

# A CASE OF PRIMARY BREAST DIFFUSE LARGE B CELL LYMPHOMA

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*Primary breast diffuse large B-cell lymphoma (DLBCL) is a rare non-Hodgkin's lymphoma with limited data. We here report a case of primary breast diffuse large B-cell lymphoma mimicking breast cancer. A 52-year-old woman had a painless mass in her right breast. Fine needle aspiration cytology and core biopsy were performed which suggested malignant features but could not confirm the specific subtype. Excisional biopsy then was conducted revealing non-Hodgkin lymphoma, which was subsequently confirmed with histopathology and diagnosed as diffuse large B-cell lymphoma (DLBCL). A chest computed tomography scan revealed a 3.5cm sized breast mass with skin thickening and modest lymphadenopathy in the ipsilateral axilla. The patient received six courses of R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone plus rituximab) chemotherapy, then whole breast radiation (30Gy in 15 fractions). At 12 months of follow-up, the patient survives with no evidence of disease. No morbidities occurred in this patient during the follow-up period. We briefly review the current practice pattern in patients with primary breast diffuse large B-cell lymphoma.*

**Keywords:** Primary breast lymphoma (PBL), DLBCL, R-CHOP.

## I. INTRODUCTION

Primary breast lymphoma (PBL) is a rare tumor that originates from lymphoid tissues. It represents only a tiny fraction of all breast malignancies.<sup>1</sup> For example, primary breast lymphoma is only 1% of all non-Hodgkin lymphoma. Moreover, the most common histology in PBL is diffuse large B-cell lymphoma (DLBCL).<sup>2</sup> Although PBL may present similar clinical and radiological signs as breast carcinoma, both treatment strategy, and outcomes differ. Because of its rarity, the treatment approach varies greatly. Rituximab, combined with chemotherapy, effectively treats primary breast diffuse large B-cell lymphoma. Rituximab effectively treats primary breast

diffuse large B-cell lymphoma and is currently considered the standard treatment approach for PBL patients with DLBCL.<sup>3</sup>

We present a case of primary breast diffuse large B-cell lymphoma treated with R-CHOP in combination with Consolidation Radiotherapy and a brief literature review of the current practice pattern of PBL patients with DLBCL.

## II. CASE PRESENTATION

A fifty-two-year-old woman presented at Hanoi Medical University hospital (in April 2020) after noticing a mass in her right breast for two months, which rapidly enlarged and caused mild pain. There were no nipple discharge or distractions, and she denied fever, weight loss, or night sweats. Past medical history was remarkable only for a *Fasciola hepatica* infection five years ago. On physical examination, the tumor was located at the upper outer quadrant of the breast of 4x5cm in size. It had an irregular border but was not attached

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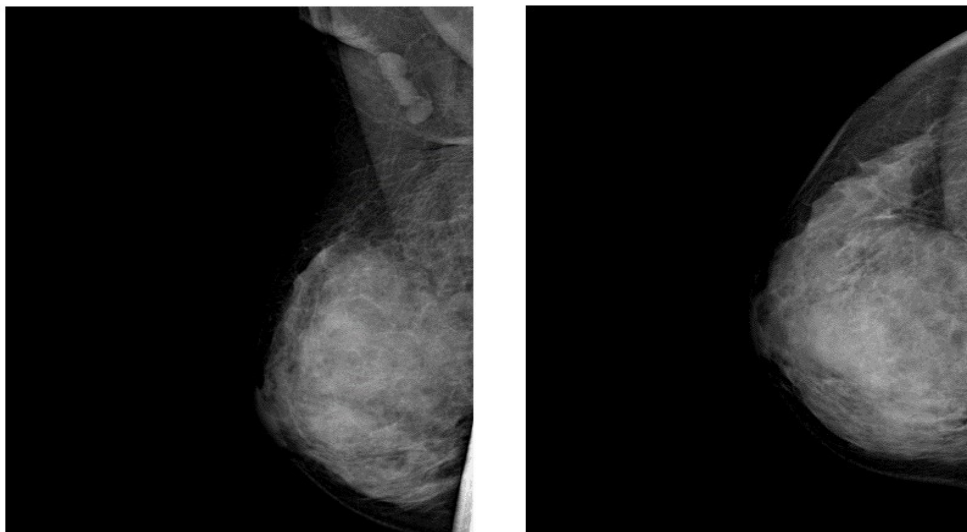
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to the chest wall and the overlying skin. A hard and movable right axillary lymph node about 1 cm in size, was also noted.

