Hematopoietic malignancies of the breast: Revisiting a rare disease

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Learning objectives

The purpose of this exhibit is to review the spectrum of hematopoietic malignancies affecting the breast and discuss the clinicopathologic features and multimodality imaging findings.

Background

Hematopoietic malignancies affecting the breast are a rare entity and include lymphoid, myeloid and histiocytic/dendritic neoplasms. The clinical presentation and imaging features often overlap with other breast malignancies as well as benign breast disorders making tissue diagnosis essential. However a combination of imaging findings in the appropriate clinical scenario can raise suspicion of a haematological malignancy and imaging plays an important role in diagnosis and work up of haematological malignancies affecting the breast. Recognition of this rare group of malignancies is important for radiologists as the management is usually non-surgical and differs significantly from other breast malignancies.

This exhibit looks at haematological malignancies involving the breast from a radiologist’s standpoint. We briefly review the clinico-pathological features of haematological malignancies and discuss the multimodality imaging findings.

Findings and procedure details

Brief overview of the clinicopathological features of hematopoietic malignancies of the breast:

LYMPHOMA:

- Most common hematopoietic malignancy affecting the breast
• Represents 0.04-0.7% of malignant breast tumors [1,2], probably a reflection of the small amount of lymphoid tissue in the breasts [3,4]
• Breast involved in 1- 2% of lymphomas
• More commonly B cell lymphomas
• Common types of B cell lymphoma involving the breast are diffuse large B cell lymphoma(DLBCL) (most common in some series) and low grade lymphomas ( MALT lymphomas and follicular lymphoma
• Can be primary or secondary:

Primary : Based on the diagnostic criteria defined by Wiseman and Liao [5] :

1. Histological evidence of a close association between mammary tissue and lymphomatous infiltrate

2. Absence of disseminated lymphoma or preceding extra-mammary lymphoma at the time of diagnosis

3. No extra-mammary disease other than ipsilateral axillary node

Secondary : Defined by presence of systemic lymphoma with concurrent or subsequent involvement of the breast

Clinical Features :

• Median age : 55 - 65 years , Burkitt lymphoma in younger patients
• Clinical symptoms : Most common painless palpable lump
• Ipsilateral axillary lymphadenopathy in upto 50% cases [6]
• Nipple retraction , discharge and skin changes - rare
• Skin changes , edema more common in T - cell lymphoma
• Bilateral synchronous disease in 10% , contralateral metachronous disease in upto 15% [7,8]
• Possible association with estrogen, autoimmune disease and breast implants [9,10]

Treatment :

• B cell lymphoma - chemotherapy +/- radiation.
• Mastectomy not recommended in DLBCL because it offers no benefit as regards survival or recurrence risk
• Role for CNS prophylaxis in aggressive forms as CNS is the most common site for relapse of PBL, breast is another site of relapse for lymphoma
• **T cell lymphoma** - Variable (chemotherapy, radiation, bone marrow transplantation, surgery)

**Prognosis :**

• 5 year survival for diffuse B cell lymphoma is 60 - 65%
• Prognostic factors: stage, bilaterality, bulk of disease > 5cm
• Outcome worse for secondary lymphoma

**LEUKEMIA :**

• Isolated breast involvement less common than systemic disease affecting breast, breast site of post stem cell transplantation relapse
• Clinical symptoms: painless breast mass most common presentation
• **Treatment**: similar to other locations, chemo +/- RT

**MULTIPLE MYELOMA / PLASMACYTOMA :**

• Exceedingly rare. Breast involvement seen in 1.5% of cases of plasmacytoma and 0.2% of breast cancers in one series [12]
• Mostly seen in cases of known plasma cell myeloma, exceptionally as an isolated extramedullary plasmacytoma
• Clinical findings: most commonly breast lump, minority of patients are asymptomatic
• **Treatment**: same as for other sites of plasmacytoma, chemo +/- RT; Role for excision in lesion limited to breast
• Primary breast plasmacytoma carries better prognosis than secondary breast involvement in multiple myeloma
• Breast involvement often represents relapse or progressive disease in known myeloma with guarded prognosis

