EJMCM

Samreen, N, et al. 2018. Leukemia Recurrence Exclusively in the Breast after Stem Cell Transplant. *European Journal of Molecular & Clinical Medicine*, 5(1), pp. 41–45, DOI: https://doi.org/10.5334/ejmcm.255

CASE REPORT

Leukemia Recurrence Exclusively in the Breast after Stem Cell Transplant

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Introduction: Leukemic involvement of the breast is extremely rare but constitutes an oncologic emergency. Imaging findings of T-Cell acute lymphoblastic leukemia (T-ALL) recurrence in the breasts have not been previously described.

Case Description: Patient is a 25 year old female who presented with symptoms of superior vena cava (SVC) obstruction secondary to a mediastinal mass status post biopsy demonstrating T-ALL, which was cluster of differentiation 3 (CD3) positive and B-cell lymphoma 2 (BCL-2), and 80% Ki-67 positive. She was treated with chemotherapy and post-treatment positron emission tomography/computed tomography (PET/CT) demonstrated resolution of mediastinal mass, with no evidence of distant disease. She underwent allogeneic hematopoietic stem cell transplant (HSCT) in first remission. Seven months post-HSCT, patient presented with a large area of tender swelling of both the breasts with biopsy demonstrating relapsed T-ALL. Radiologic findings showed bilateral breast masses on ultrasound and mammogram, which were hypermetabolic on PET/CT.

Conclusions: Breast involvement in leukemia recurrence, a very rare entity, can present with palpable masses. Mammographic findings in leukemia can include masses or architectural distortion, they are typically hyperechoic on ultrasound, and can have marked uptake on PET/CT. Oncologists, primary care providers and radiologists should be aware of leukemia presentations in the breast for prompt referral for urgent management.

Keywords: T-Cell ALL; leukemia; recurrence; breast; mammogram; ultrasound; PET/CT

Introduction

Leukemic involvement of the breast is rare, with fewer than 200 cases reported in the literature (Glazebrook et al., 2014). It may occur in isolation, in the setting of widespread disease, or in the setting of leukemic relapse as the only site. Both myeloid leukemia and lymphocytic leukemia involving the breast have been described previously (Surov et al., 2012; Bayrak et al., 2009). Acute myeloid leukemia (AML) is the most common type of leukemia presenting in breasts whereas chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL) in the breast are exceedingly rare. Acute lymphocytic leukemia (ALL) in the breast is even rarer. The median age for leukemia presentation in the breasts is 33 years (but with a wide age range of 1–80 years). Patients may present with unilateral or bilateral breast masses with or without axillary adenopathy (Glazebrook et al., 2014) in cases of breast leukemia. Typical imaging methods for diagnosis of T-ALL include a chest CT and a PET/CT. Additionally, post-allogeneic transplantation, since the patient is at increased risk of primary breast cancer, a mammogram is standard practice.

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This case report describes a case of mediastinal T-Cell lymphoblastic leukemia (T-ALL), status post hematopoietic stem cell transplant (HSCT), who had an isolated recurrence in bilateral breasts. Imaging findings of isolated T-ALL recurrence in the bilateral breasts have not been previously described in peer reviewed literature. The purpose of current report is to emphasize on the breast imaging paradigm for leukemias since acute leukemias are considered to be a medical emergency which requires prompt treatment.

Case Report

Patient is a 25 year old female who initially presented with several week history of head pressure particularly when bending over, neck, chest, and face swelling, pleuritic chest pain, fatigue, and intermittent dysphagia with a choking sensation.

Laboratory data included hemoglobin of 10.9 grams per deciliter (g/dl), white blood cells of 6.4×10^9 per liter (L), platelets of 265×10^9 per liter (L), normal serum chemistries, and an LDH of 243 units per liter (U/L). Viral studies including HIV, hepatitis B, and hepatitis C, were negative, apart from hepatitis B surface antibody positive [surface antigen negative]. A chest CT was performed which showed a large 20 cm infiltrative mediastinal mass extending from

the lower neck/thoracic inlet to the retrocrural portion of the upper abdomen, causing narrowing of the trachea, superior vena cava (SVC), right brachiocephalic vein and lower left internal jugular vein (**Figure 1a, 1b**).

