Case Report with Review of Literature

Bilateral Primary Breast Lymphoma Masquerading as Breast Carcinoma: A Rare Case Report

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Ind J Med Paediatr Oncol

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Abstract

Primary breast lymphoma (PBL) is a rare entity, accounting for roughly 0.5% of all primary breast tumors. It commonly presents as a lump, which is frequently confirmed based on histopathological findings, as it is difficult to differentiate from other breast primaries on imaging. On histopathology, the most common subtype is diffuse large B-cell lymphoma (DLBCL). Prognostic factors are age, histological grade, and stage at diagnosis. We report a case of a 44-year-old female, who came to us with a painless lump in her left breast, after having a modified radical mastectomy for a similar lump in the opposite breast, under the suspicion of carcinoma breast, 25 days ago. Postoperative histopathology report from the right breast was positive for DLBCL, similar to a tru-cut biopsy from the left breast. 18-Fludeoxyglucose-positron emission tomography (PET) scan was done, which showed no avid lesions in any other organs. The patient was started on an RCHOP chemotherapy regimen. She responded very well to the treatment. After 4 years, the patient remains disease free with no evidence of any recurrence in yearly follow-up PET scans. Awareness and clinical suspicion of PBL are critical for rapid and precise diagnosis to avoid unnecessary surgery and better treatment outcomes.

Keywords

- primary breast lymphoma
- breast carcinoma
- DLBCL
- RCHOP
- IHC

Introduction

Primary breast lymphoma (PBL) is an uncommon manifestation of non-Hodgkin's lymphoma (NHL). PBL was first defined by Wiseman and Liao and later modified by Hugh as localized involvement of mammary tissue by lymphomatous infiltrate, with the involvement of ipsilateral axillary lymph nodes being optional.[1] PBL consists of 0.05 to 0.53% of all breast cancers, making it a rare diagnosis and resulting in unnecessary surgical excision.[2] Various frequencies have been reported, but in most studies, they account for less than 1.7 to 2.2% of all extranodal lymphomas and 0.38 to 0.70% of all NHLs.[1] The most common clinical sign of breast lymphoma is a painless, unilaterally palpable breast lump. Approximately 10% of patients may have bilateral breast lumps when they are first diagnosed.[3] While the imaging features are nonspecific, they can occasionally resemble benign tumors. A tru-cut needle biopsy is typically used to establish the diagnosis. Unlike primary breast cancer, PBL does not require surgery as the primary treatment. The principal approaches to treatment are chemotherapy and radiation therapy. When positive for CD-20, targeted therapy injection rituximab is added with the chemotherapy. The clinical outcome is very good; with 80% overall survival (OS) at 5 years.[1] Only case studies and case series can be reviewed in the literature. We present a case of a 44-year-old female patient with bilateral PBL, her imaging modalities, and the management protocol for managing lymphoma as per our institution.

DOI https://doi.org/10.1055/s-0044-1791945.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

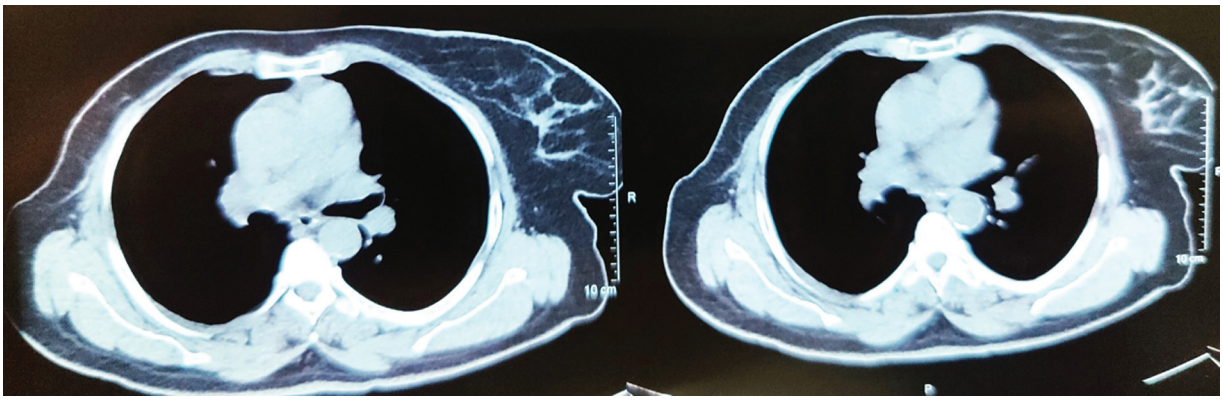

Fig. 1 Contrast-enhanced computed tomography (CT) scan showing lesion in the left breast and postop right breast.

