Case Report

Hematologic malignancies of the breast: report of three cases

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Article history:
Received 6 November 2021
Revised 31 January 2022
Accepted 1 February 2022

Keywords:
Breast lymphoma
Breast hematologic malignancies
Leukemia
Breast mass

Abstract

Involvement of the breast by hematologic malignancies is rare and remains an important diagnostic challenge for radiologists. We present the cases of 3 patients diagnosed with hematologic breast malignancies at our institutions. All cases were diagnosed by breast core biopsies, which revealed 2 cases of diffuse B-cell lymphoma and one case of myeloid sarcoma associated with acute myeloblastic leukemia (AML). This study focuses on describing the diagnostic features found on mammographic and sonographic imaging at initial presentation of lymphomas and leukemias affecting the breast.

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Introduction

Hematologic malignancy is a broad term that encompasses any neoplasm that originates from hematopoietic and lymphoid cells. Depending on the type of cells and tissues affected, they can be classified as lymphoma, leukemia, or myeloma. Although rare, hematologic malignancies can affect the breast both as primary neoplasms and secondary to systemic disease or metastasis. The most common hematologic malignancy affecting the breast is lymphoma, which only accounts for approximately 0.04%-0.7% of all breast cancer cases [1, 2]. Breast involvement in leukemia and myeloma is even more rare. Current published data on these cases are scarce and mostly consists of case reports without significant statistical information.

Unlike breast carcinomas, hematologic malignancies affecting the breast are usually not treated with surgery. Since first-line treatment differs significantly from breast carcinomas, accurate diagnosis is essential. Additionally, initial imaging of these malignancies is non-specific and differs widely posing a significant challenge for radiologists. Herein, this paper focuses on describing the initial imaging presentation of our 3 patients. In addition, we conducted a systemic literature review via PubMed and discuss our findings.

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https://doi.org/10.1016/j.radcr.2022.02.004
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Case #1

A 90-year-old female with a history of hypertension and dyslipidemia presented to her primary care physician after noticing a palpable painless mass in her left breast 2 weeks after receiving her second dose of the Pfizer SARS-CoV-2 vaccine in the left arm. A diagnostic mammogram was performed and showed a 33 mm irregularly shaped mass in the left breast at 9-o’clock, 6 cm from the nipple (Fig. 1). A targeted ultrasound of the left breast showed a 25 × 14 × 33 mm irregularly shaped mass at 9-o’clock, 6 cm from the nipple (Fig. 2) favored to correlate with the irregular appearing mass seen on mammography. BI-RADS category 5 was assigned to the left breast and core biopsy was recommended. Breast core biopsy showed aggressive diffuse large B cell lymphoma (DLBCL), non-germinal center phenotype.

diagnostic mammogram was performed and showed an oval mass with indistinct margins in the upper outer quadrant of the left breast, posteriorly at 1-o’clock and 13 cm from the nipple (Fig. 3). Breast ultrasound showed a 16 × 11 × 15 mm oval mass with indistinct borders at the site of the clinically palpable and mammographic mass (Fig. 4). A BI-RADS category 4C was assigned to the left breast and breast core biopsy was recommended.

Left breast core biopsy of the mass a week later demonstrated morphological and immunohistochemical findings consistent with diffuse large B-cell lymphoma, germinal center phenotype. Bone marrow biopsy revealed follicular lymphoma involving 20% of bone marrow cells. Positron emission tomography (PET) –computed tomography (CT) was ordered which revealed abnormal fludeoxyglucose (FDG) uptake in multiple organs and tissues including lymphomatous involvement of lung, liver, mesentery, axial and appendicular skeleton. When considered along with the previous biopsy results, these findings were consistent with diffuse non-Hodgkin’s lymphoma (Fig. 5). The patient achieved complete remission after treatment with 6 cycles of R-CHOP (R – rituximab, C – cyclophosphamide, H – doxorubicin (hydroxydaunomycin), O – vincristine (oncovin), P – prednisolone (a steroid), completed 9 months ago (Fig. 6).

Case #2

A 55-year-old female with no family history of cancer presented to the clinic after noticing a painless lump in her left breast while completing a self-breast exam in the shower. A
Fig. 2 – Transverse (A) and long views (B) of left breast ultrasound show a 25 x 14 x 33 mm irregularly shaped mass at 9-o’clock, 6 cm from the nipple. These findings correlate with the irregular mass seen earlier in the patient’s diagnostic mammogram.

Fig. 3 – Left breast diagnostic mammogram MLO view (A) and SCC view show an oval mass with indistinct margins in the upper outer quadrant posteriorly at 1-o’clock, 13 cm from the nipple (dashed circle). A palpable triangular marker in close proximity to the mass can also be seen in both images (blue arrow).

