IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 12 Ser.4 (December. 2022), PP 01-08
www.iosrjournals.org

Primary breast diffuse large B Cell lymphoma: report of 4 cases

N.ALAMI DRIDEB *, R.FELK, S.BOUCHNAFATI, M.BOUZAYD, H.MASROUR, S.SAOUDI, N OUBELKASSEM, M.OUAZZANI, Z.KHAMMAR, R. BERRADY

** Department of internal medicine and onco-hematology , Hassan the second university hospital, Fes, Morocco*

Abstract
Primary breast diffuse large B-cell lymphoma (PB-DLBCL) is the most common type of both primary and secondary lymphoma B cells, this is a rare extranodal involvement, defined by the presence of a primary lesion within the breast without extra-mammary sites of Involvement except regional node. Typically presents in middle-aged women as a unilateral palpable breast mass. Imaging is unable to distinguish lymphoma from breast cancer, which is more common; therefore, Biopsy is necessary to establish the diagnosis. Whole-body positron emission tomography-computed tomography (PET-CT) is widely used in determining clinical staging. The Treatment is chemotherapy and radiation, not surgical excision. The outcome is less favorable, however than that for epithelial breast cancer.
We report 4 cases of Primary breast diffuse large B cell lymphoma (PB-DLBCL) in different ages women illustrating clinical management.

Keywords: *breast, diffuse B cell lymphoma, chemotherapy*

Date of Submission: 01-12-2022 Date of Acceptance: 12-12-2022

I. Introduction

Primary breast lymphoma (PBL) is a rare entity representing 0.04–1% of malignant breast neoplasms and less than 1% of NHL [1], it arises from B or T breast lymphoid tissue and the B cell proliferation represents over 90% of PBL. The most common subtype of PBL is diffuse large B-cell lymphoma (DLBCL) accounting over for 50%, followed by the more indolent lymphomas, extranodal marginal zone of mucosa associated lymphoid tissue ,and follicular lymphoma [2]. Over 98% of cases occur in women [3].
We report 4 cases of Primary breast diffuse large B cell lymphoma (PB-DLBCL).

II. Case Report

CASE 1
A 27-year-old female patient, with four months history of left breast mass, gradually enlarging. At physical examination, there was a 7 cm left breast mobile masse with orange peel. The contralateral breast and the rest of the somatic exam were normal; there were no Systemic B symptoms.
Mammogram and breast ultrasound showed left retro areolar mass, oval, with discreetly macro lobed contours, blurred and irregular measuring 9.5 cm, the controlateral breast was normal.
The masse biopsy was performed and histopathology showed an undifferentiated round cell tumor process relative to high grade diffuse large B cell lymphoma with activated phenotype: CD20+, Ki67 at 80%, CD10-, diffuse Mum1 expression, CD3 expressed by the reactionel T cell.
The Full body computed tomography (CT) indicated a tumor mass of the left breast measuring 71x 95mm associated with two 13x17 mm homolateral axillary lymphadenopathy. The bone marrow biopsy was normal (figure 1).
The patient was classified as stage II E with prognostic 2 (according to the International Prognostic Index (IPI), and low to intermediate risk group.

The treatment protocol was RCHOP (Rituximab, Cyclophosphamide, DoxorubicinVincristine Prednisolone), in addition to four prophylactic intrathecal administrations of Methotrexate.
He achieved a partial response after four cycles of the RCHOP protocols, and the treatment was continued. After the sixth cycle, A 18 FDG PET-Scan showed intense hypermetabolic left breast masse Deauville 5. The biopsy confirmed a tumor proliferation of large cell B-cell lymphoma.

CASE 2

A 75-year-old female patient, menopausal at the age of 46, with 3 months history of an ulcer-budding mass in the right breast, rapidly progressive, in the context of weight loss and asthenia. At the clinical examination, a right breast was completely destroyed, with significant loss of substance and superficial necrosis ranges, bleeding easily on contact (Fig 2). The contralateral breast and lymph nodes were normal. A mass biopsy is performed; the histopathology showed undifferentiated tumor proliferation of large cells suggesting a lymphoma or carcinomatous process. The immunohistochemical revealed an expression of CD20 in tumor cells; CD3 is expressed by reactive T lymphocytes and a lack of cytokeratin, CD10, and c-myc. The Ki65 is 90%. Cervical, thoracic, abdominal ,and pelvic CT scan objectived right axillary lymphadenopathy satellites of the ulcer-budding process of a size of 17 mm long axis, abnormalities (Figures 3 and 4). The bone marrow biopsy was normal.

