CASE REPORT

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Diffuse Infiltration of both Breasts in Pregnant Women is the First Manifestation of Myeloid Sarcoma - A Case Report and Literature Review

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ABSTRACT

Myeloid sarcoma (MS) during pregnancy is rare, and cases initially presenting as bilateral breast infiltration are particularly misleading and difficult to diagnose. It is essential to differentiate MS from conditions such as mammary hyperplasia and breast cancer. We report a case of a 28-year-old woman who developed bilateral breast induration, distension, and serous discharge at seven months' gestation. The final diagnosis was MS secondary to acute myeloid leukemia. The patient is currently undergoing chemotherapy. Clinicians should increase their awareness of MS and, when necessary, recommend hematological and bone marrow cytomorphological examinations for pregnant women presenting with suspicious breast symptoms to ensure early diagnosis.

Keywords: Pregnancy; myeloid sarcoma; breast mass; acute myeloid leukemia; diagnosis

INTRODUCTION

Myeloid sarcoma (MS) is a malignant tumor composed of immature myeloid cells that forms a solid mass outside the bone marrow and disrupts the native tissue architecture. It is also known as extramedullary myeloid tumor, granulocytic sarcoma, or chloroma. MS can occur in any part of the body and typically manifests with symptoms of tissue infiltration and compression at the affected site. It most commonly involves the skin, lymph nodes, soft tissues, bones, and testes.[1] Breast involvement is rare and usually unilateral[2,3] with bilateral cases are even more uncommon.[4] We report a rare case of bilateral MS in a pregnant woman in whom diagnosis and treatment were delayed because of her pregnancy.

CASE REPORT

A 28-year-old pregnant woman presented to a local hospital at 7 months' gestation with bilateral breast swelling and clear discharge. The ultrasound finding was considered to represent a pregnancy-related breast secretion reaction and was not investigated further. After natural childbirth resulting in a healthy baby, she complained of persistent hardening and swelling of both breasts and clear nipple discharge. The patient was transferred to our hospital for further treatment.

Magnetic resonance imaging showed that both breasts appeared full, with diffuse hyperintensity on T2-weighted fat-suppressed imaging, high signal intensity on diffusion-weighted imaging, and low signal intensity on the apparent diffusion coefficient map. Contrast enhancement

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was heterogeneous, with nodular thickening of the skin and areolae bilaterally (Figure 1). 18F- fluorodeoxyglucose positron emission tomography-computed tomography (CT) showed that both breasts were enlarged, with mass-like soft-tissue densities present. The radiotracer uptake is diffusely increased and heterogeneous, with an maximum standardized uptake value of 7.4. In addition, increased radiotracer uptake in bone and muscle was observed at multiple sites throughout the body. The imaging diagnosis was malignant breast cancer with multiple bone marrow metastases and multiple soft-tissue metastases (including muscle) throughout the body (Figure 2).

Hematological analysis showed a white blood cell count of 4.62×10^9/L, a red blood cell count of 5.13×10^{12}/L, hemoglobin concentration of 141 g/L, and a platelet count of 302×10^9/L. Differential counts revealed neutrophils at 32.1%, lymphocytes at 49.2%, and monocytes at 17.4%. The D-dimer level was 1.69 mg/L. Coagulation tests showed a prothrombin time of 12.9 seconds and an international normalized ratio of 0.99. Serum lactate dehydrogenase and uric acid were elevated, at 566 U/L and 496 μmol/L, respectively.

Bone marrow aspiration demonstrated that blasts comprised 58.1% of cells and were characterized by weak CD45 expression and low side scatter. Immunophenotyping showed expression of stem/progenitor and myeloid markers (HLA-DR, CD38, CD34, CD33, CD15, MPO) as well as B-cell markers (CD19, CD22, CD79a). CD10, CD20, CD13, and CD117 were not expressed. Bone marrow cellularity was markedly increased, with granulocytic, erythroid, and lymphocytic lineages accounting for 73.5%, 1.5%, and 25.0%, respectively, all showing normal morphology. Blasts constituted 65.0%, and the peroxidase positivity was 22.0%.

To confirm the diagnosis, a breast biopsy was performed under local anesthesia. Histopathological examination revealed diffuse infiltration by tumor cells. Immunohistochemical staining showed the following profile: CD3 (–), CD5 (–), CD20 (–), CD79a (–), CD21 (–), Ki-67 (75%+), BCL-6 (60%+), MUM1 (+), BCL-2 (+++), p53 (50%+), MPO (+++), CD43 (+++), CK (–), and EMA (+). Based on these findings, a diagnosis of MS was considered.

