochemical (IHC) marker scoring by multiplying the percentage of positive staining tumor cells (1% to 100%) by the intensity of the staining (0, 1+, 2+, 3+). The intensity 0 is considered none; 1+, weak; 2+, moderate; and 3+, intense. A marker is considered positive if the H-score is 1% or greater for ER and PR. For HER2, negative staining is considered when there is no staining or less than 10% membranous staining (0) or faint/weak incomplete membranous staining in 10% or greater of tumor cells (1+). HER2 positivity is defined by 2 criteria: the presence of strong, complete membranous staining in 10% or greater of tumor cells (3+), or moderate, complete membranous staining in 10% or greater of tumor cells (2+) accompanied by a positive HER2 fluorescence in situ hybridization (FISH) result.

All cases with known ER, PR, HER2, and Ki-67 status were subtyped based on the 2013 St Gallen guidelines.[22] Molecular categorization was performed by the following guidelines: luminal A (ER-positive, PR-positive, and HER2-negative), luminal B HER2-negative (ER-positive, HER2-negative, and at least one of the following: Ki-67 of 14% or greater, PR-negative, or PR-low [<20%]), luminal B HER2-positive (ER-positive, HER2-positive, any Ki-67, any PR), HER2 overexpression (ER-negative, PR-negative, HER2-positive), and triple-negative/basal-like (ER-negative, PR-negative, HER2-negative).

In this study, the conformity of continuous variables to normal distribution was tested using the Shapiro-Wilk test. Continuous variables were summarized using the mean, median, and range, while categorical variables were expressed as frequency counts and percentages. Independent comparisons between 2 groups were conducted using the Mann-Whitney U test. Independent comparisons among multiple groups were performed using the Kruskal-Wallis test. For post hoc comparisons, the Dunn-Bonferroni test was used. The Spearman correlation test was conducted to compare 2 continuous variables. Statistical analyses were performed using SPSS software (IBM SPSS Statistics for Windows, version 21.0; IBM Corp), and a P value of < 0.05 was considered statistically significant.

RESULTS

A total of 117 female patients diagnosed with pure mucinous carcinoma of the breast were

identified from the MKA Breast Cancer Clinic database. The patient demographics (Table 1), clinical parameters (Table 2), and pathological characteristics (Table 3) of these tumors are detailed. The mean time to disease-free survival was 60.3 months (SD, 56.5; interquartile range, 37 months), and the mean time from diagnosis to death was 88.2 months (SD, 29.4; interquartile range, 15 months), with a mean follow-up time of 58.1 months. The mean patient age was 53.1 years (range, 23–89 years). Also, 47 patients (40.2%) were premenopausal, 6 (5.1%) were perimenopausal, and 64 (54.7%) were postmenopausal. The tumors were mainly located on the left side (n=66, 56.4%). Seventeen patients (14.5%) had multifocal disease.

Table 1. Patient demographics

Characteristic	Patients (N=117), No. (%)
Age, mean (SD), y	53.1 (15.0) (range, 23-89)
Menopausal status	
Premenopausal	47 (40.2)
Perimenopausal	6 (5.1)
Postmenopausal	64 (54.7)
OCP use[a]	
None	95 (81.9)
Yes, mean (SD), mo	21 (18.1) (18.9)
HRT use[a]	
None	96 (82.8)
Yes, mean (SD), mo	20 (17.2) (39.3)

OCP, oral contraceptive pill; HRT, hormone replacement therapy
[a]Data missing for 1 patient.

The mean tumor size in this cohort was 3.27 cm (SD, 2.32). A smaller tumor size was associated with fewer metastatic lymph nodes ($r = 0.26$; $P = 0.009$). A smaller tumor size was associated with a higher usage of hormone replacement therapy ($r = -0.22$; $P = 0.02$).A significant association was found between tumor size and recurrence status ($H = 6.34$; $P = 0.04$); as a result of the Dunn-Bonferroni test performed for post hoc analysis, a difference was found between the distant recurrence and nonrecurrence groups, and the mean of the nonrecurrence group was lower ($Z = -25.33$; $P = 0.01$).

