

Lymphoepithelioma-Like Carcinoma of The Breast: A Case Report

Trupti R Jansari*, Tanvi Gupta, Priti P Trivedi, Manoj J Shah

Department of Pathology, The Gujarat Cancer And Research Institute, Ahmedabad, Gujarat, India

Keywords: Breast, Differential Diagnosis, Lymphoepithelioma-Like Carcinoma.

ABSTRACT

Lymphoepithelioma-like carcinoma (LELC) is an undifferentiated carcinoma, it occurs in the organs that exclude nasopharynx, but has the same morphology as that of nasopharyngeal lymphoepithelioma. It has been described in several organs, however it is rarely seen in the breast. Due to the undifferentiated appearance of neoplastic cells and the presence of prominent lymphocytic infiltrate, LELC can wrongly be diagnosed as lymphoma and medullary carcinoma. In this case, we present the LELC of the breast in a 39 year-old woman with clinical, histological and immunohistochemical features with differential diagnosis.

***Corresponding author:**

Dr Trupti R. Jansari, Room no. 412, Histopathology department, The Gujarat Cancer And Research Institute, Civil Hospital Campus, Asarwa, Ahmedabad, Gujarat. 380016. India

Phone: +91 - 9586727494

E-mail: dr.truptijansari@gmail.com



Introduction

Lymphoepithelioma, which was first described in the nasopharynx by Regaud and Reverchon, and Schminke in 1921, is an undifferentiated carcinoma composed of malignant epithelial cells with prominent lymphoid infiltration.^[1] Lymphoepithelioma-like carcinomas (LELCs) are tumors with the same morphological features as undifferentiated nasopharyngeal carcinomas. LELCs have been reported in the salivary glands, stomach, lungs, and thymus, and less often in the skin, uterine cervix, and bladder.^[2] The cells may be arranged singly (Schminke's pattern) or in syncytial masses, nests, or cords (Regaud's pattern).^[3] Breast LELC was first reported by Kumar et al. in 1994.^[4] Although it was shown that there is a relationship between LELCs in the stomach, lungs, and salivary glands, and Epstein-Barr virus (EBV), such a relationship has not yet been observed in other organs, including the breast.^[2]

Here we present a patient diagnosed with breast LELC, its clinical, histological, and immunohistochemical features, and a discussion based on a review of the literature.

Case report

A 39 year old female presented with lump in left breast since one month, which was gradually increasing in size but was not associated with any pain or nipple discharge. Physical examination revealed firm to hard non-tender mobile lump measuring 4.0cm×3.5 cm in the upper quadrant (at 12 o'clock position) of the left breast. Axillary lymph nodes were not palpable.

Mammography showed a 42mm×36 mm dense lobulated lesion in the upper quadrant at 12 o'clock of left breast. Lesion had ill-defined margins without any evidence of significant calcification and was found to be suspicious for malignancy.

We received core needle biopsy of the lesion which was diagnosed as Lymphoplasmacytic cell mastitis with invasive carcinoma. Patient underwent lumpectomy outside and then came to this hospital for expert opinion. Microscopic examination revealed multinodular growth pattern consisting of predominantly lymphoplasmacytic cells and in between clusters of malignant cells showing syncytial pattern, having eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli. Focal area showed histiocytic giant cells [figure – 1(a-c)]. No in-situ carcinoma was identified in adjacent breast parenchyma and necrosis was absent.

Histological features favoured lymphoepithelioma-like carcinoma of the breast. Immunohistochemistry showed positivity of tumor cells for AE1, CK7 and EMA while lymphocytic population was reactive for LCA, CD20

and CD2 and negative for CD30. Estrogen receptor(ER), progesterone receptor(PR) and HER-2 neu was negative[figure – 2(a-f)].

Finally, diagnosis of LELC breast was given. For further management, left modified radical mastectomy was planned. But, unfortunately patient was lost to follow-up.

