

Lymphoepithelioma-like carcinoma of the breast

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Lymphoepithelioma-like carcinoma of the breast is a rare malignancy, with fewer than 20 cases documented in the literature. Given the paucity of reported cases, there is limited information available to guide the diagnosis and management of patients with this tumor. We present a case of a 39-year-old woman with a palpable right breast mass that was initially diagnosed by core needle biopsy as infiltrating carcinoma with prominent lymphoplasmacytic stroma. Subsequent neoadjuvant chemotherapy with docetaxel, doxorubicin, and cyclophosphamide resulted in a marked decrease in the size of the mass. After wide local surgical excision, pathology revealed a lymphoepithelioma-like carcinoma of the breast. Given the excellent treatment response, our experience may help clinicians determine future therapeutic strategies for this rare breast tumor.

Case report

A 39-year-old Hispanic female presented to our breast clinic with a 2.5-year history of a right breast lump that had been gradually increasing in size. The patient did not have associated breast pain, skin changes, nipple discharge, or a history of breast trauma. Her past medical history was significant only for hypercholesterolemia. Her menarche was at age 13, and she was gravida 2 para 1, with one miscarriage. She was 20 years old at the time of her first birth. There was no family history of breast or ovarian cancer.

Her physical exam was notable for a palpable right breast mass located in the upper inner quadrant at the 1 o'clock position, measuring approximately 2 x 3 cm. No skin changes were visualized. The left breast exam was negative. There was no palpable lymphadenopathy in the axillary or the supraclavicular regions.

A diagnostic mammogram, subsequently performed, revealed a 2.7-cm, irregular-shaped, high-density mass with

microlobulated margins at the 1 o'clock position (Fig. 1). Right breast ultrasound demonstrated a corresponding 2.7 x 2.5 x 2.5-cm, nonparallel, irregular-shaped, hypoechoic mass with heterogeneous internal echogenicity, microlobulated margins, and posterior acoustic enhancement (Fig. 2). The mass was categorized as Breast Imaging Reporting and Data System (BI-RADS) Category 4C: high suspicion for malignancy. The right axilla was sonographically negative for lymphadenopathy.

An ultrasound-guided 14-gauge core-needle biopsy was performed, with the histologic result of infiltrating carcinoma with prominent lymphoplasmacytic stroma. The tumor was 40% positive for estrogen-receptor (ER), <1% positive for progesterone-receptor (PR), and HER2/neu was negative by fluorescence in-situ hybridization (FISH) testing. A BRST-2 stain showed rare positive cells, which favored a primary breast carcinoma; however, clinical correlation and metastatic workup to exclude a primary cancer elsewhere were recommended by pathology.

Computed tomography performed for cancer staging demonstrated an irregular-shaped, heterogeneously enhancing, soft-tissue-density mass in the right breast (Fig. 3) with no evidence of metastatic disease. The patient was referred for a genetic consultation and tested negative for the *BRCA1/2* gene mutation.

Neoadjuvant chemotherapy with six cycles of docetaxel, doxorubicin, and cyclophosphamide was administered. Following completion of the neoadjuvant chemotherapy regimen, the breast mass was no longer palpable on physical exam. Only a small residual area of hypoechoogenicity

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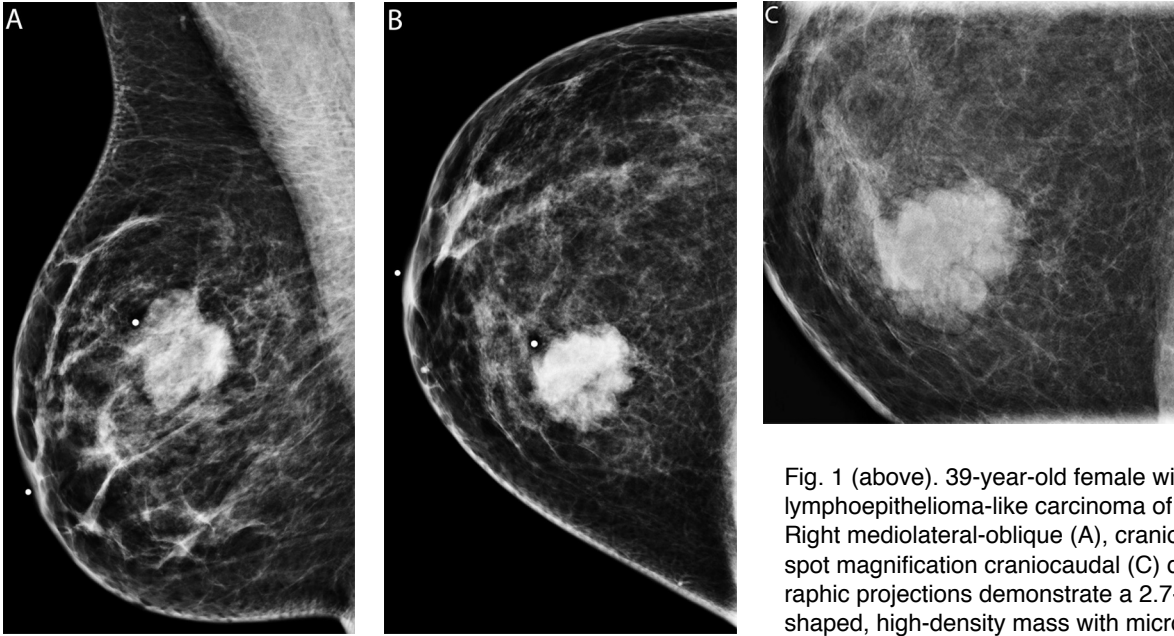