Patient underwent an ultrasound guided biopsy of the mass. Pathology showed diffuse sheets of monomorphous lymphoid cells infiltrating into the skeletal muscle, and stained positive for CD3, terminal deoxynucleotidyl transferase (TdT), and BCL-2, with a high proliferation index by Ki-67 staining of 80%. Fluorescence in-situ hybridization (FISH) showed an adverse karyotype, and t(10;11) consistent with histone lysine methyltransferase DOT1L cofactor/Phosphatidylinositol binding clathrin assembly protein (MLLT10/PICALM) fusion. The overall morphologic and immunophenotypic features were suggestive of T-lymphoblastic leukemia/lymphoma. Bone marrow biopsy done at the same time showed small abnormal immature T-cell, consistent with minimal (<5%) involvement by T lymphoblastic lymphoma/leukemia. Baseline echocardiogram was normal and the cerebrospinal fluid was negative for malignancy.

Patient subsequently underwent a PET/CT which showed extensive increased fludeoxyglucose (FDG) uptake in the large mediastinal mass extending from the lower neck at the level of the thyroid to the diaphragm (**Figure 1c, 1d**) with FDG standardized uptake value (SUV) maximum measuring 9.58. No additional uptake was seen within the abdomen or pelvis.

She was therefore diagnosed with precursor T cell ALL with symptomatic SVC obstruction. She began treatment with induction chemotherapy (Hyper-CVAD). Follow up PET/CT one month after treatment showed complete resolution of mediastinal mass consistent with marked positive treatment response. No evidence of local or distant metastatic disease was noted. She had achieved first complete remission (CR1) after 1 cycle. She subsequently completed 2 full cycles of chemotherapy followed by myeloablative HSCT from her sister.

One year later, while her immunosuppression was being tapered, she noticed breast masses which were hard and rapidly growing. Exam indicated multiple irregular masses in breasts, no axillary adenopathy, no tethering, and no nipple discharge. She underwent workup with a mammogram and ultrasound with an ultrasound guided biopsy (**Figures 2a** and **3a**). A PET/CT was also performed (**Figure 4a**).

Biopsy was sent for histopathology and flow cytometry. Upon immunophenotyping, approximately 95% of the

