Breast Lymphoma: A pictorial review

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Learning objectives

- To illustrate the imaging spectrum of primary and secondary breast lymphoma based on a series of seven patients.
- To review the imaging characteristics of breast lymphoma on a multimodality evaluation and discuss its occurrence.
- To alert the radiologist for this diagnostic entity in breast imaging.

Background

Breast Lymphoma is an unusual entity, representing approximately 0.15 - 0.7% of malignant mammary neoplasms. Approximately 1 - 2% of all lymphomas occur in the breast and sometimes it can be the first sign of a systemic disease. [1, 2]

Malignant lymphoma of the breast is classified into primary or secondary, morphologically indistinguishable at histologic analysis. The diagnosis of primary breast lymphoma is limited to patients with no evidence of a systemic lymphoma or leukemia when the breast lesion is detected and the disease should involve only the breast or the breast and ipsilateral axillary lymph nodes. Secondary breast lymphoma is slightly more common. It occur in patients with known prior disease or it is diagnosed when breast lesion, usually multiple, is found with simultaneous lesions in non-mammary organs. [1, 2, 3]

Breast lymphoma is predominantly of B-cell non-Hodgkin type, followed by follicular, T-cell, histiocytic and MALT lymphoma more rarely. [1]

A literature review focusing on the imaging patterns on different methods and a correlated radiologic-pathologic analysis of breast lymphoma cases diagnosed in our department are exposed.

Imaging findings OR Procedure details

Various imaging findings in a multimodality evaluation, including: mammography, ultrasonography (US), MRI, Gallium scintigraphy and combined PET/CT scanning played a major role throughout diagnosis workup in this series.

Case 1:

54-year-old female with a painful lump in the right breast, first noticed 1 month earlier. US image (Fig. 1) revealed an irregular hypoechoic mass with posterior enhancement.
Percutaneous core needle biopsy proved a primary diffuse large B-cell non-Hodgkin lymphoma. No other sites of disease were identified in a staging PET/CT scan (Fig. 2).

Less than 0.5% of all malignant lymphomas involve the breast primarily. The criteria for PBL are controversial; on adequate pathologic specimens, mammary tissue and lymphomatous infiltrate have to be in close association; clinically, it is defined as disease localized to one or both breasts with or without regional lymph nodes involvement. Bilateral synchronous breast lymphoma occurs in 10% of patients, and contralateral metachronous disease occurs in up to 15%. [1, 3]

Case 2:
Secondary extranodal marginal zone B-cell lymphoma of MALT type in a 61-year-old woman with known extramammary non-Hodgkin lymphoma. (Fig. 3 and 4)

Case 3:
74-year-old woman with abnormal findings in screening breast exams (Fig. 5). The lesion was classified as probably malignant and proved by percutaneous biopsy a low-grade non-Hodgkin lymphoma - extranodal marginal zone B-cell primary breast lymphoma of MALT type. (Fig. 6 and 7)

Case 4:
Female, 37-year-old, with a painful palpable breast lump in the right upper outer quadrant (UOQ) for 6 months. After mammary imaging evaluation (Fig. 8, 9 and 10), a percutaneous core needle biopsy was performed, which diagnosed primary Hodgkin Lymphoma. (Fig. 11 and 12)

Case 5:
Female, 64-year-old, with a history of stomach MALT lymphoma treated in 2006 with complete remission. After 4 years, relapses in sinuses, lungs and skin, and also presenting with a palpable breast node in the left UOQ. At imaging breast evaluation (Fig. 13 and 14), an irregular lesion was identified, proven by percutaneous biopsy a secondary MALT lymphoma.

MALT lymphoma is a non-Hodgkin type lymphoma associated with chronic inflammation. It typically occurs in the gastric mucosa or the thyroid parenchyma, and is rarely reported in the breast. Among the types of breast lymphomas, MALT constitutes a variable
subgroup with frequencies ranging from 0% to 44% in the literature. It tends to have an indolent behavior with good prognosis. [5]

Case 6:
Primary breast follicular Non-Hodgkin Lymphoma in a 68-year-old female, first presented with a palpable left breast lesion. (Fig. 15 and 16)

Case 7:
60-year-old woman with known Hodgkin lymphoma appears with a right breast lump and an ipsilateral palpable lymph nodes. Imaging findings (Fig. 17, 18, 19, 20 and 21) and percutaneous biopsy confirmed the breast involvement by Hodgkin lymphoma.

