An uncommon granulocytic sarcoma of the breast: a case report and literature review

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Abstract: Granulocytic sarcoma (GS) is an uncommon extramedullary manifestation of acute myeloid leukemia. GS is often likely to be clinically misdiagnosed as another type of primary breast cancer due to its rarity. We report an uncommon case of breast GS in a patient and review the relevant literature.

Keywords: granulocytic sarcoma, breast, misdiagnosis, immunohistochemistry

Introduction

Acute myeloid leukemia (AML) is generally considered to include a group of relatively well-defined cancers of the myeloid lineage of blood cells. In AML patients, immature leukocytes grow rapidly in the bone marrow and interfere with the production of normal blood cells. Granulocytic sarcoma (GS) is an uncommon extramedullary manifestation of AML and refers to an extramedullary mass consisting of myeloid blasts with or without maturation, which destroys the normal tissue architecture. Although myeloid sarcoma has been listed in the World Health Organization classification, it represents a unique clinical presentation of any subtype of AML, rather than being a specific subtype of AML in its own right. Myeloid sarcoma can precede or occur simultaneously with bone marrow diseases, sometimes as a manifestation during AML relapse or progression of a prior myelodysplastic syndrome or myeloproliferative neoplasm. The sites of isolated GS include the ovary, uterus, epidural region, soft tissues, peristeme, bone, and lymph nodes as well as less commonly the orbit, intestine, and mediastinum, with involvement of the breast being rare. However, several previous articles have reported on this kind of breast tumor (Table 1).

The clinical features and imaging characteristics of breast GS are not specific, and it can therefore easily be misdiagnosed as other breast tumors, such as lymphoma, carcinoma, and benign tumors, especially primary tumors with no evidence of medullary disease. Histopathological examination with immunohistochemical tests is currently the gold standard for diagnosis. Although some experts advocate the treatment of localized GS in relapsed acute promyelocytic leukemia with local radiation to the extramedullary disease site, systemic therapy is also usually required for relapsed disease. Herein, we report an uncommon case of breast GS in a patient and review the relevant literature. Written informed consent was obtained from the patient for publication of the case details and any accompanying images.

Case analysis

A 34-year-old woman attended our hospital complaining of a palpable mass in the superior lateral quadrant of her right breast. Physical examination revealed a painless and...
<table>
<thead>
<tr>
<th>Author</th>
<th>Sex/age</th>
<th>Relevant medical history</th>
<th>Symptoms</th>
<th>Other involved sites</th>
<th>Type of leukemia</th>
<th>Imaging findings</th>
<th>Treatment</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joo et al (2000)</td>
<td>Female/42</td>
<td>None</td>
<td>A mass in the left breast</td>
<td>None</td>
<td>AML-M1</td>
<td>–</td>
<td>Surgical excision and chemotherapy</td>
<td>The follow-up showed no blastic cells</td>
</tr>
<tr>
<td>Dutta Roy et al (2004)</td>
<td>Female/72</td>
<td>None</td>
<td>A left breast lump</td>
<td>None</td>
<td>GS</td>
<td>An irregular mass lesion with areas of increased echogenicity</td>
<td>Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Gündüz et al (2014)</td>
<td>Female/30</td>
<td>AML-M6</td>
<td>A palpable mass in the right breast</td>
<td>None</td>
<td>None</td>
<td>An irregular mass of the breast</td>
<td>High-dose ara-C, etoposide, and idarubicin combination chemotherapy</td>
<td>Invasive aspergillosis developed despite posaconazole prophylaxis, and she died of sepsis 25 days after chemotherapy At 26 months follow-up, the patient remains asymptomatic and there is no evidence of relapse of the disease</td>
</tr>
<tr>
<td>Gonçalves et al (2014)</td>
<td>Female/35</td>
<td>None</td>
<td>Nodule on left breast</td>
<td>None</td>
<td>–</td>
<td>A solid heterogeneous nodule</td>
<td>Chemotherapy and radiotherapy</td>
<td></td>
</tr>
<tr>
<td>Wu et al (2014)</td>
<td>Female/29</td>
<td>None</td>
<td>Masses on bilateral breasts</td>
<td>Migrating arthralgia at bilateral elbow and knee joints</td>
<td>AML-M4</td>
<td>–</td>
<td>Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Stewart et al (2015)</td>
<td>Female/46</td>
<td>AML</td>
<td>Mass on right breast</td>
<td>None</td>
<td>AML</td>
<td>A circumscribed mass in the right breast</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huang et al (2015)</td>
<td>Female/58</td>
<td>AML-M6</td>
<td>An enlarged, painless, and palpable mass in the left breast</td>
<td>None</td>
<td>AML-M6</td>
<td>A single, irregular, poorly defined mass without calcification</td>
<td>Operation and chemotherapy</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1** Previous reports of GS of the breast

