

## Extranodal primary non hodgkin lymphoma of breast: Multimodal approach to diagnosis

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### Abstract

The primary Non-Hodgkin's lymphoma of breast is rare. The primary lymphomas of breast are bilateral in younger age group and unilateral in older age group. We report a rare case of primary Non-Hodgkin's lymphoma (NHL) diffuse large B cell type of right breast with multimodal approach for diagnosis. Features of undifferentiated carcinoma were seen on fine needle aspiration cytology, histopathology with gold standard method for diagnosis showed features of aggressive malignant diffuse large cell lymphoma. Immunohistochemistry positive for CD20, MUM1 and Bcl6 provided the evidence to the histopathological diagnosis and guided us towards the poor prognosis of the malignancy by subtyping. We compare the incidence of NHL of breast at our institute with the available literature.

**Keywords:** Primary Non-Hodgkin's lymphoma of breast, diffuse large B cell type, Fine needle aspiration cytology, Immunohistochemistry.

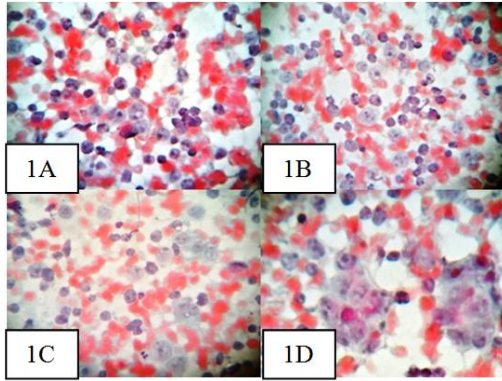
### Introduction

Primary breast lymphoma (PBL) is very rare, with incidence of 0.04 to 0.5% of all breast malignancies, it is 0.38 to 0.7 % of all Non Hodgkin Lymphomas (NHL), and between 1.7 to 2.2% of all extranodal NHL.<sup>1,2</sup> PBL and breast carcinoma show similar clinical and radiological features. Most commonly females are affected, presenting as a painless lump. We report a rare case of recurrent primary breast lymphoma and discuss the diagnosis and its incidence in our institute and compare it with the available literature.

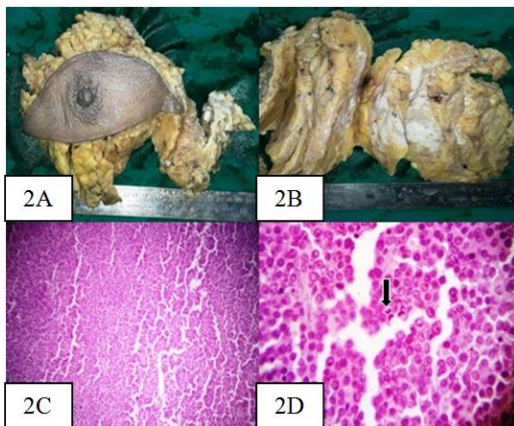
### Case History

A 52 year old female presented with progressive increasing painless lump in the right breast since 3-4 months. Clinically the lump was 5x5cm, firm to hard in consistency. The overlying skin was normal and there was no discharge from nipple. Fine needle aspiration cytology (FNAC) from breast mass showed high cellularity of malignant cells (Fig. 1) and a diagnosis of undifferentiated carcinoma was rendered; Modified Radical Mastectomy (MRM) was done. On gross examination right MRM specimen measuring 18x6x4cm with skin tag measuring 13x3cm was received (Fig. 2 A & B). Tumour involved all the four quadrants measuring 5x4cm. Cut section revealed solitary irregular mass with fleshy whitish in appearance. Axillary tail showed 14 lymph nodes, largest one measuring 3x2 cm. Microscopy revealed monotonous population of cells having pleomorphic, hyperchromatic cleaved vesicular nuclei with prominent nucleoli & scanty eosinophilic cytoplasm.

Focal area shows atypical mitosis 6-8 /hpf. Few areas showed fibrous septae separating tumour, which is infiltrating into surrounding fat. On histopathology the diagnosis of PBL was made (Fig. 2 C&D) with involvement of one lymph node. On Immunohistochemistry (IHC) the tumour cells were immunopositive for CD20, MUM1, Bcl6 and immunonegative for CD3, CD10, CD138. The Ki67 proliferative index was >60% (Fig 4). Diagnosis of Diffuse Large B cell Lymphoma (DLBL), Activated B-cell like, high grade (Hans Algorithm) was confirmed. Clinical and CT imaging evaluation did not reveal any other mass/neoplasm in the body. The patient received chemo and radio therapy at an outside hospital. Despite the treatment after 6 months the patient presented with hard lump in breast at our institute and on FNAC monomorphic malignant cells were seen. The patient further received chemo and radio therapy and for the second time after mastectomy had a swelling over the right breast region. On FNAC there were cells of malignant lymphoma and few cells showed regressive changes due to radiotherapy.