The most common mammographic feature seen in the literature was described as noncalcified solitary mass (69 - 76%), predominates in the pathologies of primary origin, followed by multiple masses, and global asymmetry (diffuse increase in breast density). Masses were most frequently lobular or irregular in shape and demonstrated indistinct margins in the majority. [1, 2, 4]

US features of breast lymphoma include a large heterogeneously hypoechoic mass with indistinct margins and overlying skin and subcutaneous edema; circumscribed hypoechoic masses, or diffuse nodular infiltration of the breast. An echogenic boundary and posterior acoustic phenomena can be found in 64% of cases, therefore posterior acoustic shadowing, frequently associated with breast carcinoma, is not a feature. [1, 2, 4]

MR imaging shows intense global heterogeneous enhancement with pattern characteristic of malignancy, like rapid initial increase and washout kinetics on dynamic contrast-enhanced images. [1, 2, 4]

Nowadays, the combination of PET/CT whole body scan play an important role in the assessment of patients with lymphoma, either initial or recurrent disease. Most tumors demonstrate avid homogeneous FDG uptake at PET/CT, with a high mean maximum standardized uptake value (mean 10.6). [1, 2]

A mammographic finding of bilateral axillary lymphadenopathy should arouse suspicion about the presence of a secondary lymphoma. Other causes of bilateral axillary lymphadenopathy include leukemia, collagen vascular diseases, nodal hyperplasia, granulomatous diseases, human immunodeficiency viruses, silicone-related adenopathy, and metastases (usually from breast, lung, thyroid cancer or melanoma). [1, 2, 4]

At histologic analysis with routine hematoxylin-eosin staining, malignant lymphoma may be confused with lobular or medullary carcinoma. In addition, inflammatory conditions of
the breast may mimic MALT-type lymphoma at histologic analysis. Fine-needle aspiration biopsy together with flow cytometry is easy and useful for initial diagnosis, but core-needle biopsy is superior for lymphoma subtyping. [1]

**Fig. 1:** US - Irregular hypoechoic mass with posterior enhancement.

**Fig. 2:** 18F-FDG-PET/CT - A focal area of increased uptake found in the right breast (SUV 11.3). No other sites of disease were identified.
Fig. 3: Mammography - Mediolateral oblique (MLO) and craniocaudal (CC) views demonstrate a high-density lobulated mass in the upper inner quadrant of the right breast.
Fig. 4: US - Well defined hypoechoic mass with slightly irregular borders and posterior acoustic phenomena.
Fig. 5: Mammography - Left mediolateral and CC mammograms show high-density focal asymmetry, with ill-defined margins in the upper inner quadrants.
**Fig. 6:** US - Hypoechoic mass with irregular borders and no posterior acoustic shadowing was identified over the corresponding area on prior mammogram.

**Fig. 7:** MRI - (a) T1-weighted axial MRI postcontrast: maximum intensity projection (MIP) image demonstrates an irregular mass with heterogeneous enhancement in the left breast. (b) T2-weighted STIR MRI image reveals heterogeneous high-signal-intensity appearance with low signal central area that may correspond to fibrosis.

**Fig. 8:** US - Well-defined hypoechoic masses with round margins and posterior acoustic phenomena, compatible with enlarged intramammary and axillary lymph nodes. They have an atypical morphology with cortical thickening and obliteration of the fatty hilum.
Fig. 9: Mammography - Right mammogram reveals an irregular round high density mass in the posterior aspect of UOQ (metallic skin marker over palpable lesion - BB).

Fig. 10: MRI - Irregular mass with homogeneous enhancement on T1-weighted three-dimensional dynamic MRI and high signal intensity on T2-weighted STIR image. Kinetic analysis shows fast and strong enhancement that peaks in the early postcontrast phase.
Fig. 11: Gallium SPECT/CT scintigraphy - radiotracer uptake in mammary lesions and axillary lymph nodes, no other sites of disease were found.

Fig. 12: PET/CT - High uptake of 18F-FDG (SUV 9.94) in the right breast lesions and axillary lymph nodes. No other sites of disease were identified.
Fig. 13: Mammography - left MLO view and spot compression depict an irregular high density mass in the left UQ over the palpable area (skin maker - BB).

Fig. 14: MRI - (a, b) T1-weighted axial MIP and sagittal MRI postcontrast image show an abnormal area of enhancement as a mass with irregular borders. (c) T2-weighted STIR image shows an irregular high signal intensity lesion.
Fig. 15: US - Well defined nodular lesion in the left breast.
Fig. 16: Mammography - Left breast CC and MLO mammograms reveals a nodular image in the lower inner quadrant (LIQ).
Fig. 17: MRI - T1-weighted post contrast 3D MIP image reveals an abnormal homogeneous enhancement in a mass located in the right breast LIQ and axillary lymph nodes enlargement.
Fig. 18: Mammography - Right ML mammogram demonstrate a dense and heterogeneous mammary tissue with non-identifiable lesion.

Fig. 19: US - Hypoechoic lesion with irregular and ill-defined borders, and no posterior acoustic phenomena.
**Fig. 20:** MRI - (a) Diffusion-weighted sequence. (b) ADC map (0,9).

**Fig. 21:** PET/CT - Multiple areas of increased 18F-FDG uptake in the right breast (SUV 6.5) and bilateral axillary lymph nodes.
Conclusion

Many features in different imaging techniques can be found in breast lymphoma. However, some cases do not exhibit characteristics that distinguish them from other malignant entities involving the breast, an overlapping pattern with the ductal carcinomas may exist. Therefore, other signs can also alert the radiologist for the diagnosis possibility of breast lymphoma, such as lymphadenopathy, cutaneous thickening and other sites of disease.

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