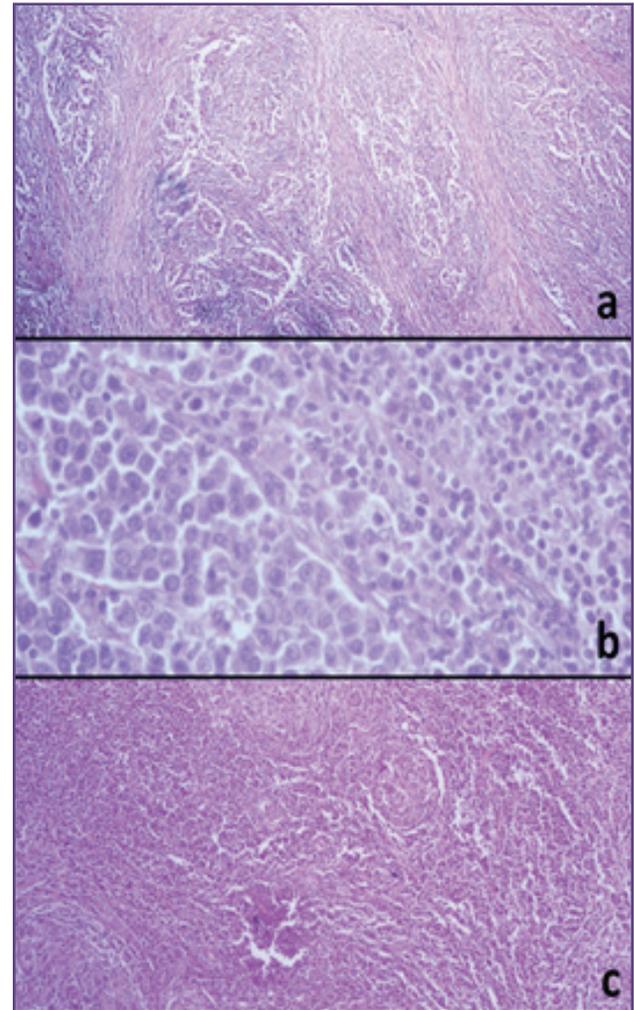


Fig. 1: Lymphoepithelioma-like carcinoma of the breast. A) Multinodular growth pattern (H&E, 10x), b) Neoplastic cells showing eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli (H&E, 40x) c) Histiocytic granuloma (H&E, 10x).

Discussion

Lymphoepithelioma is an undifferentiated carcinoma, which was originally described in the nasopharynx.^[2] LELCs are tumors that occur in all organs, except for the nasopharynx, and they have the same morphological features as nasopharyngeal lymphoepithelioma.^[5] LELCs are characterized by malignant epithelial cells, which are

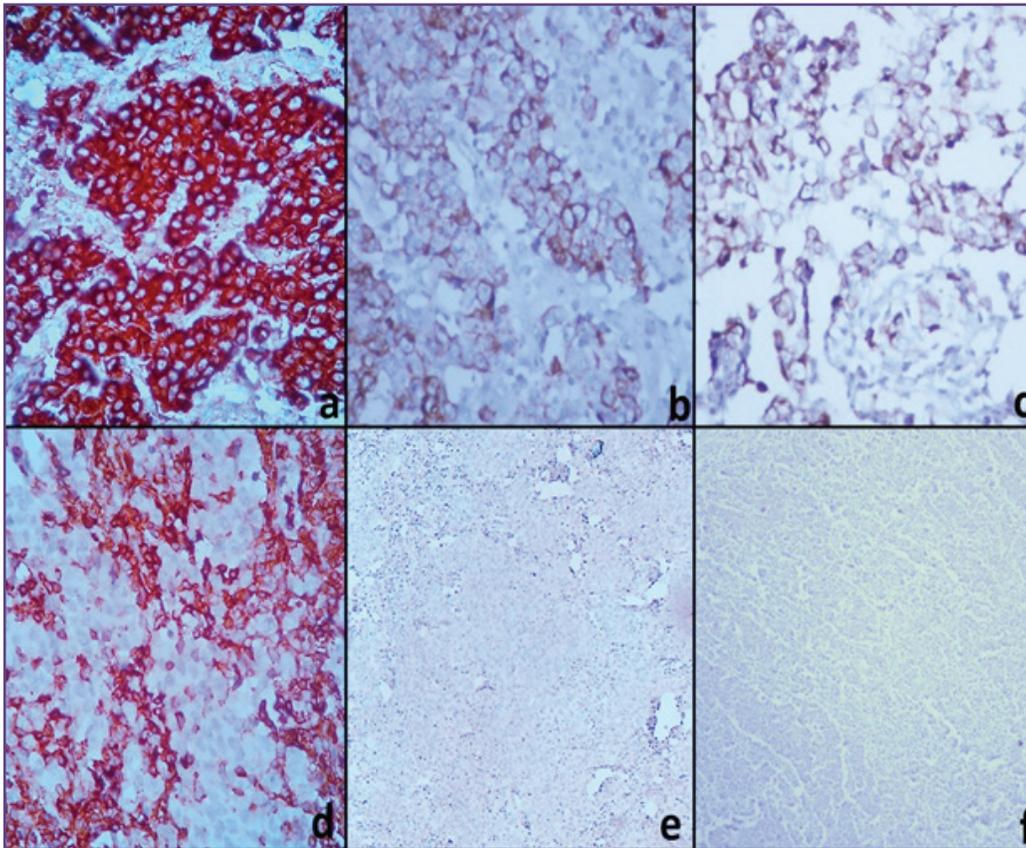


Fig. 2. IHC results. a) EMA Positive, b) AE-1- Positive, c) CK-7- Positive, d) LCA- Positive in lymphocytes, e) ER- Negative, f) PR- Negative.

in the form of islets or cords, or are syncytial in structure or scattered individually. They contain prominent lymphoid stroma. Because medullary carcinoma, atypical medullary carcinoma, and some ductal or lobular carcinomas can have prominent lymphoid stroma, they should be considered in the differential diagnosis of LELCs.^[6,7] In addition, the differential diagnosis of LELC should include Non-Hodgkin's lymphoma. Lymphomas have diffuse neoplastic proliferation of lymphoid cells, but do not have an epithelial component; however, sometimes in H&E-stained sections it can be difficult to differentiate between malignant epithelial cells and mononuclear lymphoid cells.^[7] EMA and cytokeratin stains, which are used for immunohistochemical analysis, are very useful in showing the nature of tumor epithelial cells located between lymphocytes and plasma cells.^[5,6]

LELC raised the possibility of Hodgkin disease, so called T-cell-rich B-cell lymphoma, and anaplastic large cell lymphoma. The tumor cells resembled mononuclear Hodgkin cells, especially set in the background of lymphocytes, plasma cells, and occasional eosinophils.

