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Mimicking Breast Carcinoma: Radiologic-Pathologic Correlation in a Rare Case of High-Grade B-Cell Lymphoma

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Abstract

Background: Primary breast lymphoma is a rare category of extranodal non-Hodgkin's lymphoma accounting for less than 1% of all non-Hodgkin's lymphoma and less than 0.5% of all breast cancer. It often presents radiologically and clinically as breast cancer leading to delayed diagnosis and inappropriate management. It remains a rare diagnosis that continues to challenge radiologists and clinicians. **Case Presentation:** A 45-year-old woman presented with a rapidly enlarging mass in her right breast over the past two months. She reported no skin changes, nipple discharge, or associated pain. There was no noteworthy family history or comorbidities. A large, firm, solid mass with skin deformity and attachment to the chest wall was discovered during physical examination. A large, irregular, solid, hypoechoic mass with hypervascularity was discovered by breast ultrasonography. A CT scan of the chest showed several right rib destruction and a soft tissue mass infiltrating the pectoralis muscle. A solid intradural extramedullary lesion from the C4 to L4 vertebrae showing canal stenosis and myeloid edema on a spinal MRI suggested either lymphoma infiltration or dural metastasis. Large lymphoid cells in diffuse proliferation, positive expression of CD45, CD20, and a Ki-67 proliferation index greater than 90% were found in FNAC, histopathology and immunohistochemical examination. The right breast, axilla, vertebrae, and spinal dura mater all showed high FDG uptake on PET-CT. The patient was diagnosed with high-grade B-cell non-Hodgkin lymphoma in the right breast, which had already spread to the bone and spinal cord. The R-CHOP regimen was used to start systemic therapy. **Conclusion:** Diagnostic vigilance needed in rare cases such as breast non-Hodgkin lymphoma has been emphasized. Clinically, it supports a systematic approach from a deep history and physical examination to reach a correct diagnosis. Radiologically, a homogeneous extensive mass lesion of soft tissue occupying and destroying bone without the common features associated with carcinoma such as skin in-drawing or calcification bears importance for it is not a primary source of epithelial origin. Apart from that, Initial biopsy on atypical breast masses before an operative intervention, and interprofessional collaboration for attaining an appropriate diagnosis and therapy, are crucial. Besides that, it is further expected that radiological awareness of breast lymphoma would eventually lead to better evaluation, diagnosis, management, and unnecessary procedures avoided among the clinicians and radiologists.

Keywords: Extranodal lymphoma, breast lymphoma, non-Hodgkin lymphoma, radiology, case report

Abstrak

Latar Belakang: *Limfoma payudara primer adalah kategori langka limfoma non-Hodgkin ekstranodal yang mencakup kurang dari 1% dari semua limfoma non-Hodgkin dan kurang dari 0,5% dari semua kanker payudara. Penyakit ini seringkali secara radiologis dan klinis tampak seperti kanker payudara, yang menyebabkan keterlambatan diagnosis dan penanganan yang tidak tepat. Penyakit ini tetap merupakan diagnosis langka yang terus menjadi tantangan bagi ahli radiologi dan dokter.* ***Presentasi Kasus:*** *Seorang*

wanita berusia 45 tahun datang dengan benjolan yang membesar dengan cepat di payudara kanannya selama dua bulan terakhir. Ia melaporkan tidak ada perubahan kulit, keluaran cairan dari puting, atau nyeri terkait. Tidak ada riwayat keluarga atau komorbiditas yang perlu diperhatikan. Sebuah benjolan besar, keras, padat dengan deformitas kulit dan melekat pada dinding dada ditemukan selama pemeriksaan fisik. Sebuah benjolan besar, tidak beraturan, padat, hipoekogenik dengan hipervaskularitas ditemukan melalui ultrasonografi payudara. Pemindaian CT dada menunjukkan beberapa kerusakan tulang rusuk kanan dan massa jaringan lunak yang menginfiltrasi otot pektoralis. Lesi intradural ekstramedular padat dari vertebra C4 hingga L4 yang menunjukkan stenosis kanal dan edema mieloid pada MRI tulang belakang mengindikasikan infiltrasi limfoma atau metastasis dural. Sel limfoid besar dalam proliferasi difus, ekspresi positif CD45, CD20, dan indeks proliferasi Ki-67 lebih dari 90% ditemukan pada pemeriksaan FNAC, histopatologi, dan imunohistokimia. Payudara kanan, ketiak, vertebra, dan dura mater tulang belakang semuanya menunjukkan penyerapan FDG yang tinggi pada PET-CT. Pasien didiagnosis menderita limfoma non-Hodgkin sel B tingkat tinggi di payudara kanan, yang telah menyebar ke tulang dan sumsum tulang belakang. Regimen R-CHOP digunakan untuk memulai terapi sistemik. ***Kesimpulan:*** *Kewaspadaan diagnostik diperlukan dalam kasus-kasus langka seperti limfoma non-Hodgkin payudara, dan hal ini perlu ditekankan. Secara klinis, hal ini mendukung pendekatan sistematis dari riwayat penyakit yang mendalam dan pemeriksaan fisik untuk mencapai diagnosis yang tepat. Secara radiologis, lesi massa jaringan lunak yang homogen dan luas yang menempati dan menghancurkan tulang tanpa ciri-ciri umum yang terkait dengan karsinoma seperti retraksi kulit atau kalsifikasi memiliki arti penting karena bukan merupakan sumber utama asal epitel. Selain itu, biopsi awal pada massa payudara atipikal sebelum intervensi bedah, dan kolaborasi interprofesional untuk mencapai diagnosis dan terapi yang tepat, sangat penting. Di samping itu, diharapkan kesadaran radiologis tentang limfoma payudara pada akhirnya akan mengarah pada evaluasi, diagnosis, manajemen yang lebih baik, dan menghindari prosedur yang tidak perlu di antara para klinisi dan ahli radiologi.*