Based on these clinical and paraclinical data, the diagnosis of primary breast diffuse large B cell lymphoma is retained, classified stage II E with prognostic 3, poor prognosis (R-IPI) , and high- intermediate risk group (IPI).

The treatment protocol was RCHOP, in addition to four prophylactic intrathecal administrations of Methotrexate.

The clinical course after two chemotherapy treatments was marked improvement in the initial lesion, with a tendency towards scarring (Figure 5). The patient is still under treatment, without major incidents.

CASE 3

A 69-year-old female patient, with six months medical history of the enlarging left breast lump with local pain, The clinical examination noted a 3 cm masse without inflammatory signs or nipple discharge; There were no Systemic B symptoms. The contralateral breast and the rest of the somatic exam were normal.

Left Breast Mammogram and Ultrasound confirmed tissue masse of the left breast classified ACR 4b

Histological examination of a left breast tumorectomy showed a histological and immunohistochemical Diffuse large B cell lymphoma with CD 2+, CD 10+, Mum 1+, Ki 67 to 60%, Ac anti-cytokeratin-, Bcl2-, Bcl6-, CD 15-, Cycline D1-

The cerebral, cervical, thoracic, abdominal and pelvic CT scan showed a left and axillary retro-pectoral nodes, associated with left breast thickening and infiltration of the glandular tissue underlying without nodular lesion detected. The bone marrow biopsy was normal.

She was diagnosed as PB-DLBCL, Ann Arbor stage II E. IPI 2 low to intermediate risk group

The treatment protocol was RCHOP, in addition to four prophylactic intrathecal administrations of Methotrexate. He achieved a complete metabolic response after six cycles of chemotherapy

Confirmed by an 18 FDG PET-Scan. More than 18 months later, she remains in complete remission and asymptomatic.

CASE 4

A51-year-old female, presented since 10 months a right breast painless lump increasing gradually in volume. The clinical exam finds a very inflammatory right breast with the presence of a 14 cm masse taking the whole breast, fixed to the overlying skin with crusty ulcerative areolar, oozing with pus, and right axillary lymphadenopathy, measuring 4cm.

The contralateral breast and the rest of the somatic exam were normal.

Ultrasonography breast imaging showed a solid mass occupying almost all the right breast, measuring 110 with skin invasion, and Right axillary adenomegaly, measuring 82 x 59 mm, 80 x 46 mm, and 56.5 x 41mm (Figure 6).

The Histological examination of a surgical biopsy of the right breast revealed a diffuse large B-cell lymphoma (DLBCL). The immunohistochemical staining were as follows: shows CD20+, diffuse PAX5, Ki-67 (+: 80%), anti-CD45+, anti-CK-, CD3- , CD5- , CD10-.

The patient underwent a whole-body CT scan which revealed a voluminous mass interesting the whole right mammary gland, invading the skin, measuring 88 x 132, associated with other

satellite nodules all around, as well as infiltration of breast fat retro-glandular. Two tissue masses depending on the 3rd and 4th cartilage right sterno-costal, invaded the right internal breast chain inThe two dimensions are 19 x 23 mm and 30 x 50 mm with Voluminous right axillary and pectoral ADPs, measuring for the largest 38 x 67 mm diameter (Figure 7).

She was ultimately diagnosed as PB-DLBCL, Ann Arbor stage II E. IPI 2 low to intermediate risk group. The patient was treated with 3 cycles of rituximab-cyclophosphamide, hydroxydaunomycin, oncovin, and prednisone marked by net mass reduction.

III. Discussion

The primary breast lymphoma is a rare form of extranodal lymphoma. The definition proposed by Wiseman and Liao In 1972, modified by Hugh et al in 1990, requires the presence of breast tissue in close proximity with lymphoma, no antecedent diagnosis of lymphoma, and no extramammary disease other than ipsilateral axillary nodes [4].

The prevalence of PBL in females is much higher than that in males. Sex-based Preferences were observed because estrogen plays an important role in the pathogenesis of PBL [5], the peak age of incidence in the sixth decade [6].

PBL arising from B cells accounts for up to 90% of all PBL cases and predominantly consists of the diffuse large B cell lymphoma (DLBCL), which has a high degree of malignancy and the most aggressive histological subtypes [7], The non-germinal center phenotype is more common in PB-DLBCL with usually high Ki-67 [8]. The follicular B cell lymphoma, extra-nodal marginal zone lymphoma, and Burkitt lymphoma are amongst the less common B cell variants [2].

