Case Report

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Relapsed Acute Myeloid Leukemia Presenting as Multiple Breast Masses: A Case Report

유방의 다발성 결절로 발현한 급성 골수성 백혈병 재발의 건: 증례 보고

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Hematologic malignancy of the breast is very rare. Here, we report a case of relapsed acute myeloid leukemia (AML) presenting as multiple breast masses. A 77-year-old female visited an outpatient clinic reporting palpable masses in both breasts. She had a medical history of AML, which showed complete remission after nine cycles of chemotherapy. On mammography and ultrasonography, there were multiple masses correlated with her palpable symptoms accompanied by enlarged lymph nodes. Core needle biopsy immunohistochemistry (IHC) results indicated AML and blastic plasmacytoid dendritic cell neoplasm. AML was confirmed using bone marrow biopsy. Although very rare, when a patient with a history of hematologic malignancy presents a palpable mass in the breast, clinicians should conduct proper tissue analysis, including IHC stating for leukemic markers, to guide appropriate diagnosis and treatment.

Index terms Leukemia, Myeloid, Acute; Breast; Mammography; Ultrasonography

INTRODUCTION

Breast leukemia is an extremely rare disease entity. In 1878 there was the first report about the leukemic tumor in the breast. Since then, there only have been fewer than 200 reports about metastatic breast leukemia (1). Since it is a rare disease, breast leukemic infiltration could be mistaken for other diseases, such as primary breast cancer, if we do not pay enough

attention to the patient's past medical history or any other general condition. Here we present a scarce case of the relapsed acute myeloid leukemia (AML) presenting as bilateral palpable breast masses.

CASE REPORT

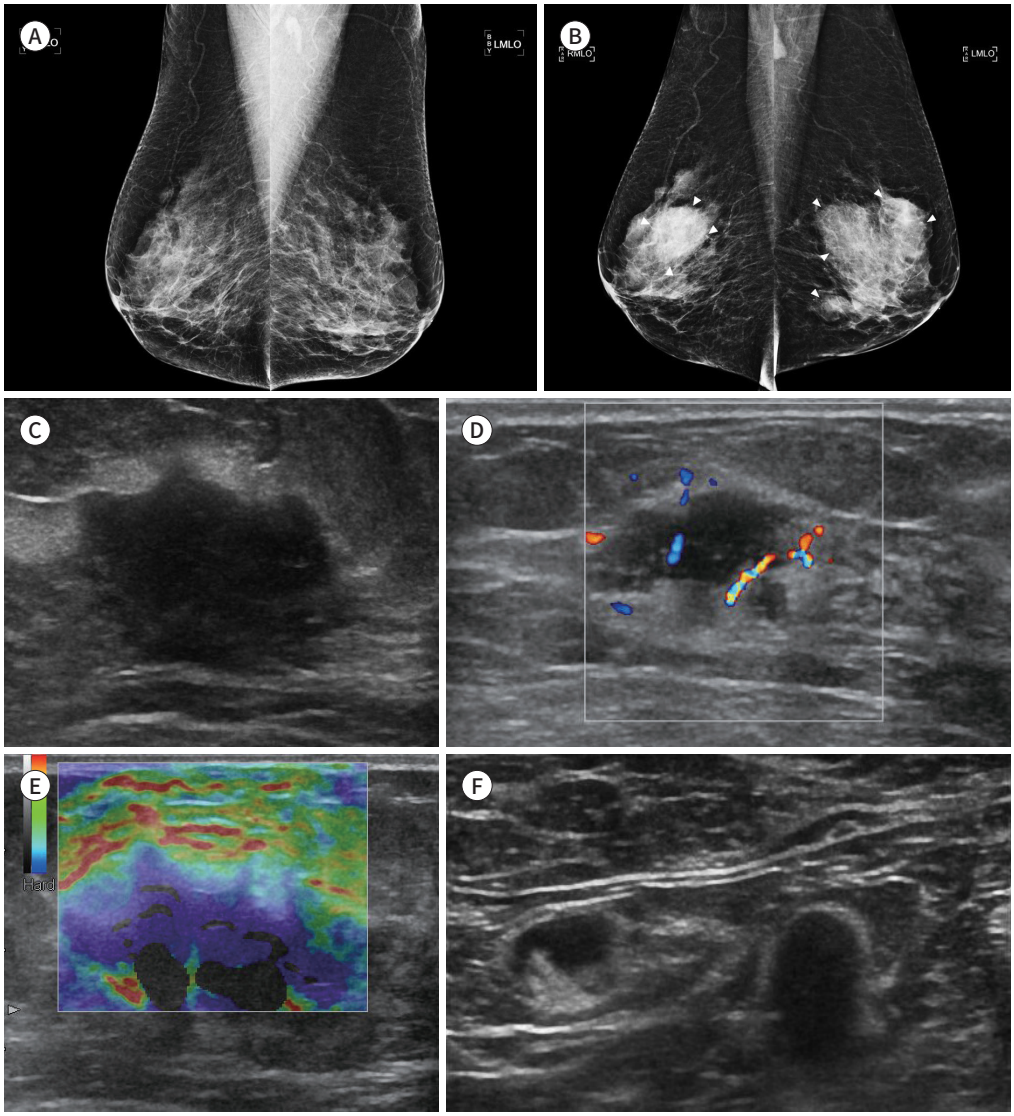
In May 2020, a 77-year-old female patient came to the emergency department due to aggravating dizziness and general weakness. The blood test revealed pancytopenia (white blood cell count 2400/μL, hemoglobin 9.7 g/dL, and platelet count 43000/μL), and an additional bone marrow (BM) biopsy showed an excess of primitive cells, where 60.4% were blast cells. Hence, she was diagnosed with AML. The patient was treated with 9 cycles of decitabine until March 2021, discontinued due to her poor general condition. After two months of off-chemo status, the follow-up BM biopsy result was reported as complete remission, as the marrow cells showed nearly normal distribution.