Case #3

A 53-year-old female with a past medical history of phyllodes tumor and DCIS treated in 2008 with left lumpectomy and radiotherapy presented to the clinic with a new mass, which she first noticed 3 weeks ago when her dog jumped on her. Patient-reported that she had a normal mammogram a couple of months ago. More recently, she had another mammogram at an outside hospital, which showed architectural distortion of the lower portion of the right breast and a mass with satellite lesions in the right breast’s upper outer quadrant. The patient received further imaging at UTMB. Right breast diagnostic mammogram showed an irregularly-shaped mass extending along the upper outer quadrant with anterior satellite masses centered along the 10-o’clock axis, 8 cm from the nipple. An irregularly-shaped mass with angular margins was also noted in the right breast at 3-o’clock, 5 cm from the...
Radiology Case Reports 17 (2022) 1384–1390

1387

Fig. 4 – Transverse (A) and long (B) views of left breast targeted ultrasound demonstrate an oval mass with indistinct margins measuring 16 × 11 × 15 mm at the site of the clinically palpable and mammographic mass at 1-o’clock, 13 cm from the nipple.

Fig. 5. (A) Maximum intensity project (MIP) images show multiple areas of abnormal FDG uptake within the axial and appendicular skeleton, liver, lung, and lymphatic system. Axial PET-CT (B) and (C) show a morphologically abnormal left axillary lymph node (red arrow) and abnormal FDG uptake within the lung fields most prominent in the right (dashed circle) and axial PET-CT (B and C) show.

The mass and adjacent satellite lesions measured approximately 10 cm in the longest mammographic AP dimension. Of note, accurate sonographic measurements of this mass were limited due to the mass extending beyond the transducer field of view (Fig. 8). A BI-RADS category 5 was assigned to the right breast and a core biopsy of the masses was recommended.

Core biopsies were taken from the 2 breast masses and an axillary lymph node, which revealed myeloid sarcoma. The patient subsequently underwent bone marrow biopsy and was also diagnosed with acute myeloid leukemia (AML). She received induction therapy and 14 days of Midostaurin as treatment. Unfortunately, on day 6/10 of chemotherapy, she presented to the ED unresponsive and pancytopenic. In the ED, she was diagnosed with NSTEMI and was found to be COVID-positive. Her condition worsened rapidly and she died shortly after.

Discussion

Hematologic neoplasms of the breast are rare, accounting for less than 1% of all diagnosed breast malignancies [1, 2]. Examples of hematologic neoplasm affecting the breast include lymphomas and leukemias. Histological examination remains the only modality capable of confirming the disease. Despite the high accuracy of pathology reports, no modality is perfect. In a small study, 7 of 41 breast hematologic malignancies (17%) were misdiagnosed as carcinomas by histologic and morphologic features [3]. The frequency of this mistake may be attributable to framing bias, since the vast majority of malignant lesions found in breast tissue are in fact carcinomas. Accurate diagnosis is especially important for breast hematologic malignancies, as these tumors often indicate diffuse disease and are treated differently from breast carcinoma. Jennings
Fig. 6 – (A) Left breast MLO view of a negative screening mammogram nine months prior. (B) Left breast MLO view of diagnostic mammogram depicts an oval mass with indistinct margins in the upper quadrant posteriorly at 1-o’clock, 13 cm from the nipple (dashed circle), a palpable triangular marker can also be seen (blue arrow). (C) Left breast MLO view of screening mammogram status post R-CHOP treatment 11 months after diagnosis. No abnormal findings are seen, except for a small biopsy marker clip at the site of the treated lesion (yellow arrow).

Fig. 7 – Right breast diagnostic mammogram CC view (A) and ML view (B) show an irregularly-shaped mass extending along the upper outer quadrant with anterior satellite masses centered along the 1-o’clock axis, 8 cm from the nipple (dashed circle). This mass and adjacent satellite masses measured approximately 10 cm in the longest mammographic AP dimension. Posterior to the mass, a bar-shaped clip can be seen (yellow arrow). An irregularly-shaped mass with angular margins is also visible in the right breast at 3-o’clock, 5 cm from the nipple (red circle).
et al. investigated treatment outcomes for primary breast lymphomas in a large case series and found that surgery (mastectomy) did not offer any therapeutic advantage. Surprisingly, radiotherapy for stage 1 node-negative disease showed increased overall survival and disease-free survival [4].

To help pathologists arrive at a correct diagnosis and ensure patients receive appropriate treatment, it is important for radiologists to include these rare malignancies in the differential for a breast mass. Clinical presentation and certain imaging findings, although non-specific, can at least raise suspicion when seen on breast imaging. To help pathologists arrive at a correct diagnosis, it is important for radiologists to obtain high-quality biopsy samples and preserve them properly. Because of the low frequency of lymphoma in the breast, it is easy to misdiagnose. According to BI-RADS criteria, all breast lesions that are category 4 or higher should be biopsied. Our 3 patients had category 4C (1) and category 5 (2) lesions, making them highly suspicious for malignancy. When sampling breast lesions, formalin is the most commonly used tissue preservative. Current ASCO/CAP guidelines recommend the use of formalin for the sake of staining the sample for hormone and growth factor receptors (i.e., estrogen, progesterone, and HER2) [5]. Conversely, RPMI is the recommended preservative agent for lesions that are suspicious for lymphoma. This is because RPMI is a better preservative for samples that may need to be analyzed by flow cytometry. However, there was little reason to suspect lymphoma in the breast based on mammographic findings in our 3 patients. Tissue samples from all three patients were still sufficiently preserved in formalin, evidenced by the fact that they were adequate for diagnosis.

