Multinodular bilateral breast lesions diagnosed as primary breast lymphoma in a young lactating woman
Mohammad Akrama, Ruquiya Afroseb, Sadaf Hayatb, Mohammed Naimb

Departments of bRadiotherapy, bPathology, J.N.Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India
Correspondence to Ruquiya Afrose, MD, Department of Pathology, J.N.Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India
Tel: 05712700201, e-mail: ruqs.afrose@gmail.com

Introduction
Primary breast lymphoma (PBL) is a rare extranodal lymphoma, accounts for about 0.04–0.74% of all malignant breast tumors and 0.7% of extranodal non-Hodgkin’s lymphomas [1]. PBL is mainly found in the female population, accounting for 95–100% of all PBL patients [2]. Diffuse large B-cell lymphoma is the most common histological diagnosis [3]. This lesion tends to follow a bimodal age distribution, with a unilateral, localized-type-resembling typical breast carcinoma affecting the older women, and a bilateral, more diffuse-type affecting the younger often puerperal or pregnant women [4]. We report an unusual presentation of PBL in a young puerperal female, which made the diagnosis a challenge.

Case history
A 24-year-old lactating female with a history of normal vaginal delivery 1 month back, presented to us with a bilateral nodular breast enlargement from the last 2 months. The patient also had a history of bilateral axillary lymph node enlargement from the last 15 days. There was associated pain, low-grade fever, and generalized weakness. Examination revealed bilateral enlarged breast with erythema and prominent vessels over the skin. There were multiple, discrete mobile nodular firm masses ranging from 3 to 6 cm in diameter involving both breasts (three in the right and two in the left breast). Nipple and areola complex were normal. Bilateral multiple mobile axillary lymph nodes were also palpable (Fig. 1). No other peripheral lymph nodes were palpable.

Ultrasound examination of the breast revealed multiple well-defined hypoechoic masses of size 3, 4, and 6 cm in the right breast and 4 and 5 cm in the left breast having predominantly solid components with perilesional inflammatory changes, and architectural

Figure 1

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distortion. Ultrasound of the abdomen and pelvis did not reveal any abnormality. An impression of bilateral breast malignant tumor with bilateral axillary lymph node metastasis was suggested.

Fine needle aspiration cytology smears from both the right and the left breast showed richly cellular monomorphic population of loosely cohesive single lymphoid cells of two to three times the size of mature lymphocytes, with moderate anisonucleosis, moderately opened-up chromatin, and fragile cytoplasm (Fig. 2a). No evidence of gland formation or intracytoplasmic mucin was seen. The ductal epithelial cells of the breast were not seen in the cytology smears. Similar cytomorphic features were also present in the aspirate from both axillary sides of lymph nodes. A cytological diagnosis of non-Hodgkin's lymphoma large cell type was given.

A core needle biopsy of the right breast revealed replacement of the breast parenchyma by diffuse sheets of monomorphic lymphoid cells (Fig. 2b). On higher magnification, the lymphoid cells showed moderate anisokaryosis, clumped nuclear chromatin, conspicuous nucleoli, and minimal amount of eosinophilic cytoplasm on a background of lymphoglandular bodies (Fig. 2b).

Immunohistochemical studies were performed on formalin fixed, paraffin-embedded blocks of the core needle biopsy specimen. The lymphoid cells expressed diffuse strong membranous positivity with antibodies against leukocyte common antigen (Fig. 2c) and CD20 (Fig. 2d), whereas negativity for CD3 and cytokeratin.

As there was no primary elsewhere as evidenced by the absence of hepatosplenomegaly and the absence of any lymph node enlargement other than bilateral axillary lymph nodes, the final diagnosis of primary diffuse large B-cell lymphoma of the breast, stage II was offered. Her baseline laboratory investigations, including bone marrow examination and ultrasound examination of the abdomen were normal. The patient was planned for systemic chemotherapy R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). However, further management and follow-up of the patient could not be carried out, as she did not turn up after first cycle of chemotherapy.

