Primary Breast Lymphoma with Aggressive Extranodal Involvement: ^{18}F-FDG PET-CT Findings of Two Unusual Cases

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ABSTRACT

Background: Primary breast lymphoma (PBL) is a rare extranodal non-Hodgkin lymphoma, accounting for less than 0.5% of all breast malignancies. Due to its rarity and nonspecific clinical and imaging features, diagnosis is often challenging, particularly in cases with dense breast tissue or atypical presentation. This report describes two cases of histologically confirmed PBL with aggressive clinical behavior and extensive systemic involvement.

Case Reports: Case1 - A 70-year-old male had bilateral breast enlargement and was diagnosed with diffuse large B-cell lymphoma.

Case 2 - A 28-year-old female with dense breast tissues had inconclusive reports in conventional imaging. The biopsy reported plasmablastic lymphoma.

Both the patients demonstrated intensely hypermetabolic bilateral breast lesions in ^{18}F-FDG PET-CT with widespread nodal and extranodal involvement, including lymph nodes, lungs, peritoneum, skin, and skeleton, consistent with advanced-stage (stage IV) disease.

Conclusion: These cases highlight the aggressive nature of certain PBL subtypes and the limitations of conventional imaging modalities. FDG PET-CT proved essential in accurately staging the disease, detecting multifocal involvement, and guiding clinical management. Early utilization of PET-CT is crucial for comprehensive disease assessment and optimal treatment planning in patients with suspected primary breast lymphoma.

Keywords: Primary breast lymphoma, ^{18}F-FDG PET-CT, extranodal involvement, advanced stage disease.

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INTRODUCTION

Primary breast lymphoma (PBL) is a rare and distinct clinicopathological entity defined as lymphoma arising within the breast tissue in the absence of prior or concurrent widespread disease at the time of diagnosis. It accounts for approximately 0.04%–0.5% of all breast malignancies and about 1%–2% of extranodal non-Hodgkin lymphomas, making it an uncommon diagnostic consideration in routine breast imaging and oncology practice (1). The rarity of PBL is largely attributed to the relatively sparse lymphoid tissue within the breast parenchyma compared to other extranodal sites (2).

PBL predominantly affects women, typically in the fifth to seventh decades of life, although cases have been reported across a wide age range. Male breast involvement is exceptionally rare due to minimal breast tissue and even less lymphoid content (3). Histologically, the majority of PBL cases are of B-cell origin, with diffuse large B-cell lymphoma (DLBCL) being the most common subtype. Less frequently encountered but clinically significant subtypes include follicular lymphoma, marginal zone lymphoma, and highly aggressive variants such as plasmablastic lymphoma (4). These aggressive subtypes are often associated with rapid disease progression, extranodal dissemination, and poorer prognosis.

Clinically, PBL most commonly presents as a painless, palpable breast mass. However, atypical presentations such as bilateral breast involvement, rapid enlargement, breast discomfort, and associated systemic “B symptoms” (fever, weight loss, and night sweats) may occur, particularly in high-grade lymphomas (5). Unlike primary breast carcinoma, skin changes, nipple retraction, and microcalcifications are less commonly observed, which may further complicate differentiation from other benign or malignant conditions (6).

Radiological evaluation of PBL poses significant challenges. Mammographic findings are often nonspecific and may demonstrate a well-defined or ill-defined mass without characteristic calcifications.

Ultrasonography typically reveals hypoechoic or heterogeneous masses but lacks specificity for definitive diagnosis. These limitations are particularly evident in patients with dense breast tissue, where lesion conspicuity is reduced and diagnostic accuracy is compromised (6). Consequently, histopathological examination with immunohistochemistry remains the gold standard for diagnosis.

In recent years, F-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET-CT) has become an indispensable imaging modality in the evaluation of lymphoma. It provides combined metabolic and anatomical information, enabling accurate detection of both nodal and extranodal disease sites (7). FDG PET-CT is highly sensitive in identifying metabolically active lesions, assessing disease burden, staging, and guiding therapeutic decisions. It also plays a crucial role in response assessment and prognostication, as increased FDG uptake often correlates with tumor aggressiveness (8).

The role of FDG PET-CT is particularly important in rare and aggressive presentations of PBL, where conventional imaging may underestimate disease extent. Early and accurate staging is essential, as management strategies differ significantly between localized and advanced disease, with systemic chemotherapy forming the cornerstone of treatment in disseminated cases (9).