Abbreviations: AML, acute myelocytic leukemia; GS, granulocytic sarcoma; MRI, magnetic resonance imaging.
relatively hard, removable mass measuring −2.6×3.5 cm, with no palpable axillary lymph nodes. Her breast had no nipple discharge, skin ulcers, orange-peel appearance, or nipple retraction. Her medical history included AML (classification: M2) diagnosed 3 years earlier, based on nasosinal space-occupying lesions. She underwent six cycles of chemotherapy with cytosine arabinoside and achieved satisfactory disease control and remission, indicated by postchemotherapy bone marrow examination. The patient had no other symptoms or signs and no relevant family history.

A mammogram showed a −2.5×2.4 cm round mass with well-defined, irregular margins in the superior lateral quadrant of the right breast, 4.5 cm from the nipple, with a thick blood vessel passing through the tumor from the chest wall. Another mass was detected in the inferior lateral quadrant of her right breast, 2.1 cm from the nipple, measuring −1.4×1.1 cm. Several axillary lymph nodes could be observed on the right side, the largest being −1.9 cm in diameter (Figure 1). Breast ultrasound clearly demonstrated a hypoechoic mass measuring −3.7×2.6 cm in the superior lateral quadrant of the right breast (Figure 2). The mass was lobulated with an unclear edge, with numerous low-speed bloodstream signals within and close to the mass (resistive index: 0.60). There was another homogenous, hypoechoic mass below the nipple, measuring −1.8×1.1 cm in diameter, with a clear edge and an irregular shape. Color Doppler flow imaging showed rich blood supply signals from the surround-

A complete blood count demonstrated a white blood cell count of 8.07×10^9/L, a neutrophil count of 5.81×10^9/L, the hemoglobin levels of 137 g/L, and a platelet count of 188×10^9/L. The results of chest radiography and abdominopelvic computed tomography were normal. Fine needle aspiration of the two tumors was performed, and inflammatory cell infiltration and granular calcification with several atypical epithelial cells in the background were identified, suggesting possible malignancy. Considering the differential diagnosis between breast cancer and lymphoma, we performed a bone marrow aspirate examination, which revealed no abnormalities. A lumpectomy was therefore performed under local infiltration anesthesia. The cut surface demonstrated two tumors, well-circumscribed in relation to the adjacent structures. The tumors were −3×3×2.5 cm and 2×2×2 cm and were located −0.5 cm apart. Based on the examination of frozen sections, the patient was diagnosed with poorly differentiated malignant tumor.

Postoperative paraffin-based histopathology showed dense myeloid cellular proliferation with breast tissue invasion. Immunohistochemical examination demonstrated that the tumor was strongly positive for myeloperoxidase, CD43, and human leukocyte common antigen (Figure 3); weakly positive for CD20, kappa, lambda, and progesterone receptor; and negative for CD79-α, CD3, CD38, CD10, CD5, CD56, AE1/AE3, estrogen receptor, and C-erbB-2. The histological features were consistent with breast GS. The patient was treated with four cycles of consolidation chemotherapy postoperatively (12 mg/m^2 idarubicin once a day on days 1 and 2, plus 1 g/m^2 cytarabine per half a day on days 1–3) and achieved remission. She was followed up by bone marrow aspiration and breast Doppler ultrasound examinations every 3 months and remained in good health at the 1.5-year follow-up.

