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ORIGINAL ARTICLE

Pure Mucinous Carcinoma of the Breast: a Clinicopathologic Analysis with 56 Patients

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Key words: breast cancer; pure mucinous breast carcinoma; lymph node status

Objective To assess recent trends and prognostic features in the treatment of pure mucinous carcinoma (PMC) of the breast.

Methods Fifty-six patients diagnosed with PMC of the breast in our hospital from December 1982 to June 2008 were included. We evaluated the general information and tumor characteristics of the patients, examined the relationship between these factors and prognosis. Fisher's exact test was applied to analyze tumor characteristics.

Results The mean age of the patients was 53.7 years. The majority of the patients presented with early stage disease. Tumor size was found not a significant prognostic factor in this study. Mean follow-up period was 39 months and no breast cancer-related deaths were identified in the patient cohort.

Conclusions PMC of the breast has a favorable prognosis. Tumor size does not appear to significantly impact survival.

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MUCINOUS carcinoma of the breast was first described in 1826, but it was and remained one of the uncommon pathological categories in breast cancer.^{1,2} It accounts for 1-4% of all breast cancers and is associated with a better prognosis than infiltrative ductal carcinoma.^{3,4} Mucinous carcinoma of the breast is further divided into pure and mixed subgroups according to the quantification of tumor cellularity. The pure type consists exclusively of tumor tissue with extra-

cellular mucin production, while the mixed type also contains other components without mucin.^{5,6} Pure mucinous carcinoma (PMC) of the breast is rare and considered to display indolent behavior. In the present study, we retrospectively reviewed the medical records of patients with pathologically proved PMC of the breast in our hospital, in order to assess the recent trends and prognostic features in the treatment of this disease.

PATIENTS AND METHODS

Patients

A retrospective review was performed with patients pre-

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senting with PMC of the breast between December 1982 and June 2008 in Peking Union Medical College Hospital. Only those with a pathological diagnosis of PMC of the breast were included. We reviewed the patients' medical records and evaluated the clinical characteristics, surgical treatment, tumor size and pathological grade, presence of hormone receptor, lymph node status, and the use of adjuvant chemotherapy, endocrine therapy, or radiotherapy.

Statistical analysis

Fisher's exact test was used to compare tumor characteristics. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using the SSPS15.0 statistical software.

RESULTS

We reviewed the medical records of 3 386 women with breast cancers diagnosed between December 1982 and June 2008 in our hospital. Among those patients, a total of 56 (1.65%) were recognized as having PMC. Patient information and tumor characteristics are listed in Table 1.

The mean age of the included patients was 53.7 ± 13.3 years (range, 26-82 years). The laterality of the lesions was right-sided in 30 (53.6%) patients and left-sided in 26 (46.4%). Twenty-four patients underwent fine needle aspiration before operation and 10 (41.6%) of them had positive results.

The mean tumor size was 2.6 cm in diameter (range, 0.3-6.5 cm). Forty-eight patients underwent modified radical mastectomy and 1 patient had mastectomy with immediate reconstruction (49/56, 88%); only 3 patients received breast-conserving therapy with adjuvant radiotherapy (3/56, 5%); 4 patients underwent lumpectomy without radiotherapy (4/56, 7%). Of the last group, 1 underwent lumpectomy with axillary node dissection and the other 3 just received lumpectomy. Fifty-three patients (95%) received axillary node dissection, of which 7 (13%) had positive results. The remaining 3 patients did not have axillary node dissection because of advanced age or significant comorbidities.

Forty-four patients had complete record of pathological stage. Histological section of carcinoma breast shows clusters of malignant cells floating in mucus pool (Fig. 1A). The majority of those 44 patients (40, 90.9%) presented with early stage disease, of which 15 (34.1%) were at stage I and 25 (56.8%) were at stage II. Only 4 (9.1%) patients were diagnosed at stage III and none at stage IV.

The mean diameter was taken as the cutoff point. The

tumor size was over the average level in 21 patients, among whom 4 showed lymph node metastasis; the tumor size was below the average level in 23 patients, in which 2 had lymph node metastasis. However, no significant association was found between tumor size and lymph node metastasis ($P > 0.05$) (Table 2).

Table 1. Patient information and tumor characteristics ($n=56$)

Characteristic	Value
Age (yr), mean (range)	53.7 (26-82)
Tumor size (cm), mean (range)	2.6 (0.3-6.5)
Tumor stage, n (%)	
T1	17 (30)
T2	26 (46)
T3	5 (9)
T4	0 (0)
Unknown	8 (14)
Lymph node status, n (%)	
Positive	7 (13)
Negative	46 (84)
Unevaluated	3 (4)
Pathological stage, n (%)	
I	15 (27)
II	25 (45)
III	4 (7)
Unknown	12 (21)
ER detection, n (%)	
Positive	24 (43)
Negative	13 (23)
Unknown	19 (34)
PR detection, n (%)	
Positive	23 (41)
Negative	14 (25)
Unknown	19 (34)
HER-2/neu receptor detection, n (%)	
Positive	2 (4)
Negative	27 (48)
Unknown	27 (48)
Primary treatment, n (%)	
Mastectomy	49 (88)
Lumpectomy with radiotherapy	3 (5)
Lumpectomy without radiotherapy	4 (7)
Systemic therapy, n (%)	
Endocrine therapy alone	10 (18)
Chemotherapy alone	17 (30)
Chemotherapy + endocrine therapy	10 (18)
None	19 (34)
Follow-up time (mon), mean (range)	39 (1-240)

ER: estrogen receptor; PR: progesterone receptor.