The resetting of lymphoid cells around the large tumor cells simulated the pattern seen in T-cell-rich B-cell lymphoma. Some of the more pleomorphic tumor cells had the characteristic nuclear features also seen in anaplastic large cell lymphoma. This resemblance was further accentuated by the focal clustering of the tumor cells. Immunohistochemistry rules out the lymphoma as a differential diagnosis.^[1]

LELCs that exhibit a syncytial growth pattern in the presence of dense lymphoid cell infiltration are sometimes misdiagnosed as medullary carcinoma. In medullary carcinoma, the tumoral margin is typically well circumscribed pushing type. Tumor cells are separated from adjacent stroma by a sharp border. Cells have high grade nuclear features and are arranged in syncytial pattern (>75%).^[5,7]

In invasive ductal or lobular breast carcinomas the inflammatory infiltrate may be observed in the stroma, however, the quantity of mononuclear infiltrate is low and not more than that observed in LELCs. Nonetheless, structural growth patterns (tubular, cribriform structures,

diffuse sheets), cytological features (monomorphic low nuclear grade nuclei, distinct cell borders, intracytoplasmic lumens), and stromal desmoplasia are helpful in differentiating ductal or lobular carcinoma with inflammatory stroma from LELC.^[7] The relationship between LELC and EBV varies by organ. The presence of the EBV genome in LELC was observed in the salivary glands, lungs, stomach, and thymus, whereas the relationship was not observed elsewhere. In terms of the relationship between EBV and breast LELC, in all previous reports of breast LELC the presence of the EBV genome, which was investigated by various methods, was not noted.^[2]

Regarding IHC studies on LELC, Kumar et al., Pesterelli et al., and Ilvan et al. reported ER and PR positivity in tumor cells,^[4,6,8] whereas Dadmanesh et al. reported that in all but 1 of their cases ER and PR positivity was not noted.^[7] Again, HER-2 positivity was observed only by Kurose et al., while the other reported cases were HER-2 negative.^[5] In a study of 6 cases by Dadmanesh et al. low molecular weight cytokeratin and EMA were positive, and high molecular weight cytokeratin and actin were negative in all the cases.^[7] In the presented case, tumor cells were positive for AE1, CK7 and EMA, while negative for ER, PR and HER-2.

As with all breast cancers, surgery is the primary therapy for LELC of the breast. Breast LELC was reported to have a good prognosis.^[2] Axillary lymph node metastasis occurred in 1 of the 6 cases reported by Dadmanesh et al., and in 1 case reported by Naidoo et al. and Pesterelli et al., whereas in the other reported cases axillary lymph node metastasis was not observed.^[1-2,7-8]

To conclude, LELC of the breast is a rare clinical entity. Pathologic diagnosis depends on a thorough histological and immunohistochemical examination. The known characteristic pathologic features of LELC ensure an appropriate diagnosis.

Funding

None

Competing Interests

None declared

References

1. Naidoo P, Chetty R. Lymphoepithelioma-like carcinoma of the breast with associated sclerosing lymphocytic lobulitis. *Arch Pathol Lab Med* 2001;125: 669-72.
2. Kucukzeybek BB, Postaci H, Ozguzer A, Yakan S, Denecli AG. Lymphoepithelioma-like Carcinoma of the Breast: A Case Report and Review of the Literature. *Int J of Hematol and Oncol*; 2011;21:115-119
3. Dinniwell R, Hanna W et al. Lymphoepithelioma-like carcinoma of the breast: a diagnostic and therapeutic challenge. *CurrOncol* 2012;19: 177-183.
4. Kumar S, Kumar D. Lymphoepithelioma-like carcinoma of the breast. *Mod Pathol* 1994;7: 129-31.
5. Kurose A, Ichinohasama R, Kanno H, et al. Lymphoepithelioma-like carcinoma of the breast. Report of a case with the first electron microscopic study and review of the literature. *Virchows Arch* 2005;447: 653-659.
6. Ilvan S, Celik V, Akyildiz EU, et al. Lymphoepitheliomalikecarcinoma of the breast: is it a distinct entity? Clinicopathologicalevaluation of two cases and review of the literature. *The Breast* 2004; 13: 522-26.
7. Dadmanesh F, Peterse JL, Sapino A, et al. Lymphoepithelioma-like carcinoma of the breast: lack of evidence of Epstein-Barr virus infection. *Histopathology* 2001;38: 54-61.
8. Pestereli HE, Erdogan O, Kaya R, Karaveli FS. Lymphoepithelioma-like carcinoma of the breast. A newly recognized subtype of lobular carcinoma. *APMIS* 2002;110: 447-450.