Case History

A 44-year-old female patient presented to the outpatient department with a complaint of a lump in her left breast for 1 year. She was referred to us by the general surgery department, after doing a modified radical mastectomy of the right breast 25 days back, under the clinical suspicion of breast carcinoma. The scar site was healed and was sent to us for further management. The patient experienced a lump in the upper inner quadrant of her right breast for 1.5 years, steadily increasing in size. It was hard, tender, and fixed to breast tissue, for which she went to a surgeon.

Our clinical examination revealed a 3×3 cm lump in the lower outer quadrant of the left breast that was hard, nontender, and mobile. A 1×1.2 cm lymph node in the left axilla was palpable, nontender, and freely mobile. There were no other palpable lymph nodes in the bilateral cervical or supraclavicular region. No hepatosplenomegaly can be appreciated during examination. The patient underwent contrast-enhanced computed tomography (CECT) scan of the thorax, which showed a lesion in the left breast with right postop chest wall (►**Fig. 1**). The postoperative histopathology report (►**Fig. 2**) for the right breast revealed a tumor composed of groups, follicles, and lobules of small round cells with scanty cytoplasm and hyperchromatic nuclei separated by fibrous septa, indicating lymphoma, with all margins and lymph nodes negative. Immunohistochemistry (IHC) was performed, as shown in ►**Table 1**.

IHC confirmed it as diffuse large B-cell NHL (DLBCL) and was CD-45 (►**Fig 3**), CD-20 positive (►**Fig. 4**). On 18-fludeoxyglucose (FDG) positron emission tomography (PET) scan, there was a $3.3 \times 2.5 \times 3.5$ cm FDG-avid lesion (standardized uptake value [SUV] 24) present in the left breast along with bilateral axillary lymph nodes, the largest being 1.6 cm in the left axilla (SUV 5.5). Tru-cut biopsy from the left breast also came out positive for lymphoma. Bone marrow was uninvolved, which was confirmed by biopsy and an 18-FDG-PET scan. Cerebrospinal fluid cytology was negative. The lactate dehydrogenase (LDH) level of the patient was 678 U/L. The patient was categorized as stage IV in Ann Arbor staging and 2 in International Prognostic Index scoring with an Eastern Cooperative Oncology Group (ECOG) score of 0.

R-CHOP regimen, that is, injection rituximab 375 mg/m^2, injection cyclophosphamide 750 mg/m^2, injection doxorubicin 50 mg/m^2, injection vincristine 1.4 mg/m^2, and tablet prednisolone 100 mg/m^2/day (day 1–5) was started and to be repeated every 21 days. The results of CECT scans of the abdomen and thorax showed that the lesion in the left breast was completely gone after four cycles of chemotherapy. Two more cycles of chemotherapy were given, completing six

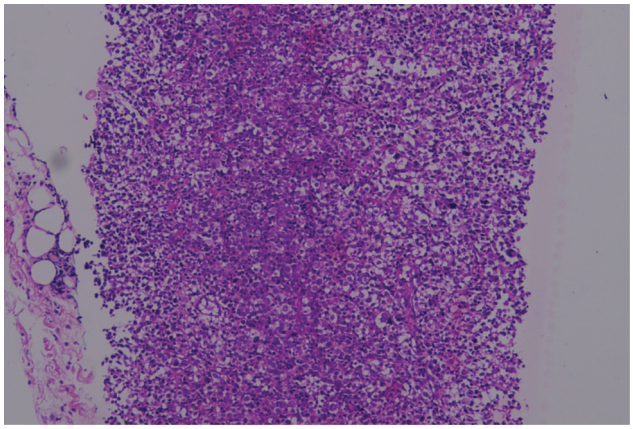

Fig. 2 Histopathology image of diffuse large B cell lymphoma (DLBCL).

Table 1 IHC markers from right breast tissue sample

IHC markers	Result
CD-20	Positive
CD-45	Positive
CD-3	Positive
CD-5	Positive
CD-10	Negative
CK-7	Negative
CK-20	Negative
HMWCK	Negative
Estrogen receptors	Negative
Progesterone receptors	Negative

Abbreviations: HMWCK, high molecular weight cytokeratin; IHC, immunohistochemistry.