**Discussion**

GS is an uncommon extramedullary manifestation of AML that occurs as a consequence of leukemic cell proliferation or migration. Hematopoietic precursor cells divide and differentiate into premature cells, which interact with fibroblasts to promote myeloid metaplasia in many nonhematopoietic tissues.\(^8,10\) AML is the most common and typical inducing and predisposing factor for GS. There have been a growing number of reports of GS (Figure 4), mostly from North America, Europe, East Asia, and South Asia (Figure 5).
The rarity of breast GS means that it is frequently misdiagnosed, most commonly as lymphoma, sarcoma, or breast carcinoma. The clinical findings of GS, including painless and painful palpable breast masses involving unilateral or bilateral breasts, are usually nonspecific, thus increasing the risk of its clinical misdiagnosis as other primary breast cancers. The breast skin may sometimes be involved, and axillary lymph nodes may be observed, while nipple discharge and retraction are not common.11–13 In the current case, an investigation of the patient’s medical history and the

![Figure 2](image_url) Breast ultrasound demonstrated a hypoechoic mass measuring ~3.7×2.6 cm in the superior lateral quadrant of the right breast.

![Figure 3](image_url) Immunohistochemical results for the resected tumor tissue.

**Notes:** (A) Hematoxylin–eosin staining; (B) Myeloperoxidase; (C) CD43; and (D) human leukocyte common antigen. Magnification: 20×.
results of bone marrow aspiration revealed no abnormalities, making a precise clinical diagnosis difficult.

The results of radiological examinations are also not specific for GS. However, if the patient has a medical history of hematological disease, especially granulocytic leukemia, GS must be kept in mind as a potential differential diagnosis. Kirubha et al have reported mammogram features, which include tumors (with or without calcification) of variable sizes, with indistinct and hazy borders. Similarly, ultrasound descriptions of breast GS are rare, though breast GS is generally depicted ultrasonographically as hypoechoic, with speculated or microlobulated margins. Breast GS may show prominent vascularity on color Doppler ultrasonography.

In our case, ultrasound examination revealed two hypoechoic lobulated tumors in the outer upper quadrant of the right breast, with marked vascularity. Magnetic resonance imaging was not employed in the current case, but Thachil et al reported that T2-weighted coronal images might show GS as hyperintense, heterogeneous, ill-defined, multiple masses relative to the breast parenchyma.

Histopathological examination together with immunohistochemical tests is the gold standard for a final diagnosis of GS, conventionally showing different degrees of myeloid differentiation. However, the histopathological characteristics are inconsistent, potentially resulting in misdiagnosis or a missed diagnosis, especially in cases of isolated, low-differentiated GS. GS can easily be misdiagnosed as various other tumors, and breast GS is often confused with infiltrating lobular carcinoma, primary breast sarcoma, Burkitt’s lymphoma, and diffuse large B-cell lymphoma. It is therefore essential to consider GS in the differential diagnosis of breast masses. Immunohistochemical tests, cytogenetic tests, and flow cytometry are useful methods for helping to reduce the misdiagnosis rate, and some molecular
b Biomarkers of GS have been identified, including CD117, CD68, lysozyme, nucleophosmin, FLT3-internal tandem duplication, and the biochemical abnormality t(8;21) inversion.9

Hematologists, oncologists, and surgeons have not yet reached a consensus regarding the optimal treatment strategies for breast GS, although lumpectomy or mastectomy with systemic chemotherapy is generally recommended.20

Imrie et al21 found that patients with breast GS who received chemotherapy had significantly longer overall survival than those without chemotherapy. In the current case, the patient received postoperative systemic chemotherapy and was in good health at the time of her 1.5-year follow-up.

Conclusion
GS of the breast is difficult to diagnose, and it is therefore difficult to make clinical decisions regarding its treatment. Although histological results play an important role in its diagnosis, they can also be confusing, especially in poorly differentiated tumors that closely mimic other neoplasms. The present study indicated that lumpectomy combined with systemic chemotherapy could result in a good outcome for patients with GS of the breast. It is therefore essential to include GS among the possible differential diagnoses for breast masses.

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Disclosure
The authors report no conflicts of interest in this work.

References