In this report, we present two cases of PBL, including a rare male patient and a young female with dense breast tissue, both demonstrating aggressive clinical behavior and extensive systemic involvement on FDG PET-CT. These cases highlight the diagnostic challenges and emphasize the critical role of PET-CT in comprehensive disease evaluation, staging, and management of this uncommon malignancy.

CASE REPORTS

Two patients with histologically confirmed primary breast lymphoma were evaluated. The first case involved a 70-year-old male who presented with progressive bilateral breast enlargement and discomfort. Ultrasonography demonstrated soft tissue masses in both breasts. Histopathological examination and immunohistochemistry confirmed diffuse large B-cell lymphoma. ^{18}F-FDG PET-CT revealed intensely hypermetabolic masses in both breasts, along with widespread nodal involvement, including axillary, mediastinal, and abdominopelvic lymph nodes. Additionally, multiple skeletal lesions demonstrated increased FDG uptake, consistent with advanced systemic disease (Figure 1 and 2).

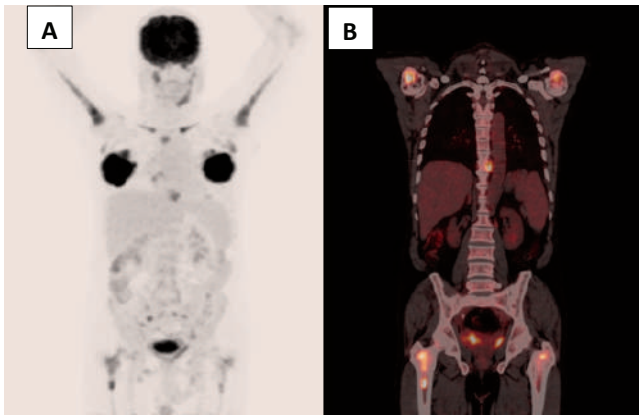

Figure 1: Maximum Intensity Projection (MIP) view (A) and coronal fused (B) view of ^{18}F-FDG PET-CT showed hypermetabolic masses in both breasts, along with widespread nodal and extranodal involvement.

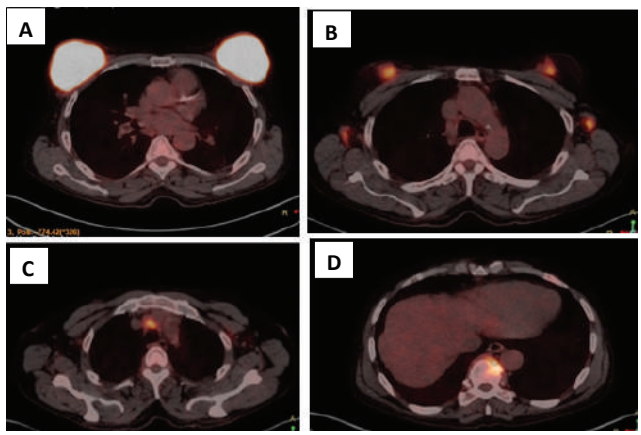

Figure 2: ^{18}F-FDG PET-CT fused axial images in a 70-year-old male showed bilateral breast enlargement with intensely hypermetabolic soft tissue masses in both breasts (A). Hypermetabolic lymph nodes in axilla (B), mediastinum (C) and skeletal (D) involvement.

The second case was a 28-year-old female presenting with breast enlargement. Mammography and ultrasonography were limited due to dense breast parenchyma, obscuring clear lesion visualization. Biopsy revealed non-Hodgkin lymphoma, and immunohistochemistry confirmed plasmablastic lymphoma, an aggressive subtype. ^{18}F-FDG PET-CT demonstrated intensely hypermetabolic bilateral breast lesions with extensive extranodal spread involving

both lungs, axillary and upper abdominal lymph nodes, skin, peritoneum, and skeletal system (Figure 3 and 4). In both cases, PET-CT findings indicated stage IV disease with multifocal involvements which reflected the aggressive nature of breast lymphoma for the both male and female patients.