Fig. 1 (above). 39-year-old female with lymphoepithelioma-like carcinoma of the right breast. Right mediolateral-oblique (A), craniocaudal (B), and spot magnification craniocaudal (C) digital mammographic projections demonstrate a 2.7-cm, irregular-shaped, high-density mass with microlobulated margins located at the 1 o'clock position at mid depth. Metallic BB markers overlie the nipple and the palpable mass on the mediolateral-oblique and craniocaudal projections.

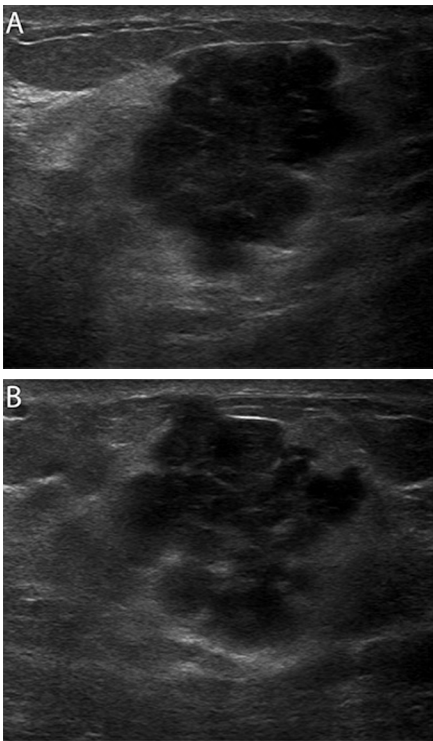


Fig. 2 (left). 39-year-old female with lymphoepithelioma-like carcinoma of the right breast. Ultrasound images in transverse (A) and longitudinal (B) orientations show a 2.7 x 2.5 x 2.5-cm, nonparallel, irregular-shaped, hypoechoic mass with heterogeneous internal echogenicity, microlobulated margins, and posterior acoustic enhancement. The mass is located at the 1 o'clock position and corresponds to the mammographic mass.