Kata kunci: *Limfoma ekstranodal, limfoma payudara, limfoma non-Hodgkin, radiologi, laporan kasus*

I. INTRODUCTION

Approximately 1.7–2.2% of all extranodal non-Hodgkin lymphomas (NHLs) and less than 1% of all breast cancers are primary breast lymphomas (PBLs). According to recent multicenter research, PBL accounts for roughly 46.7% of breast lymphomas, whereas secondary breast lymphoma (SBL) accounts for roughly 43.5%. Approximately 6.5% of cases are anaplastic large cell lymphomas (BIA-ALCL) linked to breast implants.[13,20] The average age at diagnosis for PBL is around 68.4 years, compared to 61.9 years for SBL. Overall, patients with PBL tend to have a better prognosis, with a median lymphoma-specific survival of 76.1 months, compared to 59.5 months in those with SBL.[12]

Breast lymphomas frequently manifest as painless breast lump, quickly growing masses that don't cause any systemic symptoms, making diagnosis challenging. Nonspecific radiologic features can be mistaken for breast cancer. Lesions may show up on mammograms as round or oval masses devoid of calcifications. A hypoechoic or heterogeneous mass with increased vascularity and ill-defined margins is usually visible on ultrasound. PET-CT is helpful for staging, while MRI and CT aid in evaluating local invasion and systemic spread.[9]

By emphasizing the value of multimodality imaging and histopathological confirmation in diagnosis and treatment, this case seeks to educate radiologists and clinicians about this uncommon entity. Due to its rarity, a definitive diagnosis of primary breast lymphoma requires a biopsy and immunohistochemical examination.

II. CASE PRESENTATION

A 45-year-old woman presented to the hospital with a rapidly growing lump in her right breast over the past two months. The lump was not accompanied by pain, nipple discharge, or skin changes resembling peau d'orange. The patient had no family history of breast cancer, no comorbidities, and was a non-smoker. Her psychosocial status was good. On physical examination, a sizable, firm mass was noted in the right breast, accompanied by irregular skin texture and an area of skin breakdown. The mass appeared fixed and gave the impression of adhesions to the chest wall. There was no nipple retraction or lesions in the contralateral breast. The right axillary lymph node was palpably enlarged, firm, and non-tender.