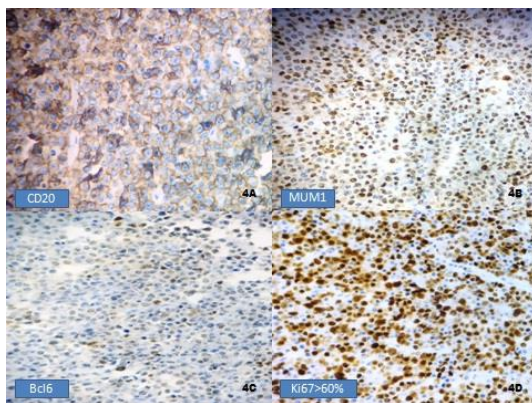


**Fig. 1:** FNAC from breast mass showing high cellularity of undifferentiated malignant cells. (PAP stain 1A & 1Bx100, 1C & 1Dx400)



**Fig. 2A & 2B:** Tumour involved all the four quadrants, solitary irregular mass, cut surface fleshy whitish appearance

**Fig. 2C & 2D:** Monotonous population of cells having pleomorphic, hyperchromatic cleaved vesicular nuclei with prominent nucleoli & scanty eosinophilic cytoplasm and mitotic figures (arrow). H&Ex100(2C), H&Ex400(2D)



**Fig. 4:** Immunohistochemistry shows tumour cells positive for CD20 (4A), MUM1 (4B) and Bcl6 (4C) The Ki67 proliferative index >60 % (4D)

## Discussion

PBL is malignant lymphoma which primarily occurs in breast in absence of previously detected lymphoma. In a retrospective five years analysis we encountered 399 (71.12%) cases of benign breast lesion, and 162 (28.88%) cases of malignant lesions. Out of these 162 malignant tumours only one case of PBL (0.6%) was observed, this is in concurrence with the data put forward by Wendy Jeanneret-Sozzi et al<sup>1</sup> and Enver Vardar et al<sup>2</sup> in their articles. The incidence of PBL is rare in breast because breast contains very less lymphoid tissue compared to other organs like lungs and intestine, where lymphomas are more common.<sup>2</sup> In Roberto Giardinis study of 33 cases of PBL it was found that, right breast (51.5%) is more involved than left (42.4%) breast.<sup>5</sup> Wiseman and Liao in 1972 reported that a diagnosis of PBL must satisfy the following criteria- adequate pathological evacuation, both mammary tissue and lymphomatous infiltrate must be in close association, the exclusion of either lymphoma or previous extra mammary lymphoma.<sup>4</sup> Clinical examination and radiological features along with screening mammography do not provide any specific characteristic to the diagnosis of PBL.<sup>5</sup> Diagnosis of PBL is exclusively made by aspiration cytology or breast excision. Histopathology and IHC are helpful in differentiating PBL from other malignancy. IHC study using CD20, MUM1, Bcl6, CD3, CD10, CD138 and Ki67 antibody markers provides evidence to the histopathological diagnosis and further helps in subtyping of the lesion. Roberto Giardini et al,<sup>3</sup> Ho Jong Jeon et al<sup>6</sup> and Mu-Tai Liu et al<sup>7</sup> studies showed DLBL as most common histologic type of PBL. Gene expression profiling described in 2000 identified two prognostic types on the basis of cell of origin, germinal center B-cell (GCB) and activated B cell (ABC) like. Recent studies showed GCB profile predicts better survival than ABC-like.<sup>8</sup> The management of PBL is based on histological grade. Cytohistological evaluation with IHC offers a better guide for therapy. Our study satisfies the multimodal approach for diagnosis and differentiation of undifferentiated carcinoma and lobular carcinoma from the PBL.

## Conclusion

We report a rare case of recurrent PBL-DLBL, involving the right breast with single axillary lymph node metastasis. Our case fulfilled the Wiseman and Liao's criteria for PBL. The diagnosis of PBL should always be confirmed by histopathology and sub typing by IHC. Further studies about PBL in Indian population are necessary to improve understanding of this disease.

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