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# Primary Bilateral Malignant Non-Hodgkin's Lymphoma of the Breast: A Case Report and **Review of the Literature**

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## **Abstract**

Primary breast lymphoma (PBL) is considered a rare clinical entity, representing approximately 0.4% to 0.5% of all breast tumors. In this report, we present a case of Primary breast lymphoma in a 19-year-old woman complaining of a lump in the right breast and a nodule in the left breast. Breast imaging pointed towards PBL which was confirmed by the results of immunohistochemistry. The case was eventually diagnosed as non-Hodgkin's type B lymphoma. The management of PBL and carcinomas is completely different. The value of preoperative diagnosis should be emphasized, as the patient avoids unnecessary surgery and begins chemotherapy earlier.

## **Subject Areas**

Gynecology & Obstetrics, Pathology

# **Keywords**

Primary Large B-Cell Lymphoma, Breast, Therapeutic Approach

# 1. Introduction

Primary non-Hodgkin's lymphoma of the breast (PNHL) is a rare entity, accounting for approximately 0.04% to 0.5% of all malignant breast tumors and forming approximately 1.7% to 2.2% of Extra-ganglionic NHL [1] [2] [3]. Their heterogeneity is reflected by various clinical, morphological, immunological and cytogenetic presentations which explain their different classifications.

Their diagnosis is based on an anatomopathological examination, however, an extension assessment is necessary to assess the importance and spread of the

lymphomatous process.

They are part of neoplasias that are considered to have a poor prognosis, but their prognosis has undergone a transformation by the progress made in therapeutic methods.

In accordance with the SCARE criteria [4], we report a case of NHL which was diagnosed during a bilateral breast tumor with a review of the literature.

#### 2. Observation

The case 19-year-old Mrs. E.S, married, mother of a child, with no notable personal or family medical history. The onset of the disease dates back to January 2018 with the appearance of bilateral breast swelling that gradually increased in size. With a conserved general state.

On inspection: right breast greatly enlarged, red, inflammatory with periareolar ulceration.

## 2.1. On Palpation

Right breast: presence of a large, hard, regular mass, occupying almost the entire right breast of 20 cm/18 cm fixed relative to the superficial plane and mobile relative to the deep plane, presence of an ulceration in the lower external quadrant, associated with a 4 cm/4 cm homolateral lymphadenopathy mobile with respect to the 2 planes.

Left breast: presence of a mass of 4 cm/4 cm astride the upper quadrants.

#### 2.2. Mammography

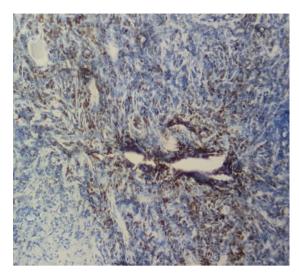
 $40 \text{ mm} \times 64 \text{ mm}$  left breast abscess, and a right breast abscess with generalized mastitis and micro calcifications requiring histological verification.

#### 2.3. Biopsy

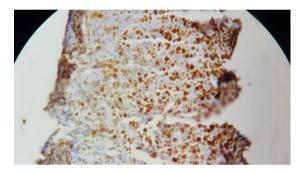
Histological examination of a Tro-cut biopsy of the right and left breast showed an undifferentiated tumor proliferation, the morphological appearance of which evokes a high-grade non-Hodgkin's malignant lymphoma in these two samples, right and left.

The immunostaining of the cells returned negative for the anti-CD3, anti-CD5, anti-CD34, anti-Tdt, anti-myeloperoxidase antibodies, and positive for the anti-CD20 (**Figure 1**) and anti-Bel2, anti-Bel6, anti-MUM1, while anti-ki 67 (**Figure 2**) antibody labeling is estimated at 70% of tumor cells.

All of the above evokes a diffuse non-Hodgkin's lymphoma with large cells of phenotype B of type non germinal center. An extension assessment including a thoraco-abdominopelvic CT and an abdominal ultrasound were carried out and revealed an enlarged liver with a liver span in the midclavicular line measuring 17 cm of regular contours with the presence of a small hypodense lesion of segment VI measuring 10.9 mm in diameter with stable appearance. An osteo-medullary biopsy was done, and showed a morphological aspect in favor of



**Figure 1.** Intense and diffuse membrane expression of anti-CD20 antibody tumor cells.



**Figure 2.** Moderate expression of 60% of anti-KI 67 anticoprs tumor cells.

hematopoietic marrow of normal richness without any specific lesions or visible tumor locations. An HIV test was also carried out and was found to be negative. The patient was therefore referred to the oncology department for treatment.

The treatment included 8 courses of chemotherapy with the R-CHOP protocol. In the third course of chemotherapy, there was a cutaneous flexibility in the right breast and a disappearance of the right axillary lymphadenopathy and also the disappearance of the nodule of the left breast. However, one month after the 6th course of chemotherapy, the patient was readmitted for worsening of the lymphomatous disease of the right breast. This became edematous, inflammatory, ulcerated, painful and infected, giving off a foul odor (Figure 3) This required a mastectomy.