The patient received the IA chemotherapy regimen, comprising idarubicin (17 mg, intravenous infusion, days 1-3) and cytarabine (0.17 g, intravenous infusion, days 1-7), along with alkalization, hydration, antiemetic therapy, and gastric-protective measures. On June 26, 2023, a follow-up bone marrow examination showed a blast cell percentage of 2.0%. Blood cell analysis results were as follows: white blood cell count, 3.28×10^9/L; red blood cell count, 3.76×10^{12}/L; hemoglobin, 99 g/L; platelet count, 68×10^9/L; lymphocyte percentage, 40.9%; and absolute neutrophil count, 1.79×10^9/L.

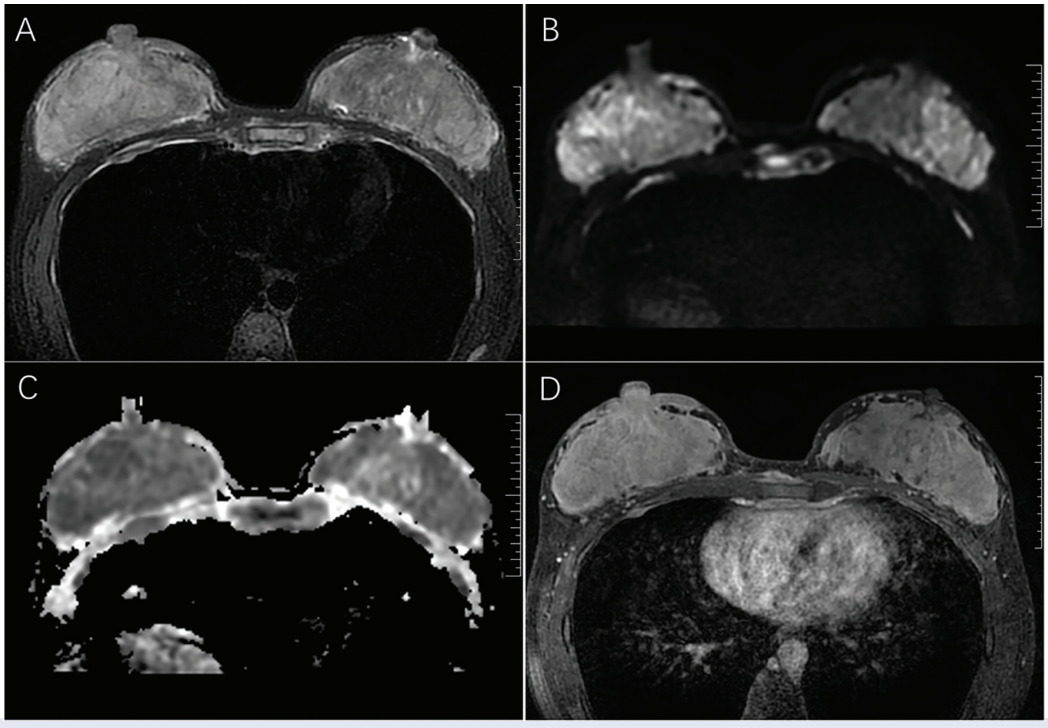

FIGURE 1: Breast magnetic resonance imaging examination, (A) T2-weighted fat-suppressed imaging shows diffuse high signal intensity in both breasts, (B) Diffusion-weighted imaging shows diffuse high signal intensity in both breasts, (C) The apparent diffusion coefficient map shows reduced signal intensity in both breasts, (D) Post-contrast imaging demonstrates heterogeneous enhancement, with skin thickening and enhancement in both breasts.

As the patient's blood parameters gradually recovered, they were discharged. Follow-up CT scans performed on July 7, 2023 (Figure 3A) and October 12, 2023 (Figure 3B) revealed a significant reduction in the breast mass.

DISCUSSION

MS commonly occurs secondary to hematologic malignancies, such as acute myeloid leukemia (AML), blast crisis of chronic myeloid leukemia, and myelodysplastic syndromes. MS can be categorized into two major types: leukemic MS - which includes extramedullary infiltration in AML or relapse following complete remission of AML. Isolated MS characterized by a solitary solid mass without accompanying bone marrow involvement.