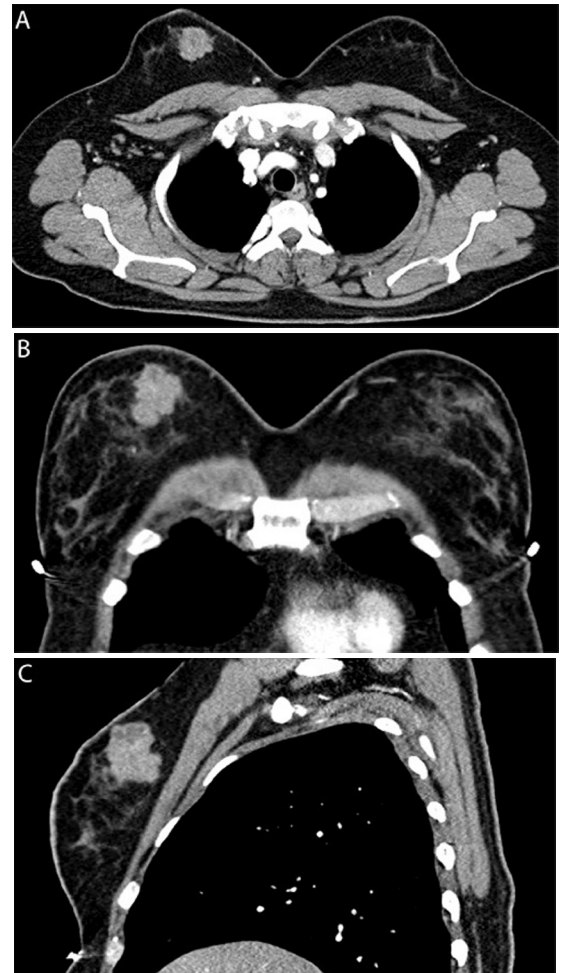


Fig. 3 (right). 39-year-old female with lymphoepithelioma-like carcinoma of the right breast. Contrast-enhanced computed tomography axial (A), coronal reformatted (B), and sagittal reformatted (C) images demonstrate an irregular-shaped, soft-tissue-density mass with heterogeneous internal enhancement in the right breast upper inner quadrant.

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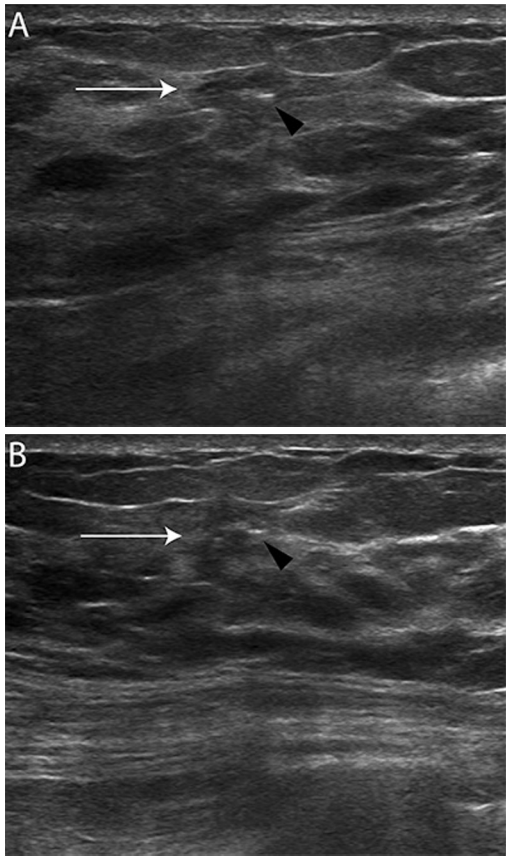


Fig. 4 (left). 39-year-old female with lymphoepithelioma-like carcinoma of the right breast. Ultrasound images in transverse (A) and longitudinal (B) orientations after administration of six cycles of neoadjuvant chemotherapy demonstrate only a small residual area of hypoechogenicity at the site of the primary tumor at the 1 o'clock location (white arrows), indicating an excellent treatment response. An echogenic focus representing the microclip placed at the time of core needle biopsy is also noted (black arrowheads).

