

Case Report

Reports of primary and secondary breast lymphoma: Our experience in King Chulalongkorn Memorial Hospital

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Abstract

We report four cases of primary breast lymphoma (PBL) and five cases of secondary breast lymphoma (SBL). We illustrate imaging findings in various imaging modalities including mammography, ultrasonography (US), magnetic resonance imaging (MRI) and positron emission tomography (PET) as well as review literature concerning this uncommon condition.

Keywords: Primary breast lymphoma, Secondary breast lymphoma, Mammography, Ultrasonography, Magnetic resonance imaging.

Introduction

Breast lymphoma, malignant neoplasm arising in lymphatic tissue in the breast, is a rare entity affecting the breast. This accounts for only 0.04-0.7% of all malignant breast tumors [1,2] Breast lymphoma can be stratified into primary breast lymphoma (PBL) and secondary breast lymphoma (SBL). PBL is defined as disease involving breast tissue in the absence of prior diagnosis of extramammary lymphoma or evidence of concurrent widespread disease except the ipsilateral axillary lymph node [3]. SBL, diagnosed when the disease is not confined to the criteria of PBL, is slightly more common than PBL accounting for 17% of metastatic disease to the breast. Distinction from breast carcinoma is important because the main modality of treatment is different and unnecessary surgical intervention can be avoided in breast lymphoma.

This review illustrates imaging findings in various imaging modalities of breast lymphoma cases including four PBL cases and five SBL cases in our institution. The radiologists should be aware of these rare entities due to possible differential diagnosis of breast mass.

Primary breast lymphoma

Case 1

A 75-year-old female presented with palpable mass in the left breast for one year. On the physical examination, the patient was found to have a large nontender mass on the left breast and palpable left axillary lymph nodes. She underwent mammography and an US examination demonstrating a large mass at the upper mid part of the left breast with a few prominent left axillary lymph nodes (Figure 1 and 2). All the findings were highly suggestive of malignancy and were scored 5 according to the Breast Imaging, Reporting and Data System (BI-RADS). The Core Needle Biopsy (CNB) revealed the diagnosis of diffuse large B cell lymphoma (DLBCL). A further CT scan of the thorax and abdomen and a bone marrow examination showed no evidence of the disease dissemination.

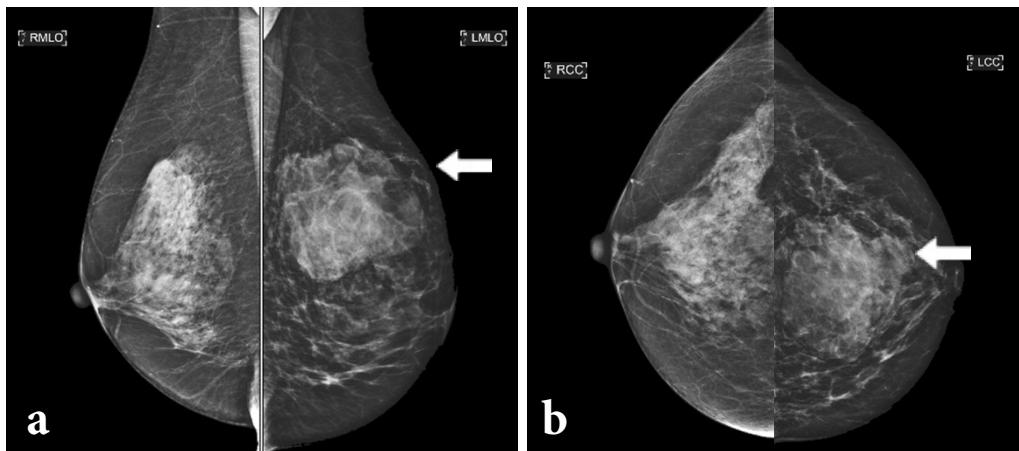


Figure 1. Mammography (a) MLO (b) CC views show a large oval circumscribed mass with equal density at the upper mid part of the left breast (arrow), measuring about 5.1x3.9x5.7cm.

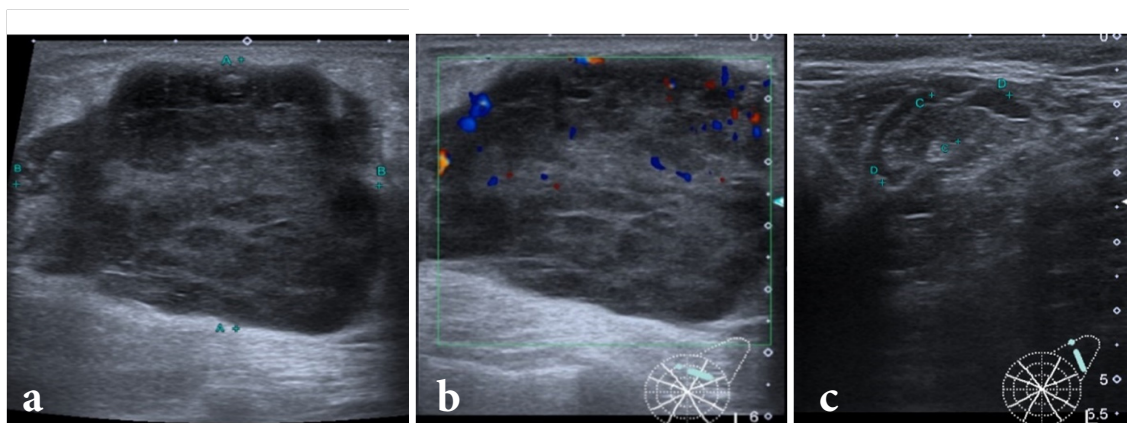


Figure 2. Ultrasound (a) gray scale (b) color Doppler US of the upper mid part of the left breast reveals a 5.1x4.2x4.7-cm oval circumscribed heterogeneous hypoechoic mass with hypervascularity. (c) US at left axilla shows a left axillary lymph node with eccentric cortical thickening.

Case 2

A 62-year-old female presented with palpable right axillary mass and right breast lumps for three months. The patient denied of B symptom. The mammography and US confirmed a huge mass occupying nearly the entire right breast and enlarged right axillary lymph node (Figure 3 and 4). She underwent further investigation with breast MRI which revealed two contiguous enhancing masses occupying nearly the entire right breast with multiple enlarged matted right axillary lymph nodes (Figure 5). US-guided CNB showed DLBCL. Staging work-up by CT scan of the chest and the upper abdomen, bone marrow biopsy and CSF examination revealed no other site of disease involvement.

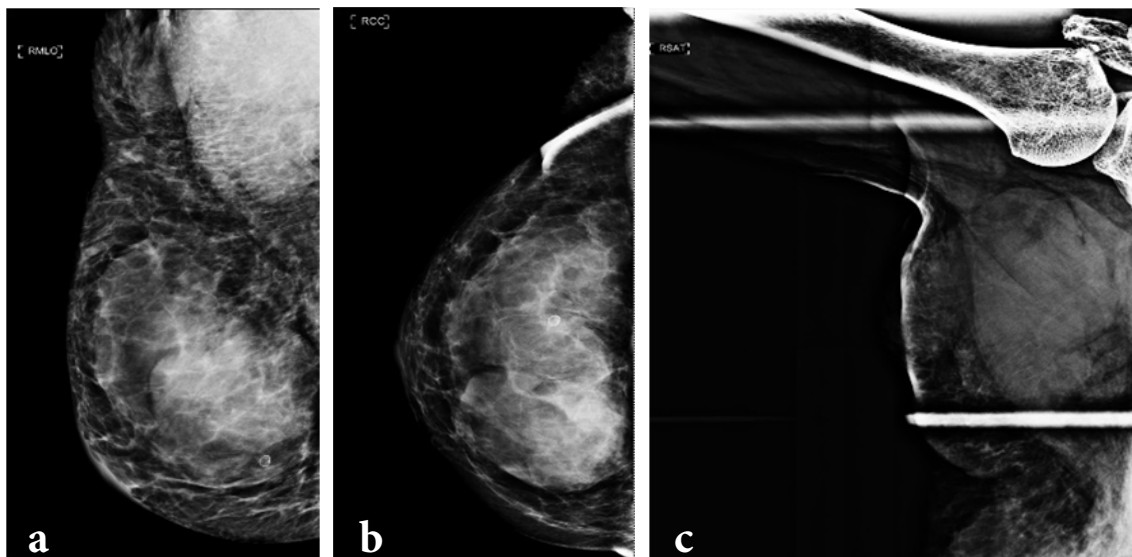


Figure 3. Mammography (a) MLO (b) CC views of right breast reveal a large oval indistinct hyperdense mass occupying nearly the entire right breast and the (c) right axillary view shows enlarged right axillary lymph node.