The clinical manifestations of MS are non-specific, with initial symptoms primarily caused by mass effect and compression. MS can occur at any age and in various anatomical locations, but cases of AML with multisite

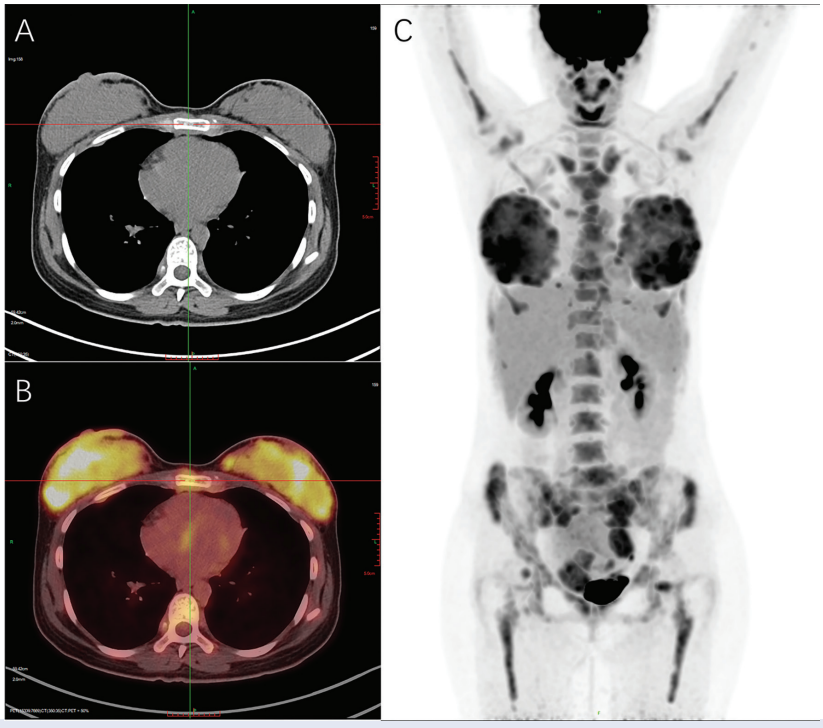

FIGURE 2: F-18 FDG PET-CT findings, (A) CT images show bilateral, dense, and full breast tissue with skin thickening, (B) PET images reveal diffusely increased but uneven radiotracer uptake in both breasts, with an SUV_{max} of 7.4, (C) Coronal maximum-intensity projection images demonstrate widespread systemic metastases.

PET: Positron emission tomography; CT: Computed tomography; FDG: Fluorodeoxyglucose; SUV: Standardized uptake value

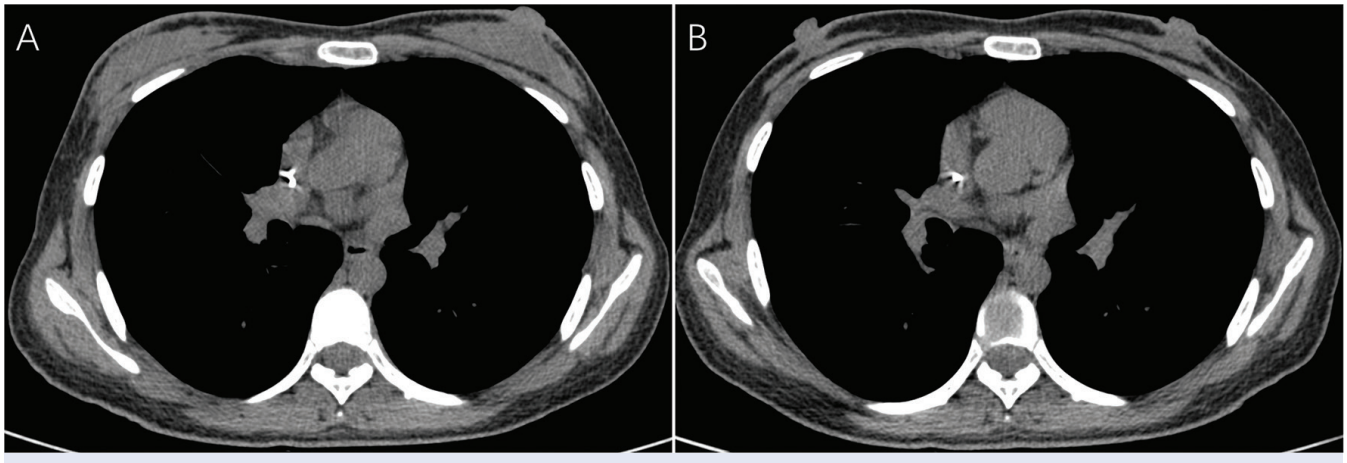

FIGURE 3: Post-treatment follow-up computed tomopraphy findings, (A) The computed tomography image reveals dense bilateral breast tissue and mild thickening of the skin, (B) The breast masses have mostly resolved.

