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# CASE REPORT: PRIMARY BREAST DIFFUSE LARGE B-CELL LYMPHOMA

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## ABSTRACT

Primary breast diffuse large B-cell lymphoma (DLBCL) is a rare entity, accounting for less than 0.5% of all primary breast malignancies and less than 1% of all non-Hodgkin lymphomas. It is often challenging to diagnosed due to its clinical and histopathological resemblance to invasive breast carcinoma. Objective to report the diagnostic journey and histopathological characteristics of a rare case of primary breast DLBCL and to highlight the importance of immunohistochemical examination in establishing an accurate diagnosis. This case report documents a 47-year-old female patient presenting with a right breast mass. The diagnosis was established through histopathological examination using Hematoxylin and Eosin (H&E) staining and immunohistochemical analysis. Initial histopathology suggested the possibility of medullary-pattern invasive breast carcinoma with a differential diagnosis of large-cell lymphoma. Immunohistochemical analysis revealed diffuse positive expression of CD20, negative expression of CK5/6 and CD3, and a Ki67 proliferation index exceeding 30%. These findings confirmed the diagnosis of primary breast DLBCL. Primary breast DLBCL is a rare malignancy that should be considered as a differential diagnosis for high-grade breast tumors. Histopathological and immunohistochemical examinations play a crucial role in ensuring an accurate diagnosis.

Keyword: breast tumor; case report; diffuse large b-cell lymphoma ; histopathology; immunohistochemistry; primary breast lymphoma

## INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is a mature B-cell neoplasm that may occur as either a primary or secondary malignancy in the breast. Primary breast lymphoma (PBL) is an uncommon entity, accounting for only approximately 0.05–0.5% of all breast malignancies and about 2% of extranodal lymphomas (Jia et al., 2018; Maccio et al., 2025). Histologically, DLBCL is the most frequently encountered subtype in PBL (Maccio et al., 2025; Zhang et al., 2017). Although rare, primary breast DLBCL poses significant clinical relevance as it often presents a diagnostic challenge, particularly in distinguishing it from invasive breast carcinoma. Epidemiologically, PBL predominantly affects middle-aged to elderly women, with male cases being exceedingly rare (Zhang et al., 2017). Clinically, patients typically present with a rapidly enlarging, painless breast mass, often lacking classic features of breast carcinoma such as nipple retraction or peau d'orange—factors that frequently lead to initial misdiagnosis (Pereira et al., 2023; Sakhri et al., 2023).

Conventional radiological imaging findings are frequently nonspecific and may further complicate differentiation from invasive breast carcinoma. Accurate diagnosis, therefore, requires comprehensive histopathological evaluation supplemented with immunohistochemical analysis. DLBCL characteristically exhibits positivity for CD20, CD79α, and BCL6, often with a non-germinal center B-cell (non-GCB) phenotype, while epithelial markers—such as cytokeratin (CK), ER, PR, and HER2—are typically negative (Maccio et al., 2025; Pereira et al., 2023). This distinction is critical, as therapeutic strategies differ substantially: primary breast DLBCL is typically treated with R-CHOP–based chemotherapy with or without radiotherapy, whereas radical mastectomy—common in breast carcinoma—is generally not indicated and offers no survival benefit (Jennings et al., 2007; Pereira et al.,

2023; Sakhri et al., 2023). This case report aims to document the diagnostic journey of a patient with primary breast DLBCL, from clinical evaluation to confirmation via histopathology and immunohistochemistry. It also underscores the pivotal role of ancillary testing in distinguishing primary breast DLBCL from invasive breast carcinoma, thereby ensuring accurate diagnosis and appropriate patient management.

## METHOD

This study is a case report that details the diagnostic evaluation of a patient presenting with a right breast tumor. The diagnostic approach integrated data from clinical examination, radiological assessment, histopathological analysis, and immunohistochemical profiling, which together are essential for distinguishing primary breast lymphoma from more common breast malignancies such as invasive carcinoma. Case reports play a critical role in documenting rare clinical entities, highlighting diagnostic challenges, and providing insight into the utility of ancillary testing methods in confirming the diagnosis and guiding appropriate management (Gagnier et al., 2013; Quintana & Collins, 2023). Data were collected from the patient's medical records, including history taking, clinical examination, and ancillary test results, and were subsequently reviewed in a descriptive and comparative manner with relevant scientific literature. The review involved analyzing the concordance of clinical finding, histopathology and immunohistochemistry findings with the characteristics of previously reported cases, thereby providing a comprehensive understanding of the diagnosis and management of the case.