The causes of PB-DLBCL remain unclear, although post-menopausal estrogen levels [9], chronic inflammatory, autoimmune diseases [10], pregnancy, and lactation [11], have been proposed as risk factors.

The Clinical manifestations are non specific, often presenting as a rapidly enlarging breast lump, painless masse mostly seen in the upper outer quadrant, multiple breast masses, diffuse breast enlargement, and/or enlarged axillary lymph nodes [8]. The right breast is involved slightly more frequently; the Cutaneous manifestations, nipple retraction, and discharge are rare [12]. Systemic type-B symptoms including weight loss, fatigue, and fever can occur in PBL. [13].

Mammographic or ultrasonographic imaging features are the most common imaging modality used to evaluate the breast, however, No distinct characteristics are known that would differentiate breast lymphoma from primary breast cancer[14]. Most CT scan lesions are also rounded or oval with circumscribed edges, with no specific signs [4], therefore needle biopsy is necessary for an accurate diagnosis.

MR imaging routinely done in women newly diagnosed breast cancer, in whom MR imaging is an appropriate next-line is imaging Study, in contrast to women with PBL [15].

After a diagnosis of PBL, 18 FDG PET-Scan is used for lymphoma staging.PET–MR imaging is currently being evaluated for its role in staging extra nodal lymphoma but is not in routine clinical use [4]

The outcome of PB-DLBCL patients can be estimated according to the International Prognostic Index IPI, or the modified age-adjusted IPI, revised IPI [16, 17]. Other adverse prognostic markers identified such as stage IIE disease poor performance, status, erythrocyte sedimentation rate > 30 mm/hr, tumor size > 4–5 cm, soluble serum IL2 > 1000U/ml, high tumor microvascular density and bilateral involvement [17].

PB-DLBCL has a high tendency to disseminate at relapse to the contralateral breast in 12–44% of cases [16], but also other extranodal sites, In particular, central nervous system (CNS), Yhim et al. found higher rates of CNS relapse (3-year cumulative incidence 23.6% vs. 1.4%, $P < 0.001$) in a matched-pair analysis of PB-DLBCL ($n = 25$) with limited stage nodal DLBCL uniformly treated with R-CHOP[18],

PB-DLBCL requires systemic treatments such as chemotherapy, radiotherapy, and immunotherapy. Interestingly, in contrast with breast parenchyma-derived neoplasms, surgery and mastectomy seem to be associated with higher rates of recurrence and poorer prognosis [8], Generally, the treatment regimen for PBL is similar to that of systemic lymphoma of similar histology. Most PBL are of the histologic subtype DLBCL, Ryan et al. demonstrated that patients treated by combined therapy had a median overall survival of 8.0 years, median progression-free survival of 5.5 years; multimodality treatment was significantly associated with longer overall survival in patients treated for primary DLBCL of the breast [16].

Owing to its aggressive nature, The most frequently administered treatment protocol for PB-DLBCL is six cycles of R-CHOP, consisting of rituximab, a monoclonal antibody targeting CD20, cyclophosphamide, doxorubicin, vincristine and prednisone followed by consolidative radiation therapy and/or five doses of intrathecal methotrexate as a prophylactic measure for central nervous system metastasis [8,13].

IV. Conclusion

Lymphoma is the most common extramammary breast cancer and occurs most often in the 5th to 6th decades Primary breast diffuse large B cell lymphoma is the most common presentation of PBL and is one of the more aggressive histological subtypes. The diagnosis of PB-DLBCL mainly depends on the pathological and immunohistochemical examination of the breast mass biopsy. The treatment is chemotherapy, radiation, and central nervous system prophylaxis.