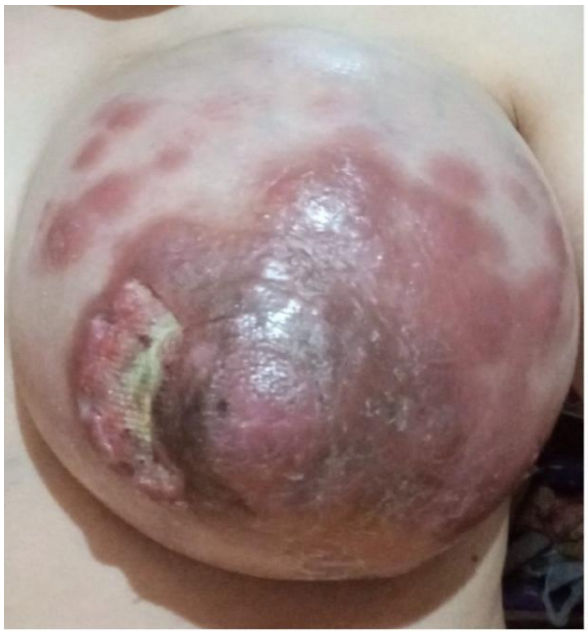


FIGURE 1. CLINICAL IMAGE OF RIGHT BREAST FROM THE PATIENT'S INITIAL SELF-EXAMINATION (TAKEN FROM THE FRONT CAMERA

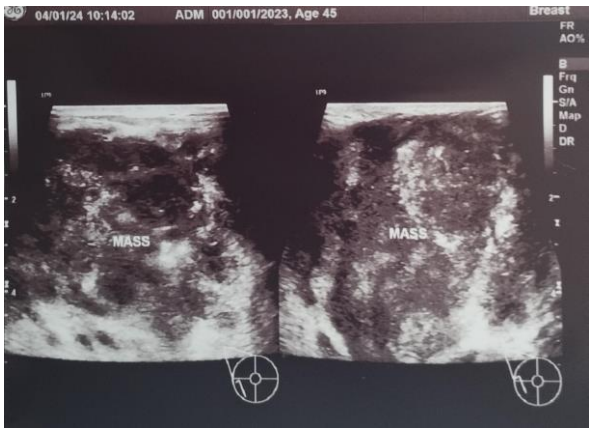
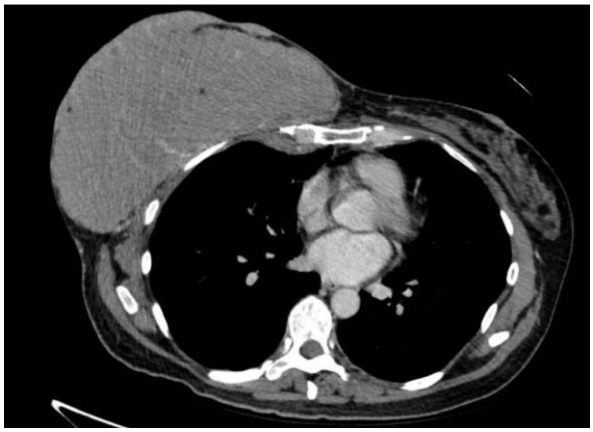


FIGURE 2. A LARGE, IRREGULAR, HETEROGENOUS ISO-HYPOECHOIC SOLID MASS, WITH INDISTINCT MARGIN, TALLER THAN WIDER (3,86X5,77CM AND

4,91X5,48CM) WAS VISIBLE ON INITIAL ULTRASOUND OF THE RIGHT BREAST



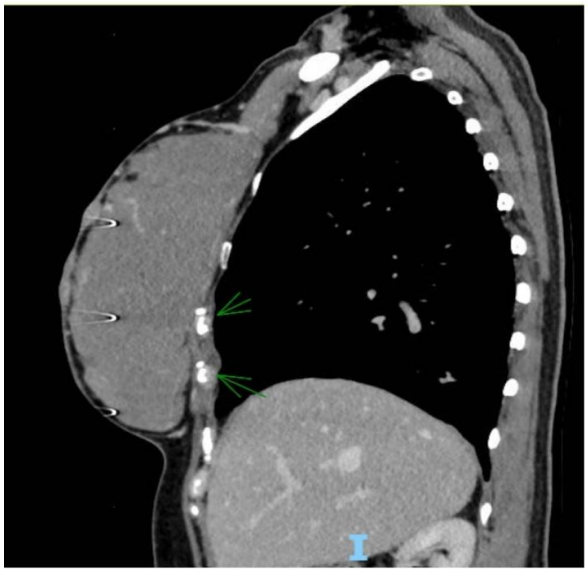
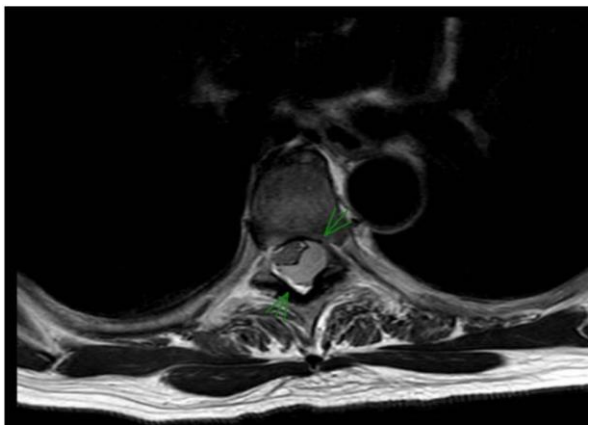


FIGURE 3. A SOFT TISSUE MASS THAT HAD PENETRATED THE PECTORALIS MAJOR AND MINOR MUSCLES AND CAUSED MULTIPLE DESTRUCTION OF THE RIGHT RIBS (ARROW) WAS DISCOVERED ON A CT SCAN OF THE CHEST