Four months later, the patient visited the breast clinic because of the palpable masses in both breasts, noticed one week ago. On physical examination, firm masses were palpated in the upper inner quadrant of the right breast and the upper area of the left breast. On the same day, mammography and breast ultrasonography were performed. At mammography, multiple hyperdense, oval masses with obscured margins were found in both breasts (Fig. 1B). These masses were new compared to her previous mammography taken three years ago (Fig. 1A). No definite microcalcification nor architectural distortion was found on mammography. On ultrasonography, multiple hypoechoic irregular masses with 1 to 4 centimeters of maximum diameter were scattered in both breasts (Fig. 1C-F). The largest mass was located at the left inner upper quadrant, measuring 3.79 cm × 2.67 cm × 2.02 cm. There were hyperechoic changes in the peritumoral space. On the left axillary level I, there were multiple enlarged lymph nodes with cortical thickening, which were highly likely to be metastatic lymph nodes. Bilateral breast masses were all classified as Breast Imaging Reporting and Data System (BI-RADS) category 5 (C5). Immediate core needle biopsies were done at the largest bilateral C5 masses and left axillary lymph node with 14 and 18-gauge needles, respectively.

Microscopic examination suggested hematolymphoid malignancy in the specimens. The immunohistochemistry (IHC) revealed that the tumors were positive for CD43, CD117, and weakly positive for CD34, CD56, and CD4. CD123 was also positive, which is highly expressed in patients with AML and also in patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), previously known as natural killer (NK) cell leukemia/lymphoma. Therefore, the pathologic diagnosis was reported as relapsed AML versus BPDCN. Her blood test showed leukocytosis (white blood cell count 20190/μL) with 59% of immature cells, which had shown normal distribution without any immature cells one month ago. Considering the patient had no definite skin lesion, where the BPDCN expresses most frequently, she was clinically judged to have a relapse of AML.

The clinician started the first cycle of the chemotherapy with a new regimen, venetoclax plus azacytidine. In the follow-up BM biopsy, there were aberrant CD7, CD 56, and CD79 expressions, so the final diagnosis was confirmed as acute myeloid leukemia in relapse. However, the patient died due to neutropenic fever, 3 months after the presentation of breast masses.

Fig. 1.Mammography and ultrasonography of both breasts.
A. A routine screening mammography in 2018 is normal.
B. On the recent 2021 mammography, the patient's report of palpable masses is correlated with multiple hyperdense, obscured, oval masses (arrowheads) in both breasts.
C. Gray-scale ultrasonography shows an irregular, hypoechoic mass with microlobulated margin and a hyperechoic change between the subcutaneous fat layer and the mass.
D. Color Doppler ultrasonography shows intratumoral hypervascularity.
E. Static elastography shows blue within mass, indicating a poorly deformable hard malignant lesion.
F. Enlarged left level I axillary lymph nodes.



This case report was approved by the Institutional Review Board of our institution and the requirement for written informed consent was waived (IRB No. 30-2022-32).

DISCUSSION

Whether as an initial presentation or as relapse after treatment, leukemic infiltration of the breast is rare. Among leukemic diseases, most cases of breast involvement occurred in

patients with AML (1, 2). A meta-analysis revealed that of 156 cases of breast leukemic involvement reported from 1969 to 2005, 107 cases were AML (68.6%) (3). Still, breast involvement is very rare among AML patients. An autopsy review reported that of 235 patients with AML, only 4 patients had breast involvement (1.7%) (4).