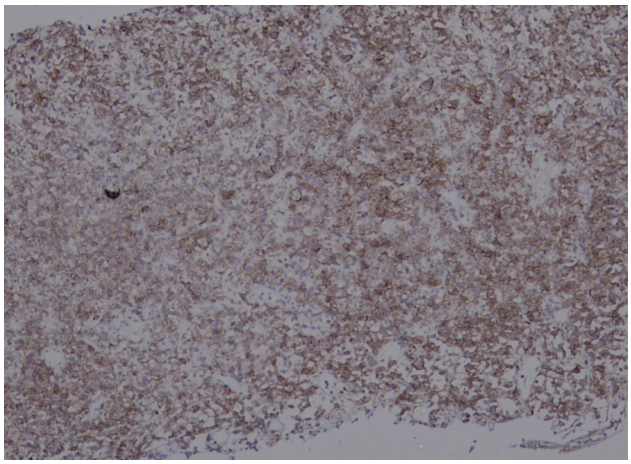

Fig. 3 Immunohistochemistry (IHC) image of CD45 marker.

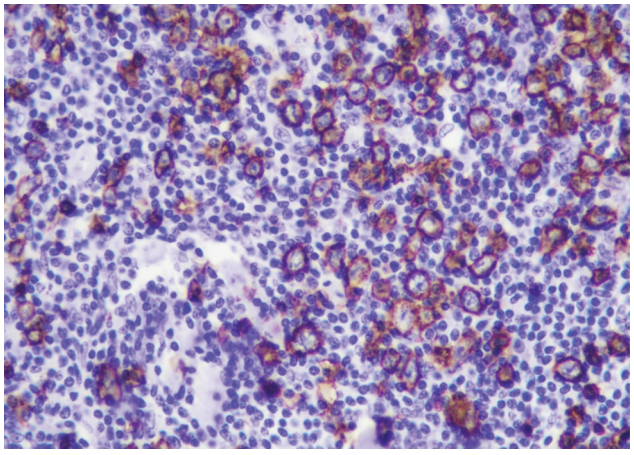

Fig. 4 Immunohistochemistry (IHC) image of CD20 marker.

cycles of the R-CHOP regimen. The patient then underwent 18-FDG-PET scans to assess any residual lesions. It demonstrated no FDG-avid lesions in the body. The patient was advised for a regular 3 monthly follow-up. The patient completed a disease-free survival of 4 years with a yearly PET scan assessment.

Discussion

PBL is rare, accounting for less than 0.5% of breast malignancies and 1% of lymphomas.[3] They typically present without systemic involvement, with only 10% presenting with a bilateral breast lump.[3] Many reports describe PBL as a painless and indolent mass, with female predominance and a median age of 60 to 65 years.[4] Weight loss, night sweats, fever, and other B-symptoms associated with systemic lymphoma are not usually found in these patients.[5] The most common mammography finding is a solitary noncalcified mass (66%) in the studies of Liberman et.al, with magnetic resonance imaging findings being nonspecific and lobulated.[6,7] The standard investigation for diagnosis, staging, and response evaluation is the 18-FDG-PET scan, which is usually intense and focused on the breast.[3] Wiseman and Liao[8] established the diagnostic criteria for PBL in 1972, and Hugh et al[9] amended them in 1990, as summarized in ►**Table 2**.

Table 2 Diagnostic criteria for PBL

Diagnostic criteria for PBL by Hugh et al
1. The primary location of disease is breast 2. No previous history of lymphoma 3. Absence of any systemic disease at diagnosis 4. With ipsilateral axillary lymph nodes being involved simultaneously with primary disease 5. Lymphoma is seen in close association with breast tissue in pathologic findings

Abbreviation: PBL, primary breast lymphoma.

