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CASE REPORT

Epithelial-myoepithelial carcinoma occurrence in the site of previously treated ductal carcinoma in situ of the breast: Imaging features with histopathologic correlation, a case report and review of the literature

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Key Clinical Message

Epithelial-myoepithelial carcinoma of the breast is an extremely rare biphasic tumor. This report documents the first case of epithelial-myoepithelial carcinoma presenting in the location of a previously treated ductal carcinoma in order to increase the awareness of this entity as a potential differential for recurrent breast lesions.

Abstract

Epithelial-myoepithelial carcinoma of the breast is an exceedingly rare biphasic tumor, seldom documented in medical literature. This report describes the first known case of this entity at the site of a previously treated neoplasm in a 75-year-old female with a history of high-grade ductal carcinoma in situ who presented with a new breast mass. Imaging demonstrated an oval shaped mass with microlobulated borders and hypoechoic echogenicity on ultrasound. Following multidisciplinary discussion, she underwent a mastectomy, revealing epithelial-myoepithelial carcinoma with metaplastic squamous cell carcinoma. The patient began chemotherapy but discontinued due to poor tolerance and neurological complications. Generally, prognosis for epithelial-myoepithelial carcinoma (World Health Organization Classification of Breast Tumors 2019, 8562/3) is highly variable, with limited available data suggesting that epithelial-myoepithelial carcinoma may follow a course similar to that of breast adenocarcinomas with both hematogenous and lymphatic spread. Treatment typically involves curative excision, though the role of axillary lymph node sampling remains under discussion. This case underscores the need for vigilance in post-treatment surveillance for breast cancer and highlights the importance of recognizing this entity in recurrent breast pathology.

KEYWORDS

breast, carcinoma, ductal, neoplasms, pathology, radiology, second primary

1 | INTRODUCTION

Multiple similarities in the embryogenic epithelial-myoepithelial cell differentiation of the salivary glands and breast tissue allows for overlap of neoplastic development of classically salivary gland tumors in the breast. While biphasic epithelial-myoepithelial lesions of the breast are uncommon and include pleomorphic adenoma, adenoid cystic carcinoma, and benign adenomyoepithelioma, malignant transformation of benign adenomyoepithelioma into epithelial-myoepithelial carcinoma (EMC) of the breast is extremely rare, with fewer than 50 reported cases in the existing literature over the past four decades.[1,2] Thus far, there have previously been no cases that bring up the possibility of EMC development following the treatment of primary breast cancer in the existing literature.

2 | CASE HISTORY/EXAMINATION

In this case, the patient is a 75-year-old gravida 2, para 1 female with a prior history of right breast ductal carcinoma in situ (DCIS), high nuclear grade, solid, and cribriform type with comedonecrosis, positive for estrogen receptor and negative or progesterone receptor with clear margins, status post prior lumpectomy, re-excision, and completion of chemoradiation with tamoxifen and 42.6 Gy over 16 fractions to the right breast approximately 6 years previously. With regards to hormonal risk factors, she was noted to have onset of menarche at 13 years of age and was 31 years of age at first parity with additional history of 5 years of remote oral contraceptive use. Of note, the patient reported a family history of bilateral breast cancer in a maternal aunt.

She then presented again to the breast surgery clinic with a new chief complaint of progressive discomfort and fullness of the right breast associated with right nipple prominence. On physical examination, the right breast demonstrated an intact lumpectomy scar, mild hyperpigmentation with breast fibrosis, and a palpable mass measuring approximately 3 centimeters at the 10 o'clock position, just superior to the previous incision.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENT)

Diagnostic mammogram was initially performed (Figure 1) and showed a concerning oval mass in the right breast at the 10 o'clock position. Ultrasound was then performed showing a mass with irregular shape, indistinct margins, and hypoechoic echogenicity (Figure 2).