systemic MS are extremely rare and are associated with a poor prognosis, as reported in the literature. Diagnosing MS in patients with a known history of AML is relatively straightforward. However, diagnosis of primary MS remains challenging, with an initial misdiagnosis rate of 75%, most commonly misdiagnosed as large-cell lymphoma. Advances in cytogenetic analysis, immunohistochemistry, flow cytometry, and fluorescence in situ hybridization have reduced the misdiagnosis rate to 25%-47%, although it remains high.[5] In this case, the patient presented with a breast mass and was initially misdiagnosed with breast cancer. Further investigation revealed the involvement of the pancreas, bone marrow, pleura, and multiple muscle and soft-tissue sites throughout the body. The definitive diagnosis was established through pathological and immunohistochemical analysis.

Histopathological examination of biopsy specimens is crucial for diagnosing MS. Morphologically, MS is characterized by myeloid cell infiltration and can be classified, based on cell origin, as granulocytic sarcoma, primitive monocytic sarcoma, or trilineage hematopoietic MS. Additionally, based on the degree of cell differentiation, MS can be categorized into blastic, immature, and differentiated subtypes. Immunohistochemical staining plays a vital role in assisting the diagnosis of MS. The most commonly expressed antigens in MS are MPO, CD34, CD43, CD45, CD56, CD68, CD117, and lysozyme; CD11, CD13, and CD33 are also frequently expressed. Among these, CD43 and lysozyme are the most sensitive markers, showing nearly 100% positivity.[5] MPO has a positive expression rate ranging from 66% to 96% and exhibits a characteristic green appearance when exposed to air.[5-7] However, some MS cases may abnormally express B-cell or T-cell markers, leading to misdiagnoses such as diffuse large B-cell lymphoma, peripheral T-cell lymphoma, or small lymphocytic lymphoma. A high Ki-67 index (typically >60%) is also common in MS. In this case, MPO, CD34, and Ki-67 were strongly positive, whereas CD3, CD5, CD20, CD79a, and CD21 were negative, ruling out B- and T-cell origins. Together with bone marrow aspiration and hematological analysis, these findings confirmed the diagnosis of MS.

Common chromosomal abnormalities in MS include MLL rearrangements, t(8;21), inv(16), and monosomies. Among genetic mutations in MS8, NPM1 is the most frequently mutated gene. Other reported cytogenetic abnormalities include the translocations t(9;11), t(8;17), t(8;16), and t(1;11), and the deletion 16q.[1,5] The clinical presentation of MS is closely linked to molecular abnormalities. Orbital MS in children is often associated with t(8;21), whereas inv(16) is related to extramedullary disease in AML, which is associated with a higher incidence of gastrointestinal and breast MS.[7-9]

MS during pregnancy poses a diagnostic challenge. During pregnancy, Cases involving the cervix, spinal cord, and stomach have been reported in which compression symptoms at the affected sites were the initial presentation.[10-12] Breast MS typically exhibits a diffuse or single-cell infiltrative growth pattern and can be classified, based on cellular differentiation5, into mature, immature, or blastic subtypes. Its single-cell infiltration pattern may mimic invasive lobular carcinoma, but MS usually does not disrupt the ductal and lobular structures of the breast. Immunohistochemistry is crucial for differentiating between these conditions.[13] Breast MS is primarily treated with chemotherapy and radiotherapy; in some cases, stem-cell transplantation may be considered. The prognosis is generally poor, making early and accurate diagnosis essential for timely and intensified treatment, which may improve long-term survival and the potential for cure.

CONCLUSION

MS presenting as bilateral breast masses is extremely rare. In pregnant women, physiological breast changes can obscure symptoms, making misdiagnosis highly likely, most commonly as mastitis, hyperplasia, breast cancer, or breast lymphoma. In patients presenting with breast masses, particularly those with suspected myeloid leukemia, MS should be considered in the differential diagnosis. Early histopathological examination and immunohistochemical analysis are recommended to establish a definitive diagnosis and to avoid treatment delays. We obtained the patient's consent.

Ethics

Informed Consent: Informed consent was obtained.

Footnotes

Authorship Contributions

Concept: W.Y., C.H., Data Collection or Processing: W.Y., Analysis or Interpretation: W.Y., C.H., Literature Search: F W.Y., C.H., Writing: W.Y.

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