A tru-cut biopsy is usually sufficient for the diagnosis of such patients without the need for immediate surgical intervention. In pre-Rituximab era, when patients used to come to doctor with a breast lump, surgical excision was performed under institutional guidelines. But with the advent of rituximab, tru-cut biopsy is sufficient for the diagnosis rather than surgery as done to our patient.[10] In a retrospective review of breast biopsy samples from 2000 to 2019, Picasso et al found that only 11/19,354 patients had PBL. Of these, 72.7% of patients had DLBCL, with mucosa-associated lymphoid tissue lymphoma and follicular lymphoma making up 18.2 and 9.1% of the cases, respectively. In terms of location, PBL was observed in the upper outer quadrant (50%), upper inner quadrant (25%), central quadrant (16.7%), and lower inner quadrant (8.8%). At the time of diagnosis, only 36.4% of cases had axillary lymph node involvement, with no cases having bilateral breast involvement.[1]

As per Joks et al,[11] DLBCL-PBL should be given six cycles of the CHOP regimen (injection cyclophosphamide 1,500 mg/m^2, injection epirubicin 100 mg/m^2, injection vincristine 1.2 mg/m^2, and tablet prednisolone 100 mg/m^2) along with injection rituximab 375 mg/m^2 in CD-20 positive patients. As per Ganjoo et al, the OS is dependent on the ECOG score and the high LDH level, whereas Lin et al emphasized the Ann Arbor stage and central nervous system (CNS) prophylaxis as playing a major influence in the relapse-free survival of patients.[12,13] The Mayo Clinic has found a significant correlation between the Ann Arbor stage and survival; with 83% OS in stage I as compared to 20% in stage II. CNS prophylaxis has no proven advantage but is beneficial in controlling relapse.[14]

In conclusion, DLBCL is the most common histopathology found in PBL. R-CHOP remains the standard of care. Our patient did not get throughly investigated before start of the treatment. CNS prophylaxis was not given to our patient, as we think it needs to be further evaluated. We need more comprehensive studies to properly understand the pattern of spread and form a consensual treatment plan for better therapeutic outcomes in extranodal lymphoma patients such as PBL.

Declaration of the Patient consent

Written informed consent was obtained from all the patients and/or guardians.

Conflict of Interest
None declared.

Acknowledgment
None.

References

1 Picasso R, Tagliafico A, Calabrese M, et al. Primary and secondary breast lymphoma: focus on epidemiology and imaging features. Pathol Oncol Res 2020;26(03):1483–1488
2 Sabaté JM, Gómez A, Torrubia S, et al. Lymphoma of the breast: clinical and radiologic features with pathologic correlation in 28 patients. Breast J 2002;8(05):294–304
3 Parashar K, Nepal P, Assaker R, Vargas J, Rosasco S. Incidentally detected Non-Hodgkin's lymphoma of the breast. A case report with review of literature. Radiol Case Rep 2020;16(01): 205–209
4 Yoneyama K, Nakagawa M, Hara A. Primary lymphoma of the breast: a case report and review of the literature. Radiol Case Rep 2020;16(01):55–61
5 Wadhwa A, Seneboutarath K. Primary lymphoma of the breast: a case series. Radiol Case Rep 2018;13(04):815–821
6 Liberman L, Giess CS, Dershaw DD, Louie DC, Deutch BM. Non-Hodgkin lymphoma of the breast: imaging characteristics and correlation with histopathologic findings. Radiology 1994;192 (01):157–160
7 Garg NK, Bagul NB, Rubin G, Shah EF. Primary lymphoma of the breast involving both axillae with bilateral breast carcinoma. World J Surg Oncol 2008;6:52
8 Wiseman C, Liao KT. Primary lymphoma of the breast. Cancer 1972 Jun;29(06):1705–1712
9 Hugh JC, Jackson FI, Hanson J, Poppema S. Primary breast lymphoma. An immunohistologic study of 20 new cases. Cancer 1990; 66(12):2602–2611
10 Giardini R, Piccolo C, Rilke F. Primary non-Hodgkin's lymphomas of the female breast. Cancer 1992;69(03):725–735
11 Joks M, Myśliwiec K, Lewandowski K. Primary breast lymphoma - a review of the literature and report of three cases. Arch Med Sci 2011;7(01):27–33
12 Ganjoo K, Advani R, Mariappan MR, McMillan A, Horning S. Non-Hodgkin lymphoma of the breast. Cancer 2007;110(01):25–30
13 Lin Y, Guo XM, Shen KW, Wang JL, Jiang GL. Primary breast lymphoma: long-term treatment outcome and prognosis. Leuk Lymphoma 2006;47(10):2102–2109
14 Ribrag V, Bibeau F, El Weshi A, et al. Primary breast lymphoma: a report of 20 cases. Br J Haematol 2001;115(02):253–256