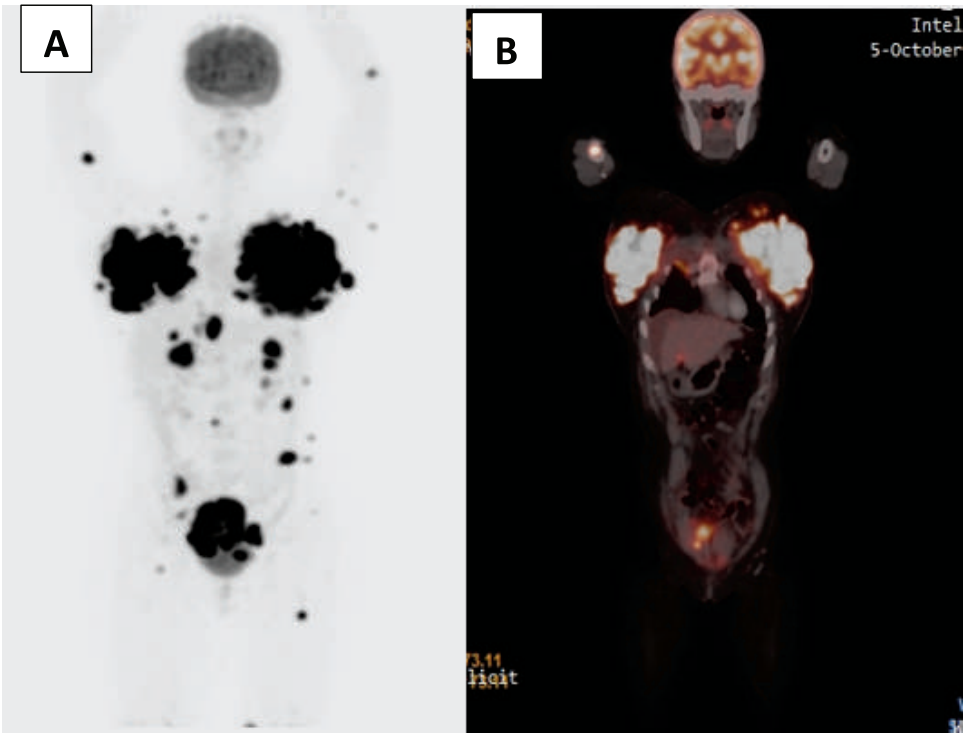

Figure 3: Maximum Intensity Projection (MIP) view (A) and coronal fused view (B) of ^{18}F-FDG PET-CT showed hypermetabolic masses in both breasts, along with widespread nodal and extranodal involvement.

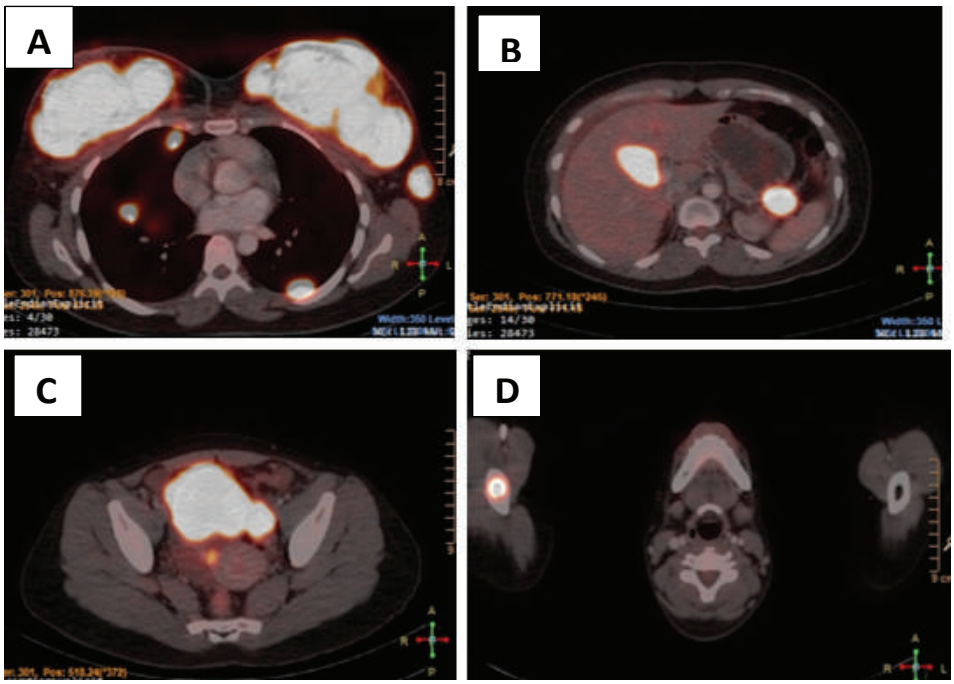

Figure 4: ^{18}F-FDG PET-CT fused axial images in a 28-year-old female presented with breast enlargement and revealed intensely hypermetabolic soft tissue masses in both breasts (A). Hypermetabolic lesions involving both lungs, axilla (A) and upper abdominal lymph nodes (B), peritoneum (C) and skeleton (D).