The association between tumor size and multifocality status ($Z = -1.97$; $P = 0.048$) suggests that patients with multifocality tend to have larger tumors. A statistically significant relationship was found between treatment and tumor size ($H = 9.61$; $P = 0.008$), as determined by the Dunn-Bonferroni test, with a significant difference observed between the adjuvant and metastatic groups, where the adjuvant group had a lower mean ($Z = -36.34$; $P = 0.009$).

Table 2. Clinical Parameters

Characteristic	Patients (N=117), No. (%)
Time to disease-free survival, mean (SD), mo	60.3 (56.5)
Time from diagnosis to death, mean (SD), mo	88.2 (29.4)
Follow-up time, mean, mo	58.1
Tumor location	
Right	50 (42.7)
Left	66 (56.4)
Bilateral	1 (0.9)
Nodal statusa	
SLND	42 (37.5)
Axillary dissection	59 (52.7)
Recurrence	
Absent	104 (88.8)
Local	1 (0.9)
Distant	12 (10.3)
Distant metastasis	
Absent	101 (86.3)
Liver	1 (0.9)
Bone	4 (3.3)
Lung	3 (2.5)
Liver and spleen	1 (0.9)
Lung and brain	1 (0.9)
Lung and pleura	1 (0.9)
Bone, lung, and liver	2 (1.6)
Bone, lung, pleura, and brain	1 (0.9)
Bone, lung, pleura, liver, and diaphragm	1 (0.9)
Bone, lung, and liver	1 (0.9)

SLND, sentinel lymph node dissection

A significant association was found between lymph node (LN) stage and recurrence status ($\chi^2 = 13.41$; $P = 0.038$). Analysis showed that 92.6% of patients with stage N0 disease had no recurrence, compared with 81.8% of those with stage N1. A strong association was also observed between LN stage and distant metastasis ($\chi^2 = 78.02$; $P = 0.003$). Furthermore, the rate of patients with no recurrence inversely correlated with advancing LN stage: 91.4% for N0, 72.7% for N1, 71.4% for N2, and 50.0% for N3. A statistically significant negative correlation was found between tumor size and ER staining percentage ($r = -0.23$; $P = 0.02$).

Forty-two patients (37.5%) underwent sentinel lymph node dissection (SLND) and 59 (52.7%) underwent axillary lymph node dissection. Recurrence was seen in 13 patients (11.2%) during follow-up, of whom 1 (0.9%) had local recurrence and 12 (10.3%) had distant recurrence. Most of the patients (101 of 117 [86.3%]) did not have metastasis. Of the remaining patients with metastasis (n=16, 13.7%), 9 had bone and 10 had lung metastasis, suggesting that the lung and bone are the most common distant metastatic sites.

Table 3. Pathological Parameters

Characteristic	Patients, No. (%)
Tumor size, mean (SD), cm[a]	3.27 (2.32)
T stage[b]	
T1	36 (31.0)
T2	62 (53.4)
T3	17 (14.7)
T4	1 (0.9)
N stage[c]	
N0	81 (72.3)
N1	22 (19.6)
N2	7 (6.3)
N3	2 (1.8)
Multifocality	
Absent	100 (85.5)
Present	17 (14.5)

[a]Data missing for 3 patients.
[b]Data missing for 1 patient.
[c]Data missing for 5 patients.

Table 4. Treatment Characteristics

Characteristic	Patients, No. (%)
Treatment modalities	
Neoadjuvant	7 (6.0)
Adjuvant	103 (88.0)
Metastatic	7 (6.0)
Treatment type (other than surgery)	
Radiotherapy[a]	69 (60.0)
Chemotherapy[b]	46 (39.3)
Endocrine therapy	105 (89.7)
Surgical procedure[c]	
MRM	47 (44.3)
SM	15 (14.2)
BCS	44 (41.5)

BCS, breast-conserving surgery; MRM, modified radical mastectomy; SM, simple mastectomy.
[a]Data missing for 2 patients.
[b]Data missing for 3 patients.
[c]Data missing for 11 patients.

The relationship between distant metastasis and LN stage was evaluated, and a significant association was found ($\chi^2 = 78.02$; $P = 0.003$); in patients with a higher LN stage, distant metastasis was seen more often. In patients with distant recurrence, the most common distant metastasis locations were the lung (16.7%) and lung, liver, and bone (16.7%). A significant relationship was found between HER2 status and distant metastasis ($P = 0.04$, Fisher exact test), with HER2 being positive in 10.6% (10 of 101) of the patients without distant metastasis and 31.3% (5 of 16) in those with distant metastasis; however, no correlation was observed with the site of metastasis.