References

[1]. Moura C , Leite MI , Parreira R , Medeiros A . Primary breast lymphoma. *J Surg Case Reports* . 2020;2020(1):1–3 .
[2]. Thomas A , Link BK , Altekruse S , Romitti PA , Schroeder MC . Primary Breast Lymphoma in the United States: 1975–2013. JNCI J Natl Cancer Inst . 2017;109(6) .
[3]. Caon J, Wai ES, Hart J, Alexander C, Truong PT, Sehn LH, et al. Treatment and outcomes of primary breast lymphoma. Clin Breast Cancer 2012;12:412–9.
[4]. Nicholson, B. T., Bhatti, R. M., &Glassman, L. (2016). ExtranodalLymphoma of the Breast. RadiologicClinics of NorthAmerica, 54(4), 711–726. doi:10.1016/j.rcl.2016.03.005
[5]. Fei Peng et al Epidemiological features of primary breast lymphoma patients and
[6]. development of a nomogram to predict survival The Breast 57 (2021) 49-61
[7]. Mason HS, Johari V, March DE, Crisi GM. Primary breast lymphoma: radiologic and
[8]. pathologic findings. Breast J 2005;11(6):495–6.
[9]. Emily R. James 1 , Roberto N. Miranda 2 , Suzanne D. Turner Primary Lymphomas of the Breast: A Review JPRAS Open 32 (2022) 127–143
[10]. Chen M , Zhou J , Qu X . Primary Breast Diffuse Large B-Cell Lymphoma in a 42-Year-Old Female: A Case Report and Review of Literature. J Med Cases . 2021;12(5):181
[11]. Teras LR , Patel AV , Hildebrand JS , Gapstur SM . Postmenopausal unopposed estrogen and estrogen plus progestin use and risk of non-Hodgkin lymphoma in the American Cancer Society Cancer Prevention Study-II Cohort. Leuk. Lymphoma. . 2012;54(4):720–725 .
[12]. Shen F , Li G , Jiang H , Zhao S , Qi F . Primary breast diffuse large B-cell lymphoma in a patient with systemic lupus erythematosus: A case report and review of the literature. Medicine (Baltimore) . 2020;99(33):e21736 .
[13]. Yin Y , Ye M , Chen L , Chen H . Giant primary breast diffuse large B-cell lymphoma during pregnancy and lactation. Breast J . 2019;25(5):996–997 .
[14]. « PrimaryBreastLymphoma: A Mimic of InflammatoryBreast Cancer ». International Journal of Surgery Case Reports 53 (1 janvier 2018): 410‑ 13. https://doi.org/10.1016/j.ijscr.2018.11.040.
[15]. Yoneyama K , Nakagawa M , Hara A . Primary lymphoma of the breast: A case report and review of the literature. Radiol Case Reports . 2021;16(1):55 .
[16]. Schillaci O, Travascio L, Lacanfora A, et al. Rare lymphoid malignancies of the breast: Report of two cases illustrating potential diagnostic techniques.J Radiol Case Rep 2012;6(12):43–50.
[17]. Houssami N, Ciatto S, Macaskill P, et al. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: Systematic review and meta-analysis in detection of multifocal and multicentric cancer. J Clin Oncol 2008;26(19): 3248–58.
[18]. Ryan G, Martinelli G, Kuper-Hommel M, Tsang R, Pruneri G, Yuen K, et al.Primary diffuse large B-cell lymphoma of the breast: prognostic factors and outcomes of a study by the International Extranodal Lymphoma Study Group.Ann Oncol 2008;19:233–41
[19]. Chan Y. Cheah, Belinda A. Campbell; John F. Seymour Primary breast lymphoma Cancer Treatment Reviews 40 (2014) 900–908
[20]. Yhim HY, Kim JS, Kang HJ, Kim SJ, Kim WS, Choi CW, et al. Matched-pair analysis comparing the outcomes of primary breast and nodal diffuse large B cell lymphoma in patients treated with rituximab plus chemotherapy. Int J Cancer 2012;131:235–43.

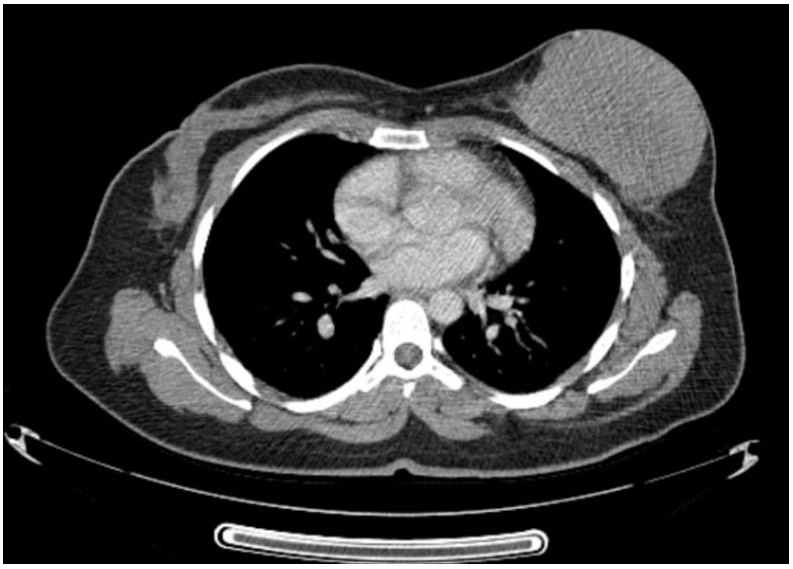

Figure 1: Case 1, pre-treatment Transverse cross-sectional thoracic CT showing scan Presence of a large tissue mass interesting the different quadrants of the left breast, enhanced by low and homogeneous after contrast injection, measuring 71 x 95 mm