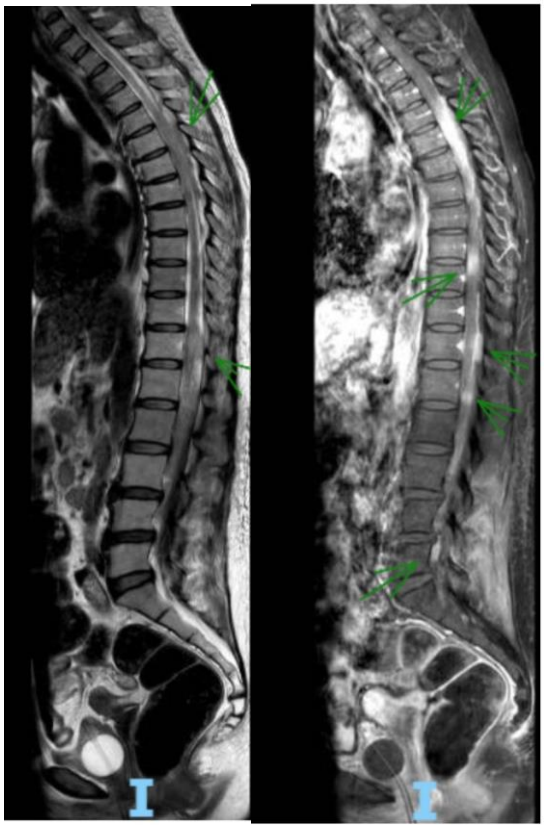


FIGURE 4. MULTIFOCAL SOLID INTRADURAL EXTRAMEDULLARY LESIONS FROM THE C4 TO L4 VERTEBRAE WERE DISCOVERED ON A SPINAL MRI. THESE LESIONS CAUSED SPINAL CANAL AND FORAMINAL STENOSIS ALONG WITH SPINAL CORD EDEMA, WHICH MAY INDICATE LYMPHOMA INFILTRATION OR DURAL METASTASIS

The patient underwent ultrasound-guided biopsy of both right breast nodules. Fine-needle aspiration cytology was conducted on the enlarged, firm mass in the right breast, revealing large, round cells with prominent nucleoli and basophilic cytoplasm arranged in a diffuse pattern. Histopathological evaluation of the biopsy specimens showed diffuse large cells, and immunohistochemistry demonstrated CD45 positivity, CD20 positivity, CD3 negativity in the atypical round cells, and a Ki-67 index exceeding 90%.

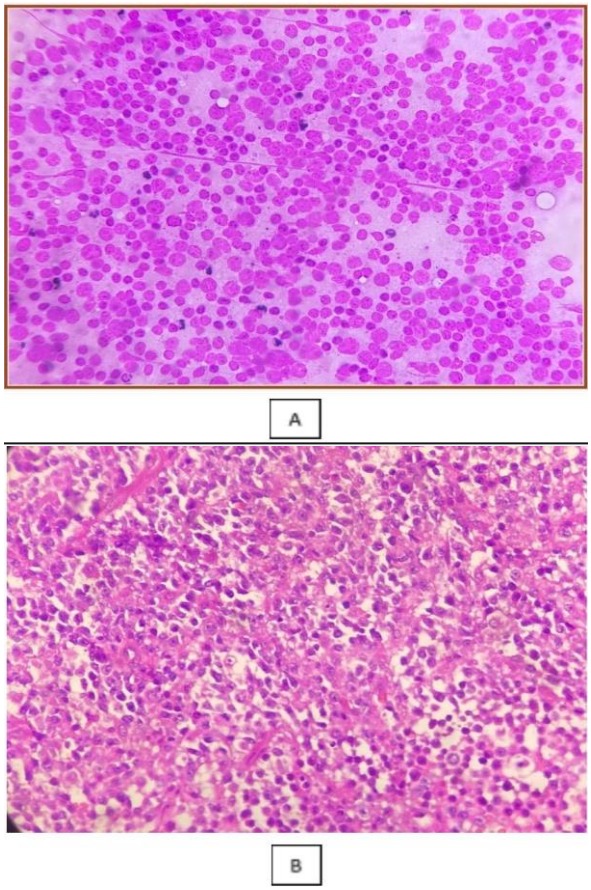


FIGURE 5. FNAC SMEAR (A) AND HISTOPATHOLOGICAL SPECIMEN FROM OPEN BIOPSY (B) SHOWED THE DIFFUSE PATTERN OF ROUND CELL TUMOR, MONOTONOUS IN SIZE, COARSE CHROMATIN AND SLIGHT CYTOPLASM (DQ AND HE, 400X).