Initial pathology results from the ultrasound-guided core needle biopsy and tumor resection returned showing nests, trabeculae, and cords of epithelial cells with moderate atypia, cribriform architecture, moderate to abundant eosinophilic to oncocytic cytoplasm and frequent mitoses (Figure 3A). These cells were positive for CK7 and C-kit by immunohistochemistry (Figure 3B). An intermixed myoepithelial cell component was present, which was highlighted by smooth muscle myosin (SMM), smooth

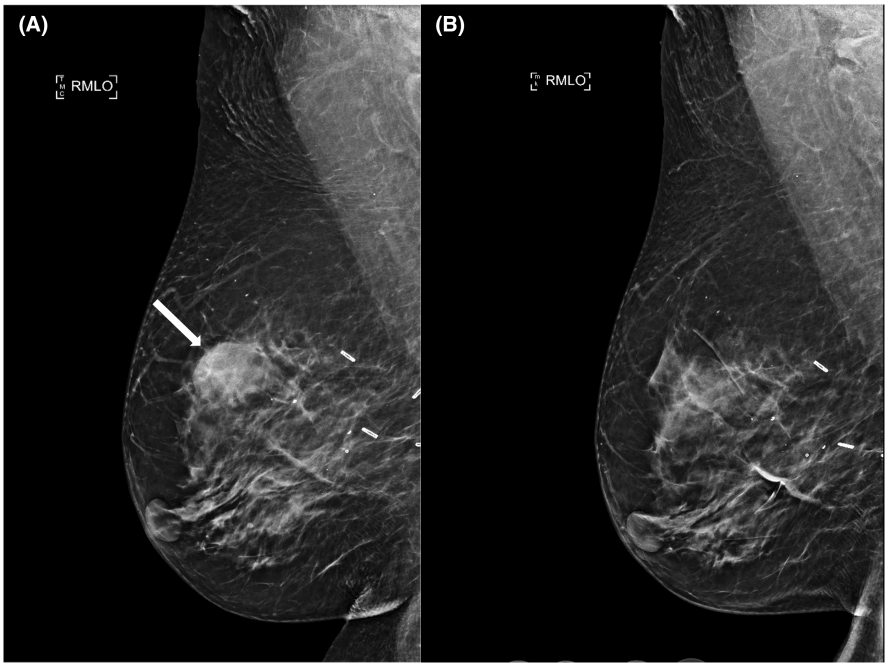

FIGURE 1 Right breast mammogram with medial lateral oblique (MLO) views (A) demonstrating a new dense, oval and indistinct mass in the upper outer quadrant, at 10 o'clock position (white arrow). (B) No mass in the region is visualized on the preceding 1-year prior mammogram.

muscle specific actin (SMSA) and p63 immunostains (Figure 3C,D). Foci of necrosis were also present. ER/PR/HER2 staining was negative, as was MUC4. At this time, the differential diagnosis provided by pathology results from limited tissue sampling included malignant adenomyoepithelioma, carcinoma ex pleomorphic adenoma, and a low-grade epithelial myoepithelial carcinoma. The case was then discussed at tumor board and multidisciplinary plan was to proceed with right breast mastectomy and sentinel lymph node biopsy with additional referral to genetic counseling.

The patient then underwent a right mastectomy (Figure 4). Following multidisciplinary discussion, radiation therapy was not recommended, and adjuvant chemotherapy was indicated with docetaxel, cyclophosphamide and pembrolizumab to reduce risk of recurrence.

Genetic testing was performed and revealed a genetic Variant of Uncertain Significance (VUS) in the *AXIN2* gene, which does not show enough evidence of association with an increased risk of cancer at this time.

Final pathology results following the right mastectomy were consistent with epithelial-myoepithelial carcinoma with component of metaplastic squamous cell carcinoma (SCC) in 10% (Figure 5A), with a tumor size of 3.2 cm, without lymphovascular or perineural invasion. Tumor arose adjacent to prior lumpectomy site (Figure 5B). All surgical margins were uninvolved, with the closest deep margin of 1.1 cm. The attached skin and nipple were free of malignancy. Additional hormone receptor testing of the epithelial-myoepithelial component showed ER low positive (1–2+, 1%–2%), PR negative, and HER2 score of 1+ (negative), while the metaplastic SCC component was ER/PR negative with a HER2 score of 0 (negative). Two sentinel axillary lymph nodes were excised, and they were both benign with no tumor identified.