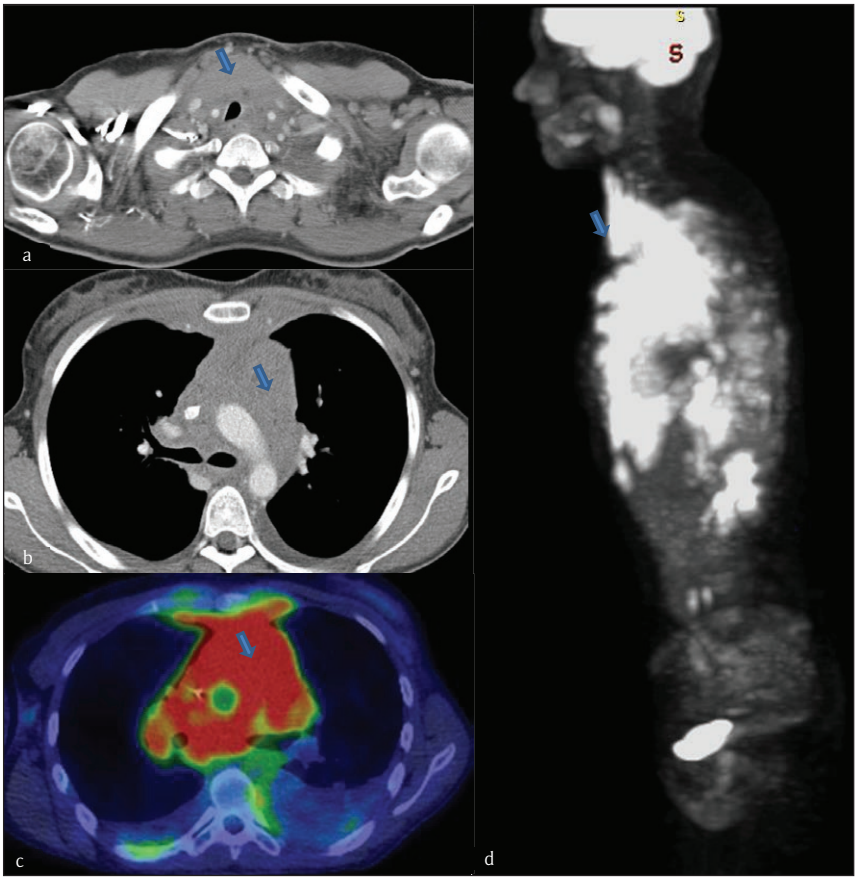

Figure 1: (a) Large infiltrative mediastinal mass (arrow) causing narrowing of the trachea, SVC, right brachiocephalic vein and lower left internal jugular vein. Left brachiocephalic vein was not visualized and felt to be compressed/occluded. **(b)** Mass involved the anterior mediastinum nodes (arrow), hilar nodes, precarinal and subcarinal nodes, pericardium, paraesophageal nodes to the level of the diaphragm. **(c)** Increased FDG uptake was noted throughout the anterior mediastinum (arrow) with an SUV maximum measuring 9.58. Bilateral pleural effusions with increased FDG uptake along the pleura were noted. **(d)** MIP demonstrating increased uptake throughout the anterior mediastinal mass, which spans from the level of the thyroid (arrow) to the diaphragm. No additional sites of disease involvement were noted in the abdomen/pelvis.

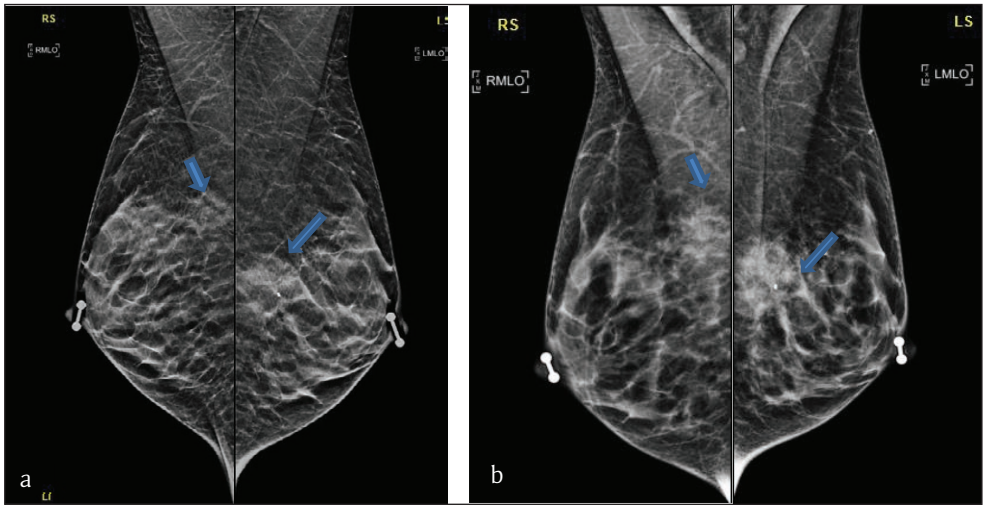

Figure 2: Mammogram **(a)** There was parenchymal asymmetry in the upper inner right breast posterior depth. There was an area of focal parenchymal asymmetry in the medial left breast middle/posterior depth, which contains a biopsy clip marking the known recurrent T-cell lymphoma. **(b)** Mammogram two weeks later demonstrated increase in size and density of the bilateral breast masses compared to two weeks prior.