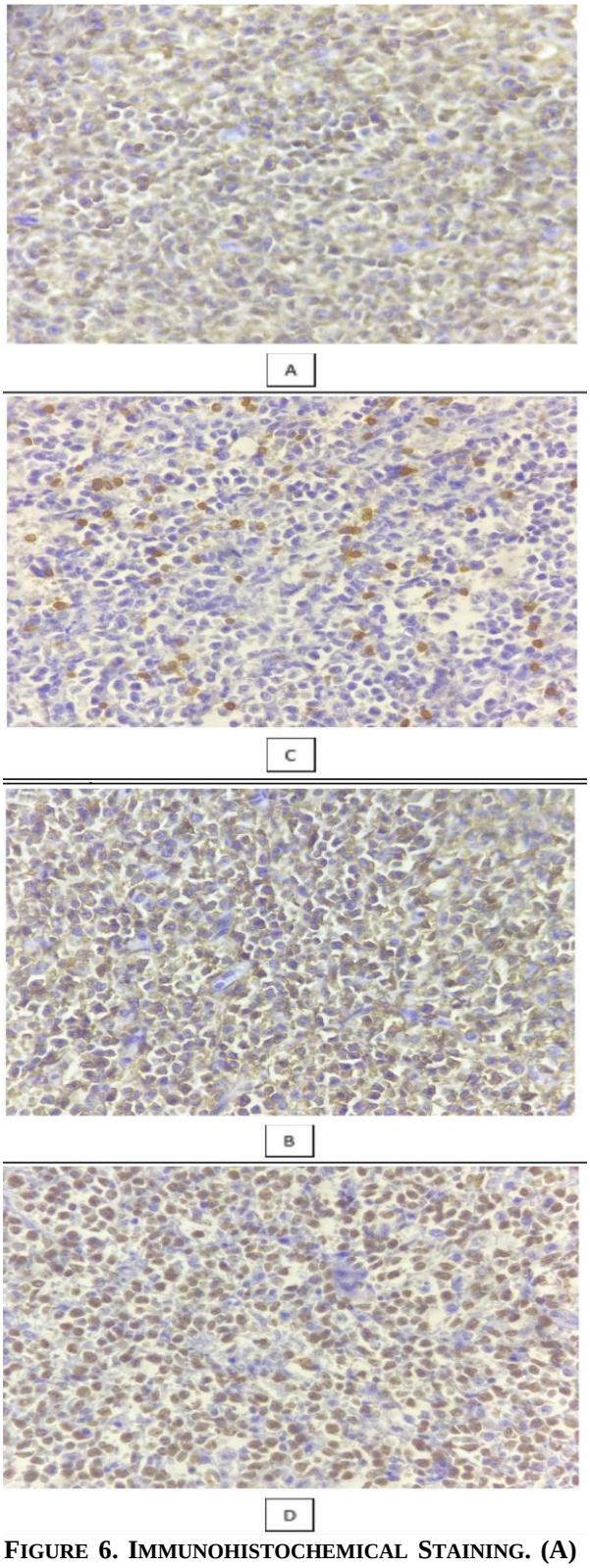


FIGURE 6. IMMUNOHISTOCHEMICAL STAINING. (A) CD45 POSITIVE IN 80% OF ATYPICAL ROUND CELL; (B) CD20 POSITIVE IN 75% OF ATYPICAL ROUND CELLS; (C) CD3 NEGATIVE IN ATYPICAL ROUND CELLS, POSITIVE IN LYMPHOCYTES; (D) KI67 POSITIVE IN MORE THAN 90% ATYPICAL ROUND CELLS WITH STRONG INTENSITY (IHC, 400X)

The final diagnosis was Diffuse Large B-Cell Lymphoma (DLBCL), a high-grade B-cell non-Hodgkin lymphoma that originated in the right breast and had extended to the bone and spinal dura mater. The patient began systemic chemotherapy using the R-CHOP protocol, with scheduled imaging to regularly monitor treatment response. Based on the Ann Arbor classification, the disease was staged as IV E, and the International Prognostic Index placed the patient in the high-intermediate risk group with a score of 3.

Following the fourth chemotherapy round, the patient showed a clinically significant improvement, and following the last chemotherapy cycle, the right breast lump dramatically shrank. For assessment, the patient subsequently had a chest CT scan.

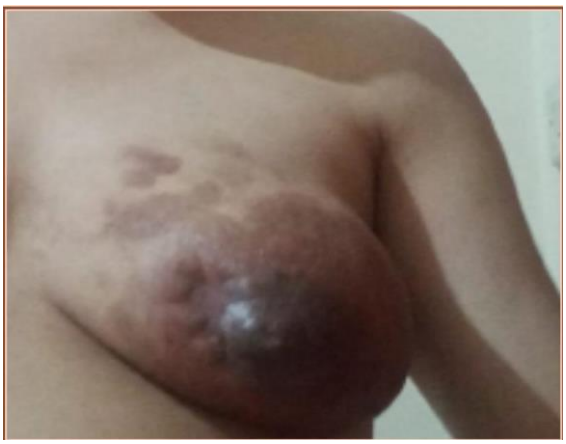


FIGURE 7. CLINICAL IMAGE OF RIGHT BREAST FOLLOWING THE FOURTH ROUND OF CHEMOTHERAPY (TAKEN FROM THE FRONT CAMERA)

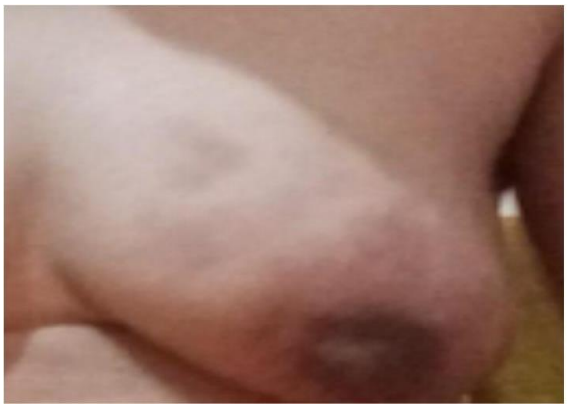


FIGURE 8. CLINICAL IMAGE OF RIGHT BREAST FOLLOWING THE FINAL ROUND OF CHEMOTHERAPY (TAKEN FROM THE FRONT CAMERA)