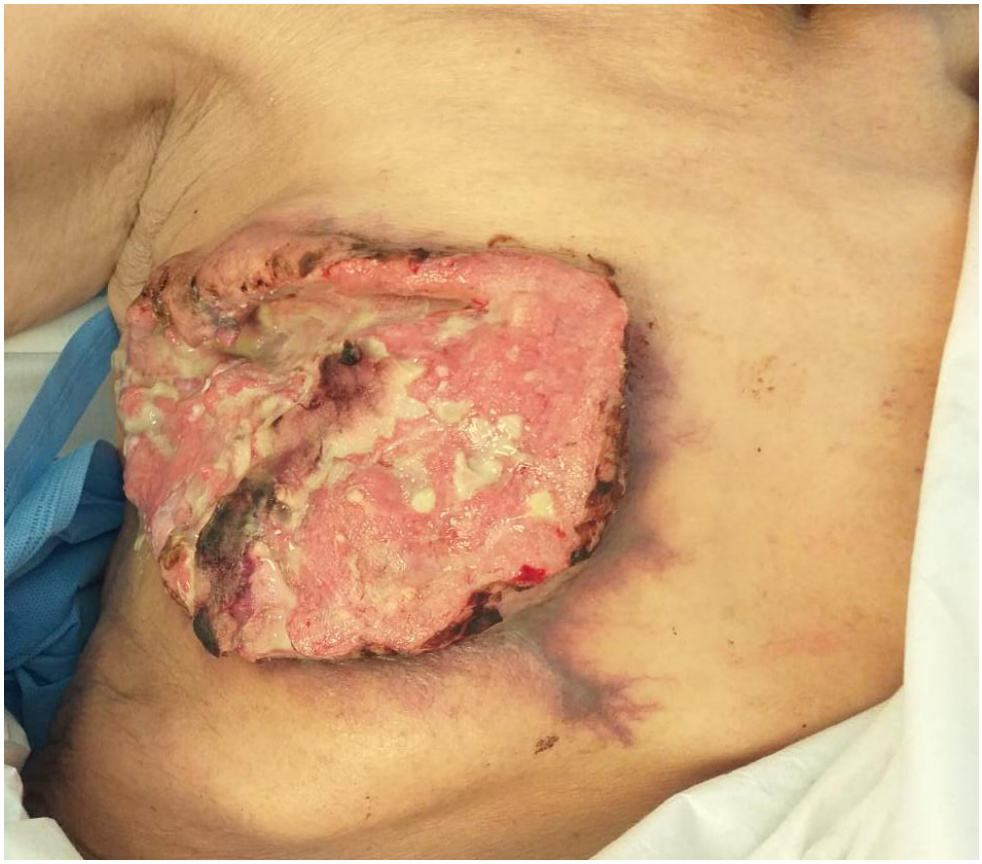

Figure 2 case 2 Ulcerobudding right breast mass with significant loss of substance resulting in total destruction of right breast and superficial necrosis ranges.