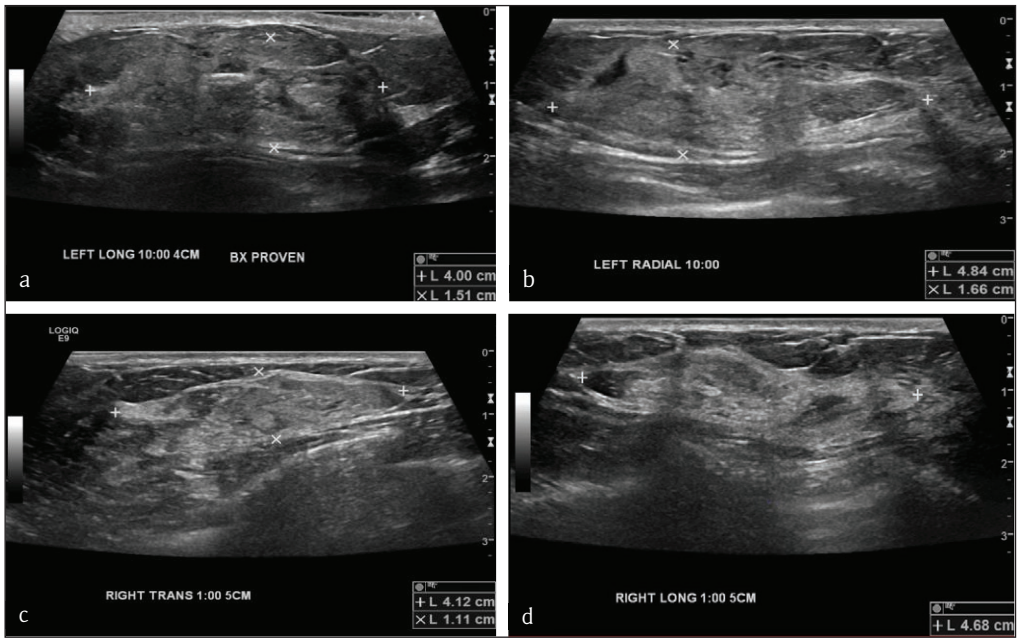

Figure 3: (a) Left breast ultrasound: Hyperechoic, heterogenous mass at 10:00, 4 cm from the nipple measured 4 cm in largest dimension **(b)** Repeat left breast ultrasound two weeks later demonstrated an increased in the size of the mass which now measured 4.8 cm in maximum dimension. There was internal vascularity within these masses. **(c, d)** Transverse (c) and longitudinal (d) images of right breast ultrasound demonstrate a hyperechoic irregular mass at 1:00, 5 cm from the nipple measured 4.7 cm in largest dimension, increased from two weeks prior where it measured 3.3 cm (not shown).

analyzed cells had dim to moderate expression of CD45, consistent with blasts. These blasts were positive for surface CD3 (dim), cytoplasmic CD3, CD5, CD7 (dim), and TdT. Immunoperoxidase studies showed CD3-positive T-cells, negative for CD30. She was diagnosed with relapsed precursor T cell lymphoblastic leukemia. There was no difference in immunohistochemistry of the relapsed tumor when compared with the primary tumor. The flow cytometry markers were similar and there were no additional cytogenetic abnormalities to suggest clonal evolution.

Urgent induction chemotherapy was offered, however, she went to Ireland for few days for a trip that was already planned which was essential for her quality of life according to her. Upon returning, patient noticed increased size of palpable breast mass and underwent repeat imaging. Imaging findings demonstrated increase in size of mass as noted on mammogram, ultrasound, and PET/CT (**Figures 2b, 3b, 3c, 3d,** and **4b**).

She was treated with nelarabine and achieved remission after 3 cycles. Repeat bone marrow biopsy was hypocellular with no evidence of T-ALL, and the FISH testing was negative for t(10;11). She had lumbar puncture with intrathecal cytarabine; and cytology was negative. Because of extramedullary isolated relapse in the breasts,

