Radiology Case Reports 19 (2024) 1764–1767

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Extramedullary relapse of acute myeloid leukemia in the breast: A radiological case report ☆

Anna Fairfax, MD, Ian Smith, DO, Brielle Paolini, MD, PhD, Rebecca Leddy, MD*

Department of Radiology, Medical University of South Carolina, Charleston, SC, USA

ARTICLE INFO

Article history:
Received 10 November 2023
Revised 12 January 2024
Accepted 23 January 2024

Keywords:
Extramedullary relapse
Acute myeloid leukemia (AML)
Breast radiology
Granulocytic sarcoma
Breast cancer

ABSTRACT

This report presents a unique case of a 42-year-old female with a history of acute myeloid leukemia (AML) who exhibited an extramedullary relapse in the breast. Given the rarity of such presentations, this case underscores the importance of considering AML in the differential diagnosis of breast lesions, especially in patients with a pertinent medical history. Additionally, this case highlights the radiological and pathological challenges in distinguishing AML from other breast malignancies. The importance of timely diagnosis and the clinical implications of such a presentation are also discussed.

Introduction

While acute myeloid leukemia (AML) primarily affects the bone marrow, extramedullary relapses are a long-term complication with a poor prognosis. Extramedullary relapse, also referred to as granulocytic or myeloid sarcoma, presenting as a single site in the breast is seldom encountered in clinical practice. Furthermore, the imaging appearance of granulocytic sarcoma can mimic several other entities including primary breast malignancies, and can pose diagnostic challenges for radiologists emphasizing the need for a comprehensive differential diagnosis. This report aims to detail the clinical, radiological, and therapeutic aspects of AML's extramedullary relapse in the breast, offering insights into the nuances that radiologists should be cognizant of to ensure timely and appropriate management.

Case

A 42-year-old female presented with a firm palpable, tender, lump in the right breast after minor trauma to the area 2 days prior. The patient had a history of acute myeloid leukemia status post autologous stem cell transplant approximately 2.5 years prior and stopped Gilteritinib (GILT) maintenance approximately 2 years prior after being determined to have

☆ Competing Interests: Ian Smith reports financial support was provided by Medical University of South Carolina. Additional authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: annakfairfax@gmail.com (A. Fairfax).

https://doi.org/10.1016/j.radcr.2024.01.067

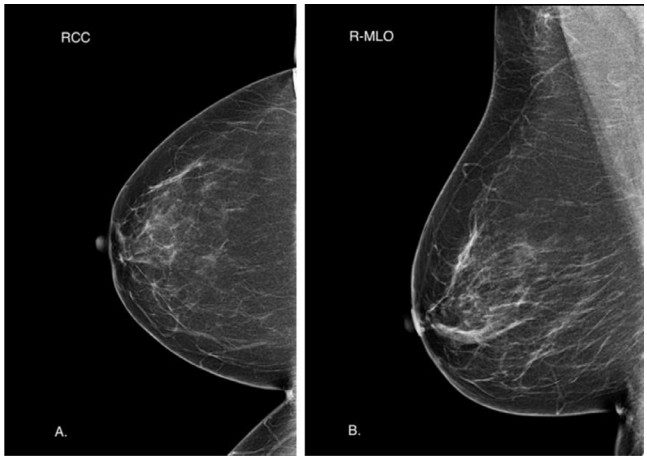

Fig. 1 – RCC (A) and R-MLO (B) negative screening exams performed approximately 5.5 months prior to Figure 2.

complete remission. There were no associated skin changes or evidence of nipple retraction. The patient had a screening mammogram performed approximately 5.5 months prior which was negative (Breast Imaging Reporting and Data System (BI-RADS) 1) (Fig. 1). Additional relevant history included menopause onset at age 40 (after stem cell transplant), and breast cancer in her paternal grandmother at age 85.

A diagnostic mammogram was performed, which demonstrated a new spiculated high-density mass in the right breast central to the nipple anterior depth (Fig. 2). This correlated on targeted ultrasound with a 3.9 cm irregular spiculated hypoechoic mass in the right breast at 7-o'clock 2 cm from the nipple (Fig. 3). Additionally, there was a prominent lymph node in the right axilla noted with uniform cortical thickening measuring up to 3mm (Fig. 4). Subsequent ultrasound-guided core biopsy of the right breast mass and right axillary lymph node was performed. Four 16-gauge core specimens were taken of both with a portion of the samples being sent for flow cytometry. Pathology demonstrated abnormal blast proliferation, compatible with extramedullary involvement by previously diagnosed leukemia of both the mass and axillary lymph node. Immunohistochemical stains of the breast mass were positive for MPO, CD45, CD79A (FOCAL, WEAK), P53 and negative for AE1/AE3, GATA3, CD3, CD20, PAX-5, which supported this diagnosis. These results were concordant with mammographic and sonographic findings and surgical/oncologic consultation was recommended.