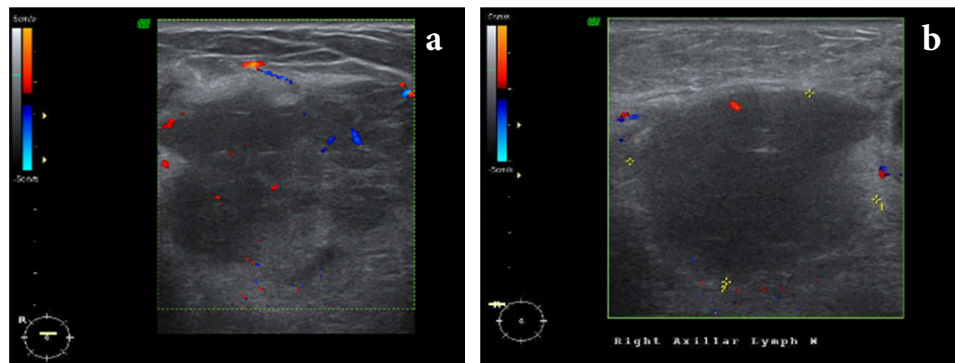


Figure 4. Ultrasound (a) color Doppler US of the upper part of the right breast and (b) color Doppler US of right axilla shows a large oval indistinct heterogeneous hypo- and hyperechoic mass with increased vascularity at the upper part of the right breast with an enlarged right axillary lymph node with the loss of fatty hilum.

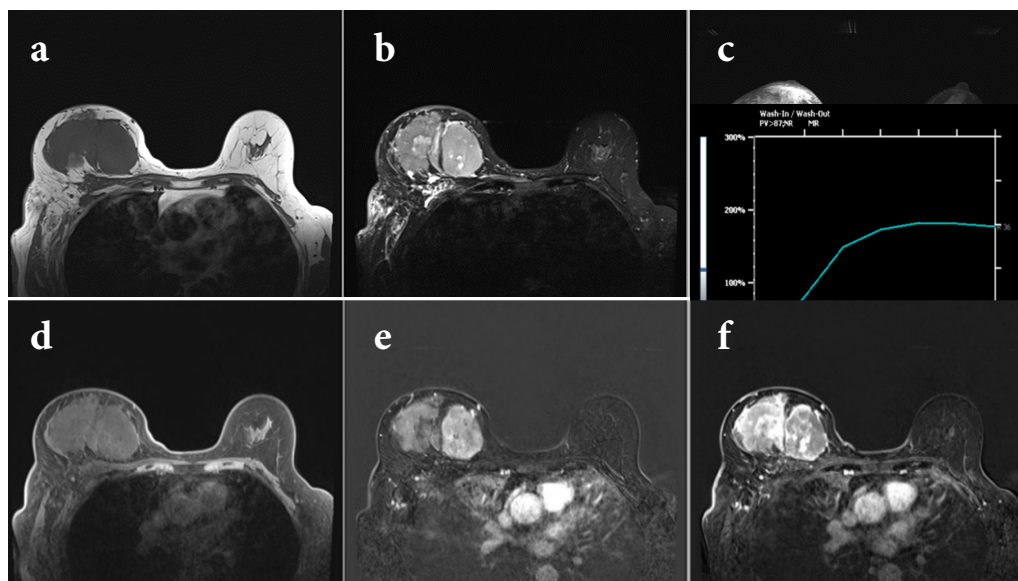


Figure 5. Breast MRI (a) T1-weighted axial image (b) T2-weighted IR axial image (c) Kinetic curve assessment (d) Fat-suppressed precontrast T1-weighted axial image (e) Fat-suppressed post contrast T1-weighted axial image with subtraction (early phase) (f) Fat-suppressed post contrast T1-weighted axial image with subtraction (delayed phase).

MRI shows two contiguous oval circumscribed enhancing masses occupying nearly the entire right breast, about 4.3x5.0x5.7 cm and 4.0x4.6x6.1 cm. These masses show heterogeneous iso-to slight hypointensity on T1-weighted image, hyperintensity on T2-weighted image, strongly heterogeneous enhancement with type II kinetic curve and restricted diffusion ($ADC=0.165-0.623 \times 10^{-3} \text{mm}^2/\text{sec}$).

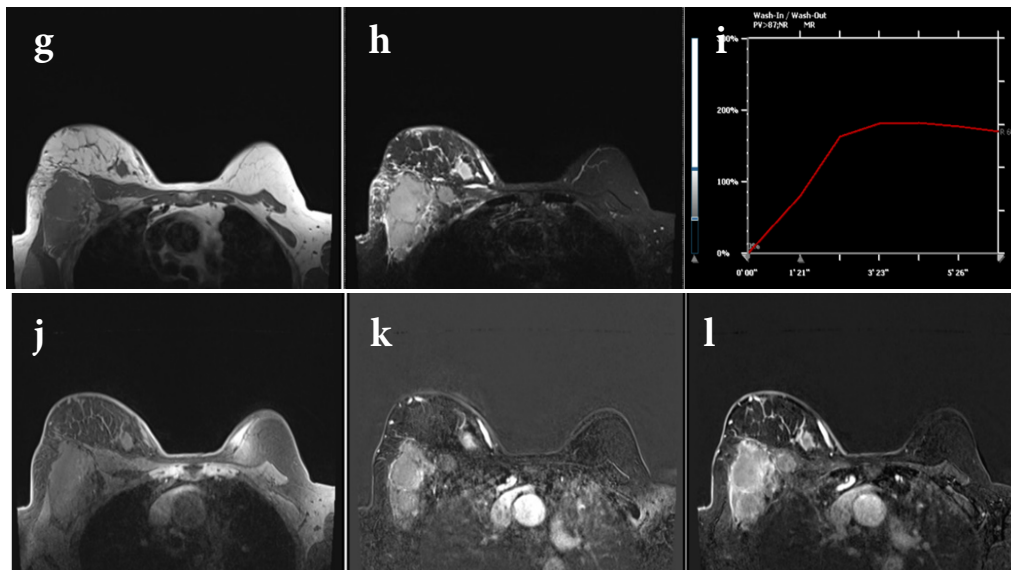


Figure 5. (continued) Breast MRI (g) T1-weighted axial image (h) T2-weighted IR axial image (i) Kinetic curve assessment (j) Fat-suppressed precontrast T1-weighted axial image (k) Fat-suppressed post contrast T1-weighted axial image with subtraction (early phase) (l) Fat-suppressed post contrast T1-weighted axial image with subtraction (delayed phase).

There are conglomerated enhancing masses with similar signal intensity to the breast masses in the right axilla, totally measuring about 8.3 x 7.2 x 11.8 cm, likely matted lymph nodes.

PET-CT after completion of chemotherapy demonstrated complete metabolic remission (Figure 6).

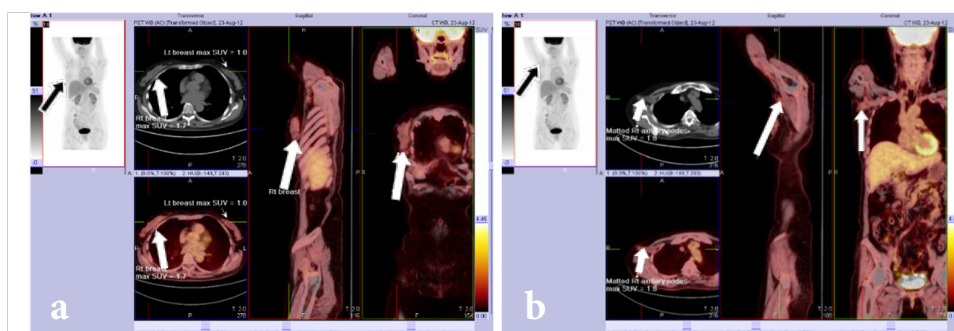


Figure 6. PET-CT after completion of chemotherapy (a) the right breast (b) the right axilla demonstrates mild thickening of the fibroglandular tissue of the right breast without definable mass and mild soft tissue thickening at right axillary region with non-significant FDG avidity (arrows), radiologically favorable complete response.

Case 3

A 43-year-old female had a rapidly growing right breast mass for two months. The patient denied of B symptom.

The mammography revealed enlargement of the right breast with global asymmetry (Figure 7. US showed a few irregular indistinct hypoechoic lesions with hypervascularity along the outer part of the right breast (Figure 8). No other evidence of metastatic disease was seen on other staging workup. The incisional biopsy of the breast mass confirmed diagnosis of DLBCL.