Table 2. Tumor size and lymph node metastasis

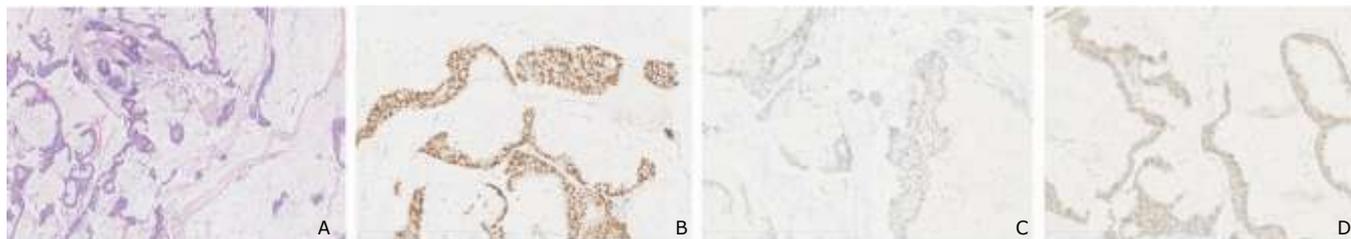
Tumor size	Lymph node metastasis		Total
	+	-	
T>2.6 cm	4	17	21
T<2.6 cm	2	21	23
Total	6	38	44

$\chi^2=0.314$, $P=0.576$ in continuity correction.

Thirty-seven patients had immunohistochemistry test for estrogen and progesterone receptors. The results were positive in 64.9% (24/37) and 62.2% (23/37) of tumors,

respectively. Twenty-nine patients had immunohistochemistry test for estrogen and HER-2 receptors, in which only 2 (6.9%) had positive results in HER-2 receptor detection (Fig. 1).

Mean follow-up time was 39 (range, 1-240) months. Three patients had distant recurrence. No known deaths related to breast cancer were identified in the studied patients. Among the four groups receiving different systemic therapies, no significant difference was found with Fisher's exact test in terms of age and tumor size ($P>0.05$) (Table 3).

**Figure 1.** Pathological findings of pure mucinous carcinoma.

A. Histological section of carcinoma showing clusters of malignant cells floating in mucus pool. HE $\times 60$

B. Immunohistochemical staining for estrogen receptor revealing nuclear staining in mucinous carcinoma. Envision $\times 400$

C. Immunohistochemical staining for progesterone receptor revealing nuclear staining in mucinous carcinoma. Envision $\times 400$

D. Immunohistochemical staining for HER-2 receptor revealing cell membrane staining in mucinous carcinoma. Envision $\times 400$

Table 3. Systemic therapy performed in the patients[§]

Systemic therapy	Age (yr)	Tumor size (cm)	Positive lymph node	Metastasis	Follow-up time (mon)
Endocrine therapy alone	60.0 \pm 14.3	1.79 \pm 1.26	0	0	44.9 \pm 54.3
Chemotherapy alone	50.1 \pm 11.4	3.06 \pm 1.51	4	0	25.8 \pm 26.1
Chemotherapy + endocrine therapy	51.5 \pm 13.5	2.90 \pm 1.84	1	1	39.0 \pm 30.1
None	54.8 \pm 13.8	2.38 \pm 1.03	2	2	45.5 \pm 65.8

§: Plus-minus values are means \pm SD.

DISCUSSION

PMC of the breast is rare. Altogether 3 386 women were diagnosed as breast cancers in our hospital between December 1982 and June 2008, and 56 of them had PMC (1.65%), which falls just within the range of 1% to 4% commonly reported in literature.^{6,7} Previous studies showed that PMC of the breast was often found in elderly women and only 1% of PMC patients were less than 35 years.^{8,9} But in the present study, 4 patients (7.1%) were under 35 years and 8 (14.2%) were under 40 years. The youngest patient was 26 years old at diagnosis. Although the sample size was small in this study, it might suggest an increase in incidence of PMC among young population.

The size of pure mucinous breast cancer at diagnosis varies widely, and the mean size in the present study was

2.6 cm. The relatively slow growth of pure mucinous breast cancer may allow diagnosis at a small size.⁶ The prognostic significance of tumor size is an especially interesting point with PMC of the breast. The statistical analysis in this study, however, did not find significant association between size and axillary lymph node metastasis. This finding should not be surprising because mucin constituted a majority of the tumor volume. Therefore, the tumor could grow to a large size without impacting survival of the patient.¹⁰⁻¹²

Of the 44 patients with complete record of pathological stage, the majority (40/44, 91%) presented at stage I or II, supporting the previous hypothesis that this disease displays indolent behavior. Modified radical mastectomy was the most frequently used surgical operation (49, 87.5%) in this study. Just as tumor size, the extent of surgery also may not significantly influence survival. Adjuvant radiotherapy and endocrine therapy after breast-conserving

therapy for mucinous cancer has become common.

Recent literature reported a high percentage of hormone receptor expression, a high rate of positive results for estrogen and progesterone receptors.¹⁰ The present study is roughly in agreement with that statement. It suggests that most patients could take endocrine therapy after surgery.

The prognosis of PMC of the breast is favorable, with good overall and disease-specific survival.¹⁰ A large retrospective comparative study showed that PMC of the breast had less aggressive behavior compared to infiltrative ductal carcinoma, and the favorable outcome still remained after 20 years.⁶ In this study the mean follow-up was 39 months and no known deaths related to breast cancer were identified in the studied patients. Three patients had distant recurrence at a mean recurrence time of 48 months, again supporting the hypothesis that pure mucinous cancers are indolent, which take longer time to recur than other invasive cancers of the breast. It may explain the fact that we have not yet observed many late recurrences.

In conclusion, PMC of the breast has a favorable prognosis. Tumor size does not appear to significantly impact survival, perhaps because the large volume of mucin may lead to overestimation of tumor burden.

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