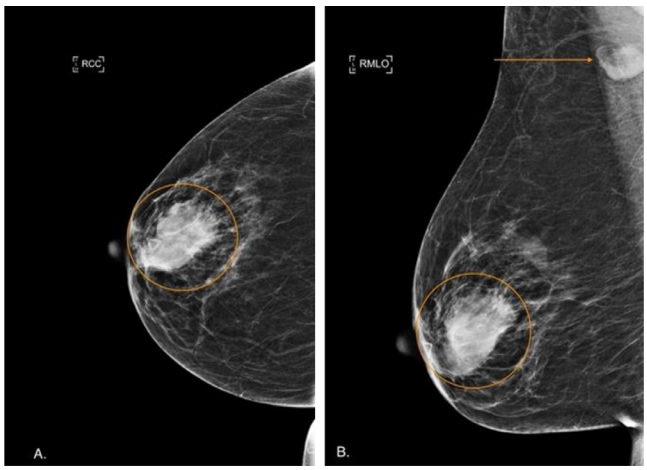

Fig. 2 – Right craniocaudal (RCC) view (A), right medial lateral oblique (R-MLO) view (B) demonstrating a new irregular high-density mass with a spiculated margin in the right breast central to the nipple anterior depth (circle). Additionally, right axillary lymphadenopathy is seen on the medial-lateral oblique view (arrow).

Further workup of the patient included PET-CT and bone marrow biopsy. PET-CT demonstrated a hypermetabolic right breast lesion and hypermetabolic right axillary lymph nodes (Fig. 5); there was additional hypermetabolic activity along the right posterior flank and right iliac bone that was thought to be secondary to recent bone marrow biopsy (not shown), otherwise, there were no additional sites of suspicious hypermetabolic disease. Bone marrow biopsy showed no evidence of acute myeloid leukemia.

The patient ultimately decided to pursue medical management for her extramedullary breast relapse and underwent subsequent systemic chemotherapy, targeted radiation, immunotherapy with donor lymphocytic infusions, and repeat autologous stem cell transplant.

Discussion

Breast involvement in AML is exceedingly uncommon [1–3]. Extramedullary relapse (EMR) may present with multi-organ involvement although it may also be localized to a single site. The most common sites of extramedullary relapse are the skin and soft tissue (including the breast), with additional sites including lymph nodes, bone, testis, ovaries, and the central nervous system [1,2,4]. In a retrospective analysis by Shem-Tov et al. [5], the incidence of isolated extramedullary relapse of AML was 5.8% with isolated breast involvement in only 6.4% of those reported cases. An additional analysis by Harris et al. [2], reported an incidence of isolated extramedullary relapse in 9% of patients with AML status postallogeneic stem cell transplant. Leukemic infiltration of the breast often suggests a propensity for further extramedullary spread and often poor prognosis [2,4,6–8]. Although extramedullary relapse has been reported to occur later than bone marrow relapse, approximately 10.1 versus 3.6 months respectively, once a single site of disease has been found, progression to other sites and bone marrow typically occurs within one year [4,5]. The survival rate after extramedullary relapse had been reported as 30% at 1 year and 12% at 2 years [2].

Radiologically, leukemic infiltration of the breast presents a diagnostic challenge. The current knowledge of radiologic features is mostly obtained from infrequent case reports and tends to vary from case to case. The mammographic and sonographic findings, such as spiculated masses or enlarged lymph nodes as in this case, can overlap with those of primary breast malignancies or metastases from other sites [7,9]. Mammographic descriptions in the literature report hyper-

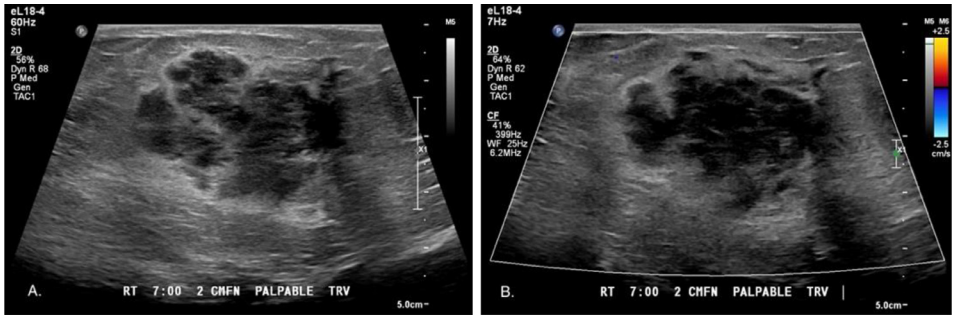

Fig. 3 – Grayscale (A) and Spectral Doppler (B) sonographic images demonstrate a 3.9 cm irregular hypoechoic mass in the right breast with spiculated versus microlobular margins at 7-o'clock 2 cm from the nipple without significant vascularity.