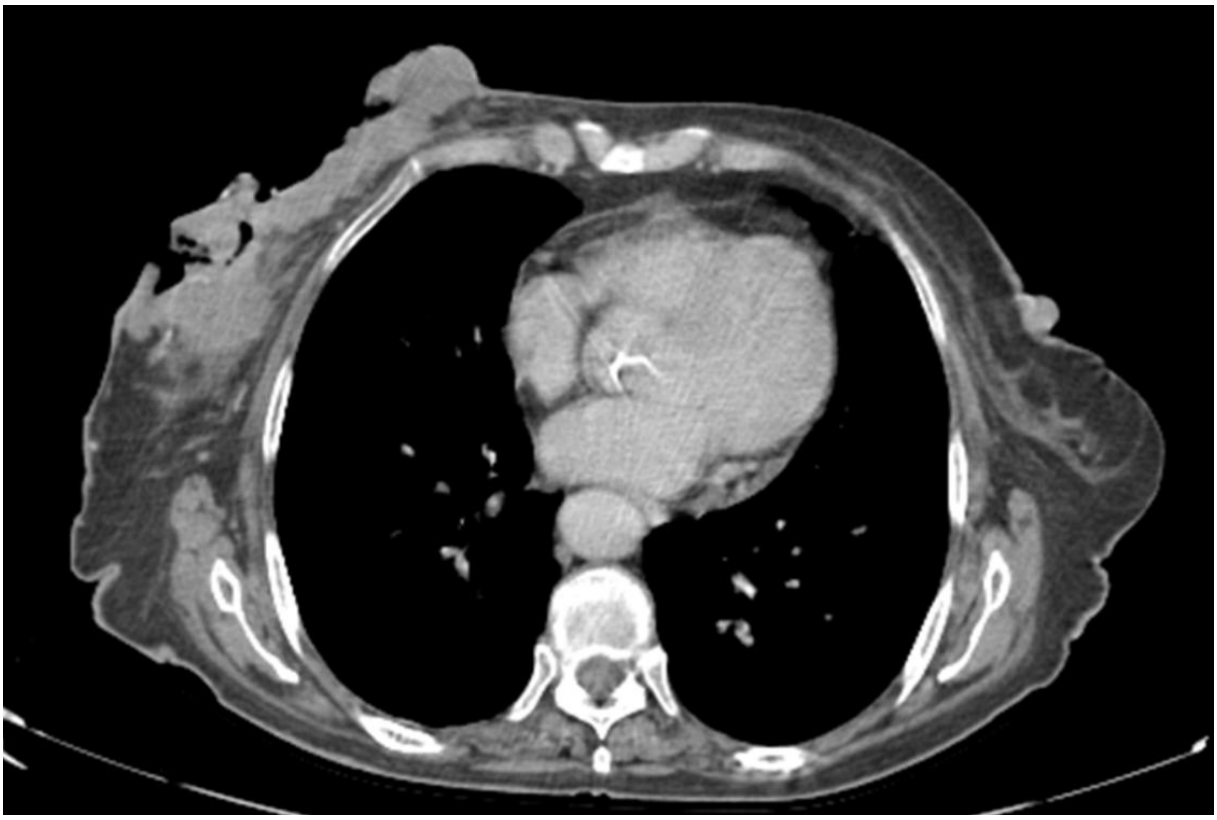

Figure 3 case 2 Transverse cross-sectional thoracic CT showing right mammary tumor mass ulcerous-budding, poorly limited, with desubstance loss, spontaneously heterodense contrast-enhanced heterogeneously after injection iodized contrast agent, occupying almost all of the breast making its measurement difficult. This mass presents an intimate contact with the pectoral muscle with respect to the separating fatty border.