All patients with a known surgical history (106 [90.6%]) underwent an R0 surgical resection. Other treatments that they received are detailed in Table 4. The relationship between therapy type and the receipt of radiotherapy was evaluated, and a significant association was found: 55.4% of those who received adjuvant therapy, 100% of those with neoadjuvant therapy, and 85.7% of those with metastatic therapy also received radiotherapy ($\chi^2 = 7.40$; $P = 0.03$).

3A significant association was found between recurrence status and receiving chemotherapy: 75% of patients with distant recurrence received chemotherapy ($\chi^2 = 8.05$; $P = 0.007$). A significant association was also found between lymph node stage and receiving chemotherapy: 29.1% of patients with N0, 64.7% with N1, 71.4% with N2, and 100% with N3 disease received chemotherapy ($\chi^2 = 15.55$; $P = 0.001$).

A significant association was found between tumor stage and receipt of chemotherapy: 25.7% of patients with T1, 41.7% with T2, 56.3% with T3, and 100% with T4 disease received chemotherapy ($\chi^2 = 7.37$; $P = 0.04$) (Table 5). A significant association was found between lymph node stage and receiving endocrine therapy: 93.8% of patients with N0, 81.8% with N1, 85.7% with N2, and 50% with N3 disease received endocrine therapy ($\chi^2 = 6.95$; $P = 0.048$). Ki-67 levels were higher in patients who received chemotherapy ($Z = -2.81$; $P = 0.005$).

Pathological prognostic markers for breast cancer in this cohort are detailed in Table 6. Three of 5 patients (60%) with HER2 FISH–positive results had HER2 IHC scores of 2+, and 2 of 5 (40%) had HER2 IHC scores of 3+. A total of 15 cases were analyzed as HER2 status positive (n=12, 3+ and n=3, 2+ with FISH-positive). All 6 patients with negative HER2 FISH results had a HER2 IHC 2+ score. Ki-67 status was available in 45 of 117 patients (38.5%). Molecular subtyping was limited by unknown HER2 status (7 of 117 [5.9%]) and Ki-67 status (72 of 117 [61.5%]). Of 117 patients, a total of 38 with known ER, PR, HER2, and Ki-67 status were subtyped as per the 2013 St Gallen Consensus guidelines[20] (Figure 1 and Supplementary Table 1). Of these 38 patients, 17 (44.7%) were classified as luminal A, 2 (5.3%) as luminal B (HER2-positive), and 19 (50%) as luminal B (HER2-negative). A demonstrative pathological section from case 11 is presented in Figure 2.

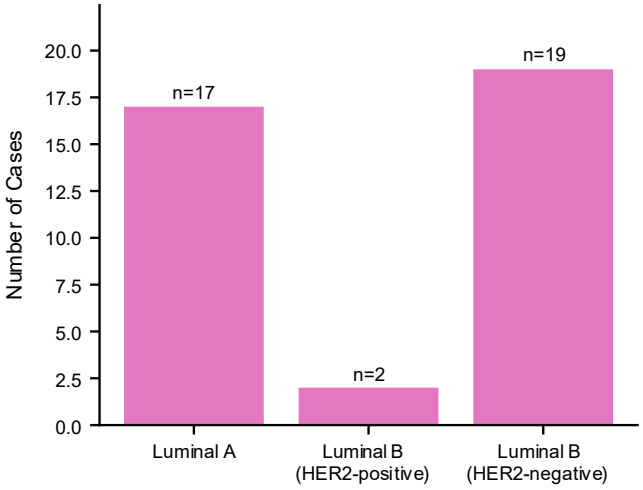

Figure 1. Molecular Subtyping of Tumors. A total of 38 cases with known estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 (HER2), and Ki-67 status were subtyped. Of these, 17 (44.7%) were classified as luminal A, 2 (5.3%) as luminal B (HER2-positive), and 19 (50%) as luminal B (HER2-negative).