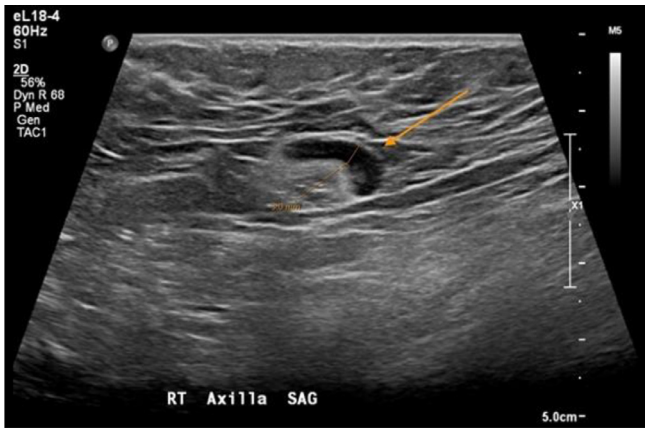

Fig. 4 – Grayscale sonographic image of the right axilla demonstrating a right axillary lymph node (arrow) with uniformly thickened cortex.

dense, round masses with microlobulated margins, typically without calcification although rarely they can exhibit microcalcifications [3]. Reports of architectural distortion are much less common. On ultrasound evaluation, lesions are typically depicted as hypoechoic with microlobulated or spiculated margins [3,9]. The differential diagnoses for these lesions is extremely broad and variable with age, including both benign and malignant lesions. This overlap in radiological findings underscores the importance of considering leukemic infiltration in the differential diagnosis and highlights the importance of investigation of the patient's medical records to find pertinent history, such as AML in this case [7,9].

Prompt and accurate diagnosis is paramount. Although is it associated with a poorer prognosis, there are no established guidelines for imaging surveillance of extramedullary relapse and follow-up typically does not include regular CT, MRI, or PET/CT [4]. As such, many patients are only diagnosed once they become symptomatic. Extramedullary relapse prognosis, although poor, has a better prognosis than that of systemic relapse; therefore, therapy should aim to prevent systemic relapse depending on the patient's overall health and previous treatment history [4,5]. Given the radiological similarities with other breast malignancies, a timely biopsy is vital. Flow cytometry, cytogenetic studies, and immunohistochemical staining for myeloid cell markers in addition to conventional histology aids in preventing misdiagnosis and confirming diagnosis, as extramedullary relapse in the breast can mimic other malignancies such as lymphoma, sarcoma, and primary breast carcinoma [6,7]. Molecular annotation of ex-

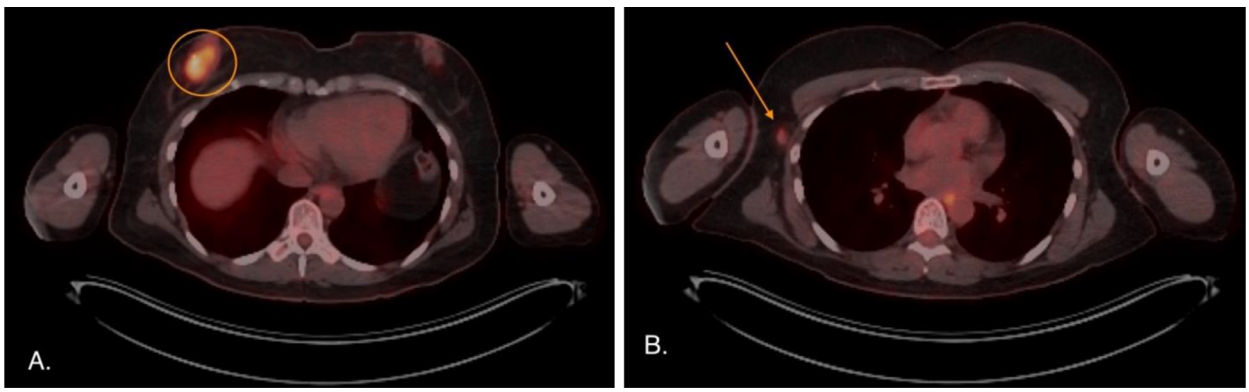

Fig. 5 – PET-CT demonstrates a hypermetabolic right breast lesion (circle) with a maximum SUV of 4.7 (A) and a small mildly hypermetabolic right axillary lymph node (arrow) with a maximum SUV of 2.2 (B).

tramedullary AML has shown that up to 52% of patients with extramedullary AML have potentially targetable mutations, which also brings up the possible benefit of site-specific next-generation sequencing for personalized targeted therapy [10].