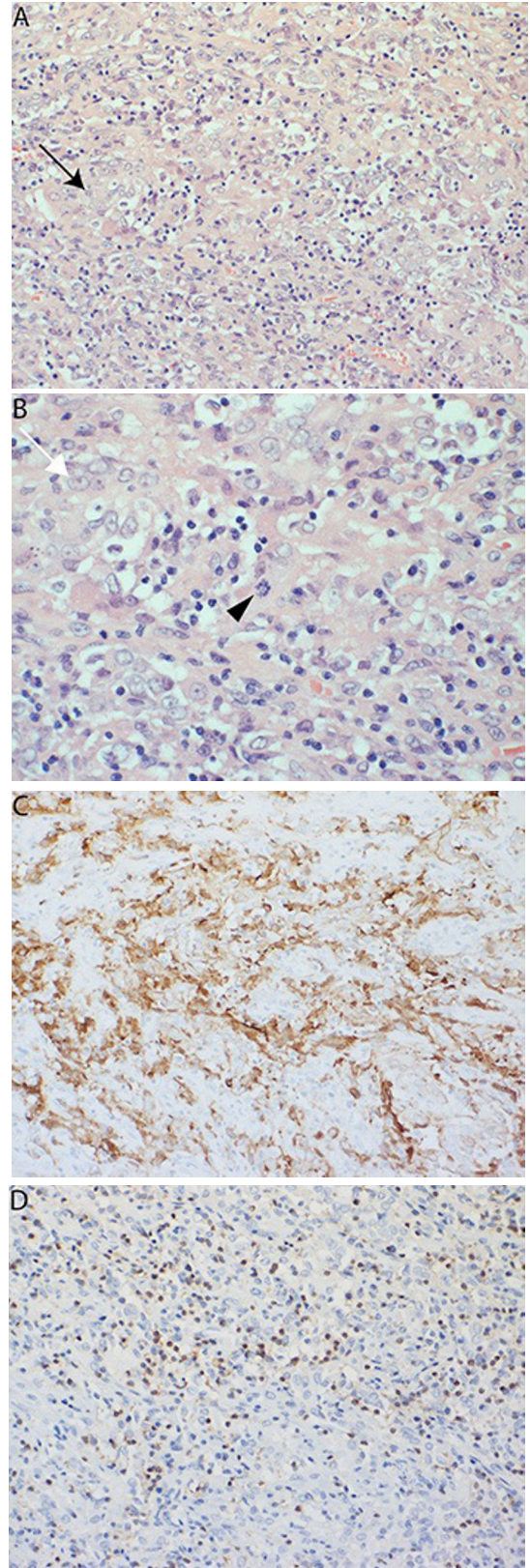


Fig. 5 (right). 39-year-old female with lymphoepithelioma-like carcinoma of the right breast. Photomicrograph of tissue samples from the wide local excision specimen. Hematoxylin and eosin stain, 20X (A) demonstrates cords of undifferentiated neoplastic cells (arrow) with a prominent lymphocytic stromal infiltrate. Hematoxylin and eosin stain; 40X (B) shows large tumor cells (arrow) with poorly defined cytoplasmic borders, pleomorphic and vesicular nuclei, and nucleoli. Lymphocytic infiltrate is present throughout the tumor. A mitotic figure can be seen in the center of this image (arrowhead). Staining with CAM 5.2; 20X (C) shows neoplastic cells positive for the CAM 5.2 keratin marker. CD3 immunohistochemistry staining; 20X (D) demonstrates infiltrating lymphocytes highlighted by the CD3 marker.

could be seen on a subsequent ultrasound examination, indicating an excellent treatment response (Fig. 4). Surgical therapy consisted of a needle-localized wide local excision and a sentinel lymph-node biopsy.

The right breast wide local excision specimen showed one small nodular focus of residual tumor measuring 4 mm. Microscopic examination revealed poorly defined nests and cords of undifferentiated epithelial cells with a prominent lymphoplasmacytic infiltrate (Figs. 5A, B). Immunohistochemical staining of the neoplastic cells demonstrated positivity for epithelial markers CAM 5.2 (Fig. 5C), HMW, and CK7. These cells were negative for Epstein-Barr virus Latent Membrane Protein. The lymphocytes were predominantly CD3-positive (Fig. 5D) with focal CD20 positivity. These findings, including the morphology

and immunohistochemical staining profile, were consistent with the diagnosis of lymphoepithelioma-like carcinoma of

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Table 1. Differential diagnosis of LELC of the breast

Lesion	Imaging modality			
	Mammography	Ultrasound	CT	MRI
Invasive carcinoma of the breast	<ul style="list-style-type: none"> • High-density, irregular-shaped mass with ill-defined or spiculated margins • Less commonly circumscribed mass • Pleomorphic fine linear or branching microcalcifications • Architectural distortion • Parenchymal asymmetry 	<ul style="list-style-type: none"> • Hypoechoic solid irregular-shaped mass with nonparallel orientation and posterior acoustic shadowing • Less commonly circumscribed mass • Complex solid and cystic mass • Sonographic distortion 	<ul style="list-style-type: none"> • Irregular-shaped enhancing soft-tissue-density mass • Less commonly circumscribed mass 	<ul style="list-style-type: none"> • T2WI: Usually hypointense mass • T1WI CE: Heterogeneous or rim enhancing mass with fast initial and washout delayed phase kinetics
Metastasis	<ul style="list-style-type: none"> • Single or multiple round, oval or irregular-shaped mass(es) with circumscribed or ill-defined margins 	<ul style="list-style-type: none"> • Single or multiple hypoechoic round, oval or irregular-shaped solid or cystic mass(es) with indistinct or microlobulated margins 	<ul style="list-style-type: none"> • Single or multiple, usually enhancing soft-tissue-density mass(es) 	<ul style="list-style-type: none"> • T2WI: Hyper-, iso-, or hypointense mass(es) • T1WI CE: Usually enhancing mass(es) with fast initial and washout delayed phase kinetics
Lymphoma	<ul style="list-style-type: none"> • Single or multiple circumscribed or ill-defined mass(es) • Architectural distortion • Parenchymal asymmetry 	<ul style="list-style-type: none"> • Hypoechoic solid circumscribed or ill-defined mass(es) • Sonographic distortion 	<ul style="list-style-type: none"> • Enhancing soft-tissue mass(es) • Often associated with bilateral axillary lymphadenopathy 	<ul style="list-style-type: none"> • T2WI: Usually hyperintense mass(es) • T1WI CE: Heterogeneously enhancing mass(es) with fast initial and washout delayed phase kinetics
LELC of the breast	<ul style="list-style-type: none"> • Irregular high-density mass with microlobulated margins • Circumscribed mass • Poorly defined mass or focal asymmetry 	<ul style="list-style-type: none"> • Solid hypoechoic mass with microlobulated margins and posterior acoustic enhancement • Area of subtle abnormal parenchyma 	<ul style="list-style-type: none"> • Heterogeneously enhancing soft-tissue-density mass • Low-density mass 	<ul style="list-style-type: none"> • No data available
Abbreviations: CE = contrast enhanced; LELC = lymphoepithelioma-like carcinoma; T1WI = T1-weighted imaging; T2WI = T2-weighted imaging				

