Original Article

Sonographic presentations of metaplastic breast cancers

Yi-Chen Lai\textsuperscript{a,b}, Chih-Yi Hsu\textsuperscript{b,c}, Yi-Hong Chou\textsuperscript{a,b}, Chui-Mei Tiu\textsuperscript{a,b,d,e}, Ling-Ming Tseng\textsuperscript{d,e}, Hsin-Kai Wang\textsuperscript{a,b}, Hong-Jen Chiou\textsuperscript{a,b}

\textsuperscript{a} Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
\textsuperscript{b} National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC
\textsuperscript{c} Department of Pathology and Laboratory Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
\textsuperscript{d} Department of Radiology, Lotung Poh-Ai Hospital, Lotung, Ilan, Taiwan, ROC
\textsuperscript{e} Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Received December 30, 2011; accepted March 30, 2012

Abstract

Background: Metaplastic carcinoma of the breast (MPCB) is a rare breast cancer. We reviewed sonographic findings for MPCB. Methods: Grayscale ultrasonography (US), color Doppler US (CDUS), and spectral Doppler US (SDUS) findings for 10 patients with MPCB breast were retrospectively reviewed. Results: The prevalence of MPCB was 3.9\% among cases of breast cancer in our hospital. All patients had a rapidly growing palpable breast mass. The mean lesion size was 5.7 cm. On US, the lesion shape was most commonly gently lobulated (90\%); only one showed an irregular shape (10\%). The lesion shape was most commonly circumscribed (90\%). Nine tumors had an abrupt boundary and one had an indistinct boundary. Lesion echogenicity was hypoechoic and very hypoechoic (40\%), hypoechoic (30\%), or very hypoechoic, hypoechoic, and hyperechoic (30\%). All our cases had cystic parts with posterior acoustic enhancement, representing necrosis or hemorrhage. CDUS showed peripheral, central and marginal color flow signals. The resistivity index (RI) of tumor vessels in the lesions ranged from 0.7 to 1.3. The axillary lymph nodes were enlarged on US and were positive for metastasis in three cases (30\%). Conclusion: MPCB is a rare rapidly growing tumor. US findings included gently lobulated, complex mass lesion with cystic parts and posterior acoustic enhancement, representing necrosis or hemorrhage. Increased color flow signals and relative high RI of the feeding arteries were also seen. Copyright © 2012 Elsevier Taiwan LLC and the Chinese Medical Association. All rights reserved.

Keywords: Breast cancer; Color Doppler ultrasound; Grayscale ultrasound; Metaplastic carcinoma

1. Introduction

Metaplastic carcinoma of the breast (MPCB) is a very rare breast cancer, accounting for less than 1–5\% of all breast cancers.\textsuperscript{1–3} It encompasses purely epithelial carcinoma and mixed epithelial and mesenchymal carcinoma.\textsuperscript{4} The objective of this study was to retrospectively review ultrasonographic (US) findings for MPCB, including grayscale US, color Doppler US (CDUS), and spectral Doppler US (SDUS), over a period of 10 years.

2. Methods

A total of 10 pathologically proven MPCB cases were encountered from 2002 to 2011 in Taipei Veterans General Hospital. Preoperative US studies of the breasts and axillae were performed in 10 patients. US was performed using high-resolution linear transducers. The sonograms were analyzed retrospectively by three experienced radiologists. The MPCB shape and margin were described according to the American College of Radiology Breast Imaging Reporting and Data

* Corresponding author: Dr. Chui-Mei Tiu, Department of Radiology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: cmtiu@vghtpe.gov.tw (C.-M. Tiu).
System (ACR BI-RADS) - Ultrasound, First Edition; 2003. The MPCB echogenicity was classified as cystic, very hypoechoic, hypoechoic, or hyperechoic. When a lesion showed echogenicity minimally less than that of subcutaneous fat, it was defined as hypoechoic. If the echogenicity of a lesion was very weak and much less than that of subcutaneous fat, the lesion was defined as very hypoechoic.

Histopathological studies were reviewed by one breast pathologist (C.-Y.H.). The subtype, chondroid matrix, cystic part, calcification, and hormone receptors for the lesions and the lymph node status were also reviewed and documented.