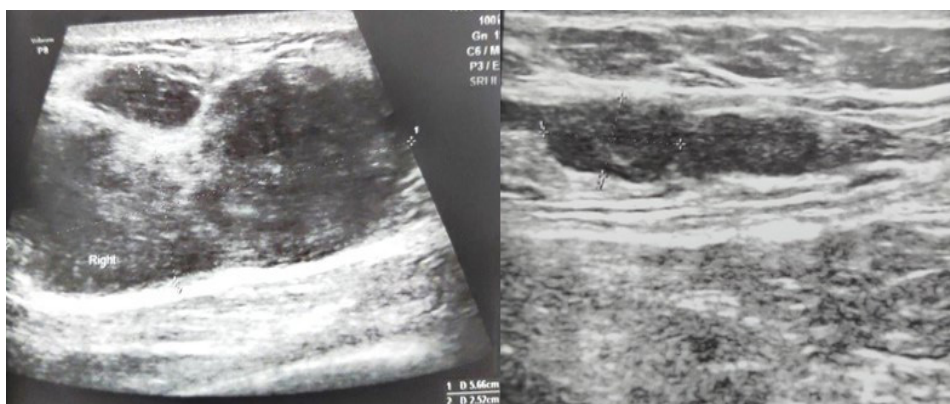
Under ultrasound examination, we documented a hypoechogenic and rare tumor located between 10 and 2 o'clock, hyper vascularized on Doppler ultrasound. There was a high-density mass with micro-calcifications on a mammogram, 30x35 millimeters in size and graded as BIRADS-4b (**Figure 1**). In addition, there were several right axillary lymph nodes with loss of fatty hilum, the largest was 6x15mm

in size (**Figure 2**).

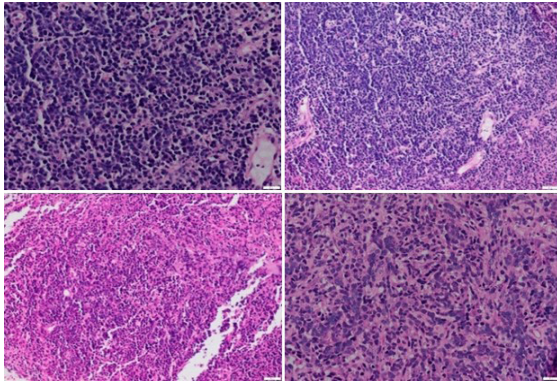
We then performed a core biopsy for a pathological diagnosis however the result just illustrated some malignant feature which was not confirmed as a specific histological subtype. an excisional biopsy was performed subsequently. The specimen showed tumor cells with large and hyperchromatic nuclei, prominent nucleoli, and a thin rim of cytoplasm. The histological diagnosis (the H&E result- the test kit was supplied by "Thermo fisher scientific" company) suspected non-Hodgkin