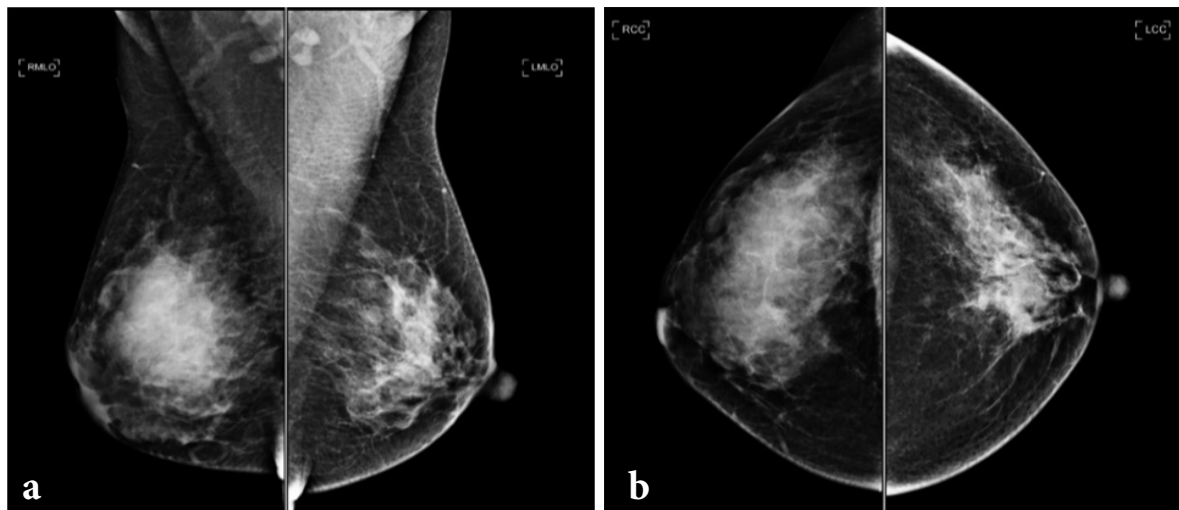


Figure 7. Mammography (a) MLO (b) CC views reveals enlargement of right breast with global asymmetry.

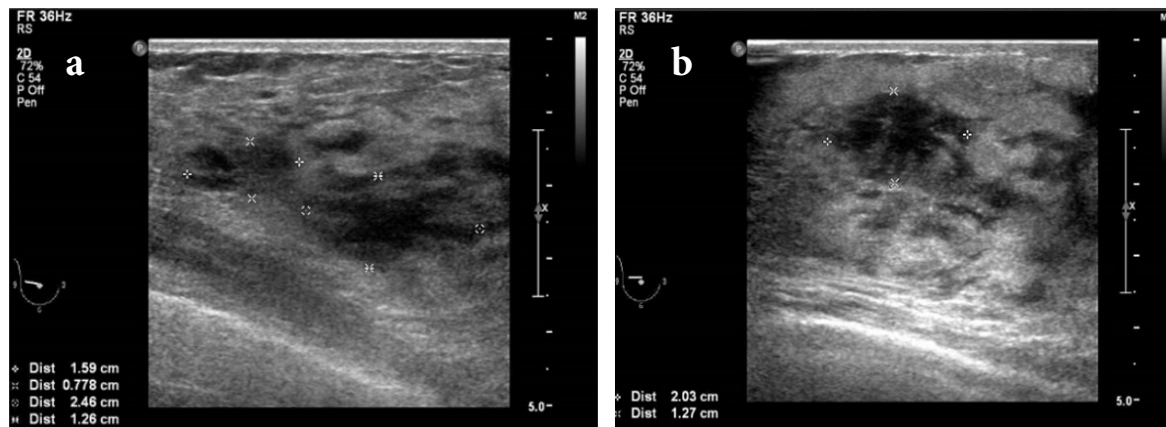


Figure 8. Ultrasound (a) and (b) gray scale US of the upper outer part of the right breast shows a few irregular indistinct hypoechoic lesions along the outer part and the central region of the right breast, measuring up to 2.5x1.3 cm. Increased echogenicity of overlying subcutaneous fat is also noted.

Case 4

A 30-year-old female presented with palpable mass on the right breast for four months. Initial US demonstrated a circumscribed mass at the upper mid part of the right breast (Figure 9). The mammography and US performed two months after the initial study revealed a much increased size of the mass in the right breast (Figure 10 and 11). US-guided CNB of the breast mass confirmed diagnosis of DLBCL. CT scan of the chest and the whole abdomen and bone marrow biopsy revealed no other site of disease involvement.

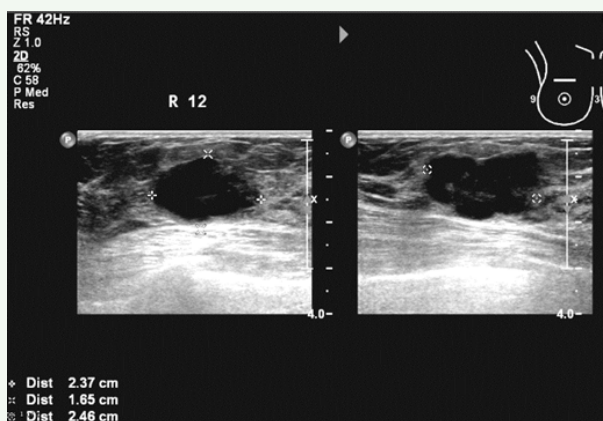


Figure 9. Gray scale US at the upper mid part of right breast reveals a 2.4x1.6x2.5-cm oval circumscribed mixed hypo- and hyperechoic mass.

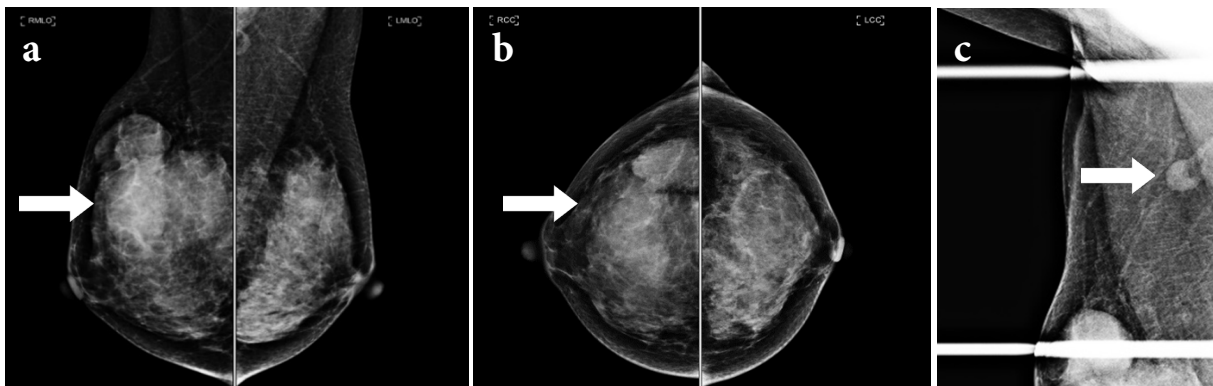


Figure 10. Mammography (a) MLO (b) CC views of the right upper mid to the upper outer quadrant shows a large oval circumscribed mass with equal density at the right upper mid to the upper outer quadrant (arrow). (c) the right axillary view shows a few right axillary lymph nodes with thickened cortex (arrow).

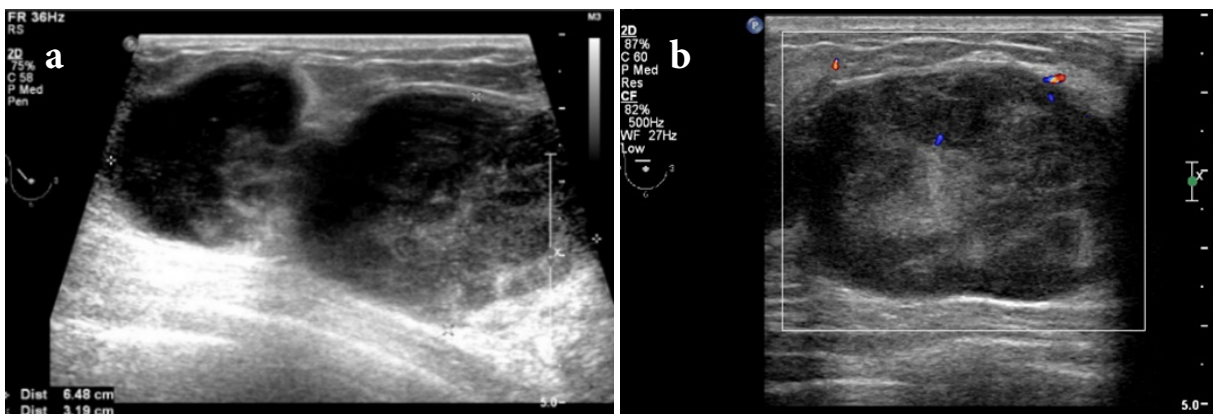


Figure 11. Ultrasound (a) gray scale and (b) color doppler US at the right upper mid to the upper outer quadrant shows a 6.5x3.2x2.3 cm oval lobulated mixed hypo- and hyperechoic mass with minimal increased vascularity, which is increased in size from the initial study.