## RESULT

A 47-year-old female patient presented with a chief complaint of a palpable mass in the right breast. She reported no masses in other locations and had no history of previous tumors. An excisional biopsy was performed, and the tumor tissue was sent to the Anatomical Pathology Laboratory. The received biopsy specimen measured 3 x 1.5 x 1.5 cm and weighed 10 grams. The tissue was partially covered by a 3 x 1.5 cm segment of skin. Upon sectioning, a grayish-white mass with ill-defined margins was observed. Histopathological examination using routine Hematoxylin and Eosin (H&E) staining revealed tissue lined by stratified keratinized squamous epithelium. The dermis comprised edematous fibrous collagenous stroma containing proliferating tumor cells with oval-to-round nuclei exhibiting moderate-to-high pleomorphism, partially vesicular hyperchromatic nuclei with prominent nucleoli, scant cytoplasm, and a high mitotic rate reaching 15 mitoses/mm². The tumor cells were arranged in a dense, diffuse, and syncytial pattern without distinct tubular structures. Additionally, inflammatory cell infiltration comprising lymphocytes, histiocytes, polymorphonuclear leukocytes (PMNs), and plasma cells was observed within the edematous fibrous collagenous stroma, along with epidermal invasion. The microscopic findings initially suggested a malignant round-cell tumor, with a preliminary impression of medullary-pattern invasive breast carcinoma and a differential diagnosis of large-cell lymphoma. Immunohistochemical analysis was performed to confirm the final diagnosis.

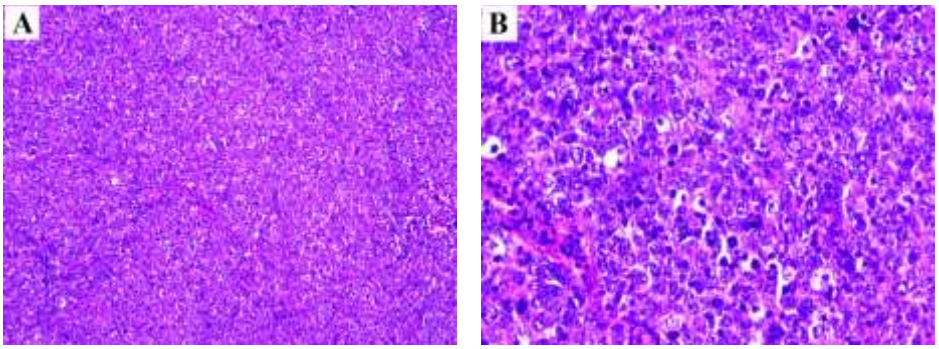


Figure 1.Morphological features of the breast specimen shows a diffuse round cell proliferation. Low power magnification 100x, H&E (A). High power magnification, 400x, H&E (B).

The immunohistochemical profile of the tumor mass demonstrated diffuse positive expression of CD20, negative expression of CD3, and an increased Ki67 proliferation index exceeding 30%. Based on histopathological and immunohistochemical findings, the tumor in the right breast was diagnosed as Diffuse Large B-Cell Lymphoma (DLBCL).

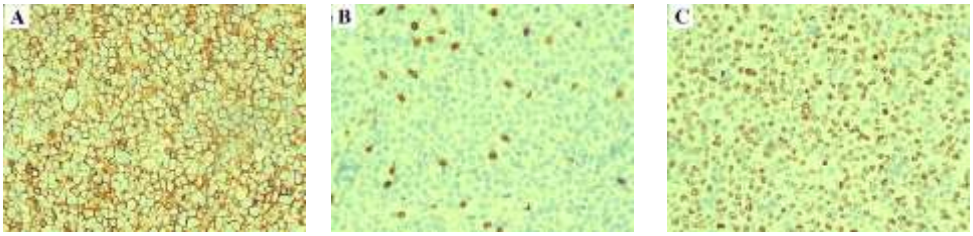


Figure 2. Immunohistological profile shows diffuse CD20 expression. CD20, 400X (A). CD3, 400X (B), Ki67 proliferation index (C).