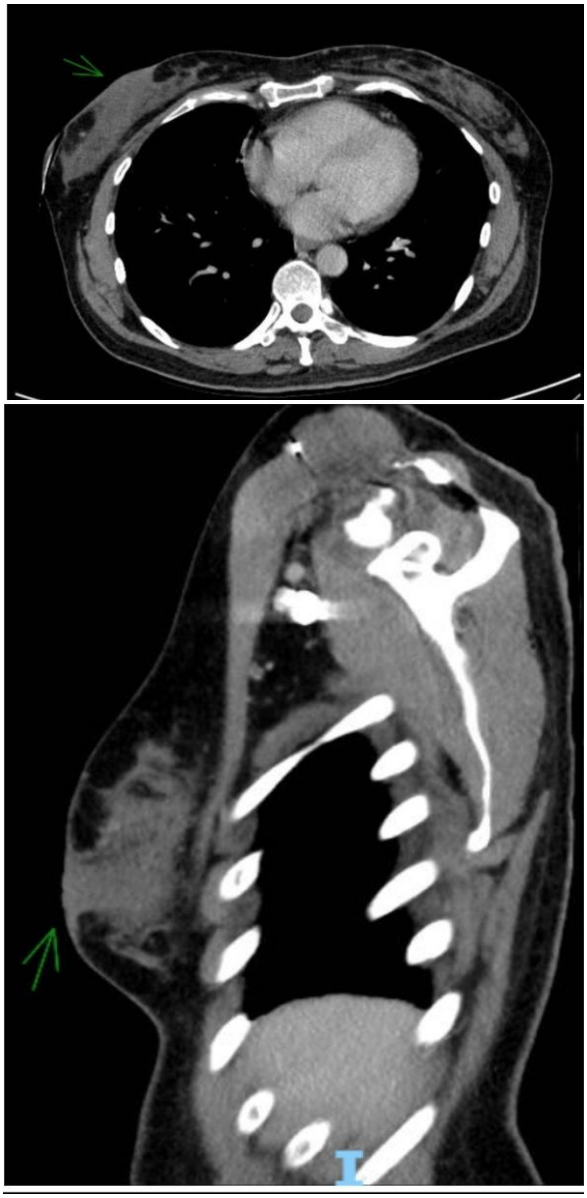


FIGURE 9. CT SCAN RESULTS OF THE THORAX FOLLOWING THE FINAL ROUND OF CHEMOTHERAPY

III. DISCUSSION

Breast lymphomas are a rare type of localized extranodal lymphoma and are categorized as either Primary Breast Lymphoma (PBL) or Secondary Breast Lymphoma (SBL). In 1972, Wiseman and Liao established the clinical criteria for diagnosing PBL, which include: (a) sufficient pathological assessment, (b) the presence of mammary tissue directly associated with the lymphomatous

infiltration, (c) absence of widespread lymphoma except for possible simultaneous involvement of lymph nodes on the same side, and (d) no previous history of lymphoma.[15] Lymphomas that involve the breast but do not satisfy the diagnostic requirements for primary breast lymphoma (PBL) are categorized as secondary breast lymphoma (SBL). There are no morphological features that reliably distinguish PBL from SBL. PBL itself is exceptionally rare, making up only 0.04–0.5% of all breast tumors and roughly 1–2% of extranodal lymphomas. In contrast, secondary breast involvement by lymphoma is encountered more frequently.[12]

The scarcity of breast lymphoma is likely due to the small amount of lymphoid tissue present in the breast, especially when compared with organs like the gut or lungs, where primary lymphomas are far more prevalent. Both PBL and SBL show a consistent tendency to affect the right breast more often, though the reason for this pattern remains unclear. These lymphomas occur predominantly in women, and most patients—regardless of whether the disease is primary or secondary—are diagnosed between the ages of 40 and 67.[13] The most common histologic subtype is Diffuse Large B-Cell Lymphoma (DLBCL), followed by MALT lymphoma. The exact cause is unknown, but some studies have linked PBL to immunodeficiency and autoimmune diseases. This disease tends to grow rapidly but responds to chemotherapy. Because of its rarity, clinicians are still unaware of the possibility of lymphoma as a cause of breast masses, leading to delayed diagnosis or misdiagnosis as breast carcinoma.[11]