**Imaging Findings :**

**LYMPHOMA :**
• Involves a multimodality approach for lesion identification, staging and follow up
• **Mammography and ultrasound**: form mainstay of imaging breast involvement
• **CT and F-18 FDG PET CT**: for staging and follow up of disease
• **MRI breast**: not routinely used in the diagnosis but may have a role in select cases

**Mammography**:

• Most common findings: **solitary non calcified circumscribed or indistinctly marginated ovoid or round mass**, some show microlobulated margins [10,13] Fig. 1 on page 9, Fig. 2 on page 10; can have multiple masses Fig. 3 on page 10

• **Spiculations, calcifications, architectural distortion uncommon** (cf. invasive ductal carcinoma) [14,15]; large painless mass without distortion or spiculation may provide a clue Fig. 4 on page 11

• Less common: **Focal / global asymmetry**

**Diffuse infiltrative form** - edema, increased reticulations, skin thickening Fig. 5 on page 12

• Often associated with **axillary lymphadenopathy** Fig. 5 on page 12

**Ultrasound**:

• Most common: **hypoechoic or heterogenous circumscribed or indistinctly marginated solid mass** [7,10,14,15] (Fig. 1 on page 9, Fig. 2 on page 10, Fig. 3 on page 10, Fig. 4 on page 11, Fig. 6 on page 13)

• Other findings: heterogeneous echotexture, posterior acoustic enhancement, **presence of echogenic rim or onion peel like surrounding rim** (thought to represent lymphedema) (Fig. 3 on page 10, Fig. 7 on page 14); **diffuse nodular infiltration or diffusely raised echogenicity** (Fig. 8 on page 15)
• **Posterior acoustic shadowing not usually seen** (cf. invasive ductal carcinoma)

• **Subcutaneous /skin involvement: - seen in T cell lymphoma** (Fig. 5 on page 12)
  • US shows skin thickening and multiple indistinct irregular hyperechoic subcutaneous masses which may contain internal tubular branching hypoechoicnecities [16,17]

**MRI:**

• Role of MRI breast in lymphoma not established

• Most lymphomas are seen as **oval masses with irregular margins** showing mild heterogeneous or homogenous internal enhancement and low ADC coefficient. Spiculated margins may be seen in some lesions reflective of infiltrative growth pattern. Rim enhancement is uncommon [18, 19]

• **Kinetic enhancement pattern is variable,** most show rapid initial enhancement and delayed plateau or washout

• Non mass like enhancement is a less common presentation

• May be more sensitive in detecting multifocal or multicentric lesions of breast lymphoma with a possible role in follow up of lymphomas

**CT and 18 FDG PET CT:**

• Routinely used for **staging and follow up** of lymphomas (Fig. 1 on page 9, Fig. 2 on page 10, Fig. 4 on page 11, Fig. 8 on page 15)

• Most lymphomas show **avid uptake on 18 FDG PET** with a high mean standardized uptake value (Fig. 1 on page 9, Fig. 2 on page 10, Fig. 8 on page 15)

**Primary Vs Secondary breast lymphoma on imaging:**

• Often **difficult to distinguish** based on routine breast imaging
- Bilateral axillary lymphadenopathy and breast edema could indicate secondary lymphoma

- Breast involvement and absence of other sites of disease on CT/PET CT suggestive of primary lymphoma

Imaging differentials of breast lymphoma:

- Include both benign and other malignant breast disorders

- The differentials for lymphoma presenting as a circumscribed mass would include a wide range of diseases range from common benign lesions such as fibroadenoma to malignant neoplasms presenting as circumscribed masses eg. invasive ductal carcinoma, medullary carcinoma, malignant papillary lesions, metastases.