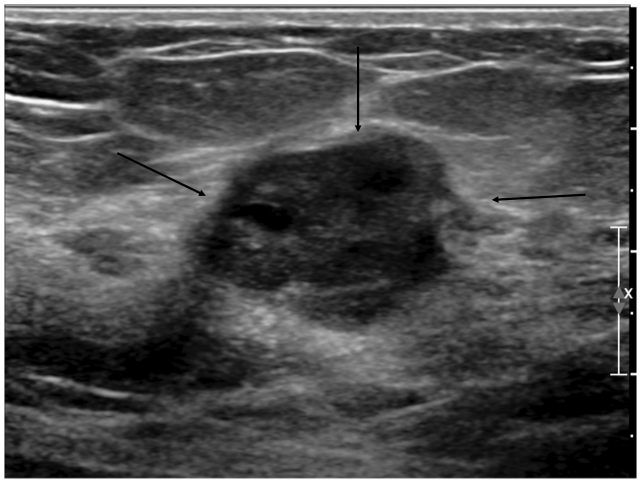

FIGURE 2 Ultrasound was performed demonstrating an oval shape, indistinct and microlobulated margins, with hypoechoic echogenicity (black arrows) in the upper outer quadrant of the right breast at 10 o'clock position. Biopsy was performed under sonographic guidance yielding a malignant neoplasm with epithelial-myoepithelial differentiation.

4 | OUTCOME AND FOLLOW-UP (CONCLUSIONS AND RESULTS)

The patient healed well following right mastectomy without postoperative complications. Thus far, the patient has completed one cycle of docetaxel-cyclophosphamide, which was dose-reduced to assess tolerance. After completion of this cycle, the patient noted overall poor tolerance to this chemotherapy and additionally developed symptoms which were assessed by Neurology to be compatible for amyotrophic lateral sclerosis or other neuromuscular disorder. As a result, following shared decision-making, the decision to forego further chemotherapy with continued monitoring was made.

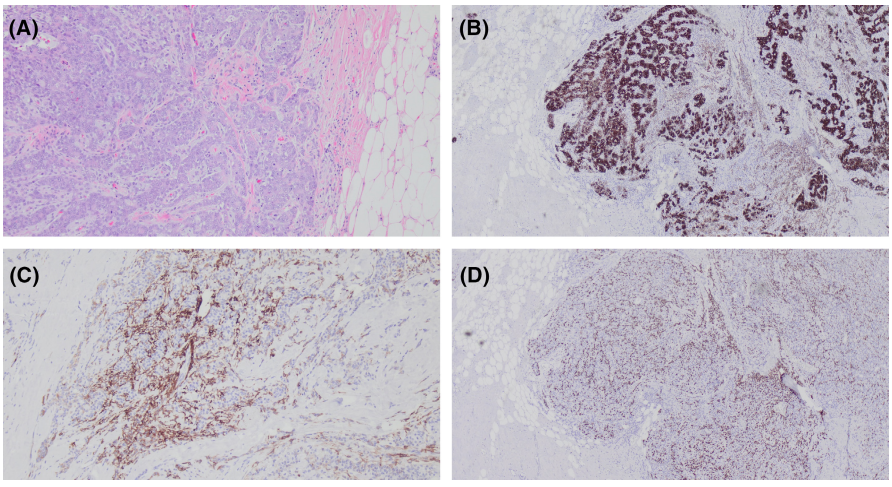

FIGURE 3 Epithelial-myoepithelial carcinoma staining results from tumor resection. (A) Frequent mitotic figures present. H&E, ×100. (B) CK7 immunostain highlights epithelial component. ×40. (C) SMM positive in myoepithelial component. ×100. (D) p63 immunostain is positive in myoepithelial component. ×40.

