

Metaplastic breast carcinoma composed of epithelial–myoepithelial carcinoma and squamous cell carcinoma

A case report

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Abstract

Rationale: Metaplastic breast carcinomas are a group of breast malignancies with varying histomorphological characteristics and prognoses. The tumor composed of epithelial–myoepithelial carcinoma and squamous cell carcinoma was not reported previously.

Patient concerns: An 81-year-old woman presented with a palpable nodule in the left breast for 4 days. The ultrasonography showed multinodular growth and focally indistinct borders. Owing to her advanced age and possible early clinical staging, primary tumor resection was performed. One year later, a small and slow growing subcutaneous nodule was found under the incision of the left breast. Ultrasonography revealed an irregular, cystic and solid, hypoechoic mass with circumscribed borders.

Diagnoses: Microscopic examination of the primary tumor revealed epithelial–myoepithelial carcinoma and squamous cell carcinoma. The former had a variety of architecture patterns, including nests, lobulations, papillary and tubular structures, and the latter showed varying morphological features, from squamous pearls to spindle cells. The recurrent tumor showed only epithelial–myoepithelial carcinoma with more aggressively malignant features than those seen in the primary tumor.

Interventions: An extensive resection of the left breast mass was performed for the recurrent tumor. The patient did not receive any adjuvant chemotherapy or radiation therapy because of the patient's advanced age.

Outcomes: The patient has been followed up for 1.5 years after second surgery without evidence of tumor recurrence and metastasis.

Lessons: Wide local excision with adequate margins is recommended for elderly patients with metaplastic breast carcinoma composed of epithelial–myoepithelial carcinoma and squamous cell carcinoma.

Abbreviation: EMC = epithelial–myoepithelial carcinoma.

Keywords: breast, epithelial–myoepithelial carcinoma, metaplastic carcinoma, squamous cell carcinoma

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1. Introduction

Metaplastic breast carcinoma encompasses a group of neoplasms characterized by the differentiation of neoplastic epithelium into squamous cells or mesenchymal elements.^[1,2] These neoplasms may be a complex admixture of carcinomatous and metaplastic areas. Squamous cell carcinoma is 1 of the most common metaplastic breast carcinomas, and spindle cells are commonly observed at the invasive front of the tumor. Malignant myoepithelioma, which includes carcinomas derived from the luminal epithelium, or myoepithelium, and epithelial–myoepithelial carcinoma (EMC), is also classified under metaplastic carcinoma.^[3] Herein, we report an extremely rare case of metaplastic breast carcinoma composed of EMC, and squamous cell carcinoma. To our knowledge, this is the first case report of these 2 tumors occurring together in a single mass.

2. Case presentation

An 81-year-old woman presented with a palpable nodule in the left breast without obvious pain, or discomfort for 4 days. A physical examination revealed a firm oval mass in the upper inner quadrant of the left breast measuring 4.0 cm in diameter. There was no redness or orange peel-like appearance of the skin. The nipple was normal, and no nipple discharge was observed. Ultrasound examination revealed a suspicious round, heterogeneous mass, measuring 3.8 cm × 2.8 cm × 2.4 cm with focally, indistinct borders. Additionally, 3 small hypoechoic masses