Secondary breast lymphoma

Case 1

A 27-year-old female had a history of a painful palpable left breast lump for three months and purulent discharge from the left nipple. The mammography revealed enlargement of the left breast with global asymmetry, diffuse trabecular and skin thickening (Figure 12). US showed an irregular indistinct hypoechoic mass with hypervascularity occupying the central part of the left breast with a few adjacent smaller lesions and increased echogenicity of overlying subcutaneous fat (Figure 13). Several enlarged left axillary lymph nodes were also found. The condition was initially suspected for an infectious or inflammatory process such as breast abscess or idiopathic granulomatous mastitis. The patient was sent home with antibiotic treatment.

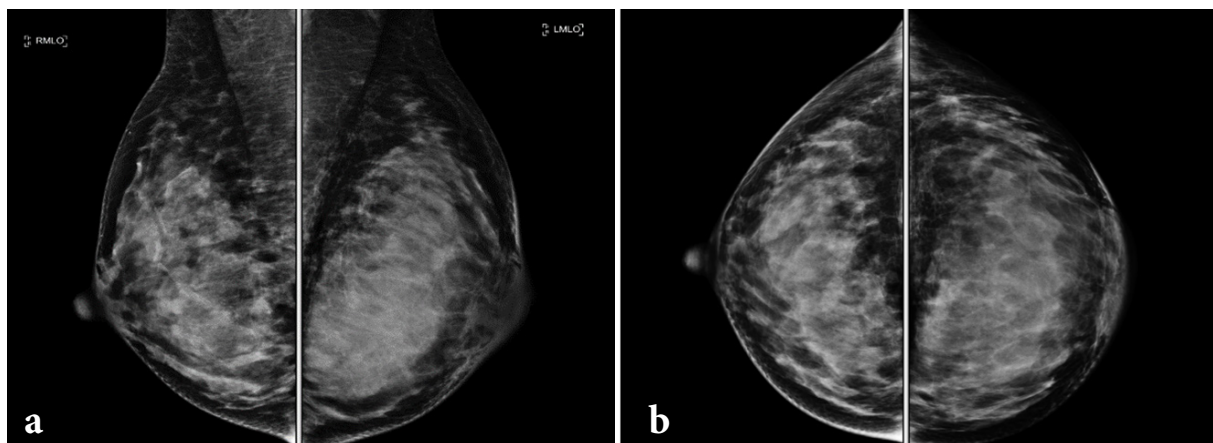


Figure 12. Mammography (a) MLO (b) CC views shows enlargement of the left breast with global asymmetry, trabecular thickening and mild skin thickening involving nipple-areolar-complex.

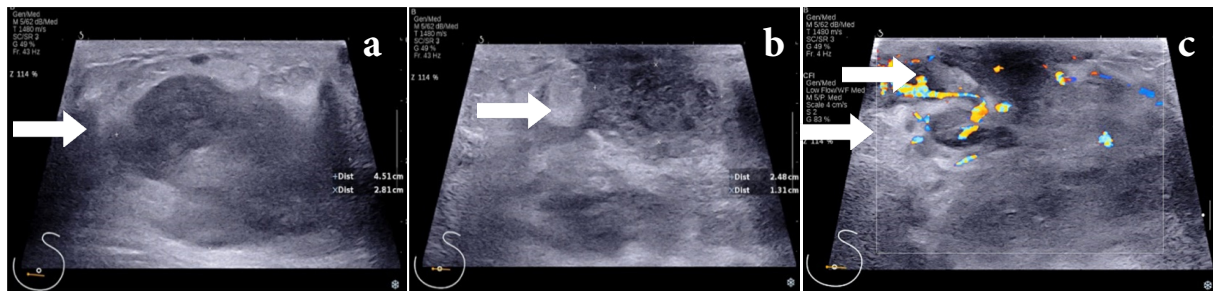


Figure 13. Ultrasound (a) gray scale US at the central part of the left breast (b) gray scale and (c) color doppler US at the left subareolar region reveals an irregular indistinct hypoechoic mass with hypervascularity occupying the central part of left breast, about 4.5x2.8 cm, with a few indistinct smaller lesions at the left subareolar region (arrows).

Follow-up US study about 2 weeks later revealed the increased size of a few irregular indistinct infiltrative hypoechoic masses at the left subareolar region and the left lower inner quadrant with a new lesion at the left outer mid part (Figure 14).

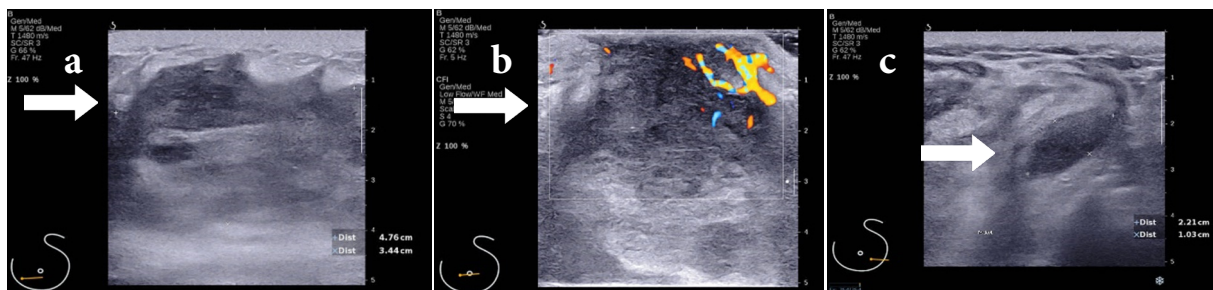


Figure 14. Ultrasound (a) gray scale US at left lower inner quadrant and (b) left subareolar region reveals the increased size and extension of a few irregular indistinct infiltrative hypoechoic masses (arrows). Some liquefaction parts are suspected. (c) Gray scale US at the left outer mid part reveals a 2.2x1.0 cm new mass (arrow). There is surrounding increased echogenicity of subcutaneous fat and skin thickening.

The patient underwent further breast MRI demonstrating multiple ill-defined conglomerated enhancing masses of various sizes occupying nearly the entire left breast, showing heterogeneous enhancement with type III kinetic curve (Figure 15). There were associated skin involvement and left nipple retraction. Multiple enlarged left axillary lymph nodes were seen.

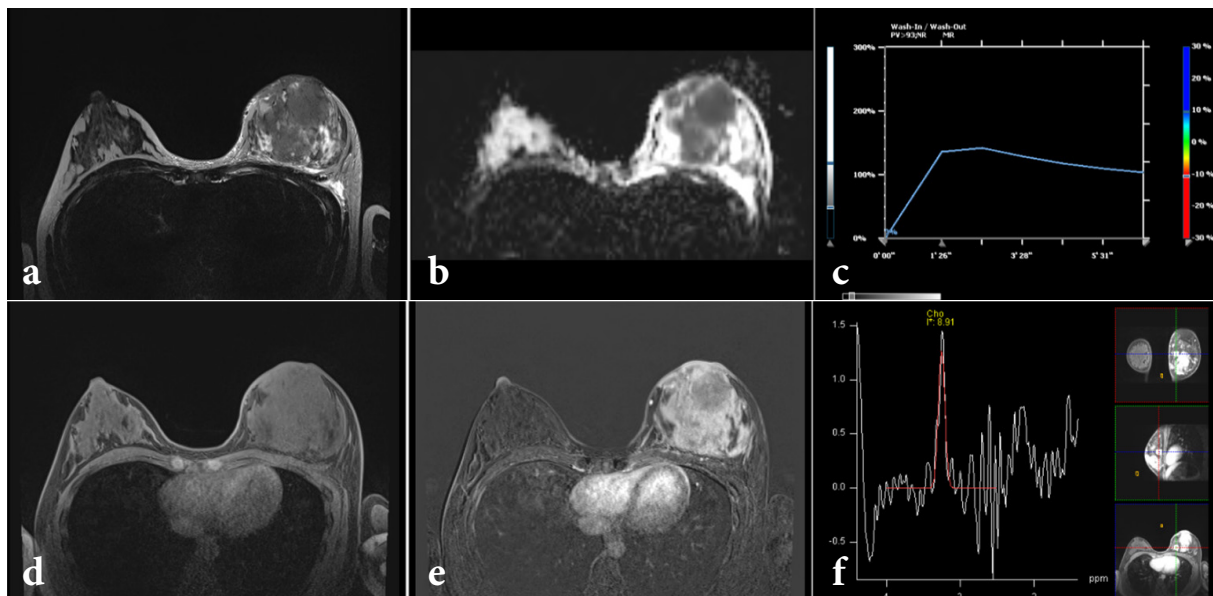


Figure 15. MRI breast (a) T2-weighted axial image (b) ADC (c) Kinetic curve assessment (d) Fat-suppressed precontrast T1-weighted axial image (e) Fat-suppressed post contrast T1-weighted axial image with subtraction (delayed phase) (f) MR spectroscopy.