Table 6. Pathological Prognostic Parameters

Characteristic	Patients, No. (%)
ER status[a]	
Positive	105 (90.5)
Negative	11 (9.5)
PR status[a]	
Positive	92 (79.3)
Negative	24 (20.7)
HER2 IHC[b]	
0	84 (76.3)
1+	3 (2.7)
2+	11 (10.0)
3+	12 (11.0)
HER2 FISH[c]	
Positive	5 (45.5)
Negative	6 (54.5)
ER statusa	
Positive	105 (90.5)
Negative	11 (9.5)

ER, estrogen receptor; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemical; PR, progesterone receptor. [a]Data missing for 1 patient. [b]Data missing for 7 patients. [c]Not performed for 106 patients.

Table 5. Treatment by T and N Stage

	T stage, %				*P* value	N stage, %				*P* value
	T1	T2	T3	T4		N0	N1	N2	N3	
Endocrine therapy	32.4	53.3	13.3	1.0	0.22	93.8	81.8	85.7	50	0.048
Chemotherapy	25.7	41.7	56.3	100	0.04	29.1	64.7	71.4	100	0.001

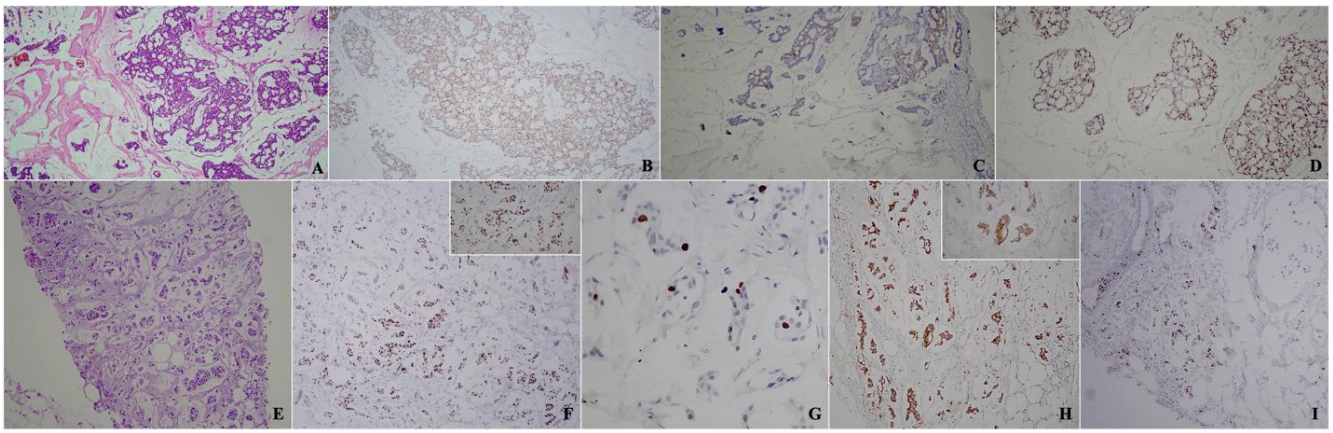

Figure 2. Example of Pure Mucinous Breast Carcinoma (PMBC) With Corresponding Stains. Histologic images from case 1 (A-D) and case 19 (E-I). **A,** Tumor cells in extracellular mucin (hematoxylin-eosin, original magnification ×400). **B,** Tumor cells were 95% strongly positive for estrogen receptor (original magnification ×40). **C,** Tumor cells were 70% strongly positive for progesterone receptor (original magnification ×400). **D,** Ten percent of the tumor cells showed staining for Ki-67 (original magnification ×400). **E,** Tumor cells in extracellular mucin (hematoxylin-eosin, original magnification ×400). **F,** Tumor cells were 90% strongly positive for estrogen receptor (original magnification ×40; inset, original magnification ×400). **G,** Tumor cells were 60% strongly positive for progesterone receptor (original magnification ×400). **H,** Tumor cells were positive (3+) for human epidermal growth factor receptor 2 (HER2) (original magnification ×40; inset, original magnification ×400). **I,** Fifteen percent of the tumor cells showed staining for Ki-67 (original magnification ×400).