## DISCUSSION

Primary breast diffuse large B-cell lymphoma (DLBCL) is a rare neoplasm, accounting for only 0.38–0.70% of all non-Hodgkin lymphomas and less than 0.5% of breast malignancies, with approximately 53% of cases classified as DLBCL (Jia et al., 2018; Zhang et al., 2017; Maccio et al., 2025). According to the World Health Organization, diagnostic criteria for primary breast lymphoma include confinement of the tumor to the breast, with or without ipsilateral lymph node involvement, and histological confirmation of diffuse proliferation of atypical B-cells (Li et al., 2012; Alkerata et al., 2024). Clinically, the disease often presents as a unilateral palpable mass without specific features, making it difficult to distinguish from primary breast carcinoma (Maccio et al., 2025). Radiologically, primary breast DLBCL lacks pathognomonic findings, as ultrasound, mammography, and MRI cannot reliably differentiate it from carcinoma, which emphasizes the crucial role of tissue biopsy and ancillary testing (Gluskin et al., 2020; Parashar et al., 2021).

Histopathologically, the differential diagnosis includes triple-negative breast carcinoma, metastatic malignancies, melanoma, and angiosarcoma. Therefore, immunohistochemical profiling is essential. Key markers such as CD20 confirm B-cell lineage, whereas cytokeratin, HMB45, S100, and ERG help exclude other mimics (Bellizzi, 2020; Quintana & Collins, 2023). Fine-needle aspiration may provide initial clues but is generally inadequate for accurate subtyping. Instead, core needle or excisional biopsy remains the preferred diagnostic approach, offering sufficient material for both histological and immunohistochemical analyses (Aviv et al., 2013; Alkerata et al., 2024). In the present case, the tumor was initially suspected to be triple-negative breast carcinoma, underscoring the diagnostic challenges, as misclassification has been documented in previous reports (Chen et al., 2021; Guo et al., 2022; Lokesh et al., 2013).

Therapeutic strategies for primary breast DLBCL have shifted over time. Historically, mastectomy was frequently performed; however, accumulating evidence demonstrates no survival benefit from surgical resection and suggests that it may even worsen prognosis (Jennings et al., 2007). Current guidelines recommend systemic chemotherapy as the standard of care, with the R-CHOP regimen being the most widely used, sometimes in combination with radiotherapy (Aviv et al., 2013; Pereira et al., 2023). Prognosis depends on multiple factors, including stage at presentation, nodal involvement, and International Prognostic Index (IPI) score. Population-based studies report a 5-year overall survival rate of 60–70%, highlighting the importance of early recognition and accurate diagnosis (Jia et al., 2018; Maccio et al., 2025). Although the mean age of onset is around 70 years, our patient was 47 years old, which aligns with reports of younger-onset cases described in the literature (Chen et al., 2021; Guo et al., 2022; Lokesh et al., 2013). This case reinforces the need for awareness among clinicians and pathologists that primary breast DLBCL, while rare, should always be considered in the differential diagnosis of breast tumors.

## CONCLUSION

Primary breast diffuse large B-cell lymphoma (DLBCL) is a rare but clinically significant malignancy that must be considered in the differential diagnosis of breast tumors. Because its clinical and radiological presentation often mimics invasive breast carcinoma, accurate diagnosis relies heavily on the integration of morphological evaluation and immunohistochemical analysis. Establishing the correct diagnosis is essential, as the therapeutic approach for breast lymphoma differs substantially from that of breast carcinoma. While breast carcinoma is typically managed with surgical intervention, primary breast DLBCL requires systemic immunochemotherapy as the cornerstone of treatment. Early recognition and precise diagnostic confirmation not only prevent unnecessary surgical procedures but also enable timely administration of appropriate therapy, ultimately improving patient outcomes and long-term prognosis.

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