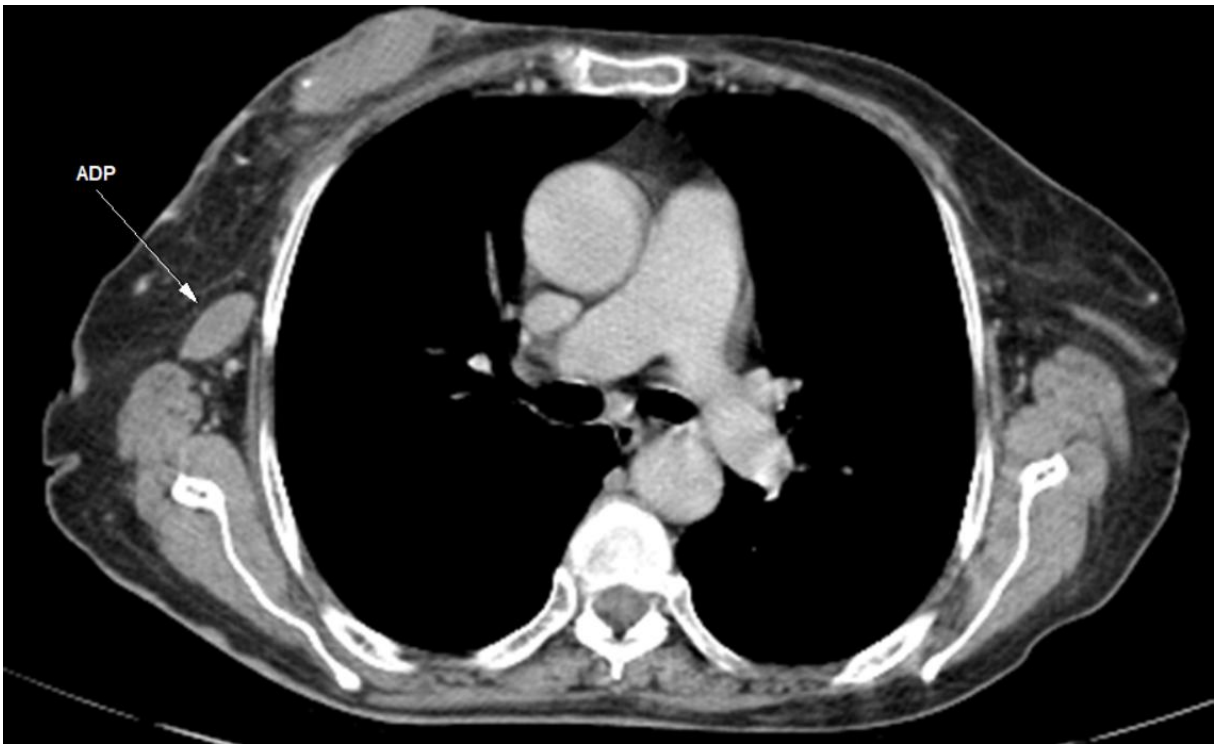

Figure 4 case 2 CT slice objectifying homolateral axillary lymphadenopathy to the 17 mm long axis breast tumor