In general, image findings of breast leukemia are non-specific. On mammography, breast leukemia is most commonly seen as multiple, often bilateral, noncalcified, circumscribed or indistinct masses (1). Architectural distortion is less common. On ultrasonography, the characteristics of breast masses could vary, from hypoechoic to mixed heterogeneous echogenicity, from oval to irregular shapes, with microlobulated or indistinct margins (1, 5). The mass frequently shows internal vascularity in the doppler study. Our case showed irregular masses with indistinct, microlobulated margins and hyperechoic periphery, which was consistent with the ultrasonographic features described in recent case report of primary hematologic malignancy of the breast (6). Our case showed hard on static elastography, whereas a previous study reported a solitary mass with intermediate on shear wave elastography in AML relapse case (7). This difference might be due to size and number differences, as our case showed multifocal, bigger lesion size.

When a patient complains of a palpable breast mass, it is not easy to consider leukemia as a possible diagnosis. However, according to a meta-analysis, 42.4% of breast leukemic involvement were relapsed cases after therapy or stem cell transplantation (59/139 patients) (3). Therefore, the clinician must investigate the patient's history thoroughly.

Our patient visited the clinic with bilateral breast palpable hard masses, the relatively most frequent type of manifestation of breast leukemic involvement. As she achieved complete remission of AML recently, the clinician and the radiologist initially considered the AML relapse as the primary differential diagnosis. Therefore tissue confirmation via core needle biopsy was immediately performed.

The treatment for the extramedullary relapse of acute leukemia is not established. In most cases, a systemic approach with chemotherapy is recommended (4). Surgery or radiation therapy alone is inadequate for breast leukemia, as the lesions tend to involve bilateral breasts with multiple masses. Our patient also received chemotherapy, but just one cycle because she suffered from neutropenic fever. Therefore, it was hard to evaluate the efficacy of the chemotherapy in our case.

The leukemic breast involvement suggests the further extramedullary spread, particularly in soft tissues, including the gynecologic tract. Once disseminated, the extramedullary disease is resistant to therapy, so the leukemic breast involvement implies a poor prognosis. However some authors claimed the importance of intensive chemotherapy aimed at cure because there have been a few cases where the long disease-free survival was achieved up to 3, 4, and more than 12 years after chemotherapy (4). Even so, an intensive chemotherapy regimen might not be ideal in relapsed patients because they have a higher probability of having a poor general condition or weak immunity due to the previous chemotherapy. There was a case report where a 34-year-old female patient with relapsed AML involving breast received chemotherapy, but died of respiratory failure within one year of treatment (8).

In conclusion, we presented an extremely rare case of the relapsed AML presenting as bilateral palpable breast masses. Nevertheless, when the patient has a history of acute leuke-

mia, it should be considered in the differential diagnosis. The proper radiologic investigation and a pathologic tissue confirmation, including IHC stating for the leukemic markers, should be done for the appropriate treatment.

Author Contributions

Conceptualization, C.A.J.; data curation, all authors; investigation, S.P.; resources, S.P.; writing—original draft, S.P.; and writing—review & editing, C.A.J., L.J.Y.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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유방의 다발성 결절로 발현한 급성 골수성 백혈병 재발의 건: 증례 보고

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유방을 침범하는 혈액종양은 굉장히 드물게 보고되었다. 우리는 유방의 다발성 결절로써 재발한 급성 골수성 백혈병의 증례를 보고하고자 한다. 77세 여자 환자가 양측 유방의 촉지되는 다발성 결절로 외래를 내원하였다. 환자는 급성 골수성 백혈병(acute myeloid leukemia; 이하 AML)으로 진단받고 9차례의 항암치료 이후 완전 관해가 된 병력이 있었다. 유방 촬영과 유방 초음파에서 환자의 촉지성 병변이 영상의학적으로 확인되었으며 액와부 림프절 종대도 동반되었다. 총생검으로 얻은 검체는 면역화학염색을 통해 AML과 blastic plasmacytoid dendritic cell neoplasm의 형태를 보였으며 추후 진행한 골수 생검에서 AML로 확인되었다. 이렇듯 굉장히 드물지만, 혈액암의 병력을 가진 환자가 유방의 촉지성 종괴로 내원하였다면 담당의는 적절한 조직검사 및 면역화학검사로 정확한 진단을 하여 환자가 적절한 치료를 받도록 해야 한다.

서울특별시 보라매병원 영상의학과