- The differentials for lymphoma presenting as a diffuse infiltrative disease with edema (Fig. 5 on page 12, Fig. 8 on page 15) would include inflammatory breast carcinoma, diffuse infiltrative metastases and mastitis.

- Presence of subcutaneous masses or nodules more common in lymphoma

- Architectural distortion, calcifications and spiculations seen in breast carcinomas are absent in lymphoma

- Dilated ducts and fistulous tracts not a feature of lymphoma (cf. mastitis)

LEUKEMIA:

Mammography: most commonly seen as solitary or multiple masses with circumscribed/irregular/ill defined margins. Diffuse infiltrative pattern or distortion less common [11]
**Ultrasound**: most commonly hypoechoic or heterogeneous lesions with irregular or lobulated margins [11,20] (Fig. 9 on page 16)

**MRI**: no established role, described findings include T2 hyperintense lesions with heterogenous enhancement

**MULTIPLE MYELOMA / PLASMACYTOMA**:

**Mammography**: Most commonly round or oval masses, may be solitary or multiple (Fig. 10 on page 17)

Diffuse infiltration of the breast less common

**Ultrasound**: Homogenous hypoechoic masses, less commonly heterogenous mixed hypoechoic and hyperechoic masses [12] (Fig. 10 on page 17)

**Diagnosing haematological malignancies of the breast**:

- Imaging findings vary and often overlap with both benign and other malignant breast disorders

- Should be considered in the differential diagnosis of breast lesion in a known case of haematological malignancy

- If there is no prior haematological malignancy the diagnosis is usually made by tissue sampling which forms the mainstay of diagnosis in both primary and secondary breast involvement.
• Tissue sampling usually done by imaging guided core biopsy. While this is superior to fine needle aspiration, undersampling and heterogeneous histopathological features are some of the potential difficulties. Excisional biopsy be considered for some cases.

• The role of imaging is crucial in lesion identification, tissue sampling, disease staging and post treatment follow up.

Images for this section:

**Fig. 1:** Fig 1. Primary breast B cell lymphoma. A 64 year old lady with a palpable right breast lump and no significant past history. Mammogram (right craniocaudal view (A) shows a partly circumscribed partly obscured ovoid isodense right retroareolar mass (arrow); seen on US as a heterogeneous irregular mass with mild acoustic enhancement (B). US guided 14G core needle biopsy showed diffuse large B cell lymphoma. 18 FDG PET CT showed avid uptake within the mass, no other site of uptake was seen in the body (C) in keeping with a primary breast lymphoma. Staging CT (D) showed the mass (arrow) with no other site of disease seen on the CT, follow up CT post chemotherapy (E) showed reduction in the size of the mass (arrow).

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Fig. 2: Radiological findings in a patient with primary breast diffuse large B cell lymphoma (DLBCL). Mediolateral (A) and craniocaudal (B) mammograms of the left breast show a partially obscured mass in the upper outer quadrant (arrows). No associated distortion or calcifications seen. (C) Composite US demonstrates a circumscribed ovoid hypoechoic mass with echogenic centre and no posterior shadowing. (D) Axial contrast CT scan shows an irregular rim enhancing left breast mass with low density centre and perilesional stranding (arrow). (E) PET CT shows an FDG avid mass.

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**Fig. 3:** Synchronous bilateral primary breast lymphoma in a 62 year old woman who presented with a palpable mass in the right breast and screen detected nodule in the left breast. Craniocaudal and mediolateral oblique mammograms (A) of the right breast shows a round, dense mass with circumscribed margins in the upper outer quadrant (arrow). (B) A small, well-defined mass is also seen in the left upper outer quadrant on mammograms (arrow). (C) Composite US of the right breast showed a complex mixed cystic-solid mass and (D) US of the left breast showed a hypoechoic lesion with a thick hyperechoic rim and without posterior acoustic shadowing phenomenon. Histopathology of the bilateral breast masses revealed diffuse large B cell lymphoma.