DISCUSSION

The mean age in our cohort was 53.1 years. Patients in this study were mostly postmenopausal (54.7%), similar to other studies in the literature[8,9,22]; however, a significant number of patients in our study (40.2%) were also premenopausal. Komenaka *et al.*[23] reported that PMBC cases in their cohort were predominantly right-sided; however, in our study, PMBC tumors were more often on the left side (56.4%). In our study, the mean tumor size was 3.27 cm, with a range of 0.2 to 10.2 cm. Additionally, larger tumor sizes have been reported in the literature[24]; the reason behind undiagnosed large-sized tumors may be the significant mucin content of these tumors, which causes fewer solid components and results in nonpalpable lesions during physical examination. Several studies have shown no significant difference in tumor size between MBC and invasive ductal carcinoma,[25,27] but mixed mucinous breast carcinoma may present in larger sizes compared with PMBC.[10,13] Di Saverio *et al.*[2] reported that tumor size is one of the prognostic factors but is less significant than nodal status and age, while based on the findings of Komenaka *et al.*,[23] tumor size may not be considered a prognostic factor. In the era of digital pathology and artificial intelligence, identifying the size of mucin content and separating it from the total size diagnosed via radiology using these advanced tools may lead to a more precise determination of tumor size. In this study, tumor size showed a positive correlation with both relapse and multifocality. However, because our cohort was not categorized based on mucin content and PMBC was analyzed as a single category, we were unable to assess tumor size differences in relation to mucin content.

Although there are some contradictions in tumor size, studies in the literature agree that nodal status is the most important prognostic factor for [13,16]MBC.[25,26] and that mixed mucinous breast carcinoma is strongly associated with the presence of lymph node metastasis with poor prognosis and lower overall survival compared with PMBC.[27,28] Emiroglu *et al.*[29] reported that lymph node metastasis usually occurs in patients younger than 50 years ($P = 0.01$) and that patients 50 years or older are more likely to receive chemotherapy or radiotherapy ($P = 0.002$). In our study, the most common stage was T2 (53.4%); 27.7% of the patients had metastatic lymph nodes, and 37.5% received SLND, while axillary dissection was performed in 52.7% of the patients. A randomized clinical trial revealed that in patients with T1 or T2 invasive breast cancers without palpable axillary adenopathy and 1 or 2 metastatic sentinel lymph nodes, axillary dissection may not be necessary, as the 10-year overall survival for this group of patients treated with SLND was noninferior to the rate in the patients treated with axillary dissection.[30] Because PMBC does not usually invade lymph nodes, axillary lymph node staging by resection may not be necessary.[27,31] In our study, although survival analysis was not performed, a significant association was found between LN stage and distant metastasis status ($\chi^2 = 78.02$; $P = 0.003$). A significant association was also found between LN stage and recurrence ($\chi^2 = 13.41$; $P = 0.038$). Among patients with lymph node metastasis, the average disease-free survival was 55.26 months.

In our study, patients most commonly underwent modified radical mastectomy (44.3%) or breast-conserving surgery (41.5%), and 88.8% received adjuvant therapy. Anan *et al.*[32] recommended that breast-conserving surgery is suitable for patients with PMBC when it is not invading the skin. Another study suggested a treatment modality with adjuvant radiotherapy and endocrine therapy after breast-conserving surgery and sentinel lymph node biopsy for mucinous carcinoma.[33] Only 17 (13.3%) of 128 cases of mucinous breast cancer received chemotherapy, and 48 (37.5%) received radiotherapy in the study by Wu *et al.*[19] However, 60% of the patients in our cohort received radiotherapy, 39.3% received chemotherapy, and almost all (89.7%) received endocrine therapy. Park *et al.*[34] reported that treatment with adjuvant chemotherapy may not need to be utilized in patients with MBC with favorable risk factors. In addition, several studies have suggested that the Ki-67 proliferation marker may further help in the decision to undergo chemotherapy[18].[18,1919] Also, for the objective of assessing prognosis and guiding systemic therapy choices in ER-positive/HER2-negative early-stage breast cancer, multiple multigene assays analyzing tumor genomic profiles or molecular biomarkers have been designed, including the Oncotype DX (21-gene recurrence score), MammaPrint (70-gene signature), and PAM50; however, data on the application of these tests in PMBC and mixed mucinous breast carcinoma remain scarce. We were not able to perform a comparative analysis with recent publications, as our study did not have access to data regarding these tests in our patient cohort.