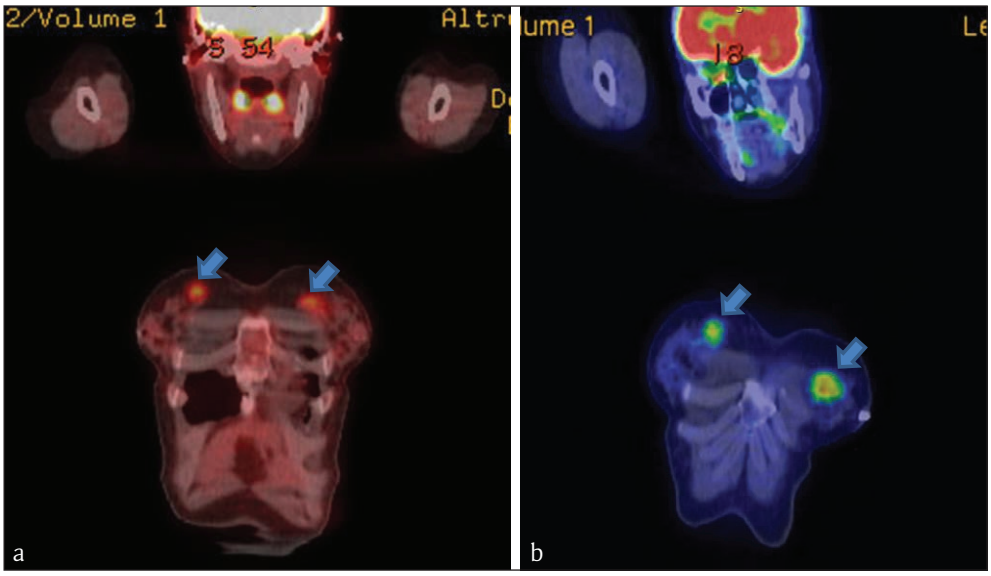

Figure 4: (a) Initial PET/CT: There was irregular soft tissue nodularity within the medial aspect of the left breast (SUV max 4.9) and medial aspect of the right breast (SUV max 3.0). Findings were in keeping with bilateral breast recurrence of lymphoblastic leukemia. **(b)** Repeat PET/CT: Increased size and FDG activity within the bilateral breasts metastases.

she underwent total body irradiation along with breast irradiation. Patient underwent second allogeneic HSCT from her sister's peripheral blood stem cells. A second allogeneic transplant for relapsed cases of T-ALL is not an uncommon practice in young patients when a matched donor is available. A three year follow up demonstrates no evidence of recurrence.

Discussion

Most patients with leukemia in the breast present with a palpable mass and discomfort. A little more than half of cases in one series had solitary lesions identified with the median size of lesion being 3.5 cm (range, 0.6–11 cm). On mammogram, breast leukemia commonly as a hyperdense mass with microlobulated margins. Microcalcifications are rare. Diffuse infiltration of the breast parenchyma or architectural distortion may also be seen.

Sonographically, primary breast leukemia may present as single or multiple heterogeneous hypoechoic masses and majority have indistinct or microlobulated margins (Glazebrook et al., 2014). In a particular case series, two patients with acute leukemia demonstrated masses with irregular shape, non-circumscribed margins, and heterogeneous echogenicity with a significant echogenic component (Bayrak et al., 2009). No axillary adenopathy was seen in either patient with acute leukemia in the case series. In our case, imaging findings of leukemia recurrence in the breast presented similarly to imaging findings noted in primary breast leukemia. Unlike lymphoma, in leukemia, patients can have a marked PET response to chemotherapy without significant reduction in size, which can indicate persistent aggressive disease.

The case also highlights the rapid increase in size which occurred in the leukemia recurrence over just a two week period. Treatment is typically chemotherapy and/or radiation with allogeneic HSCT as a curative modality in aggressive cases like hers. It is imperative to refer patients who are diagnosed with leukemia via breast biopsy to hematologists urgently, since unlike other solid cancers, the acute leukemias require immediate chemotherapy with induction. Our patient had a good response to treatment with resolution of bilateral breast masses.

Conclusion

Imaging findings of acute leukemias in breasts have been described previously but literature is lacking on metastatic deposits from leukemia. No prior case reports have identified imaging findings of T-Cell ALL recurrence in the breasts. This case highlights imaging features that are seen in recurrence of leukemia in the breasts bilaterally as noted on mammogram, ultrasound, and PET/CT.

Competing Interests

The authors have no competing interests to declare.

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How to cite this article: Samreen, N, Hashmi, SK, Conners, AL, Bhatt, A and Glazebrook, KN. 2018. Leukemia Recurrence Exclusively in the Breast after Stem Cell Transplant. *European Journal of Molecular & Clinical Medicine*, 5(1), pp. 41–45, DOI: https://doi.org/10.5334/ejmcm.255

Accepted: 07 August 2018 **Published:** 15 August 2018

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