Although there are no clear established guidelines for clinical decision-making in the treatment of extramedullary relapse of AML after allogeneic stem cell transplantation, treatment often involves a combination of systemic chemotherapy, immunotherapy with donor lymphocyte infusions, repeated transplant, and localized treatments such as radiation based on the patient's overall health and previous treatment history [1,4–6,8].

Conclusion

In conclusion, while extramedullary relapse of AML in the breast is rare, it presents significant diagnostic and therapeutic challenges. Radiologists play a pivotal role in the early recognition and diagnosis of such cases. The overlap of radiologic findings with other breast malignancies underscores the significance of a thorough clinical history and the need for a multidisciplinary approach. Prompt workup including histologic, immunohistochemical, and flow cytometry testing should be performed to ensure timely diagnosis and optimal patient management.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used OpenAI's language processing tool, ChatGPT, to assist in the editing process, limited to enhancing the paper's readability and grammatical correctness. It is important to clarify that the core components of this case report were conceived and generated entirely by the authors. We affirm that the intellectual contributions of the authors have been preserved, and the manuscript represents an original work by the authors. The authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Patient consent

The authors attest that the patient provided written informed consent for the use of their medical images for educational and scientific purposes.

REFERENCES

[1] Cunningham I. Extramedullary sites of leukemia relapse after transplant. Leuk Lymphoma 2006;47(9):1754–67. doi:10.1080/10428190600632857.
[2] Harris AC, Kitko CL, Couriel DR, Braun TM, Choi SW, Magenau J, et al. Extramedullary relapse of acute myeloid leukemia following allogeneic hematopoietic stem cell transplantation: incidence, risk factors and outcomes. Haematologica 2013;98(2):179–84. doi:10.3324/haematol.2012.073189.
[3] Surov A, Wienke A, Abbas J. Breast leukemia: an update. Acta Radiol 2012;53(3):261–6. doi:10.1258/ar.2011.110470.
[4] Clark WB, Strickland SA, Barrett AJ, Savani BN. Extramedullary relapses after allogeneic stem cell transplantation for acute myeloid leukemia and myelodysplastic syndrome. Haematologica 2010;95(6):860–3. doi:10.3324/haematol.2010.025890.
[5] Shem-Tov N, Saraceni F, Danylesko I, Shouval R, Yerushalmi R, Nagler A, et al. Isolated extramedullary relapse of acute leukemia after allogeneic stem cell transplantation: different kinetics and better prognosis than systemic relapse. Biol Blood Marrow Transplant 2017;23(7):1087–94. doi:10.1016/j.bbmt.2017.03.023.
[6] Byrd JC, Edenfield WJ, Shields DJ, Dawson NA. Extramedullary myeloid cell tumors in acute nonlymphocytic leukemia: a clinical review. J Clin Oncol 2006;24(20):3278–85. doi:10.1080/10428190600967022.
[7] Fernandes Vieira V, Vo QD, Bouquet de la Jolinière J, Khomsi F, Feki A, Hoogewoud HM. Granulocytic sarcoma presenting as a palpable breast lump. Front Surg 2017;3:67. doi:10.3389/fsurg.2016.00067.
[8] Li Y, Xie YD, He SJ, Hu JM, Li ZS, Qu SH. Breast and dorsal spine relapse of granulocytic sarcoma after allogeneic stem cell transplantation for acute myelomonocytic leukemia: a case report. World J Clin Cases 2022;10(7):2315–21. doi:10.12998/wjcc.v10.i7.2315.
[9] Kim SJ, Kim WG. Sonographic features of a myeloid sarcoma of the breast as a relapse of acute myeloid leukemia after stem-cell transplantation: a case report. Am J Case Rep 2019;20:612–19. doi:10.12659/AJCR.915453.
[10] Ball S, Knepper TC, Deutsch YE, Samra W, Watts JM, Bradley TJ, et al. Molecular annotation of extramedullary acute myeloid leukemia identifies high prevalence of targetable mutations. Cancer 2022;128(21):3880–7. doi:10.1002/cncr.34459.