The anatomo-pathological study of the right breast showed a large necrotic malignant tumor with round cells compatible with malignant lymphoma. The tumor measures 23.8 cm, and excision limits pass into healthy tissue, the closest of which (external limit) remains at 1 mm.

The patient was re-referred to the hematology department for additional treatment.



**Figure 3**. Right breast ulcerated and infected with areas of necrosis.

#### 3. Discussion

Lymphomas are the most common hematological cancers, but the association of the breast with lymphomas is rare and, with primary breast lymphoma (PBL) is even more rare, forming approximately 0.04% to 0.5% of all primitive breast cancers and about 0.85% to 2.2% of extra lymph node lymphomas (1).

The rarity of breast lymphoma may be related to the relatively small amount of lymphoid tissue present in the breast compared to the intestine or lung in which primary lymphomas are much more common (4).

This cancer generally affects women; however, male cases have been reported [5].

The risk factors for non-Hodgkin's lymphoma (NHL) are still not well understood, but multiple factors are implicated: certain viruses (HIV, Epstein-Barr, hepatitis C, etc.), immunosuppression, autoimmune diseases and certain exposures. environmental factors like dioxin [5]. Clinicians who manage breast cancer should be aware of this rare entity to detect its clinical presentation and management, which is completely different from breast carcinoma cases.

Clinically, most often breast lymphomas manifest as an enlarged, painless breast mass that mimics breast cancer [6], but they generally tend to be larger than epithelial cancers. Skin retraction, discharge from the nipple, appearance of orange skin, appearance of an inflammatory breast tumor simulating carcinomatous mastitis (as was the case with our patient) are uncommon signs of breast lymphoma. While a considerable proportion of around 24% of these patients do not develop any signs or symptoms at the time of diagnosis [7].

Axillary lymphadenopathy is often found, NHL should also be suspected when lymphadenopathy is in an unusual lymph node area such as inguinal,

however, our patient did not have lymphadenopathy other than the homolateral axillary lymph node.

The mammography systematically performed with the presence of any breast nodule is non-specific. It often shows a limited mass of homogeneous density of benign appearance, evoking a cyst, a fibro-adenoma or a phyllode tumor. The most common mammographic abnormality is a non-calcified breast mass with marginal or indistinct edges. Rarely, an ultrasound shows an inflammatory syndrome [8] [9] [10]. Global asymmetry is another form of PBL detected by mammography in a third of the patients reported in the study by Wadhwa and Senebouttarath [8] and associated with high-grade lymphomas. The differential diagnosis includes carcinoma, inflammatory carcinoma, sarcoma, fibroadenoma, breast dysplasia, breast abscess and acute mastitis [11] [12].

Only histological examination of the tissue, preferably by echo-guided biopsy puncture, can confirm the diagnosis of NHL [1]. Generally, the diagnosis of NHL is easy, but there are certain points which deserve to be underlined: the mammary lymphoma does not offer any histological characteristic because of its localization; the extemporaneous study involves a significant risk of error; mastectomy right away is to be avoided.

Mastectomy is not the primary choice of treatment of PBL and the role of surgery should be limited to a biopsy to establish the correct histological diagnosis, leaving the curative treatment to radiotherapy and chemotherapy [13]. In the case we are reporting, the patient had undergone a mastectomy due to the rapid and aggressive course of the disease and the secondary infection under chemotherapy. Once the diagnosis is made, a certain number of biological examinations is necessary including HIV serology, imaging (x-ray, scan, MRI), endoscopy and biopsy, to clarify the diagnosis, assess the extent of the lymphoma, the clinical impact and the general condition of the patient. Breast cancer, however, presents some particularities in the context of the HIV / AIDS disease: it appears in younger women, it is bilateral and more aggressive with an early metastatic course [14].

According to international literature, the treatment methods for breast lymphomas should not be different from other lymphomas of the same stage and of the same histological classification. Mastectomy and other excision procedures should be avoided as the definitive mode of treatment is systemic chemotherapy and / or radiation therapy, these malignancies being remarkably chemosensitive and radiosensitive [3].

Currently, the majority recommends chemotherapy based on: Rituximab, Cyclophosphamide, Hydroxyadriamycin, Oncovin, Prednisone (R-CHOP) [1] [15].

The prognosis for primary or secondary mammary lymphomas is considered poor with 5-year survival rates varying from 9 to 85% [16] [17] [18]. The most important prognostic factor is the histological subtype and clinical stage at the time of diagnosis, according to the Ann Arbor system.

#### 4. Conclusion

Non-Hodgkin's lymphoma of the breast is a rare anatomoclinical entity. The radiographic and clinical aspects are not specific; the diagnosis is only made based on histopathology. Lymphomas in patients with HIV/AIDS are generally highly malignant. Studying larger series could better determine their treatment and improve their management.

## **Conflicts of Interest**

The authors declare no conflicts of interest regarding the publication of this paper.

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