the breast.

Five out of five sentinel lymph nodes removed were negative for tumor involvement. Final staging was ypT1aN0M0, Stage IA. Postoperative adjuvant radiation therapy was administered. Given the ER-positive tumor and premenopausal status of the patient, antihormonal therapy with tamoxifen was also initiated. To date, there is no evidence of local or distant recurrence after 2 years of followup.

Discussion

Lymphoepithelioma-like carcinoma (LELC) is a malignancy that microscopically resembles nasopharyngeal lymphoepithelioma.

While LELC can occur in many organ systems, this entity rarely occurs in the breast. Kumar and Kumar (1) published the first instance of LELC of the breast in 1994, and since then fewer than 20 cases of this tumor have been documented in the literature (2-13). The age of initial presentation of the previous cases ranged from 37 to 69 years (2-13). At this time, the etiology of LELC of the breast remains unknown. LELC tumor cells in other organ systems have been associated with varying degrees of Epstein-Barr virus (EBV) genome expression; however, there have been no documented cases of EBV detected in LELC of the breast (2).

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The clinical and imaging findings of LELC of the breast are similar to that of other primary breast malignancies. Clinically, LELC of the breast often presents as a palpable breast mass. The mammogram may show a high-density, irregular-shaped mass with microlobulated margins, a circumscribed mass, or a poorly defined mass that can appear mammographically as a focal asymmetry (3, 4). Sonographic evaluation may demonstrate a solid hypoechoic mass with microlobulated margins and posterior acoustic enhancement, or an area of subtle abnormal parenchyma (4, 5). Computed tomography may reveal a heterogeneously enhancing or low-density mass (6). Previously documented tumor sizes ranged from 1 cm to 4 cm at the time of diagnosis. Four prior cases have noted metastatic lymph node involvement; therefore, thorough examination of the axillary and supraclavicular regions is important to identify potential lymphadenopathy (6).

The differential diagnosis of LELC of the breast based on clinical and imaging findings includes primary invasive breast cancers, metastasis, and lymphoma (Table 1). Once tissue has been obtained, the differential diagnoses are usually narrowed to lymphoma and medullary carcinoma. Histologically, LELC of the breast can appear similar to lymphoma due to the presence of undifferentiated cancer cells surrounded by a prominent lymphocytic infiltrate. Medullary carcinoma is also a consideration, because LELC of the breast shares a similar cellular morphology. Application of immunohistochemistry and careful investigation of the tissue architecture are helpful in distinguishing these entities (6).

Since LELC of the breast is so rare, limited information is available to direct optimal oncologic management. All reported instances in the literature have been treated surgically, either with wide local excision or mastectomy, and with or without adjuvant radiotherapy. Chemotherapy had been used in three previous cases; however, only one therapeutic regimen has been described in the literature (cyclophosphamide, epirubicin, and 5-fluorouracil), and this was administered only after the patient presented with chest-wall recurrence (5, 7, 8). This patient later developed lung metastasis (7). One patient was found to have developed LELC of the contralateral breast three years after the initial diagnosis. The remaining cases demonstrated no evidence of disease at the time of followup (range: 3-72 months).

To our knowledge, there has been no documented use of neoadjuvant chemotherapy prior to surgical treatment of LELC of the breast. Our case demonstrated excellent treatment response to a neoadjuvant chemotherapy regimen of docetaxel, doxorubicin, and cyclophosphamide prior to breast-conserving surgical excision. Given the paucity of previous cases to guide physicians encountering this entity, our experience may help facilitate future management decisions.

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