**Figure 1. Mammography images of the patient**



**Figure 2. Ultrasound images of the tumor and right axillary lymph nodes**

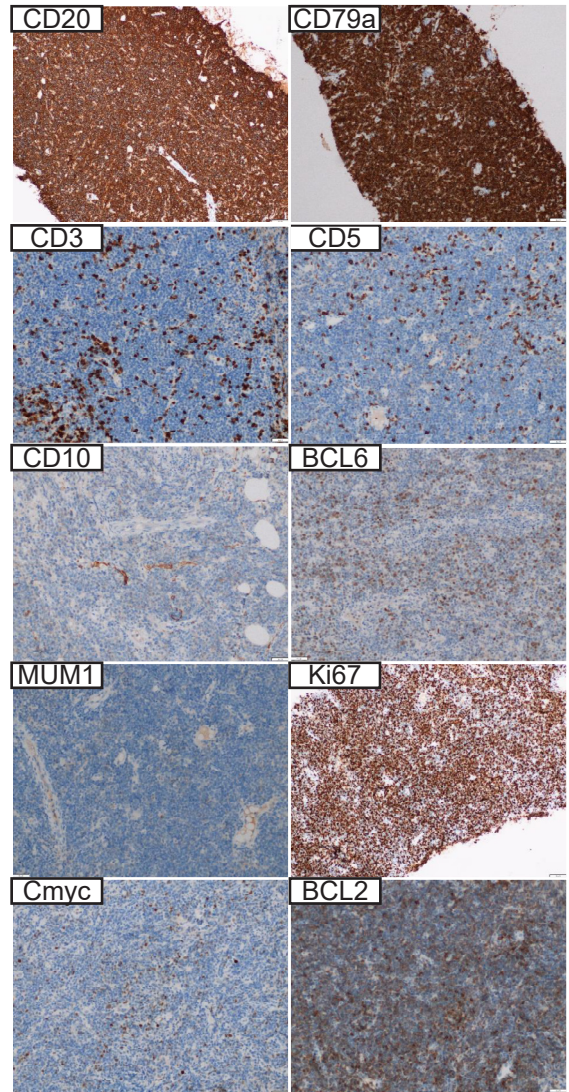


**Figure 3. Histological specimen of the tumor by hematoxylin and eosin stain**

lymphoma which is rare in breast; therefore we discussed with pathologists and performed the immunohistochemical examination. On immunohistochemical examination, the tumor was positive with CD20, CD79a, BCL6, Ki67 (80%) and scattered positive with BCL2, while negative with CD5, CD3, CD10, c-Myc, and Mum1 (Roche test kit). The final diagnosis was, therefore, germinal center diffuse large B cell lymphoma. The Ki67 index was 80% (**Figure 3, 4**).

A PET-CT demonstrated several nodes and masses that were FDG-avid and accounted for almost the entire right breast, the largest of which was 40x70 millimeter in size and had a SUVmax of 11. In addition, DG-avid lymph nodes with individual diameters of about 1 to 2cm were found at both axillae and below the aortic arch (**Figure 5**). Bone marrow aspiration and biopsy were performed and revealed a hypercellular bone marrow with no evidence of lymphomatous infiltration. Therefore, the stage of the disease was IIAE.

The patient received six courses of R-CHOP (cyclophosphamide (750mg/m<sup>2</sup> day 1), doxorubicin (50mg/m<sup>2</sup> day 1), vincristine (1.4mg/m<sup>2</sup> day 1, max dose 2mg), and prednisolone (100mg day 1 to 5) plus Rituximab (375mg/m<sup>2</sup> ngày 1)) followed by



**Figure 4. The tumor was positive with CD20, CD79a, BCL6, Ki67 (80%) and scattered positive with BCL2, while negative with CD5, CD3, CD10, c-Myc, and Mum1**

30Gy of Whole Breast Radiation. After three courses of R-CHOP, the follow-up chest CT showed decreased size of the right breast mass (3.5cm x 1.8cm) and right axillary lymph node (15 mm x 10 mm). After six courses of R-CHOP, the follow-up chest CT showed no visible mass in the breast or axilla. The patient was placed under close observation.



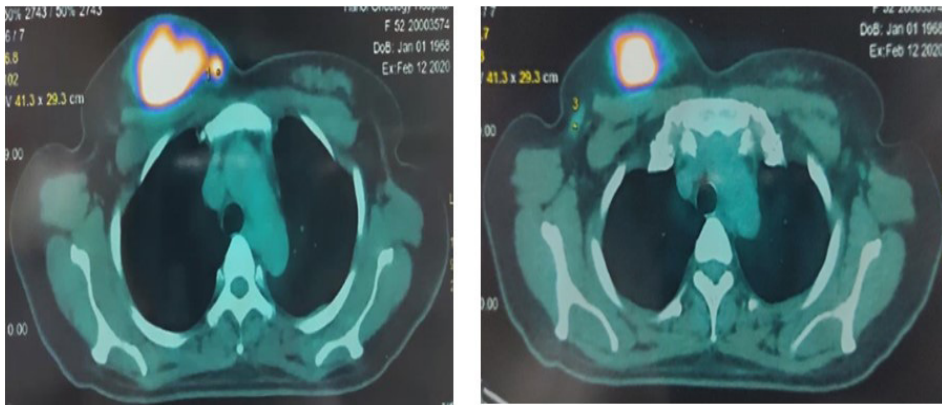


Figure 5. PET/CT images had conducted before treatment

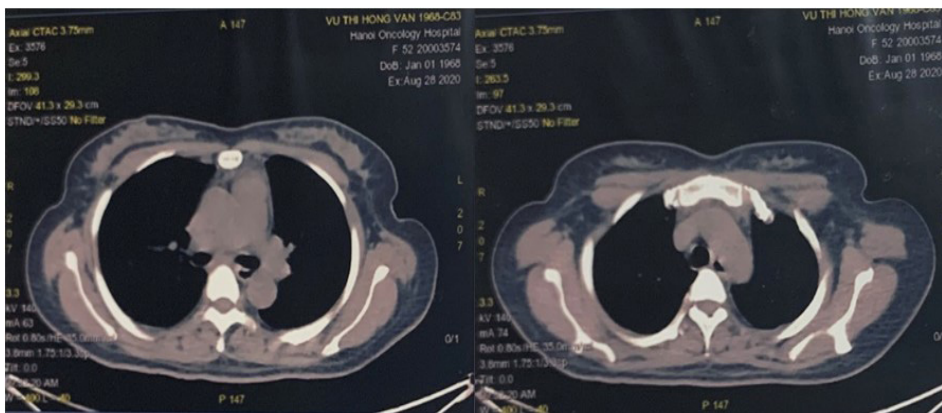


Figure 6. PET/CT images were performed two months after treatment

The PET/CT was performed two months after treatment. There was no evidence of disease (**Figure 6**). At the 12 months follow up, the patient survives with no evidence of disease and with no morbidities associated with chemotherapy.