There are multiple ill-defined conglomerate enhancing masses of various sizes occupying nearly the entire left breast, up to 5.0x4.4 cm, mainly at the left central region, showing isointensity on T1-weighted image, mild hyperintensity on T2-weighted image, heterogeneous enhancement with type III kinetic curve enhancement. The lesions show restricted diffusion ($ADC\ 0.299 \times 10^{-3}/mm^2$) with elevated choline peak (8.91).

US-guided CNB of left breast mass confirmed diagnosis of DLBCL. CT scan of the chest revealed enlarged bilateral axillary and mediastinal lymph nodes and left pleural effusion. PET/CT after completion of chemotherapy demonstrated complete metabolic response of disease (Figure 16).

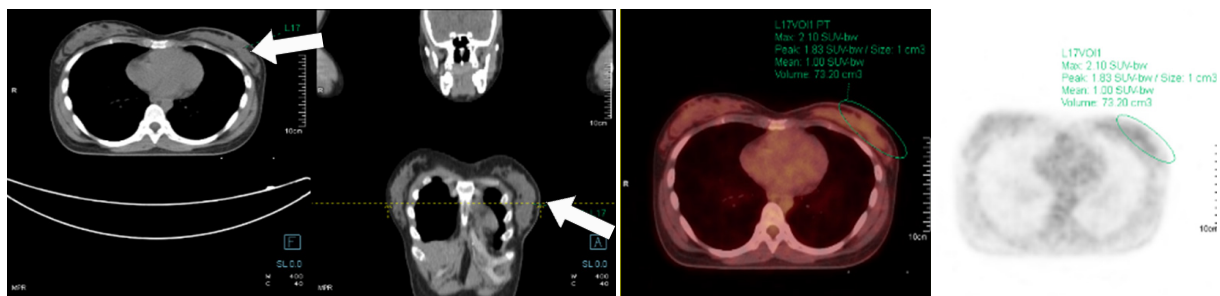


Figure 16. PET/CT after completion of chemotherapy shows mild left fibroglandular tissue thickening with non-significant mild F-18 FDG uptake.

Case 2

A 58-year-old female presented with a palpable left breast mass and bilateral axillary masses for six months. She also had generalized lymphadenopathy, weight loss and progressive dyspnea. The mammography revealed a partially obscured hyperdense mass at the left upper outer quadrant, US showing a round circumscribed hypoechoic mass with increased vascularity. Multiple bilateral axillary lymphadenopathies were seen (Figure 17 and 18). US-guided CNB of left axillary lymph nodes revealed follicular lymphoma. Staging CT examination also revealed multiple generalized lymphadenopathies, splenomegaly and bilateral pleural effusion. Bone marrow biopsy demonstrated disease involvement.

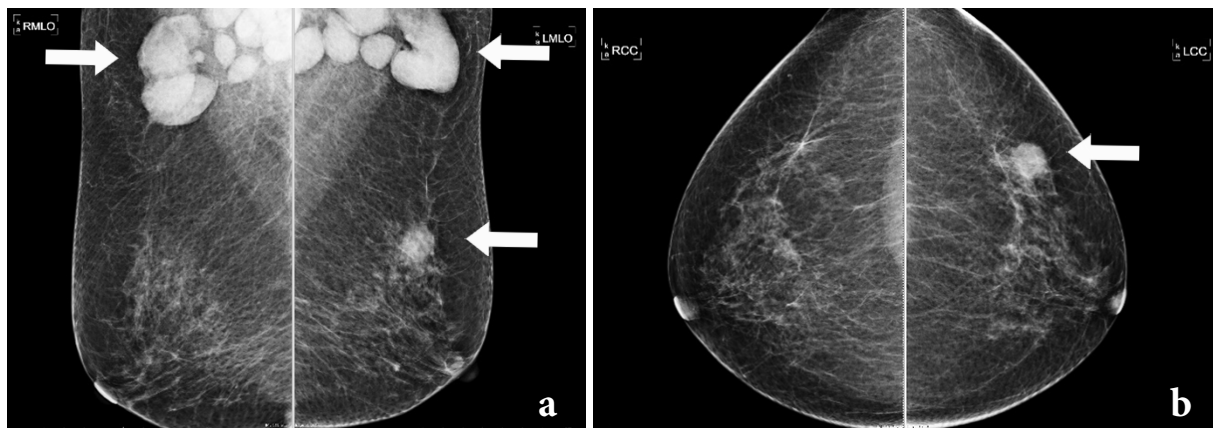


Figure 17. Mammography (a) MLO (b) CC views reveals a 1.9x1.6x2.1-cm partially obscured hyperdense mass at the left upper outer quadrant. Multiple enlarged bilateral axillary lymph nodes are observed.

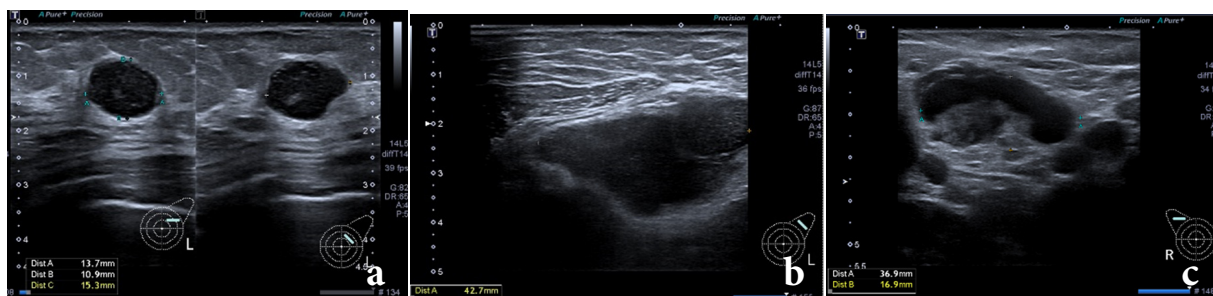


Figure 18. Ultrasound (a) gray scale US of the upper outer quadrant of the left breast shows a 1.4x1.1x1.5-cm circumscribed hypoechoic mass. Gray scale US at (b) left and (c) right axillary regions shows multiple bilateral axillary lymphadenopathies, up to 4.3 cm.

Case 3

A 65-year-old female presented with mass in right nasal cavity for about six months. Biopsy of intranasal mass revealed DLBCL. Staging CT examination revealed several enhancing bilateral breast masses, several subcutaneous masses at the chest wall and the abdominal wall, right perinephric and gastric involvement (Figure 19).

The patient underwent mammography and US demonstrating several irregular indistinct masses at both breasts (Figure 20 and 21). No pathological examination of the breast masses was performed. Bone marrow biopsy revealed disease involvement. Mammography and US performed after 6th cycle of chemotherapy revealed the overall decreased size with some showed complete resolution of masses in both breasts.

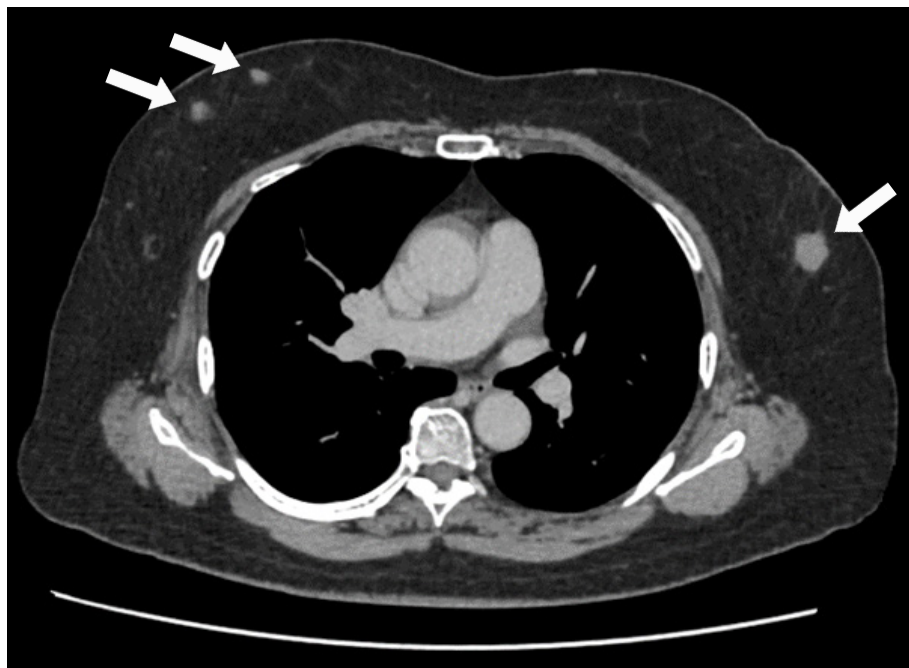


Figure 19. Axial contrast enhanced CT scan of the chest shows several enhancing bilateral breast masses.