From a clinical standpoint, breast lymphomas commonly present as enlarging breast masses that are associated with pain in up to 25% of cases. On rare occasions, nipple retraction, discharge, and skin thickening or edema may also be seen [6]. One of the cases reported in our series presented for examination of a palpable breast lump and one case presented with unilateral breast pain and nipple discharge. Clinical presentation can vary significantly in leukemia involving the breast. Masses secondary to systemic disease or metastasis may present with symptoms associated with the type of leukemia. For example, myeloid sarcoma associated with AML may present with symptoms of fatigue, recurrent infections, and easy bruising. These symptoms result from an overproduction of ineffective white blood cells and an underproduction of other types of blood cells. Therefore, these hallmark symptoms of leukemia would not be expected in a case of primary breast carcinoma. In the case of our patient with myeloid sarcoma, she had bone marrow involvement (AML) at initial presentation but denied any other symptoms besides a painless breast mass. Therefore, her cancer was thought to be a breast carcinoma until proven otherwise after biopsy. On the other hand, isolated breast leukemic involvement almost always presents as a painless mass in the absence of systemic symptoms. This type of cancer is even harder to distinguish from breast carcinoma by clinical presentation alone.

Fig. 8 – Ultrasound images of the two right breast masses biopsied. (A) Trans view and (B) long view of a 43 mm irregularly shaped mass that correlates with the mammographic finding seen at 3-o’clock, 5 cm from the nipple. Lastly, figure (C) trans view and (D) long view show an irregularly shaped mass extending outside of the transducer field of view. This correlates with the mammographic finding seen along the 10-o’clock axis, 8 cm from the nipple.
Mammographic imaging findings of breast lymphoma and leukemia are nonspecific and may resemble any other breast malignancy or benign mass. For breast lymphomas, the most common abnormality found on mammograms is a solitary circumscribed or spiculated breast mass with no calcifications [7]. Breast leukemia most commonly presents with one or more of the following mammographic findings: a hyperdense mass with microlobulated margins, diffuse infiltration, and architectural distortion. For both breast lymphomas and leukemias, multiple masses are a less common presentation and, when present, are usually associated with secondary or metastatic disease [8]. Only one of the cases in this series was a primary tumor and its initial presentation on mammography was an irregularly shaped mass without calcifications. The other 2 cases in this series were metastatic. On diagnostic mammography, the AML/myeloid sarcoma presented as multiple masses and the DLBCL presented as a non-calcified, irregularly shaped mass.

The most common sonographic imaging findings for breast lymphomas reported in the literature include a hypoechoic, solid oval, or round mass with circumscribed or indistinct margins, and a hyperechogenic, mixed echo, or pseudocystic pattern [7]. On ultrasound, a cystic and solid round mass was seen in the first lymphoma case and a hypoechoic oval mass in the second case. Lastly, multiple irregularly shaped masses with microlobulated margins were seen on breast ultrasound of the patient with AML associated myeloid sarcoma. These latter findings were similar to the findings in breast leukemias reported in a study by Surov et al. According to this study, a single or multiple homogeneous hypoechoic masses with indistinct or microlobulated margins was the most common ultrasound finding in breast leukemias [8].

Conclusion:

Diagnosis of hematologic breast malignancies remains an important challenge for radiologists. Breast imaging usually reveals non-specific findings that can be easily misdiagnosed as breast carcinoma or even as benign lesions. In the cases of our three patients, BIRADS criteria successfully identified the patients’ breast lesions as malignant. However, BIRADS cannot be heavily relied on to identify malignant lymphomas and leukemias since the criteria were developed using data on breast carcinoma. Although there are no specific imaging findings for hematologic neoplasms of the breast, a holistic approach that takes into account the patient’s age, medical history, clinical presentation, and imaging features can be helpful. In the instance that a patient has a pre-existing lymphoma or leukemia, biopsy tissue samples should be preserved in RPMI so that the sample may be examined by flow cytometry if necessary. If there is no reason to suspect lymphoma, then useable samples can be preserved in formalin the same as breast carcinoma tissue samples. However, if flow cytometry needs to be performed to identify the type of lymphoma, new biopsy samples will need to be obtained and preserved in RPMI or another flow cytometry-compatible solution. If a patient is found to have a hematologic malignancy in their breast, follow-up imaging with PET-CT should be ordered immediately. In our patients with DLBCL of the breast, there was diffuse lymph node involvement shown on PET-CT. If there is reason to suspect bone marrow involvement, a bone marrow biopsy should be ordered for the patient as well. For example, the frequent concurrence of myeloid sarcoma with AML should lead a clinician to rule AML in or out if a myeloid sarcoma is found within the breast.

Patient consent

The patients reported in the manuscript signed the informed consent/authorization for participation in research which includes the permission to use data collected in future research projects including presented case details and images used in this manuscript. A copy of the signed consent is kept on file in the patient electronic records.

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