DISCUSSION

PBL is an uncommon extranodal lymphoma that poses significant diagnostic and clinical challenges due to its rarity, heterogeneous presentation, and overlap with more common breast malignancies. According to the diagnostic criteria proposed by Wiseman and Liao, PBL is defined by the presence of lymphoma within the breast tissue with or without ipsilateral lymph node involvement, in the absence of prior systemic lymphoma at initial presentation (8). However, as demonstrated in the present cases, a subset of patients may already have disseminated disease at the time of diagnosis, reflecting aggressive tumor biology rather than true localized origin.

Diffuse large B-cell lymphoma, identified in the male patient, represents the most frequent histological subtype of PBL and is known for its rapid proliferation and tendency for systemic spread (4). The second case, involving plasmablastic lymphoma, is particularly noteworthy due to its rarity and highly aggressive clinical course. Plasmablastic lymphoma is often associated with a high proliferative index, frequent extranodal involvement, and poor prognosis, even with intensive chemotherapy (9). The presence of such aggressive histological variants likely explains the extensive nodal and extranodal dissemination observed in both patients.

Clinically, PBL may mimic primary breast carcinoma; however, certain distinguishing features exist. Rapid bilateral breast enlargement, as seen in both cases, is relatively uncommon in carcinoma but can occur in lymphoma due to diffuse infiltration. Additionally, the absence of typical features such as spiculated margins, architectural distortion, and microcalcifications on imaging may provide subtle clues favoring lymphoma over carcinoma (6). Nevertheless, imaging findings are often nonspecific, and definitive diagnosis relies on histopathological and immunohistochemical evaluation.

Conventional imaging modalities, including mammography and ultrasonography, have inherent limitations in the evaluation of PBL. Mammography may fail to detect lesions in dense breast tissue, as encountered in the female patient, while ultrasonography lacks specificity in differentiating lymphoma from other solid breast masses (6). These limitations underscore the importance of advanced imaging techniques in such cases.

^{18}F-FDG PET-CT has emerged as a cornerstone in the evaluation of lymphoma due to its ability to provide whole-body metabolic and anatomical assessment in a single examination. In both cases presented, PET-CT not only confirmed intense metabolic activity within the breast lesions but also revealed extensive nodal and extranodal involvement, including lymph nodes, lungs, peritoneum, skin, and skeletal system. Such comprehensive disease mapping is essential for accurate staging, particularly in aggressive lymphomas where disease extent may be underestimated by conventional imaging (10).

The detection of widespread extranodal involvement in these patients corresponds to stage IV disease, which has significant implications for management and prognosis. Unlike primary breast carcinoma, where surgery often plays a central role, the treatment of PBL is primarily systemic, typically involving combination chemotherapy with or without radiotherapy (11). Therefore, accurate staging using PET-CT is crucial in guiding appropriate therapeutic strategies and avoiding unnecessary surgical interventions.

In addition to staging, FDG PET-CT provides valuable prognostic information. High FDG uptake is generally associated with increased tumor aggressiveness and higher proliferative activity (12). Furthermore, PET-CT plays a pivotal role in response assessment following therapy, enabling early identification of treatment failure or residual disease, which is particularly important in aggressive subtypes such as DLBCL and plasmablastic lymphoma.

The cases presented here highlight several important clinical insights. First, PBL should be considered in the differential diagnosis of rapidly enlarging breast masses, particularly when bilateral or associated with systemic features. Second, aggressive histological subtypes may present with widespread disease at initial diagnosis. Finally, FDG PET-CT is indispensable for accurate staging, prognostication, and management planning in such patients.

CONCLUSION

Primary breast lymphoma is a rare but clinically significant entity that may present with aggressive and widespread disease. These two cases demonstrate extensive nodal and extranodal involvement at presentation, consistent with advanced-stage lymphoma. Conventional imaging may be insufficient, particularly in dense breast tissue. ^{18}F-FDG PET-CT plays a critical role in accurate staging, revealing the full extent of disease and guiding therapeutic decision-making. Early recognition and comprehensive imaging are essential for optimal management of this rare malignancy.

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