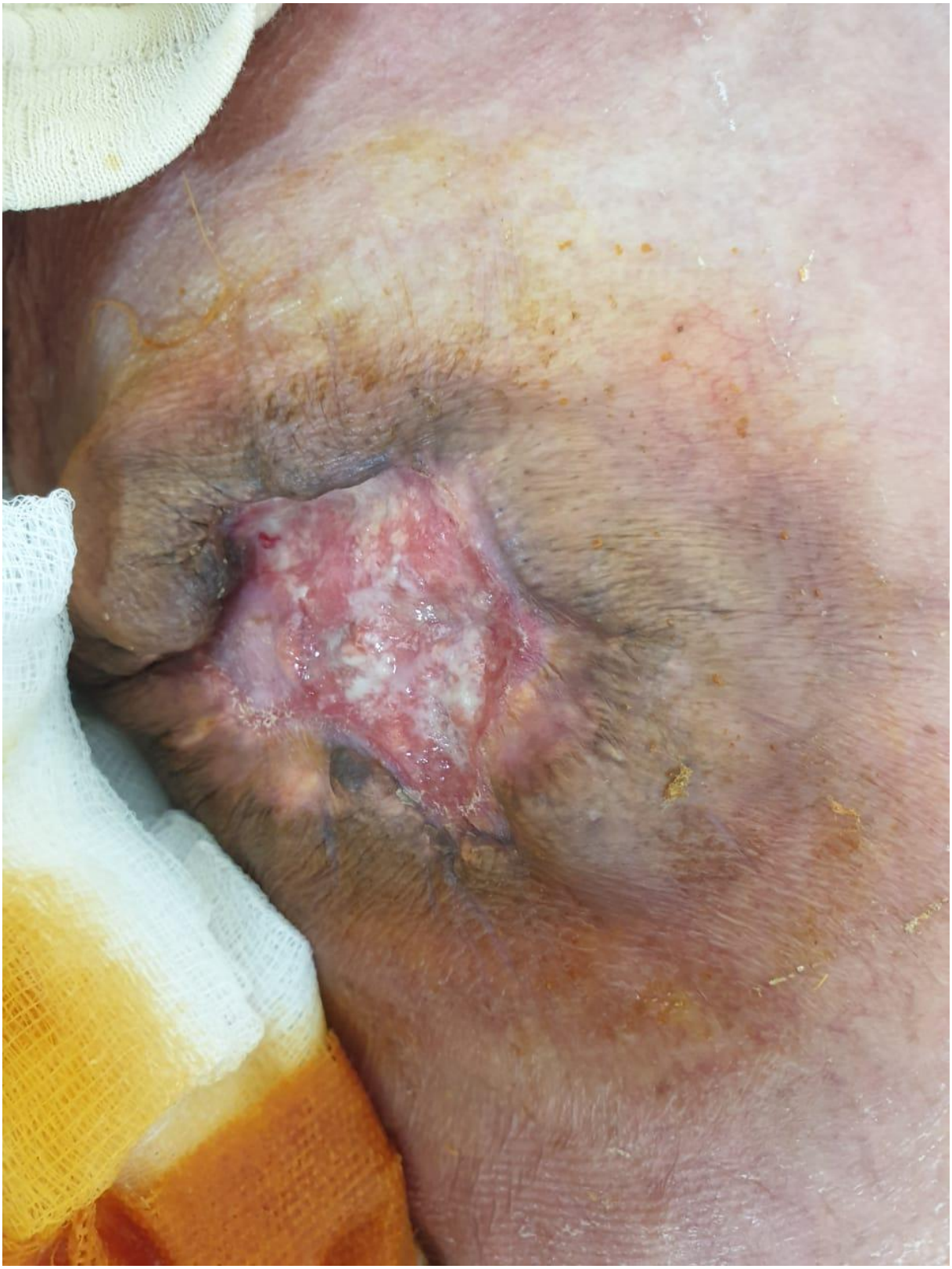

Figure 5 case 2: Breast mass evolution after 2 R-CHOP cures. There is a reduction in tumor size with a closer bank and a clean fibrinous bottom.

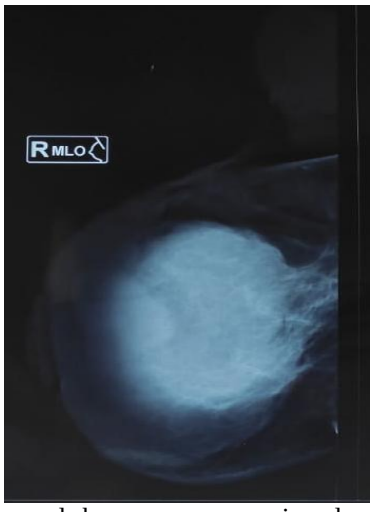

Figure 6 cases 4: pre-treatment Ultrasound shows mass occupying almost all of the right breast, hypoechoic echostructure heterogeneous, irregular contours, measuring 110 mm, with skin invasion.

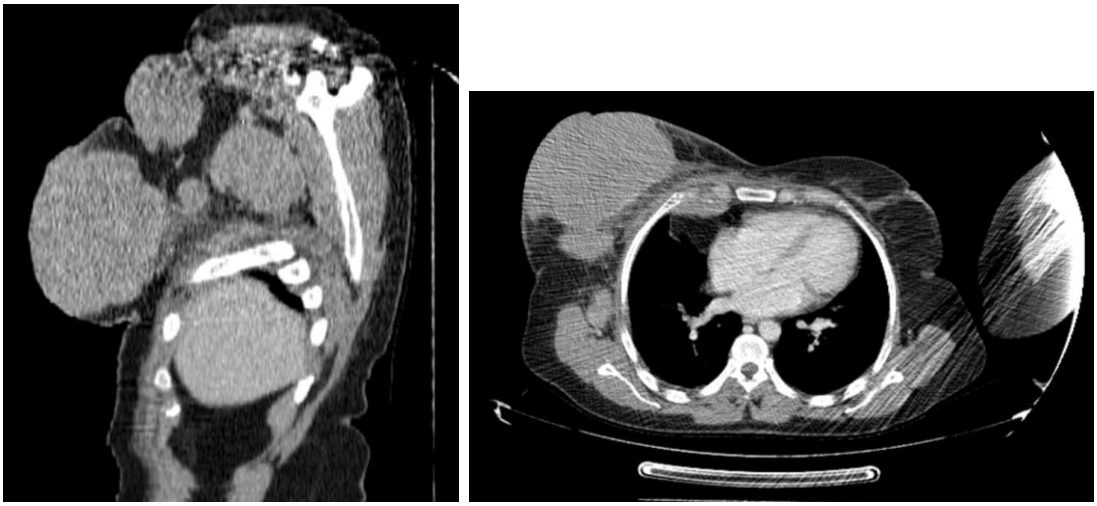

Figure 7 cases 4: CT scan shows Voluminous mass interesting the whole right mammary gland,invading the skin, measuring 88 x 132,associated with other

satellite nodules all around, as well as infiltration of breast fatretro-glandular. Two tissue masses depending on the 3rd and 4th cartilage right sterno-costal, invading the right internal breast chain inThe two dimensions are 19 x 23 mm and 30 x 50 mm with Voluminous right axillary and pectoral ADPs, measuring forthe largest 38 x 67 mm diameter.

N.ALAMI DRIDEB, et. al. "Primary breast diffuse large B Cell lymphoma: report of 4 cases." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(12), 2022, pp. 01-08.