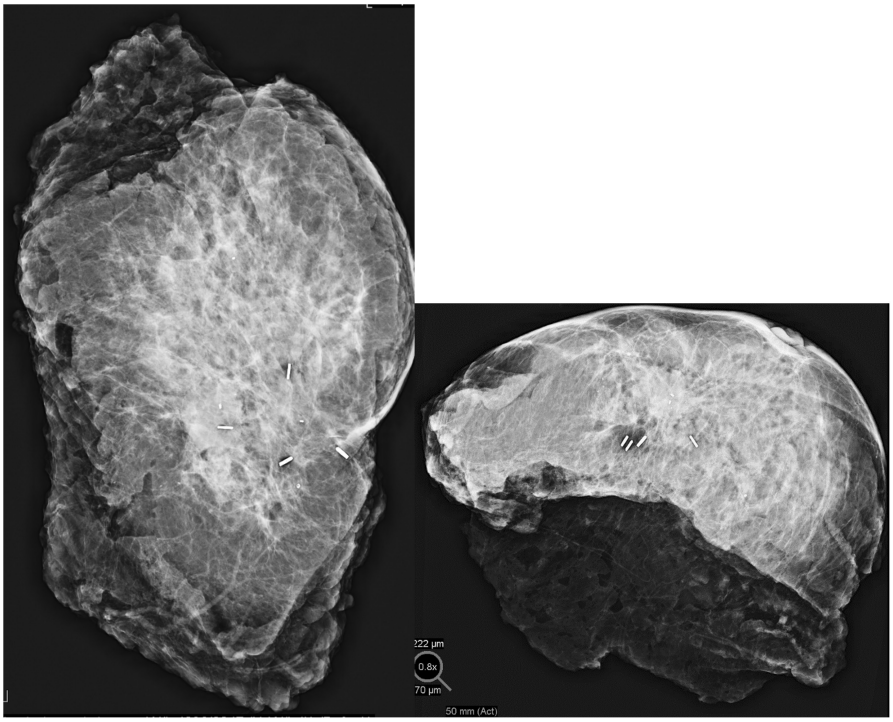

FIGURE 4 Right breast mastectomy specimen. The final pathology result was epithelial-myoepithelial carcinoma with a component of metaplastic squamous cell carcinoma.

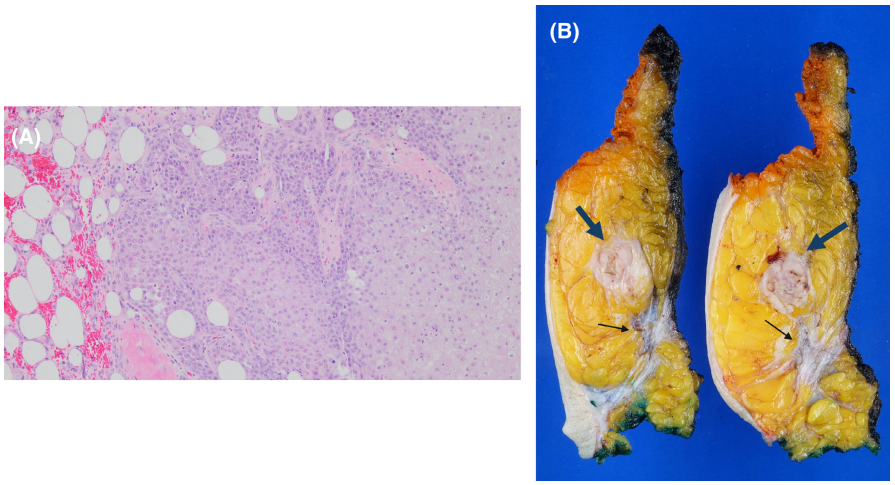

FIGURE 5 Pathology results following subsequent mastectomy and tumor resection. (A) Metaplastic component. H&E, ×100. (B) Surgical specimen. Tumor (thick arrows) adjacent to prior lumpectomy site (thin arrows).

5 | DISCUSSION

Epithelial-myoepithelial carcinoma of the breast is a rare malignant mixed biphasic tumor with epithelial and myoepithelial components which may present as a new or recurrent palpable mass with associated generalized discomfort. Epithelial and myoepithelial cells are part of the breast ductal-lobular epithelial lining and have different functions. They share a common progenitor cell, but they have different functions and express different proteins. The epithelial cells consist of an inner layer of cells and have the function of milk production and conduction. The myoepithelial cells consist of a semi-continuous outer layer, supporting the basal membrane, separating the epithelium from the surrounding stroma and have the function of contraction. Epithelial cells stain for CK 7, 8, 18, and 19 and myoepithelial cells stain for CK 5/6, 14, 7, SMA, calponin, SMM-HC, and p63, which help differentiate these the cell population of lesions.