**Discussion**

All cases of breast lymphomas reported in the literature may not have been truly primary, because secondary involvement of the breast is often difficult to rule out. Wiseman and Liao [5] proposed a criterion to diagnose PBL, which were further modified by the International Extranodal Lymphoma Study Group. According to International Extranodal Lymphoma Study Group, the specific criteria for the diagnosis of PBL include the following [6]:

1. No other organ except the breast is involved as primary site of tumor
2. A history of previous lymphoma or evidence of widespread disease absent at the time of diagnosis,
3. Patients with lymphoma demonstrated to have close association with breast tissue shown in the pathologic specimens, and
4. Patients with ipsilateral lymph nodes may be involved if they develop simultaneously with the primary breast tumor.

This definition of PBL indicates that PBL comprises only tumors in stage I (lymphoma limited to the breast) and stage II (lymphoma limited to the breast and ipsilateral axillary lymph nodes), excluding those originating outside of the breast. Our case fulfilled the criteria of stage II PBL of B-cell lineage and was clinically similar to the case reported by Illés [7] and Kirkpatrick et al. [8].

Clinically, breast lymphoma presents as painless, rapidly growing, unilateral breast mass with or without axillary lymph node involvement and is difficult to distinguish from breast carcinoma. PBL tends to be larger in size at the time of diagnosis compared with breast cancer, but it cannot be regarded as a distinguishable feature. Skin retraction, erythema, peau d’orange appearance, and nipple discharge are rare in PBL compared with breast carcinoma [6]. Rarely, PBL presents as inflammatory breast carcinoma or breast abscess. On imaging, these lesions usually appear as well-circumscribed

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**Figure 2**

(a) Monomorphic population of atypical lymphoid cells, Pap (×400).
(b) H&E (×400).
(c, d) Lymphoid cells showing strong membranous positivity for leukocyte common antigen (LCA) and CD20.
homogenous hypoechoic mass with absence of signs of breast malignancy such as microcalcification, spiculation, and distortion of surrounding tissue [6,9].

In pregnancy and lactation, PBL is usually bilateral, more aggressive, and progresses to advanced stage of disease within a short span of time suggesting hormonal influence over tumor growth [10]. Similar presentation was found in our patient, having a history of 2-months duration and, when presented, the tumor had already involved both the breast and axilla in the form of multiple large nodular masses. This is in contrast to that reported in other cases, in which PBL was presented as single nodule or diffuse mass. Nipple retraction or peau d’orange appearance was not found in our case, favoring the diagnosis of lymphoma over carcinoma.

Almost all PBLs have a B-cell lineage, and 40–70% of these are diffuse large B-cell lymphoma [3]. In young pregnant or lactating women the morphology mimics Burkitt’s lymphoma or Burkitt-like lymphoma. However, follicular lymphoma, lymphoblastic lymphoma, lymphoplasmacytic lymphoma, peripheral T-cell lymphoma, and true histiocytic lymphoma are also reported in PBL [11]. We did not find cytoplasmic vacuolation, high mitotic count or starry sky appearance in our case, which is usually observed in Burkitt’s lymphoma.

The treatment of primary non-Hodgkin breast lymphoma is similar to that used for other lymphomas and depends on the histological type. The most effective combination therapy reported in the literature is radiotherapy and three to ten cycles of treatment with R-CHOP [12].

**Conclusion**

Possibility of lymphoma in the differential diagnosis of breast masses is not usually placed by attending clinician. It is important to diagnose PBL accurately to avoid unnecessary surgery and to conserve breast, as primary treatment of PBL is chemoradiation. Fine needle aspiration cytology is simple, rapid, reliable, and cost-effective procedure, whereas core biopsy of the breast lesion aids further in resolving the diagnostic dilemma and is required for accurate diagnosis of the lesion.

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**References**