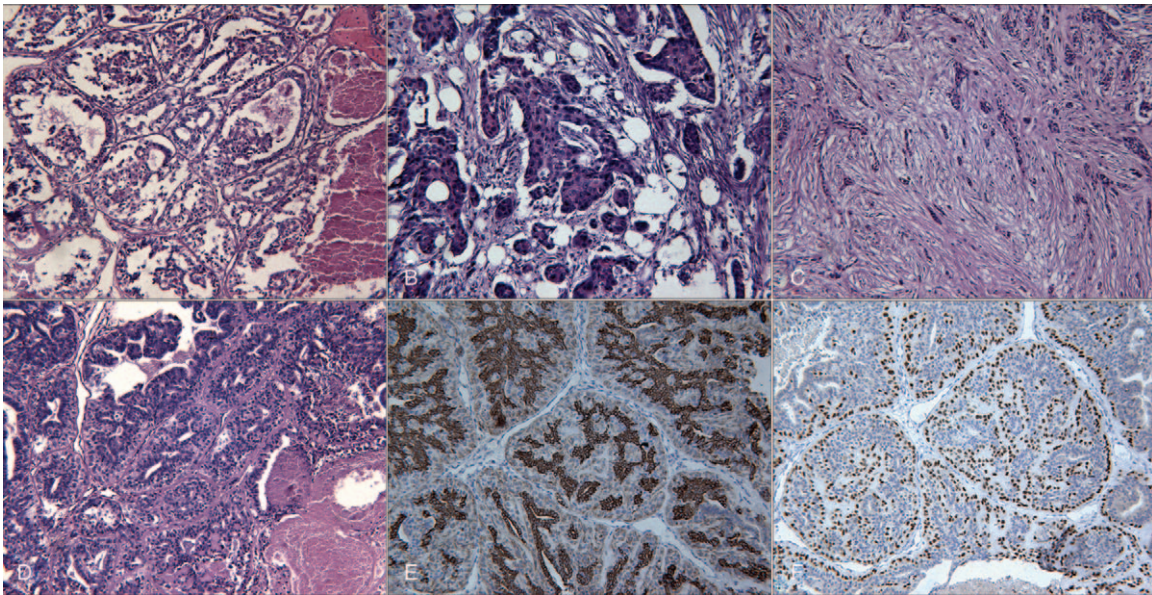


Figure 1. Morphological characteristics of the lesions. (A) the primary EMC showed an atypical proliferation of layers of myoepithelial cells around glandular epithelium-lined spaces presenting a tubular gland-like appearance. Necrosis was observed (HE, $\times 200$). (B) squamous cell carcinoma infiltrated the adjacent stroma in the form of cords and nests (HE, $\times 200$). (C) spindle-cell squamous cell carcinoma was detected (HE, $\times 200$). (D) the recurrent tumor specimen showed extensive hyperplasia of neoplastic myoepithelial cells with obvious atypia (HE, $\times 200$). (E) glandular epithelial cells in the recurrent tumor were immunoreactive for 34 β E12 (immunohistochemical staining, $\times 200$). (F) myoepithelial cells in the recurrent tumor were positive for P63 (immunohistochemical staining, $\times 200$). EMC = epithelial–myoepithelial carcinoma

(measuring 0.2 – 0.6 cm in diameter) were found around the largest mass. Simultaneously, swollen lymph nodes of the left armpit were found. Therefore, provisional diagnosis of the left breast cancer was made. Owing to her advanced age, and possible early, clinical staging, primary tumor resection was performed, and more aggressive therapy and any post-operative adjuvant therapy were not received.

The tissue sample was fixed with 10% neutral formalin, embedded in paraffin, and sectioned. The sections were stained with hematoxylin, and eosin, and immunohistochemistry. The primary tumor specimen was composed of EMC, and squamous cell carcinoma with closely, adjacent location. The EMC showed varying architectural patterns, including nests, lobulation, papillary, and tubular structures. The nest-like, or lobulated structures were separated by thin fibrous tissue, which was characterized by the unbalanced proliferation of layers of myoepithelial cells around glandular epithelium-lined spaces presenting a crack-like or tubular gland-like appearance (Fig. 1 A). The relatively, uniform myoepithelial cells were round, or polygonal, and usually, had clear cytoplasm, and a round nucleus with small nucleoli. In the area of spare myoepithelial cells, the tumor showed obvious tubular gland-like structures, and focal intraductal papillomas. The lumens were lined with a monolayer of inner epithelial cells with eosinophilic cytoplasm. Both the inner and outer cells had medium-sized atypical nuclei. We detected approximately, 4 mitotic figures per 10 high-power fields. Invasive growth and extensive necrosis of the central area were observed. The squamous cell carcinoma infiltrated the adjacent stroma in the form of sheets, cords, and nests, eliciting a conspicuous focal stromal reaction (Fig. 1 B). The infiltrating squamous elements varied in their degree of squamous differentiation, from obvious squamous pearls to spindle cells (Fig. 1 C). Immunostaining assays for the estrogen receptor, progesterone receptor, and Her2/neu were all negative in both

neoplastic elements. The pathological diagnosis of metaplastic breast carcinoma composed of EMC and squamous cell carcinoma was made.