The development of breast lymphoma—particularly high-grade B-cell types such as Diffuse Large B-Cell Lymphoma (DLBCL)—is thought to arise from the proliferation of malignant B cells that originate in germinal center or post-germinal center lymphoid tissue. In primary breast lymphoma, this malignant process may be triggered by chronic antigenic stimulation, disturbances in immune regulation, or activation of oncogenes like BCL2, BCL6, and MYC. Additionally, genetic alterations and changes within the tumor microenvironment can enhance the tumor's aggressiveness and promote infiltration of breast tissue.[3]

Primary malignant lymphoma of the breast (PLB) is a rare but very important differential diagnosis of a breast lump. A high degree of clinical suspicion is required for an early and prompt diagnosis of primary breast lymphoma so as to avoid unnecessary mastectomies.[8] Ultrasonography usually shows breast lymphomas as uniformly hypoechoic oval or round masses with prominent vascularity and minimal posterior shadowing. In many cases, patients present with a painless enlarging breast lump that can resemble breast cancer, although lymphomas often appear larger than typical epithelial tumors. Signs such as skin distortion, nipple discharge, or a peau d'orange pattern are uncommon. Interestingly, nearly one-quarter of patients—about 24%—have no noticeable symptoms or clinical findings when the disease is first detected.[13]

On mammography, breast lymphoma most often appears as an intramammary mass that is round or oval with well-defined or slightly lobulated borders and typically lacks calcifications. In primary breast lymphoma, the lesion is usually single and relatively large, whereas secondary breast lymphoma more often presents with several smaller masses. Less frequently, the imaging may show distortion of the normal breast architecture. Enlarged intramammary lymph nodes can also be observed.[21]

Breast lymphoma is also radiologically similar to carcinoma of the breast, as it often manifests as an unilateral solid mass. There are, however, major differences.

Radiologically, carcinomas typically show spiculation, microcalcifications, or distortion of the tissue architecture. Whereas lymphomas tend to be well-defined, homogeneous, and do not cause skin or nipple retraction. The increased calcification is also uncommon for lymphomas. Lymphomas might grow very rapidly but do not cause pain with possible axillary enlargement in the absence of a clear primary lesion in breast tissues. Lymphoma lesions on breast MRI (if it is performed) appear to show rapid post-contrast enhancement that is associated with washout characteristic of epithelial malignancy. However, there can be help to differentiation between lymphoma and carcinoma by absence of central necrosis, calcification, and skin retraction. The axillary lymph nodes show a common involvement but are typically enlarged homogeneously rather than having a diminished fatty hilum, as seen in metastatic carcinoma.[20] Such misclassification causes unnecessary surgery such as mastectomy when the primary treatment for lymphoma is chemotherapy. It is, therefore, very crucial for radiologists and clinicians to incorporate lymphoma in their differential diagnosis of breast masses, especially in atypical cases.[19]

When evaluating the cytology of a painless breast lump, primary breast lymphoma should always be included in the differential diagnosis. Confirmation, however, requires histopathology and immunohistochemistry[1], with histopathology being the diagnostic gold standard. A core needle biopsy is preferred because it provides enough tissue for both microscopic and IHC studies. Under the microscope, high-grade B-cell lymphomas like DLBCL show sheets of large abnormal lymphoid cells with vesicular nuclei, coarse chromatin, and little cytoplasm. Numerous mitotic figures are typically present, reflecting the tumor's aggressive nature.[7,11]

In the current WHO classification of hematopoietic and lymphoid tumors, DLBCL is divided into DLBCL not otherwise specified (DLBCL NOS) and several defined subtypes. DLBCL NOS typically shows large, atypical lymphoid cells that are CD3-negative, CD20-positive, and have a Ki-67 proliferation index above 80%. To further determine the cell of origin (COO), the Hans algorithm is used, which evaluates CD10 (cutoff 30%), BCL-6 (cutoff 30%), and MUM1 (cutoff 30%). The presence of a double-expressor profile is confirmed by assessing BCL-2 (cutoff 50%) and c-MYC (cutoff 40%). Additionally, Epstein–Barr virus–positive DLBCL can be identified through EBV in situ hybridization (EBV-ISH).[5] In this patient, cytology via FNAC, histopathological assessment from an open biopsy, and basic immunohistochemical testing for B-cell markers and tumor grading were completed, leading to the diagnosis of high-grade B-cell non-Hodgkin lymphoma. Thus, integrating histologic examination with a thorough IHC panel is essential for establishing an accurate diagnosis and guiding optimal treatment decisions.[22]

The management depends on the histological subtype, disease extent and individual patient and chemotherapy seems to be the most acceptable option, alone or in combination with surgery and radiotherapy.[8] Current literature indicates that lymphomas affecting the breast should be managed in the same way as other lymphomas of comparable stage and histologic type.[18] Although chemotherapy remains the cornerstone of therapy, the disease is still considered incurable. The R-CHOP regimen—consisting of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone—remains the standard treatment. Rituximab, an anti-CD20 monoclonal antibody, significantly enhances chemotherapy effectiveness and improves outcomes in B-cell lymphomas.[17]

