# Palliative surgery for giant mucinous carcinoma of the breast in an elderly patient: A rare case report

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Abstract. Mucinous breast carcinoma (MBC) is relatively rare, accounting for <10% of all breast cancers in women. These tumors are usually slow-growing and exhibit less aggressive characteristics compared with other types of breast cancer. Between 1989 and 2016, 55 patients underwent surgery for MBC at the Shiga Medical Center for Adults (Moriyama, Japan). The 10-year disease-free survival (DFS) and overall survival rates were 94.5 and 100.0%, respectively. Specifically, the 10-year DFS rates of pure MBC (PMBC) and mixed MBC were 97.7 and 83.3%, respectively. We herein report the case of a sizeable mucinous carcinoma causing rupture of the skin and bleeding due to tumor pressure. Palliative surgery was performed in order to remove the bleeding source after a total of 5 months of preoperative endocrine-based therapy. In conclusion, palliative surgery improved the patient's quality of life and may be a viable option for PMBC patients. The aim of the present study was to review the characteristics and management of these tumors, particularly in elderly patients.

# Introduction

Mucinous breast carcinoma (MBC) of the breast is a special type of breast cancer that is characterized by the presence of carcinoma cells surrounded by large amounts of extracellular mucin (1). MBC may be encountered in all age groups, and the median age at presentation is 50-57 years (2-4). MBC comprises approximately <10% of all invasive breast cancers. This type of tumor has an overall better prognosis and a

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Abbreviations: MBC, mucinous breast carcinoma; PMBC, pure type mucinous breast carcinoma; MMBC, mixed type mucinous breast carcinoma; IDC, invasive ductal carcinoma; OS, overall survival; DFS, disease-free survival

*Key words:* breast cancer, mucinous carcinoma, palliative surgery, elderly

higher incidence among peri- and post-menopausal patients. Pathologically, there are two main subtypes of MBC, namely pure type MBC (PMBC) and mixed type MBC (MMBC) (1). PMBC in particular is known to have a favorable prognosis compared with invasive ductal carcinoma (IDC) (4-9). We herein report a case of a giant MBC causing rupture of the skin and bleeding due to tumor pressure, and review the characteristics and palliative management of these tumors, particularly in elderly patients.

# **Case report**

A 81-year-old Japanese woman presented to the outpatient clinic of the Department of Breast Surgery of the Shiga Medical Center for Adults (Moriyama, Japan) in January 2016 with a history of rapid enlargement of a right breast mass. The patient had noticed a mass 10 years prior. There was no family history of breast cancer. On physical examination, a large nodular mass was identified, measuring 18x15 cm, involving the entire right breast (Fig. 1A). There were also palpable right axillary lymph nodes, with the largest measuring 4x3 cm. The left breast was normal. A computed tomography (CT) scan revealed a large heterogeneous solid mass with axillary lymph node metastases (Fig. 1B); however, there was no evidence of distant metastasis.

PMBC with axillary lymph nodes metastases was diagnosed by core needle biopsy and fine-needle aspiration cytology. The patient received letrozole endocrine therapy as a primary systemic therapy, as she declined surgery. Soon after endocrine therapy initiation, the patient visited our emergency room due to continuous bleeding from lacerated skin caused by tumor pressure. The patient was found to be anemic (red blood cells  $2.98 \times 10^{12}/\mu$ l, hemoglobin 8.4 g/dl), due to tumor neovascularization and intratumoral bleeding.

Laboratory data revealed marked elevation of the serum tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen 15-3 (CA15-3) to 175.1 ng/ml and 196.0 U/ml, respectively.

After 4 months, the tumor had increased in size, and the patient was started on exemestane and tegafur plus uracil (UFT<sup>®</sup>; Taiho Pharma, Tokyo, Japan), as the tumor was considered difficult to control by endocrine therapy alone. The patient's advanced age was taken into consideration when selecting a chemotherapy regimen, in order to preserve her quality of life (QOL). A large clinical trial of UFT-based



Figure 1. (A) On physical examination, the patient presented with a large nodular mass, measuring 18x15 cm, with severe disfigurement of the right breast. The contralateral breast was normal. (B) A computed tomography scan revealed a heterogeneous solid mass and lymph nodes metastases.