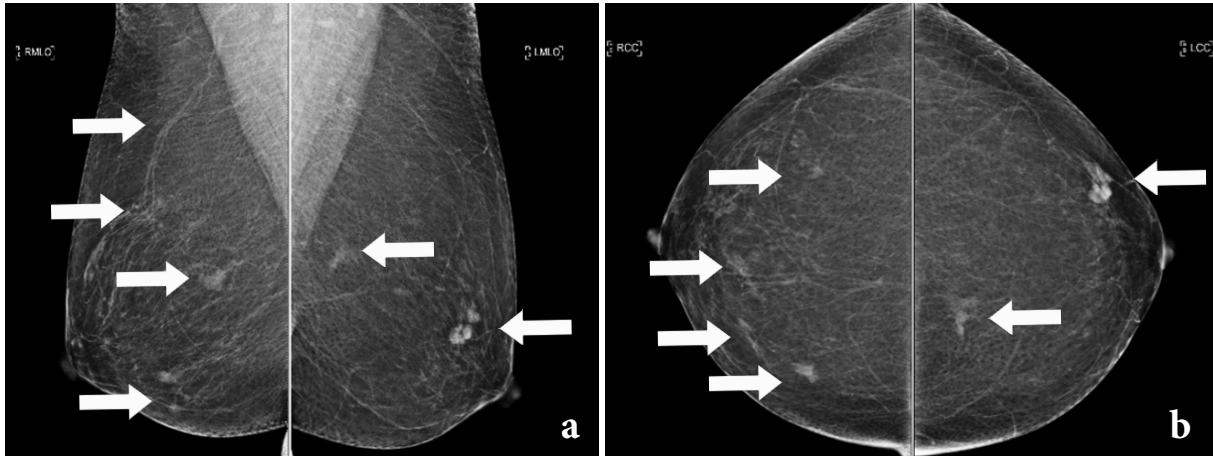


Figure 20. Mammography (a) MLO (b) CC views reveal several irregular indistinct masses with equal and high density in both breasts.



Figure 21. Ultrasound gray scale US at (a) and (b) the outer mid part of the left breast (c) the lower mid part of right breast reveals several irregular indistinct hypoechoic masses in both breasts, up to 1.9x0.6x1.9 cm.

Case 4

A 53-year-old female presented with a palpable left breast lump for one month. She denied of B symptoms. The mammography and US revealed circumscribed mass at the left lower inner quadrant (Figure 22 and 23). The patient underwent excisional biopsy which confirmed diagnosis of DLBCL. CT scan revealed liver dissemination.

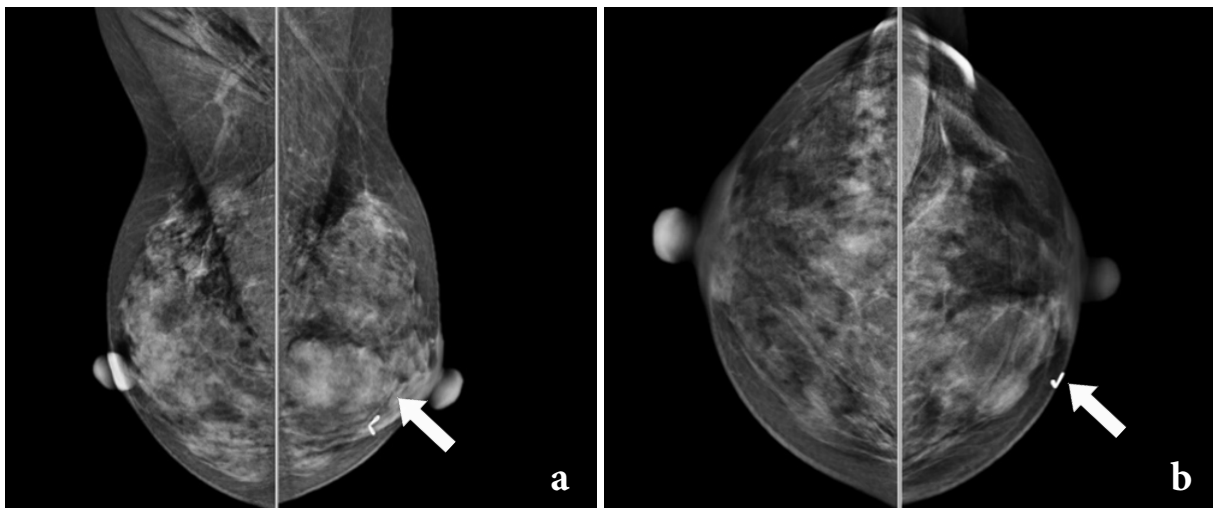


Figure 22. Mammography (a) MLO (b) CC views reveal oval circumscribed mass with equal density at the left lower inner quadrant (arrow).

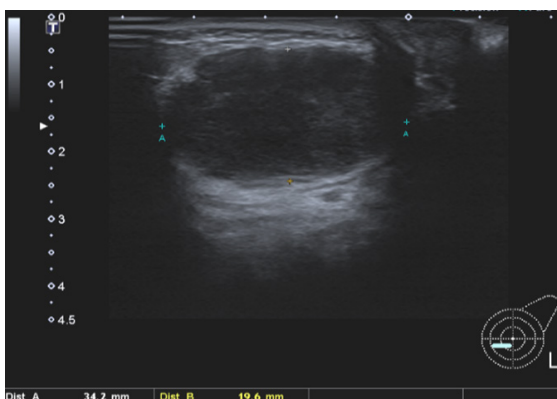


Figure 23. Ultrasound gray scale US of lower inner quadrant of left breast shows a 3.4x2.0-cm oval circumscribed hypoechoic mass.

Case 5

A 70-year-old female presented with a palpable left breast lump and a left axillary mass for three months. The mammography revealed a partially indistinct hyperdense mass at the left upper inner quadrant with skin and trabecular thickening (Figure 24), US showing a partially indistinct hypoechoic mass (Figure 25). Multiple enlarged left axillary lymph nodes were presented.

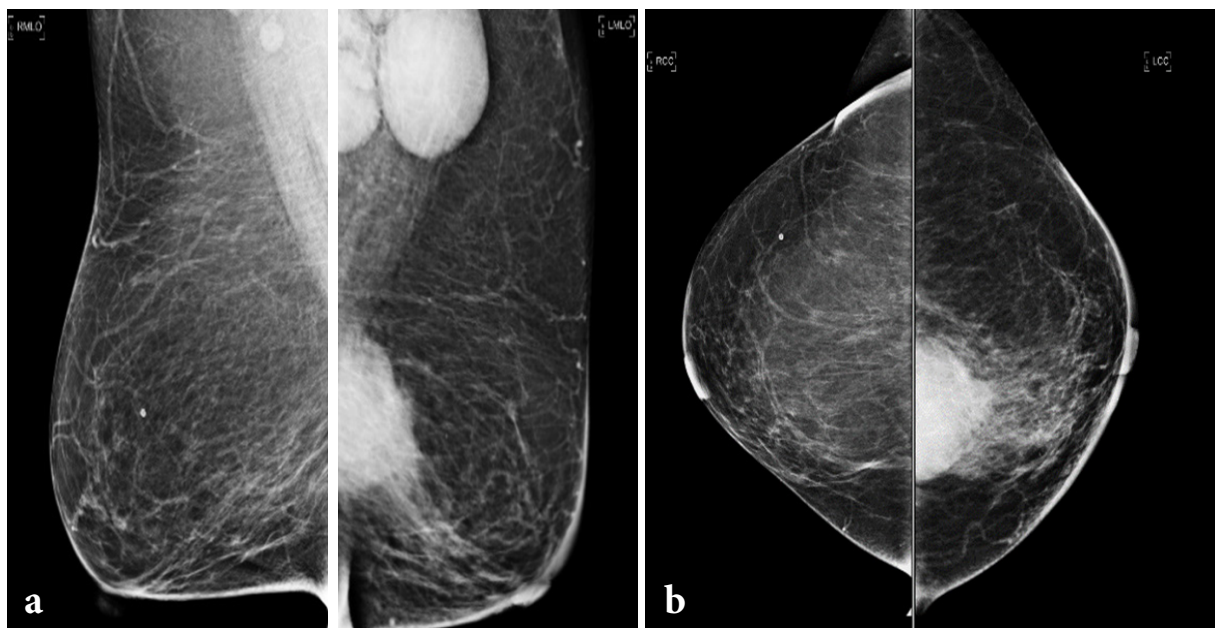


Figure 24. Mammography (a) MLO (b) CC views reveal oval circumscribed mass with equal density at the left lower inner quadrant (arrow).