Our results showed that 90.5% of PMBCs were positive for ER and 79.3% for PR. These findings align with other studies stating that PMBC is often ER- and PR-positive[2,9,35], suggesting that these tumors are mostly hormone receptor–positive. In our cohort, HER2 positivity was seen in a total of 15 cases (12.8%) (n=12 HER2 IHC 3+; n=3 HER2 IHC 2+, HER2 FISH–positive). Although it is not a common practice to perform HER2 FISH testing in 3+ IHC cases, we performed HER2 FISH in two 3+ IHC cases

at the patients' request. Of 38 molecularly subtyped cases, the most common type seen in our cohort was luminal B (HER2-negative) (50%).

Studies show that PMBC has an excellent overall and disease-free survival[2,23,31] and has a better prognosis than mixed mucinous breast carcinoma[36]; however, some studies suggest that the favorable prognosis of PMBC is temporary and tends to recur after 10 years[2] and late distant metastasis may occur.[37] Komenaka *et al.*[23] reported 5-year and 10-year disease-specific survival rates of 95.3% and 79.4% for PMBC, respectively. According to our results, PMBC tends to involve the bones when it metastasizes compared with other organs. These results indicate that despite the indolent behavior of PMBC, it is crucial to clinically follow up patients with PMBC for an extended period.

The primary limitation of our study was its retrospective, single-center design involving 117 patients with PMBC, which accounts for approximately 1.46% of more than 8000 patients with breast cancer in the private MKA Breast Cancer Clinic Database. Additionally, studies from Korea and China showed that PMBC is predominant in Asian populations.[26,40] These results contradict those reported in the study by Barkley *et al.*,[33] in which 90% of their cohort consisted of white patients. Although there was a predominance of white patients (43%) in the study by Sood et al.,1 race was not a significant predictor of recurrence-free survival.1 Unfortunately, we could not explore the diversity of PMBC, as our data only consisted of PMBC cases in a Turkish cohort. Another major limitation in our study was that molecular subtyping was limited by the unknown HER2 status (n=7) and Ki-67 status (n=72). The clinicopathologic and genetic heterogeneity of PMBC has been recognized. Although we could not perform any molecular tests, some studies in the literature show promising results. For example, Yim et al.3 performed whole-exome sequencing in 8 PMBC cases and reported that *HYDIN* (88%) was the most frequent somatic mutation, followed by *IGSF3* (38%); however, these were not pathognomonic for PMBC. Alternatively, Pareja *et al.* [11] suggested that *GATA3*, *KMT2C*, and *MAP3K1* were frequently mutated in PMBC. Despite these limitations, our study provides unique insights while supporting the existing knowledge in the literature.

CONCLUSION

In conclusion, PMBC is a rare entity typically diagnosed in older women. Tumors present in a wide variety of sizes, are usually hormone receptor–positive, have low expression of HER2, have low rates of nodal and distant metastasis, and have high overall and disease-free survival rates. Our results show that although it is rare, PMBC tends to metastasize to the lung and bone compared with other organs. Breast-conserving surgery and modified radical mastectomy are the most common choices of surgery for PMBC. Administration of radiotherapy and endocrine therapy following surgery is preferred. The use of adjuvant chemotherapy requires a comprehensive investigation of favorable risk factors and Ki-67 status. Finally, prospective studies with larger cohorts may help provide a better understanding of the tumor biology of this rare disease.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ETHICAL CONSIDERATIONS

This study was approved by the Ethics Committee of Ankara City Hospital #1, Ankara, Turkey (ethics code E1-23-3571), and was carried out according to the ethical principles of the Declaration of Helsinki, ensuring patient privacy and confidentiality.

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DATA AVAILABILITY

The data supporting this study's findings are available on request from the corresponding author. However, due to privacy or ethical restrictions, the data are not publicly available.

AI DISCLOSURE

AI tools were used only for language editing. The authors take full responsibility for the content.

AUTHOR CONTRIBUTIONS

KA: Conceptualization, Methodology, Investigation, Writing – Review & Editing; GG: Conceptualization, Methodology, Investigation, Writing – Review & Editing; SIS: Methodology, Investigation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing; YK: Investigation, Formal Analysis, Writing – Review & Editing; SS: Formal Analysis, Writing – Original Draft, Writing – Review & Editing.

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