Figure 2. Pathological results of the postoperative specimen. (A) The excised mass was sized 18x15 cm. (B) Histological analysis of the surgical specimen. The diagnosis of pure type mucinous breast carcinoma was made using hematoxylin and eosin staining (left panel: Magnification, x100; right panel: Magnification, x400).

postoperative chemotherapy conducted in Japan (NSASBC-01 trial) demonstrated that UFT is useful for the treatment of intermediate-risk patients (10). At 4 weeks after the patient was started on second-line therapy, there was no significant reduction in the breast tumor. Finally, the patient consented to receive simple mastectomy. Despite the lymph node metastases, the axillary nodes were not removed, as this was

a palliative surgery aiming to remove the bleeding source. The main purpose of the treatment for this patient was not to completely remove the macroscopically visible tumor, but maintain the patient's QOL and avoid breast cancer-related death. The surgically resected tumor was 1.96 kg in weight and 17.8 cm in diameter (Fig. 2A). The surgical margin of the breast was clear, but metastatic lymph nodes remained in the

axilla. On histological analysis, the tumor was classified as a PMBC with mucinous differentiation in the histologically high-grade intraductal component, as determined by the accumulation of intraductal mucin (Fig. 2B).

The patient's anemia subsided after the bleeding source was removed (red blood cells  $4.14 \times 10^{12}/\mu$ l, hemoglobin 12.5 g/dl). In addition, the tumor marker levels significantly decreased (CEA from 175.1 to 13.6 ng/ml, and CA15-3 from 196.0 U/ml to 32.7 U/ml) following mastectomy (Fig. 3). The patient remained well without evidence of distant metastasis after the surgery and, despite the metastatic axillary lymph nodes, lymphedema or neuropathy of the right arm has not appeared thus far (last follow-up, May 2017). The patient provided consent regarding the publication of the case details and associated images.

The medical records of 55 MBC patients were retrospectively reviewed. Between 1989 and 2016, all the patients who underwent breast surgery at the Shiga Medical Center for Adults were investigated and  $\chi^2$  tests were used to analyze qualitative data. Overall survival (OS) was defined as the period from the date of diagnosis to the date of the last follow-up or death from any cause, and disease-free survival (DFS) was defined as the period from the date of diagnosis to occurrence of any event, such as disease progression, relapse, recurrence or death. Kaplan-Meier estimates were used to calculate OS and DFS using Stat Mate V for Win & Mac Hybrid software (ATMS, Tokyo, Japan).

#### Discussion

MBC represents 1-7% of all breast cancers (1,3,4) and is classified by the World Health Organization into two subtypes: i) PMBC if the non-mucinous component is <10% and ii) MMBC if the non-mucinous component comprises 10-49% of the tumor. PMBC may be subtyped into a hypocellular variant (PMBC-A), exhibiting a tubular, cribriform, cord-like, micropapillary or papillary growth pattern, and a hypercellular variant (PMBC-B), growing in solid nests (1). It is generally accepted that PMBC has a favorable prognosis compared with IDC (2-9).

MMBC is mainly associated with lobular or ductal neoplasia (*in situ* or invasive), and a proportion of these tumors exhibit neuroendocrine differentiation. However, a specific percentage has not been clearly established for the diagnosis of MMBC. Due to the distinct clinicopathological characteristics of PMBC and MMBC, there may be a prognostic difference between the two types.

Locally advanced MBC is relatively rare. However, it was previously reported that there is no correlation between tumor size or subtype and prognosis in PMBC-A or PMBC-B. However, MMBC is known to have a prognosis similar to that of IDC. It has also been reported that breast-conserving surgery is effective for MBC due to their low local recurrence rate (3,7,11).

In order to select the optimal therapy in rare cases, such as elderly patients with locally advanced MBC, our experience with this disease and the previous related literature was reviewed.