One year later, a small subcutaneous nodule was found under the incision of the left breast. This nodule was freely, mobile, and grew gradually, to approximately 2.5 cm in diameter in 2 years after the first surgery. Ultrasonography revealed an irregular, cystic, and solid, hypoechoic mass with circumscribed borders (Fig. 2). An extensive resection of the left breast mass was

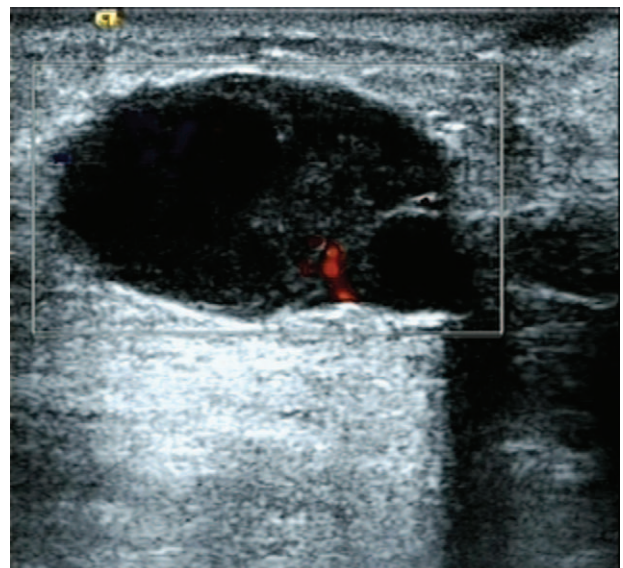


Figure 2. Ultrasonography of the left breast showed a hypoechoic nodule with increased internal doppler flow.

performed. The resected mass measured 2.5 cm × 2.5 cm × 2.0 cm, and had a partially, rough surface. The cut section showed cystic, and solid areas, with light yellow liquid, and necrosis. Any adjuvant therapy was not performed after the second surgery, and she has been followed up for 1.5 years without evidence of tumor recurrence, and metastasis.

Microscopic examination of the specimen resected in the second surgery showed characteristics of EMC with extensive hyperplasia of neoplastic myoepithelial cells (Fig. 1 D). These tumor cells showed more atypia and mitotic figures than that in the first specimen. Obvious necrosis was also observed. However, squamous cell carcinoma was not found in the second sample. Glandular epithelial cells were immunoreactive for 34βE12 (Fig. 1 E), while myoepithelial cells were positive for P63 (Fig. 1 F), SMA, and S-100. Pathological diagnosis of tumor recurrence was confirmed.

3. Discussion

In this article, we have reported a case of EMC associated with squamous cell carcinoma in an elderly woman. EMC of the breast is a rare disease characterized by the simultaneous proliferation of ductal epithelial, and myoepithelial cells, both of which show malignant features. EMC usually, occurs in elderly women. Xu et al.^[4] reviewed 16 cases of EMC with the mean age of 60 years (range, 36–86 years), and the mean tumor size of 28.8 mm (range, 3–50 mm). Tumor recurrence occurred in 25% of patients, while lymph node or distant metastases occurred in 50% of patients with the median metastasis time of 2 years.^[4] EMC is occasionally accompanied by other breast malignancies. Simpson et al.^[5] reported a case of malignant adenomyoepithelioma of the breast with osteosarcoma and invasive ductal carcinoma. Herein, we firstly, reported a case of metaplastic breast carcinoma composed of EMC and squamous cell carcinoma. The patient had no apparent symptoms, except for a palpable nodule located in the left breast. Local recurrence occurred 1 year after the excision of the primary tumor, and microscopic examination of the recurrent tumor revealed only EMC.

The exact etiology of metaplastic breast carcinoma is obscure. The majority of cases are sporadic without the familial aggregation. The histogenesis of EMC is also unclear. However, it has been suggested that stem cells in the terminal ductal lobular units of mammary tissue with intermediate epithelial/myoepithelial differentiation give rise to the tumor.^[6] The tumor evolves from adenosis with, or without myoepithelial hyperplasia, then progresses to benign adenomyoepithelioma, which transforms into a malignant tumor like pure myoepithelial carcinoma, or adenomyoepithelioma with malignant components.^[6] Although the histogenesis of squamous differentiation, or squamous cell carcinoma of the breast is far from being fully, understood, the most widely-held view is that squamous differentiation is the result of myoepithelial histogenesis from precursor multipotent cells that have a propensity to differentiate into both luminal epithelial, and myoepithelial cells.^[7] Therefore, EMC and squamous cell carcinoma may have the same original precursor.