### III. DISCUSSION

The infrequency of this malignant tumor may be because there is less lymphoid tissue in the breast than other organs, such as the intestines and lungs, where primary lymphomas are common.<sup>4</sup> PBL was traditionally defined as localized lymphoma to one or both breasts with or without regional lymph nodes such as ipsilateral axillary and/or SCLNs.<sup>5</sup> The most common pathological diagnosis in PBL

is DLBCL. The differential diagnosis of PBL includes primary breast cancer, inflammatory breast cancer, fibroadenoma, phyllodes tumor, pseudolymphoma, metastatic disease, and benign breast neoplasm.<sup>6-8</sup> DLBCL is the most common histopathological type of PBL. Other occasional histological types are follicular lymphoma, mucosa-associated lymphoid tissue lymphoma, Burkitt's lymphoma, and Burkitt-like lymphoma.<sup>9</sup> The peak age of PBL is usually the sixth decade, as was in our case, varying among various ethnic groups with the median age in the East Asian countries being approximately ten years (45 – 53 years) younger than that in the Western countries (62 – 64 years).<sup>10</sup> PBL was reported more frequently in the right breast with

a ratio of 3:2, as was in our case.<sup>11,12</sup> Yoshida *et al.* reported that PBL is usually non-GCB type, warning of a poor prognosis. However, it was not in our case.<sup>13</sup> Primary DLBCL of the breast has distinct clinicopathological characteristics in that it has the propensity to reoccur in the opposite breast, other extranodal sites, and the CNS. Jeanneret-Sozzi *et al.* for PBL reported that the 5-year overall survival (OS) rate is 53%, lymphoma-specific survival is 59%, disease-free survival is 41%, and local control rate is 87%.<sup>14</sup>

An anthracycline-based regimen is the mainstay of the treatment of PBL, with CHOP being the most frequently used regimen as in other nodal forms of DLBCL. Very few studies have been conducted to evaluate the role of Rituximab in the management of PBL-DLBCL. In a study conducted by Avilés *et al.*, the risk of CNS was improved with rituximab.<sup>15</sup> However, the Consortium for Improving Survival of Lymphoma study failed to show a positive effect on OS and progression-free survival (PFS) with the addition of Rituximab. This same study demonstrated that treatment with less than four cycles of chemotherapy decreased the 5-year PFS and OS. The study conducted by Avilés *et al.* was the only randomized trial using radiotherapy in primary breast-DLBCL (PB-DLBCL).<sup>15</sup> In this trial, patients were randomized into three arms: Radiotherapy only (45 Gy to breast and its lymphatic drainage), chemotherapy only (six cycles of CHOP every 21 days), and combined modality treatment (CMT) (six cycles of CHOP every 21 days, followed by radiotherapy of 30 Gy). This study was stopped early because an interim analysis revealed a higher CR and OS and a lower relapse rate in the CMT arm. These superior CMT results were supported by the International Extranodal Lymphoma Study Group (IELSG) observations,

which demonstrated superior outcomes for the subgroup of patients with anthracycline-based regimens and radiotherapy.<sup>11</sup>

Regarding the role of surgery, the IELSG data showed that radical mastectomy was associated with an increased risk of death. CNS relapse is noted in only 5% of PB-DLBCL patients. Some trials demonstrated that the addition of Rituximab to chemotherapy decreased the rate of CNS relapse.<sup>16,17</sup> The authors of the IELSG study concluded that routine CNS prophylaxis is not required for patients with PB-DLBCL. Our patient received six cycles of R-CHOP and 30Gy of Radiation with complete response, with no CNS prophylaxis given. At present time, our patient is under surveillance for the past 12 months with no evidence of locoregional or distant relapse.

#### IV. CONCLUSION

This report presents a case of PBL treated differently with Breast carcinoma (R-CHOP in combination with radiotherapy). There are no specific clinical or radiological diagnostic features of PBL. Therefore the majority of patients are initially approached as primary breast carcinoma. However, the H&E test and Immunohistochemical test might assist the oncologists effectively to make the correct diagnosis. Surgery should be minimally invasive and for the diagnostic purpose, either a core needle or an excisional biopsy should be sufficient.

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