Between 1989 and 2016, 55 patients underwent breast surgery for mucinous carcinoma at the Shiga Medical Center for Adults. The mean patient age was 63 years (range, 37-85 years). Following surgery, the patients received thera-



Figure 3. Tumor marker levels before and after treatment. TM, tumor marker; CEA, carcinoembryonic antigen; CA15-3, carbohydrate antigen 15-3.



Figure 4. Kaplan-Meier estimates of (A) DFS and (B) OS of MBC patients. DFS, disease-free survival; OS, overall survival; MBC, mucinous breast carcinoma; PMBC, pure type MBC; MMBC, mixed type MBC.

pies administered according to the National Comprehensive Cancer Network guidelines, version 1.2015 (12).

Prior to 2,000, selective estrogen receptor modulator (SERM) therapy was selected for pre- and post-menopausal patients with estrogen receptor (ER)-or progesterone receptor (PgR)-positive cancer. Endocrine therapy was mainly administered for 2 years. However, in patients with high risk of recurrence, such as node-positive patients or those with tumors sized >5 cm, 5-year endocrine therapy with 2 years of UFT was used prior to 1995, after which time 5-year hormonal therapy became the standard. Since 2000, aromatase inhibitors were used in post-menopausal hormonal receptor (HR) -positive patients for 5 years after surgery. Intravenous chemotherapy was administered in HR-negative patients and highly node-positive patients.

The 10-year DFS and OS were 94.5 and 100.0%, respectively (Fig. 4). The 10-year DFS of PMBC and MMBC was 97.7 and 83.3%, respectively. The clinicopathological characteristics are summarized in Table I. Statistically significant

# Table I. Clinicopathological variables of patients with mucinous breast carcinoma (n=55).

Variables	MBC, no. (%)	
	PMBC (n=43)	MMBC (n=12)
Age (years, mean ± SD)	59.19±14.12	59.25±15.24
Tumor size (mm, mean $\pm$ SD)	26.97±28.70	32.00±19.64
Number of positive LN (mean $\pm$ SD)	0.22±0.58	$1.25 \pm 3.14$
Sex		
Female	42 (97.7)	12 (100.0)
Male	1 (2.3)	0 (0.0)
Axillary LN status		
Negative	36 (83.7)	8 (66.7)
Positive	6 (14.0)	4 (33.3)
Unknown	1 (2.3)	0 (0.0)
TNM stage		
I	19 (44.2)	4 (33.3)
II	22 (51.2)	6 (50.0)
III	2 (4.6)	2 (16.7)
ER status		
Positive	27 (62.8)	9 (75.0)
Negative	6 (14.0)	1 (8.3)
Unknown	10 (23.2)	2 (16.7)
PoR status		
Positive	22 (51 2)	7 (58 3)
Negative	11 (25.6)	3 (25.0)
Unknown	10 (23.2)	2 (16.7)
HER2 status		
Positive	1 (2 3)	1 (8 3)
Negative	18(419)	7 (58 3)
Unknown	24 (55 8)	4 (33 4)
Vi 67 avpragion 04	21 (0010)	(0011)
~20	16 (37.2)	5 (41 7)
>20	2(47)	0(00)
Unknown	25 (58 1)	7 (58 3)
Droost surroum	25 (50.1)	7 (50.5)
Mastastomy	10 (44 2)	7 (58 2)
Breast conserving	19(44.2) 24(55.8)	5(41.7)
	24 (55.8)	5 (41.7)
Axillary surgery	11 (25 ()	2 (25.0)
Avillary lymph node dispertion	11(25.6)	3 (25.0)
No avillary surgery	28 (03.1) 4 (0.3)	3(00.7)
	4 (9.3)	1 (8.3)
Chemotherapy	22 (74.4)	7 (59.2)
No	32 (74.4)	7 (58.3)
ies Lietzeur	8 (18.0) 2 (7.0)	4 (33.4)
	5 (7.0)	1 (8.5)
Radiotherapy		
No	18 (41.8)	6 (50.0)
res	23 (53.5)	2 (16.7)
UNKNOWN	2 (4.7)	4 (33.3)
Anti-HER2 target therapy		
No	42 (97.7)	11 (91.7)
Yes	1 (2.3)	1 (8.3)

