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Primary non-Hodgkin's lymphoma of breast – A rare cause of breast lump

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ABSTRACT

We, here, report a case of primary breast lymphoma in a 59 years old female. The diagnosis was suspected on fine needle aspiration cytology and confirmed on excision biopsy of the tumor. Histology and immunophenotyping were in accordance with non-Hodgkin's diffuse large B-cell lymphoma. The patient has been planned for adjuvant chemoradiation. The management and outcome of primary breast lymphoma and carcinoma are totally different. Early and prompt diagnosis of primary breast lymphoma is of utmost importance to avoid unnecessary mastectomies. Fine needle aspiration cytology supplemented by immuno-cytochemistry can be applied as a reliable and cost-effective tool in the early diagnosis of primary breast lymphomas, while histopathology and immunohistochemistry are conclusive.

1. Introduction

Malignant lymphoma is a neoplasm which originates in lymphatic tissue. Primary non-Hodgkin's lymphoma of the breast is very rare and a distinct possibility in the diagnosis of breast malignancies, accounting for only about 0.1 to 0.5% of all reported malignant breast tumors and for 1.7–2.2% of extra nodal NHL [1]. There are various kinds of breast lymphomas, but the most common is the B cell non-Hodgkin's lymphoma. At presentation, most patients are clinically thought to have breast carcinoma and the diagnosis of lymphoma is made at FNAC or at histopathology of the excised breast lump as in our case. In terms of clinical prognosis, an early diagnosis of a low grade or stage I lymphoma will generally give the best outcome. The management is by surgery, chemotherapy and radiotherapy alone or usually in various combinations depending on the histological subtype, disease extent and individual patient. In view of the rarity of the lesion, the case is being reported with review of literature.

2. Case report

A 59 years old female from rural area presented to our outpatient department with a lump in left breast for previous 7 months with no constitutional symptoms. There was no complaint of pain or nipple discharge. On local examination, a firm to hard lump of about 1.4 × 1.0 cm in upper outer quadrant of left breast and fixed to the overlying skin was found. There was no history of trauma. Rest of the systemic examination was within normal limits.

USG showed a cystic lesion measuring 1.3 × 1.2 cm with wall calcification at 2 o'clock position in left breast. On mammography, there was a small oval radio-opaque lesion with irregular margins in upper outer quadrant of left breast with maintenance of retroareolar space (Fig. 1). Fine needle aspiration cytology (FNAC) smears prepared from the lump showed it to be a lymphoproliferative disorder with few groups of duct epithelial cells with degenerative changes in background of lymphoid cells, many of which were immature/atypical including few cleared forms, lymphoglandular bodies and RBCs (Fig. 2). On Excision biopsy of the lump, there was dense infiltration by sheets of lymphoid cells; on immunohistochemistry (IHC), cells were diffusely positive for LCA and CD20, focally positive for CD5 and negative for CK, synaptophysin, ER, PR and Her 2 neu receptors. Investigations showed Hb 10.4 g/dl, with normal total and differential leukocyte counts and platelet count. ESR 40 mm in 1st hour. Liver and kidney function tests were within normal limits. Chest X-ray and USG abdomen were normal. So, a provisional diagnosis of lymphoproliferative disorder was made. Histopathological examination of the tumor confirmed the diagnosis to be the primary breast non-Hodgkin's diffuse large B-cell lymphoma (DLBC NHL). On immunohistocytochemistry (IHC)

CD 20: Diffusely positive
CD 5: Focally positive
CK: Positive in ducts (Figs. 3 and 4).
The patient is on regular follow-up, doing well and has been planned for adjuvant chemoradiation.

3. Discussion

Primary breast lymphoma (PBL) is defined pathologically as the presence of lymphomatous infiltrate in normal breast tissue in a patient with neither previous nor concurrent non-Hodgkin's lymphoma at

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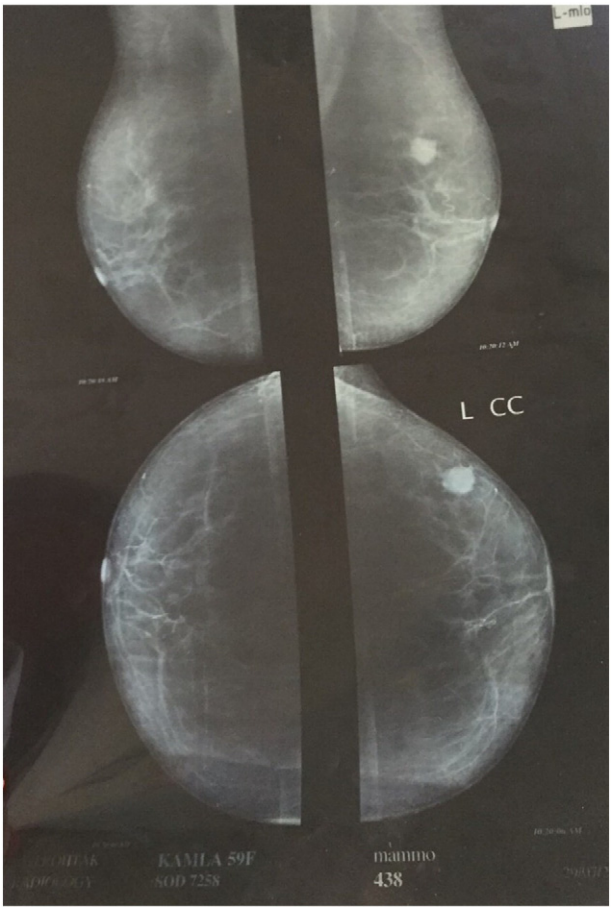