3. Results

From 2002 to 2011, the total number of breast malignancies was 3962 according to the cancer registration system in Taipei Veterans General Hospital. Among these, 10 cases were MPCB. The MPCB prevalence was therefore 3.9%. Table 1 lists clinical information and pathological findings for the 10 patients. All patients presented with a palpable breast mass.

The duration between observation of a palpable mass by the patient and medical consultation varied from 6 days to 2 years. One patient had previous contralateral breast cancer and underwent total mastectomy 19 years before. The average patient age was 55 years (range 36–81). The mean longest dimension of the lesions was 5.7 cm (range 1–15).

Table 2 lists US findings for the 10 lesions. The echogenicity of the lesions was hypoechoic and very hypoechoic (4/10), hypoechoic (3/10), or very hypoechoic, hypoechoic and hyperechoic (3/10) (Figs. 1–5). The lesion shape was gently lobulated (9/10) or irregular (1/10) (Figs. 1, 2, and 4). All our cases had cystic areas with posterior enhancement. The cystic areas were either central (2/10) or peripheral (3/10), and five patients had both central and peripheral cystic areas. Calcifications were found in four patients (4/10). In lesions with measurable calcification, the size range was 0.4–1.2 mm (0.7 ± 0.3 mm). Only one lesion presented with large calcific areas that were actually ossifications. CDUS was performed on all lesions, and SDUS was performed for eight patients. Seven lesions showed central, peripheral, and marginal color.

Table 1
Clinical information and pathological findings for ten patients.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Location</th>
<th>Chief complaint and physical findings</th>
<th>Treatment</th>
<th>Stage</th>
<th>Subtype</th>
<th>ER/PR/HER2</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>81</td>
<td>Left</td>
<td>Palpable mass for 2 y, recently enlarged</td>
<td>MRM</td>
<td>T3N1M1</td>
<td>Adenocarcinoma with SCM</td>
<td>−/−/−</td>
<td>Local recurrence and lung metastasis; expired</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>Right</td>
<td>Large palpable mass for 2 y, recently enlarged</td>
<td>MRM</td>
<td>T2N1M1</td>
<td>Adenocarcinoma with SCM</td>
<td>−/−/−</td>
<td>Pleural, lung and liver metastasis; expired</td>
</tr>
<tr>
<td>3</td>
<td>44</td>
<td>Right</td>
<td>Palpable mass for 1 mo</td>
<td>BCS, adjuvant C/T</td>
<td>T2N0M0</td>
<td>Carcinoma with CD</td>
<td>−/−/−</td>
<td>No recurrence</td>
</tr>
<tr>
<td>4</td>
<td>84</td>
<td>Right</td>
<td>Painful mass for 1 mo</td>
<td>BCS</td>
<td>T1N0M0</td>
<td>Carcinoma and OD</td>
<td>+/+/-NA</td>
<td>No recurrence</td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>Right</td>
<td>Palpable mass for 6 d</td>
<td>MRM</td>
<td>T1N0M0</td>
<td>Adenosquamous carcinoma</td>
<td>−/+/+</td>
<td>No recurrence</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>Left</td>
<td>Large palpable mass for 1 mo, recently enlarged</td>
<td>MRM, adjuvant C/T</td>
<td>T3N0M0</td>
<td>Adenocarcinoma with SCM</td>
<td>−/−/+</td>
<td>No recurrence</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>Left</td>
<td>Palpable mass for 1 mo</td>
<td>MRM and C/T</td>
<td>T2N0M0</td>
<td>Adenosquamous carcinoma</td>
<td>−/−/+</td>
<td>No recurrence</td>
</tr>
<tr>
<td>8</td>
<td>57</td>
<td>Left</td>
<td>Large palpable mass for 1 y</td>
<td>MRM and C/T</td>
<td>T4N1M0</td>
<td>Carcinoma with CD</td>
<td>−/−/−</td>
<td>No recurrence</td>
</tr>
<tr>
<td>9</td>
<td>45</td>
<td>Right</td>
<td>Large palpable mass for 1 y</td>
<td>BCS, adjuvant C/T</td>
<td>T3N0M0</td>
<td>Carcinoma with CD</td>
<td>−/−/−</td>
<td>No recurrence</td>
</tr>
<tr>
<td>10</td>
<td>36</td>
<td>Right</td>
<td>Painful mass for 3 wks</td>
<td>MRM</td>
<td>T2N0Mx</td>
<td>Adenocarcinoma with SCM</td>
<td>−/−/−</td>
<td>No recurrence</td>
</tr>
</tbody>
</table>