There is no surgical treatment option for breast lymphoma because, unlike carcinoma, it is not advanced beyond primary surgical resection. Therefore, systemic chemotherapy, owing to the high sensitivity of this malignancy to systemic chemotherapy, remains the definitive treatment, and mastectomy and other wide excisional procedures should be avoided. In specific circumstances, radiation can be administered postoperatively as adjunct therapy, particularly to patients with local disease or to those with residual disease after chemotherapy.[10]

The advancement in patient therapy response is monitored through the use of advanced imaging like PET-CT or MRI coupled with traditional methods in evaluating the extent of lesions and their systemic involvement.[16] Within therapy response assessment, the evaluation of IHC expression and systemic stages for differentiation and classification is required to estimate the therapy breadth and depth.[4]

The outlook for breast-involved lymphomas, whether primary or secondary, is generally poor, with reported 5-year survival rates varying widely from 9% to 85%.[2,13] According to the Ann Arbor staging system, the key determinants of prognosis are the histological subtype and the stage of disease at the time of diagnosis.[6]

Many case studies have indicated that Diffuse Large B-Cell Lymphoma (DLBCL) is the primary subtype in the primary breast lymphoma. Jennings et al. (2007), for example, reviewed 92 patients retrospectively and found that most patients did well on CHOP-based chemotherapy, with or without rituximab, and that surgery had no prognostic value.[10] In a separate publication, Surov et al. (2012) accentuated the peculiarities of breast lymphoma and the need to include this diagnosis when dealing with atypical breast tumors. In this case, the probable diagnosis based on imaging was fibroadenoma, while the core biopsy revealed a diagnosis of lymphoma.[21]

On the other hand, in our case, the imaging features along with the response to R-CHOP were in line with the literature, but the case's originality lay in the unilateral presentation having rapid growth and lacking clinical suspicion of lymphoma.

For radiologists, pathologists and clinicians, this case offers a number of crucial lessons that can improve awareness and diagnostic precision. First, the significance of taking lymphoma into account when making a differential diagnosis for breast masses, particularly in patients whose breast masses do not show the typical signs of carcinoma, such as spiculation, skin retraction, or microcalcifications. Second, if the diagnosis is still unclear, radiological imaging should be paired with a thorough clinical evaluation and, if necessary, a biopsy. Third, radiologists need to be able to identify common patterns that are suspicious of lymphoma, such as a solid mass on mammography without architectural distortion or a homogeneous, hypoechoic mass with distinct borders on ultrasound.

To avoid needless procedures, clinicians must be aware that primary surgery is not necessary for the treatment of breast lymphoma. For a quick and precise diagnosis and timely start of systemic therapy, radiologists, pathologists, and hematologist-oncologists must work together in a multidisciplinary manner. The management of uncommon cases like breast lymphoma also highlights the importance of an evidence-based strategy and good interprofessional communication.

IV. CONCLUSION

Primary breast lymphoma especially represents foreign high-grade B-cell types, and should be recognized as a rare, but clinically significant entity by radiologists

and clinicians. The fact that its nonspecific imaging features mimic the much more common breast malignancy, invasive ductal carcinoma, strengthens the argument for maintaining a high index of suspicion; particularly when there is a large, rapidly growing, well-defined breast mass without classic carcinoma features such as calcifications or spiculations.

Imaging multimodalities like ultrasound, CT, MRI, and PET are vital in determining the extent of tumors, regional or distant involvement, and biopsy guidance. Histopathological confirmation via core needle biopsy and immunohistochemistry remains the gold standard. Early, accurate differentiation from epithelial breast cancers can save patients from needless surgeries and afford best systemic treatment, including R-CHOP chemotherapy.

The significant point of this case is that history should be integrated with imaging and pathological data in order to make the right diagnosis. Even considering that breast lymphoma is rare among patients, it is important that increased awareness among the radiologist and referring clinicians make it a possibility to realize its diagnosis for the investment of patients' outcome.

V. KEY LEARNING POINTS

- When making a differential diagnosis of atypical breast masses, especially those that are growing quickly and do not exhibit the typical characteristics of carcinoma, always include lymphoma.
- Even in primary presentations, there may be extensive involvement, including of the vertebral and dural structures; tissue confirmation should not be delayed.
- In order to identify non-epithelial breast cancers and prevent needless surgical procedures, radiologists and oncologists should work closely together.

VI. PATIENT CONSENT

The patient provided written informed consent, which included consent for the use of imaging and anonymized clinical data for scholarly publications. The report's nature, the kinds of data that would be shared, and the reason for publishing in a peer-reviewed medical journal were all explained to the patient. Every attempt was made to guarantee patient privacy and ethical compliance.

VII. CONFLICT OF INTEREST

Regarding the publication of this case report, the authors affirm that they have no conflicts of interest. This manuscript has been interpreted, written, and submitted without any influence from financial, personal, or institutional affiliations. Each author declares that they have no conflicting interests to reveal. No conflicts of interest are disclosed by the authors.

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