Mammographically, typical imaging features in the few cases of reported epithelial-myoepithelial carcinomas typically show irregular non-calcified mass with microlobulated margins and parenchymal distortion, with microcalcifications being reported only in one published case at this time. On ultrasound, presentation usually is as a solid, hypoechoic, frequently oval mass, again with microlobulated or irregular margins. The lesion may additionally show posterior acoustic enhancement and hypervascularity.[3] While there are even fewer cases reported on MRI, at least one reported case in literature suggests these lesions may appear as T2 isointense, heterogeneously enhancing mass with malignant washout kinetics as well as potential

foci of internal necrosis.[3,4] While there is limited data on the MRI presentation of these lesions in the breast, given the pathologic similarities between salivary gland and breast epithelial-myoepithelial carcinomas, the radiologic findings share some overlap with the appearance of these tumors in the salivary gland.

Some examples of benign epithelial and myoepithelial lesions are myoepithelial hyperplasia, collagenous spherulosis, adenomyoepithelioma, and pleomorphic adenoma. Some examples of malignant epithelial and myoepithelial lesions are adenoid cystic carcinoma and malignant adenomyoepithelioma. This latter could be an adenomyoepithelioma with carcinoma or epithelial-myoepithelial carcinoma, depending on the nature of the malignant component. There are some difficulties in the differentiation with spindle cell metaplastic carcinomas, due to overlap in histologic and immunophenotypic features. An EMC with rhabdoid features has been reported[1] and there is some data indicating that these tumors might be related to HRAS and PIK3CA.[5]

Most of the reported cases were in females with a mean age of 64 years old, with a median size of 3.5 cm[5,6] but there is a report of an EMC arising in a 37-year-old patient.[7]

While previously considered to be a low-grade malignancy, prognosis has been reported to be highly variable, as it may follow a similar course to adenocarcinoma of the breast with multiple cases reporting potential for local invasion, distant metastases or recurrence after excision of primary lesion.[6,8] Review of the existing literature suggests that the degree of atypia, tumor size, tumor appearance, and the percentage of mitotic figures may be used to gauge the malignant potential of the lesion, with size greater than 16 mm having an increased risk of presenting with underlying metastatic disease.[5,8] In addition, expression of the cell cycle regulators p53 and Ki-67 were associated with a worse prognosis, similar to its salivary gland counterpart.[7,8]

Given the rarity of this diagnosis, there is a dearth of existing literature for treatment options. To date, this is the first reported case of an EMC within the site of previously treated DCIS. While multidisciplinary discussion is typically required, existing management primarily comprises curative excision following appropriate surgical clearance if caught at an early stage, as was performed in this case.[5,6] The consensus on whether axillary lymph node sampling is indicated is not yet well established, though this is frequently performed if there is concern for metastatic disease.

6 | CONCLUSION

In summary, this case report documents the first known instance of EMC arising at the site of a previously treated primary tumor. EMC, though extremely rare, should be considered in the differential diagnosis of recurrent breast lesions, especially in patients with a history of breast cancer. The variable prognosis and potential for metastasis and recurrence underscore the need for accurate diagnosis and appropriate management. Curative excision remains the primary treatment, and multidisciplinary discussion is essential for optimizing patient outcomes. Increased awareness and further research into EMC will aid in better understanding and managing this rare malignancy.

AUTHOR CONTRIBUTIONS

Jessica Hui: Visualization; writing – original draft; writing – review and editing. **Xin Zhan:** Conceptualization; writing – original draft; writing – review and editing. **Amani Bashir:** Visualization; writing – original draft; writing – review and editing. **Fabiana Policeni:** Conceptualization; writing – review and editing. **Su Kim Hsieh:** Conceptualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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