### Table I. Continued.

Variables	MBC, no. (%)	
	PMBC (n=43)	MMBC (n=12)
Endocrine therapy		
No	11 (25.6)	2 (16.7)
Yes	29 (67.4)	9 (75.0)
Unknown	3 (7.0)	1 (8.3)
Arm lymphedema		
No	39 (90.7)	12 (100.0)
Yes	1 (2.3)	0 (0.0)
Unknown	3 (7.0)	0 (0.0)

MBC, mucinous breast carcinoma; PMBC, pure type MBC; MMBC, mixed type MBC; SD, standard deviation; LN, lymph node; TNM, tumor-node-metastasis; ER, estrogen receptor; PgR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

differences were not observed between the characteristics of PMBC and MMBC. Of note, a male patient was included in the data. Although male MBC is rare, it has been previously reported (13-15).

Of the 55 patients, 3 developed recurrence. One patient had stage I, ER<sup>+</sup>/PgR<sup>+</sup>/HER2<sup>-</sup> PMBC, and developed intramammary local recurrence 2 years and 7 months after breast-conserving surgery, followed by bone metastases at 8 years and 9 months after the operation. Second-line letrozole with zoledronic acid were continued, and the patient maintained stable disease at the last follow-up visit (May 2017). The remaining 2 patients experienced lung metastases: One patient had stage I ER+/PgR-/HER2- MMBC, and developed multiple lung metastases 5 years and 4 months after the surgery. At the last follow-up visit (June 2017) the patient had progressive disease, controlled by 8th-line weekly paclitaxel. The second patient had stage IIIA (pt3n1M0) ER+/PgR+/HER2- MMBC, and developed lung and parasternal lymph node metastases 2 years and 2 months after the surgery. Surprisingly, at the last follow-up visit (May 2017) the patient had achieved clinically complete response by multidisciplinary therapy.

One of the PMBC patients suffered from arm lymphedema following axillary lymph node dissection. In the data presented herein, the incidence rate of patients who underwent axillary lymph node dissection was 2.8%, which is relatively lower compared with previous reports (5.3-54.0%) (14,16,17). The incidence rate of postoperative complications such as pain, lymphedema, numbness or motility disorders differs between sentinel node biopsy and axillary lymph node dissection (16,17). It has been reported that chemotherapy with taxanes and radiation covering the breast and supraclavicular region were independent risk factors for lymphedema (18,19). Generally, MBC is potentially resistant to chemotherapy or radiotherapy (1,2,4). The combination of chemotherapy and radiation therapy with axillary dissection is infrequently selected, even in locally advanced MBC, and we recommend that it is avoided.

Consistent with previous reports, the postoperative recurrence rate was higher in MMBC compared with PMBC (5,7-9). Since distant metastasis is rare, particularly in PMBC, some reports observed no association between tumor size (2,5,8) or lymph node status (8) and prognosis. It is considered that relapse develops after a long-term disease-free period, indicating that elderly PMBC patients do not always require aggressive chemotherapy or radical surgery. Even in patients with axillary lymph node metastasis, it may be considered a viable option to obtain sufficient symptom improvement by palliative rather than radical surgery.

If axillary lymph node status is not correlated with prognosis in PMBC, the main purpose of axillary surgery is staging and dissection may be omitted.

As in the present case, axillary lymph node dissection is not always considered necessary, as there was no complaint of arm edema or pain due to tumor pressure, and the patient continues systemic therapy after surgery. The patient's severe anemia improved immediately after the removal of the main tumor. Given the characteristics of PMBC, it is less likely to lead to immediate tumor-related death, and the possibility of arm edema due to direct vascular invasion from axillary lymph nodes is low.

In conclusion, palliative surgery may be a viable option, particularly for elderly patients with locally advanced PMBC, in order to maintain their QOL.

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