There are no well-defined criteria for the diagnosis of EMC due to the rarity of this tumor. Microscopically, it can appear either as obvious atypical myoepithelial cells, and glandular epithelial cells with high cellularity, and increased mitotic activity throughout the tumor, or as an area of obvious malignant components arising in an adenomyoepithelioma. The microscopic criteria to diagnose EMC in this setting must include the presence of definitive malignant epithelial, and myoepithelial components, high

cellularity, and cytological atypia, an increased mitotic rate (>3 mitoses/10 high-power fields), areas of necrosis, local invasion, and satellite foci. Additionally, breast adenomyoepitheliomas measuring over 2 cm should be treated as potentially, malignant.^[8–10] Furthermore, the diagnosis of EMC is usually, difficult owing to its varying histology, which includes tubular, lobulated, and papillary structures. Besides benign adenomyoepithelioma, several lesions should be considered in the differential diagnosis. EMC and adenoid cystic carcinoma are both rare malignant epithelial–myoepithelial tumors of the breast. The latter is associated with a characteristic cribriform architecture, the formation of true glandular spaces, and pseudolumina, and the histologically, distinct invagination of the stroma. The myoepithelial cells in adenoid cystic carcinoma tend to be smaller, and more basaloid than those in EMC, and the arrangement of epithelial, and myoepithelial cells is less irregular in adenoid cystic carcinoma than in EMC. On immunohistological examination, CD117 can be detected in the epithelial cells of adenoid cystic carcinoma but not in those of EMC. When papillary structures are prominent, EMC can resemble sclerosing intraductal papilloma. The latter usually, shows glandular structures that contain a typical dual cell layer of epithelial, and myoepithelial cells within a central area of dense scar-like fibrosis, and are surrounded by a thick fibrous wall. Myoepithelial cell proliferation is usually, not prominent in sclerosing intraductal papilloma.

EMC has the propensity to recur locally, and to metastasize. Although, the morphological features of the tumor that predict the potential of local recurrence, and/or metastasis are not well established, a more solid structure, cellular pleomorphism, high mitotic activity, necrosis, invasion of the surrounding tissue, and association with other types of malignant tumors (such as invasive ductal carcinoma and undifferentiated carcinoma) are thought to be the most important predictors of recurrence risk.^[9,11] Local recurrence usually, occurs between 8 months to 5 years after the initial excision, and is related to high-grade malignancy, multinodular growth, intraductal extension giving rise to satellite nodules away from the main tumor, or incomplete excision. Metastases rarely, occur in the axillary lymph nodes, and are more frequently, reported in the lungs, brain, thyroid, chest wall, and even abdominal cavity.^[4,8,10] In our patient, recurrence occurred 1 year after the primary excision, and consisted of the EMC component only. This may be related to the multinodular growth of the primary tumor demonstrated on ultrasonography. The recurrent tumor showed a more aggressively, malignant appearance, with more myoepithelial cells, nuclear pleomorphism, and atypia, mitotic figures, and more obvious necrosis than the primary tumor. The evidence of relapse again was not found 1.5 years after second extensive resection, therefore, wide local excision with adequate margins is recommended for metaplastic breast carcinoma patient with advanced age.

4. Conclusions

Herein, we have reported for the first time a rare case of metaplastic breast carcinoma composed of EMC and squamous cell carcinoma. The patient had no apparent symptoms except for a palpable nodule in the left breast. Ultrasonography revealed multinodular growth and focally indistinct borders. Local recurrence occurred 1 year after the excision of the primary tumor. Microscopic examination of the second specimen revealed only the EMC component, and a more aggressively malignant

appearance than the primary tumor, with more myoepithelial cells, nuclear pleomorphism, and atypia, mitotic figures, and obvious necrosis. Therefore, wide local excision with adequate margins is recommended for metaplastic breast carcinoma patient with advanced age.

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Author contributions

JZ, PFL and JWB designed the study, collected clinical data, and clinical interpretation, and performed the histological evaluation. XFD and PZ participated in literature search. KNL and PFL drafted the manuscript. All authors read and approved the final manuscript.

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