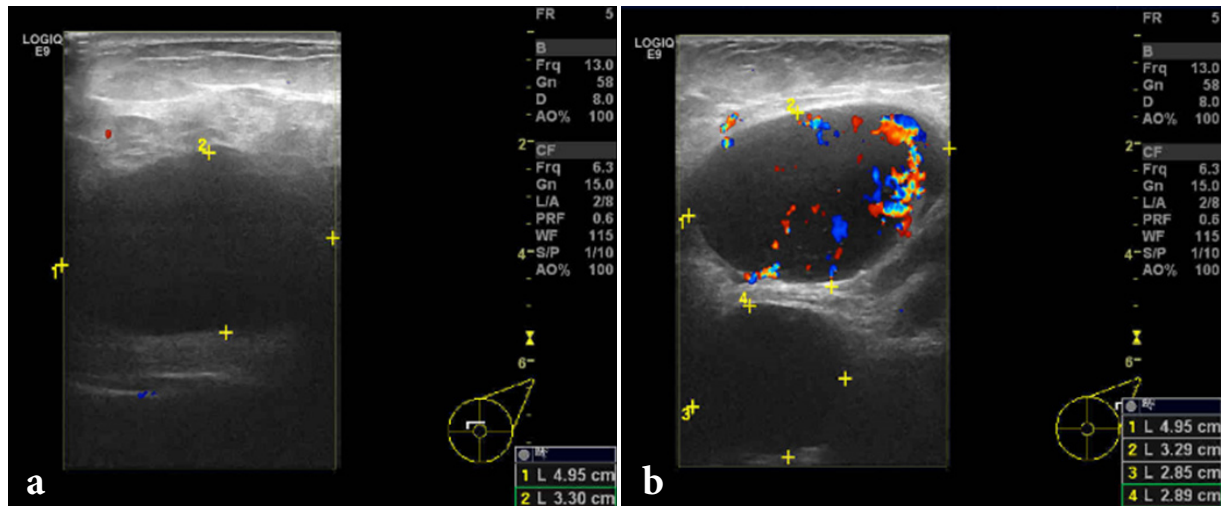


Figure 25. Ultrasound (a) gray scale US of the upper inner quadrant of the left breast reveals a 5.0x3.3-cm round partially indistinct hypoechoic mass and (b) color doppler US at the left axilla reveals left axillary lymphadenopathy.

The patient underwent breast MRI examination demonstrating a circumscribed thick rim-enhancing mass with type II kinetic curve pattern. The mass showed restricted diffusion and increased choline peak on MRS (Figure 26).

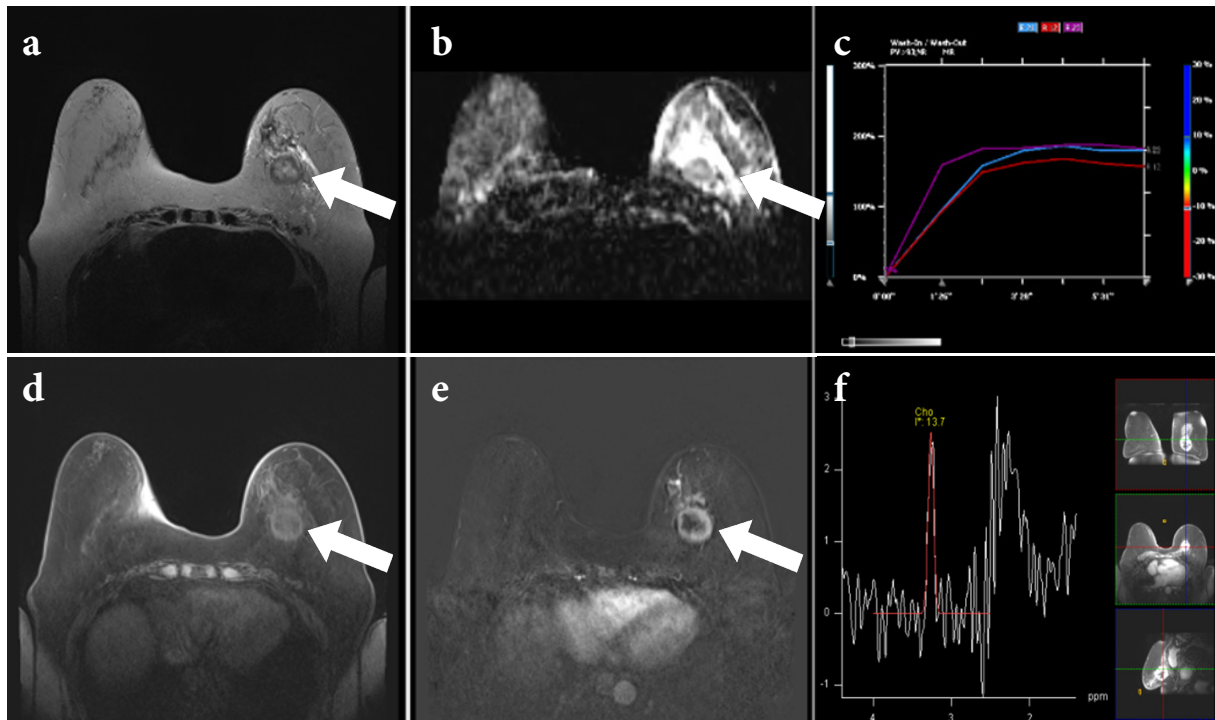


Figure 26. MRI breast (a) T2-weighted axial image (b) ADC (c) kinetic curve assessment d. Fat-suppressed precontrast T1-weighted axial image (e) Fat-suppressed post contrast T1-weighted axial image with subtraction (delayed phase) (f) MR spectroscopy.

Breast MRI reveals a circumscribed thick rim-enhancing mass at the left inner mid part, showing heterogeneous iso- to slight hypointensity on T1-weighted image, iso- to hyperintensity on T2-weighted image, irregular rim enhancement with type II kinetic curve pattern. The mass shows restricted diffusion (ADC $0.685 \times 10^{-3} / \text{mm}^2$) and an elevated choline peak on MRS (13.7).

The US-guided CNB of left axillary lymph node revealed DLBCL. Staging work-up revealed generalized lymphadenopathy, hepatic, splenic and bone marrow involvement. After completion of chemotherapy, there was an decreased size of the mass in the left breast with non-significant FDG-avidity, representing a complete metabolic response. PET/CT performed after complete remission for six months showed disease recurrence at the left breast, enlarged right external iliac nodes and inguinal nodes (Figure 27).

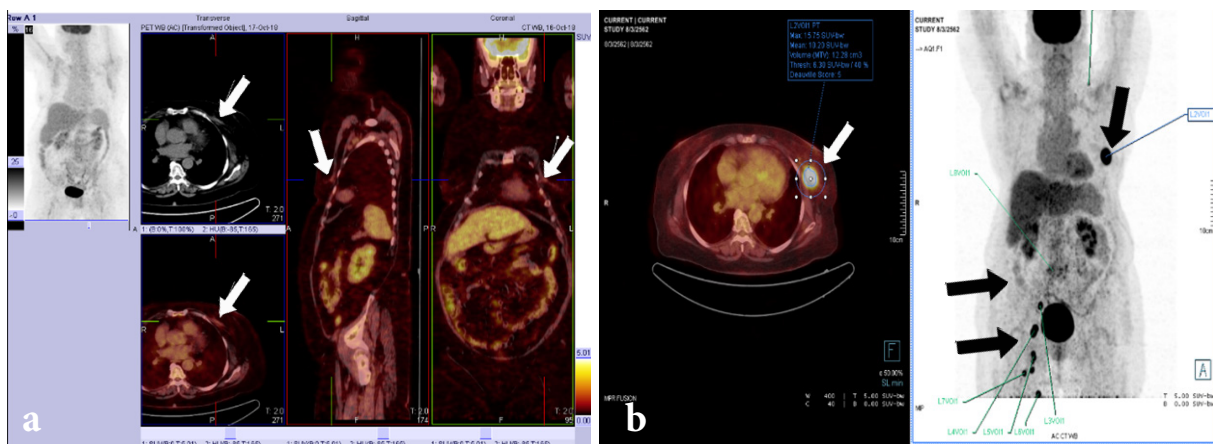


Figure 27. (a) After completion of CMT, there was a decreased size non-significant FDG-avid mass in the left breast (arrows), representing a complete metabolic response. (b) PET/CT performed after complete remission for six months revealed a new 2.6x3.8x3.0-cm circumscribed FDG avid mass at the left breast (SUVmax =15.75), representing recurrence of disease.