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Fig. 4: A 47 year old woman presented with a right breast mass. Cranio-caudal (A) and mediolateral oblique (B) mammograms show a partially obscured large mass in the central right breast without architectural distortion, speculation or calcifications (arrows). US shows a well circumscribed lobulated predominantly hypoechoic mass (C). Axial contrast enhanced CT shows a isodense homogenously enhancing lesion without mass effect (arrow) (D). DLBCL was diagnosed on core needle biopsy

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Fig. 5: Fig 5. A 71 year old woman presented with bilateral breast enlargement and axillary adenopathy. She was known to have peripheral T cell lymphoma. (A) Cranio-caudal and (B) medio-lateral oblique mammograms of both breasts show coarsened trabecular markings of the parenchyma with skin thickening. Bilateral enlarged dense axillary lymph nodes are also seen (arrows). (C) Bilateral breast US showed diffusely echogenic breast parenchyma and skin thickening. No focal lesion was identified. (D) US of both axillae show enlarged lobulated hypoechoic lymph nodes with loss of fatty hilum. A punch biopsy of the right breast peri-areolar skin revealed atypical T-lymphocyte infiltrate.

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**Fig. 6:** Fig 6. Secondary breast lymphoma. A 23 year old patient with known B cell lymphoblastic leukemia with newly diagnosed right breast lump. This was seen on the ultrasound as an ovoid circumscribed hypoechoic mass, an appearance similar to a fibroadenoma in this age group. The history however provides clue to the diagnosis of lymphoma and this was confirmed on US guided 14 G core needle biopsy

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Fig. 7: Fig 7. A palpable left breast mass in a 22 year old patient with acute pre-B lymphoblastic leukemia. Longitudinal grey-scale US image shows a rounded circumscribed predominantly hyperechoic mass for which histopathology revealed B lymphoblastic leukemic involvement.

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**Fig. 8:** Fig 8. A 45 year old woman with relapsed refractory DLBCL presented with right breast enlargement. US (A) of the right breast shows diffuse increased parenchymal echoes with minimal overlying skin thickening. NO discrete mass is seen. Mammography could not be performed as the right breast was huge and tender. Contrast enhanced axial CT (B) shows profound diffuse unilateral right breast enlargement without focal mass. (C) and (D) PET CT images show discrete FDG avid lesions within the right breast (arrows). Biopsy of the right breast confirmed a diagnosis of diffuse B cell lymphoma.

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Fig. 9: Radiological findings in a 33 year old female with known acute myeloid leukemia and bilateral palpable breast masses. (A) US of the right breast and (B) US of the left breast demonstrates heterogeneous hypoechoic lesions (arrows) with indistinct margins without posterior acoustic shadowing. (C) PET scan demonstrates several FDG avid in both breasts (arrows). A small left sided pleural is noted. Histopathology of the bilateral breast masses revealed diffuse involvement by blast cells of myeloid lineage (myeloid sarcoma)

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Fig. 10: Asymptomatic bilateral plasmablastic multiple myeloma in a 57 year old woman with first screening mammography. (A) Bilateral MLO views show dense breasts with partially obscured masses in the upper breasts (arrows). (B) US of the right breast and (C) US of the left breast show corresponding circumscribed complex cystic masses with posterior acoustic enhancement.

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Conclusion

• Hematopoietic malignancies affecting the breast are a rare entity and have overlapping clinical and radiological features with other breast malignancies and benign breast lesions

• Identification is important as the treatment is significantly different from other primary breast cancers

• Should be considered in the differentials of breast lesions in a patient with a known haematopoietic neoplasm

• Presence of subcutaneous involvement or a large mass without spiculations/distortion/calcifications and with associated axillary lymphadenopathy may provide a clue to the diagnosis of lymphoma

• Though the diagnosis is based on biopsy and histopathological examination, imaging is important for lesion identification, guiding biopsy for tissue diagnosis, staging and follow up.

Personal information

References