BCS = breast-conserving surgery; CD = chondroid differentiation; C/T = chemotherapy; ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; MRM = mastectomy; NA = not available; OD = osseous differentiation; PR = progesterone receptor; SCM = spindle cell metaplasia.

Table 2
Sonographic findings for metaplastic carcinoma.

<table>
<thead>
<tr>
<th>Case</th>
<th>Size (cm)</th>
<th>Shape</th>
<th>Echogenicity</th>
<th>Grayscale ultrasound</th>
<th>Doppler ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PE</td>
<td>Cal</td>
</tr>
<tr>
<td>1</td>
<td>3.1 × 2.7</td>
<td>Gently lobulated</td>
<td>Mixed pattern</td>
<td>Peripheral</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>3.5 × 2.8</td>
<td>Irregular</td>
<td>Very HE and HE</td>
<td>Peripheral, central</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>3.5 × 3.8</td>
<td>Gently lobulated</td>
<td>Very HE and HE</td>
<td>Central</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>1.4 × 1.1</td>
<td>Gently lobulated</td>
<td>Very HE and HE</td>
<td>Central</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>4.1 × 3.4</td>
<td>Gently lobulated</td>
<td>HE</td>
<td>Peripheral</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>11.5 × 7</td>
<td>Gently lobulated</td>
<td>Mixed pattern</td>
<td>Peripheral</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>3 × 2.8</td>
<td>Gently lobulated</td>
<td>Very HE and HE</td>
<td>Peripheral, central</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>15 × 10</td>
<td>Gently lobulated</td>
<td>Mixed pattern</td>
<td>Peripheral, central</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>5.6 × 4.8</td>
<td>Gently lobulated</td>
<td>HE</td>
<td>Peripheral, central</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>6.3 × 3.6</td>
<td>Gently lobulated</td>
<td>HE</td>
<td>Peripheral, central</td>
<td>+</td>
</tr>
</tbody>
</table>

Cal = calcification; HE = hypochoic; Mixed pattern = mixed hypo-, iso-, and hyperechoic; NA = not available; PE = posterior enhancement; RI = resistive index.
flow signals (70%), and two of them showed only peripheral color flow signals (20%). The average RI of the lesions was 0.88 (range 0.7–1.3) (Figs. 1–3).

Seven patients underwent total mastectomy and three patients received breast-conserving surgery. All patients underwent axillary lymph node dissection. Lymph node involvement was positive in three cases. Five patients received adjuvant or neoadjuvant chemotherapy.

Microscopy studies were reviewed and the specific metaplastic components were identified. Table 1 outlines the pathology findings. The subtypes included purely epithelial carcinoma in six cases (adenoaquamous carcinoma in two, and adenocarcinoma with spindle cell metaplasia in four) and mixed epithelial and mesenchymal carcinoma in four (carcinoma with chondroid differentiation in three, and carcinoma with osseous differentiation in one). Enlarged axillary lymph nodes demonstrated on US were histologically confirmed as metastasis in three patients.

Estrogen receptor (ER) and progesterone receptor (PR) status was reviewed for all patients. Only one lesion was ER-positive. All lesions were PR-negative. Human epidermal growth factor receptor 2 (HER2) status was reviewed in nine patients. Three were positive.

Eight patients were disease-free until 2011. One patient developed local recurrence 18 months after surgery and died of lung metastasis. The other expired due to lung and liver metastasis 18 months after surgery.