Fig. 1. Mammogram showing a small oval radio-opaque lesion with irregular margins in upper outer quadrant of left breast with maintenance of retroareolar space.

another site, although involvement of ipsilateral axillary lymph node enlargement may be present [2]. It is a rare tumor and often present as an innocuous lump. PBL shows a wide age distribution with a bimodal peak; with younger population showing bilateral involvement and older population showing unilateral involvement [3]. The majority of breast lymphomas are of the non-Hodgkin's lymphoma type (PBNHL). It usually affects women in their fifth or sixth decade of life. The most common symptom of PBL is a palpable lump; less frequently, it may present as diffuse breast enlargement. There is usually unilateral involvement, but bilateral cases have also been reported [2]. Wiseman and Liao are credited with first defining the clinical criteria for the classification of PBL [4]. The specific criteria for the diagnosis of PBL include:

1. The clinical site of presentation is the breast.
2. A history of previous lymphoma or evidence of widespread disease are absent at diagnosis.
3. Lymphoma is demonstrated with close association to breast tissue in the pathologic specimen.
4. Ipsilateral lymph nodes may be involved if they develop simultaneously with the primary breast tumor.

On ultrasound, PBNHL often presents as a hypoechoic area with circumscribed or microlobulated margins demonstrating increased vascularity [5]. The typical mammographic appearance of PBNHL consists of a solitary, noncalcified, circumscribed or indistinctly marginated mass with adjacent lymphadenopathy. Less commonly, diffuse increased parenchymal density with skin thickening is observed [2]. MRI may be more sensitive and accurate in representing and detecting multicentric lesions.

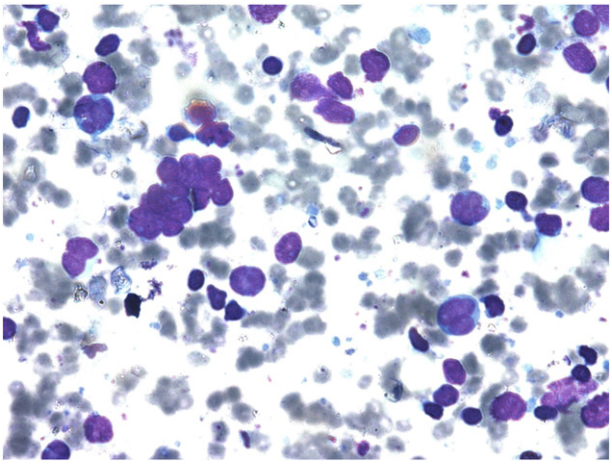

Fig. 2. FNAC breast lump showing few groups of duct epithelial cells with degenerative changes in background of lymphoid cells, many of which were immature/atypical including few cleared forms, lymphoglandular bodies and RBCs (400×).

The clinical presentation and radiology of breast lymphoma and carcinoma are similar. Both present as painless enlarging breast lump. On mammogram lymphoma may lack the irregular border of infiltrating carcinoma and more than half exhibit no calcification. Pathology remains the gold standard to differentiate these two malignancies. Histopathology, IHC and/or flow cytometry are helpful in differentiating primary breast lymphoma from other tumors [6].

All histological types of lymphoma have been described. Primary breast lymphomas are most commonly B-cell lymphomas; approximately one-half are diffuse large B-cell lymphoma (DLBCL). Indolent histologies, follicular non-Hodgkin's lymphoma or extranodal marginal zone (MALT) lymphoma occur less commonly. More than 80% of PBL are B-cell lymphomas, mostly CD20 +. The most frequent histopathologic types are: diffuse large B-cell lymphoma (DLBCL) which accounts for up to 50% of all PBL, follicular lymphoma (FL) – 15%, MALT lymphoma – 12.2%, Burkitt's lymphoma (BL) and Burkitt-like lymphoma 10.3%. Other histological types of PBL include marginal zone lymphoma (MZL), small lymphocytic lymphoma (SLL), and anaplastic large cell lymphoma (ALCL). These lymphomas have been shown to be of a non-germinal centre B-cell phenotype with a high proliferation index and are thought to be associated with a poor outcome. Although less common than breast carcinoma, PBL is often clinically indistinguishable from other breast tumors. Although primary breast lymphoma and carcinoma may appear similar clinically and radiographically, their treatments and outcome differ radically. Also because of the rapid growth of lymphoma, it is very important to distinguish primary breast lymphoma from carcinoma in early stages [7].

The management of Primary Non-Hodgkin's lymphoma of breast is based on histologic grade. Patients with low grade disease can be managed with local therapy alone. The role of chemotherapy in this group is unclear. Patients with intermediate or high grade disease have better out come if chemotherapy is included.

Disagreement regarding the treatment of such disease stems from its rareness, with small case reports; consequently, randomized controlled trials or clinically controlled trials cannot be carried out. The prognosis varies, as do the applied treatment modalities, which include surgery, radiotherapy and chemotherapy used alone or in combination.

Mastectomy has been a common component of PBL therapy for decades and remains a frequent treatment choice in some reports. Several studies found that mastectomy offered no benefit in the treatment of primary breast lymphoma [5,7,8]. Ideally, surgery should be limited to a biopsy to establish the correct histological diagnosis, leaving the treatment with curative intent to radiotherapy and chemotherapy.