Discussion

Breast lymphoma is the rare manifestation of extranodal non-Hodgkin's lymphoma (NHL). We describe our experience of breast lymphoma seen at our institution including four cases of PBL and five cases of SBL.

Most of these cases presented with a painless palpable breast mass, except two cases of SBL: one with a painful breast mass and one with a right nasal mass. Five of the nine cases exhibited a palpable ipsilateral axillary lymph node including one of SBL cases who also had palpable contralateral axillary lymph node. Similar to the previous literature, the most common presentation of breast lymphoma is a painless enlarging palpable mass with minority of patients may exhibit pain (4-25%) and ipsilateral lymphadenopathy (30-40%) [1]. Other uncommon manifestations are breast enlargement, erythema, and edema [2,3]. Nipple retraction and nipple discharge are rare, unlike in breast carcinoma [1].

Solitary mass is the most common presentation in both PBL and SBL. Multiple masses are found in less than 10% and bilateral lesions are found in about 10%, which are more common in SBL [3,4]. Most of our patients exhibit a unilateral solitary breast mass and only one case of SBL had multiple bilateral breast masses.

One of our SBL cases reported weight loss, whereas none of PBL cases had any constitutional symptom. One case of SBL manifested with generalized lymphadenopathies. B symptoms are rarely associated with breast lymphoma, especially in PBL [2]. B symptoms and generalized lymphadenopathies may help suggesting the diagnosis of the secondary form.

The median age of the patients in this series was 58 years, ranging from 27 to 75 years, comparable with most common presenting age at 5th to 6th decades with a broad range of age reported in previous literature [2,4].

Various imaging modalities have a role in evaluation in breast lymphoma including mammography, ultrasonography (US), MRI and PET/CT scanning.

Mammography: The most common mammographic feature in our case series was a solitary breast mass with a circumscribed or indistinct margin. The masses were predominantly oval and round in shape. Most of the masses exhibited high and equal density while none of them exhibited calcifications. Less common features seen in our patients were global asymmetry and skin and trabecular thickening.

Similar findings have been reported in several studies. The most common presentation on mammography is a noncalcified solitary mass (69-72%). The mass is predominantly round or oval in shape and has an indistinct or circumscribed margin. Hyperdense appearance is depicted in more than 80% of breast lymphomas [3-5]. Less common features have been described, including multiple masses (3-9%), global asymmetry or diffuse increased density (9-16%), skin thickening or edema (up to 8%) or no abnormality on mammography (9%) [3-5].

Ultrasonography: Our patients mostly presented with an oval or irregular mass with circumscribed or indistinct margins, corresponding to the appearance on mammography. The mass was a hypoechoic or mixed echogenic appearance. One of SBL who initially suspected of infectious/inflammatory condition demonstrated a marked hypoechoic appearance on US suspected of liquefied portion mimicking abscess. The vascularity assessed by doppler US was available in eight of our patients, all of which demonstrated increased vascularity. Associated posterior acoustic enhancement and no posterior acoustic features were seen. None of the patients demonstrated posterior acoustic shadow.

Our cases demonstrated comparable findings on US as mentioned in literature. Breast lymphomas usually present as hypoechoic or isoechoic masses with a circumscribed margin or a diffuse infiltrative appearance with indistinct margins. An almost anechoic mimicking fluid-filled lesion has also been described. The mass usually demonstrates increased vascularity at doppler US (55-64%) [4]. No acoustic feature or posterior acoustic enhancement is also a typical feature [5].

Surov et al found no significant differences in the mammographic or US features between PBL and SBL masses [5]. However, masses in PBL tend to have less number, less-defined margins, and a greater diameters than those observed in SBL [3,5].

Dynamic contrast material–enhanced MR imaging:

Breast MRI images were available in three of our patients (one case of PBL and two cases of SBL). Two cases showed circumscribed masses and one case showed ill-defined masses. All lesions exhibited heterogeneous iso-to slight hypointensity on T1-weighted image and heterogeneous hyperintensity on the T2-weighted image with heterogeneous or rim enhancement. All masses showed rapid initial increased signal intensity over 100% as compared with pre-contrast signal intensity. There was type II kinetic curve enhancement in two patients and type III in one patient. All masses showed restricted diffusion on ADC mapping. MR spectroscopy was performed in two patients which showed an elevated choline peak (8.91-13.7).

Our results were consistent with previous studies, with mass as the main appearance of breast lymphoma on MRI. The mass typically appears as iso to a hypointense mass on T1-weighted images, heterogeneously hyperintense on T2-weighted images, intense and heterogeneous enhancement. Type II kinetic curve enhancement is the most common pattern, followed by type III kinetic curve enhancement [4,5]. No significant differences in MRI features were detected between PBL and SBL [6]. MRI maybe useful in extension evaluation and detect multifocal and multicentric disease that might be underestimated on other imaging modalities.

PET/CT scan:

PET/CT scan has a role during initial staging of lymphoma, evaluating the treatment response or detecting recurrence of the disease. Intense hypermetabolism with F18–fluorodeoxyglucose (FDG) avidity is a typical feature, with a mean maximum SUV of 10.6 reported in the case series by Yang et al [4].

Two of our cases underwent PET/CT scan for evaluating the treatment response without a baseline pretreatment scan. PET/CT scan after completion of chemotherapy revealed a radiologically complete response. In one case of SBL, PET/CT scan had a role in detecting tumor recurrence, showing relapsed disease with a hypermetabolic activity at the left breast and distant lymph nodes.

There is no definite radiological difference between lymphoma and breast carcinoma. However, lymphoma should be considered as differential diagnosis of a mass lacking suspicious calcification, architectural distortion, spiculated border, or desmoplastic reaction on mammogram which are frequently seen in breast carcinoma [3,5]. Breast lymphoma typically does not exhibit posterior acoustic shadow on US which is a common feature in breast carcinoma [4].

Some particular clinical and radiological patterns help distinguish between the PBL and SBL (Table 1). Clinical or imaging finding of bilateral breast masses or bilateral axillary lymphadenopathy should raise concern about the presence of a secondary lymphoma. However, the causes of bilateral axillary lymphadenopathy are of broad range including leukemia, collagen vascular diseases, nodal hyperplasia, granulomatous diseases, human immunodeficiency viruses, and metastases.

Patients may present with clinical manifestations and imaging pattern mimicking inflammatory diseases. One case of SBL presented with a painful palpable breast mass accompanied with purulent nipple discharge and nipple retraction. The US examination revealed an irregular infiltrative lesion with a marked hypoechoic pattern resembling a fluid-filled lesion. The patient was initially misdiagnosed of an infectious or inflammatory breast condition. Complicated cysts with internal movable echoes or fluid-fluid level or fistulous tract toward skin are helpful features on US in differentiating the inflammatory condition from other breast conditions [6].

Histologic examination is essential for confirmation of diagnosis since the clinical and radiological features are not pathognomonic. Distinction of PBL from SBL also remains a diagnosis of exclusion which needs through diagnostic evaluation including staging CT examination, CSF examination and bone marrow biopsy [7].

Table 1. *Clinical and radiological patterns guide towards the primary and the secondary breast lymphoma.*

	PBL	SBL
Clinical presentation		
- Sign and symptom	palpable mass	palpable mass
- B symptoms	exceeding rare	may be present
- Multiplicity	unilateral, solitary	unilateral, solitary > multiple
- Axillary lymph node involvement	ipsilateral	ipsilateral or bilateral
- Generalized lymphadenopathy	none	may be present
- Previous diagnosis of hematologic malignancy	absence	may be present, breast mass representing metastatic or recurrent disease
Imaging		
Mammography, US, MRI	larger size, more indistinct margin	bilateral axillary lymphadenopathy multifocal, multicentric, bilateral lesions

Conclusion

This small case series illustrates the imaging spectrum of breast lymphoma presented at our institution. Despite the rarity, lymphoma should be considered as a differential diagnosis for the breast mass. Radiologic features combined with the clinical context and tissue diagnosis are essential for accurate diagnosis of lymphoma. Multimodality imaging also plays an important role in staging, follow-up, and detection of recurrence of breast lymphoma.

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