4. Discussion

MPCB is the rarest breast malignancy of ductal origin. According to the cancer register in our hospital, the prevalence is 3.9% among breast malignancies. This is close to the average incidence reported in the literature. MPCB is divided into two groups: (1) purely epithelial carcinoma, including squamous carcinoma, adenoaquamous carcinoma, and adenocarcinoma with spindle cell metaplasia; and (2) mixed epithelial and mesenchymal carcinoma, including carcinoma with chondroid differentiation, carcinoma with osseous differentiation, and carinosarcoma.
MPCB is not usually associated with hormone receptors. ER was negative in nine of our patients, and PR was negative in all our patients. Three of the tumors were positive for HER2.

Cystic areas found in MPCB can be a result of necrosis or hemorrhage. All of our cases showed the presence of cystic areas that correlated with pathological findings for necrosis or hemorrhage. When in areas without fluid spaces, the tumors showed hypercellularity on histological examination, which contributed to their the relative hypoechoogenicity and posterior acoustic enhancement. When in areas without fluid spaces, the tumors showed hypercellularity on histological examination, which contributed to their the relative hypoechoogenicity and posterior acoustic enhancement.

The microcalcification pattern can be used as a criterion to differentiate ductal carcinoma in situ (DCIS) and MPCB. Usually, US-detectable microcalcifications in DCIS are smaller (~0.1 mm), while calcifications in MPCB are larger (~0.7 mm). In addition, other echo features differ between MPCB and DCIS. Grayscale US findings for MPCB include a gently lobulated complex mass with cystic areas and posterior acoustic enhancement, while DCIS usually shows a poorly defined margin and an intermediate posterior acoustic phenomenon.

One of the 10 tumors contained ossifications. The pathological subtype of this case was carcinoma with osseous differentiation. Care is needed to avoid mistaking this MPCB subtype for calcified fibroadenoma on US. The relatively rapid growth, cystic areas, and hypervascularity of this MPCB subtype may be helpful in differentiating it from calcified fibroadenoma, which is slow-growing and has little or almost no vascularity.

RI values reported for benign tumors were 0.6 ± 0.11, 0.62 ± 0.095, and 0.62 ± 0.095, and values for malignant tumors were 0.75 ± 0.07, 0.74 ± 0.097, and 0.7. Although there is some controversy, the RI of malignant tumors is considered to be significantly higher than that of benign tumors. SDUS was performed on eight lesions in our study. The average RI was 0.88, which is higher than values reported for benign tumors and for breast cancers (not otherwise specified). The high RI may be due to high tumor stiffness.

Three of our patients presented with positive axillary lymph nodes. This incidence is similar to that in other studies (~12.5–40%). Distant metastasis may occur without positive axillary node metastasis. Hematogenous metastasis is more frequent than lymphangitic spreading. Two of our patients developed distant metastasis, including lung metastasis.
Fig. 3. Case 3. Carcinoma and chondroid differentiation. (A) Grayscale ultrasound (US) reveals a heterogeneously hypoechoic mass with a gently lobulated shape (large arrows), a cystic necrotic area (small arrows), and posterior enhancement (arrowheads). (B) Color Doppler US shows increased color flow signals (arrowheads) in the mass. (C) Histopathological examination demonstrates large chondromyxoid areas (stars) corresponding to cystic necrosis on US (hematoxylin and eosin stain, 100×). The peripheral part of the tumor shows vascular proliferation (arrowheads). (D) Spectral Doppler US shows a high resistive index (0.8; arrowheads) in the feeding artery.

Fig. 4. Case 4. Carcinoma and osseous differentiation. (A) Grayscale ultrasound (US) reveals a heterogeneously hypoechoic mass with a gently lobulated shape (large arrows) and coarse calcification (small arrows). (B) Histopathological examination also shows calcified zones (arrowheads; hematoxylin and eosin stain, 100×).
calcifications may be found in the subtype carcinoma with osseous differentiation. On CDUS and SDUS, hypervascularity and high RI are frequently seen. Although these US features are not pathognomonic in the diagnosis of MPCB, this unusual entity should be included in the differential diagnoses when a relatively large breast tumor with the above-mentioned US manifestations is encountered.

References