DIAGNOSIS IN ONCOLOGY

Arthur Skarin, MD, Consultant Editor

Myeloblastoma (Chloroma) in Leukemia

CASE 1. GRANULOCYTIC SARCOMA (CHLOROMA) OF THE BREAST

A 41-year-old woman was diagnosed with acute myeloblastic leukemia in April 1997. The leukemia was classified as acute myeloblastic leukemia 4 with abnormal eosinophils (French-American-British classification), and both the inversion 16 and the CBF-beta/MYH11 transcript were detected. The initial presentation was associated with hyperleukocytosis, splenomegaly, and specific infiltration of cervical lymph nodes without involvement of the CNS. Complete remission was achieved in May 1997, and the patient received two intensive courses of consolidation chemotherapy. A first marrow relapse occurred in May 1998. A second remission was obtained after treatment with a combination of high-dose cytarabine and idarubicin. Bone marrow transplantation with an HLA-identical sibling donor was performed during the patient's second complete remission.

In December 1999, a palpable breast mass was discovered associated with an enlarged axillary lymph node. The lateral mammogram disclosed a dense, rounded, and spiculated mass of 3 cm in diameter with irregular margins and skin retraction (Fig 1). Ultrasound showed a nonhomogeneous hypoechoic mass, irregular in shape with ill-defined margins and posterior acoustic shadow. A subsequent thoracic abdominal computed tomography scan showed the spiculated mass to contain a small foci of necrosis. The adjacent skin was thickened. No other abnormality was detected. On magnetic resonance imaging

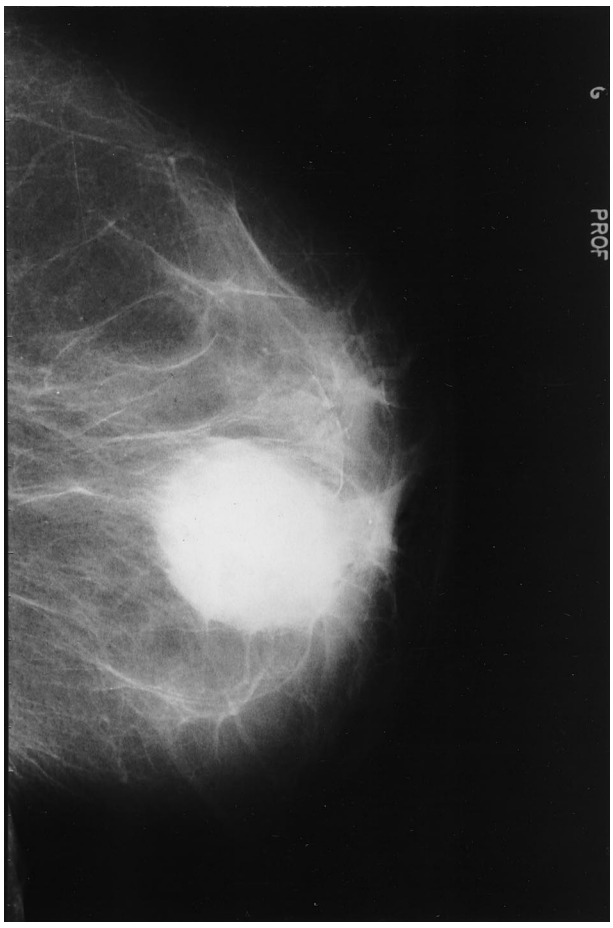

Fig. 1

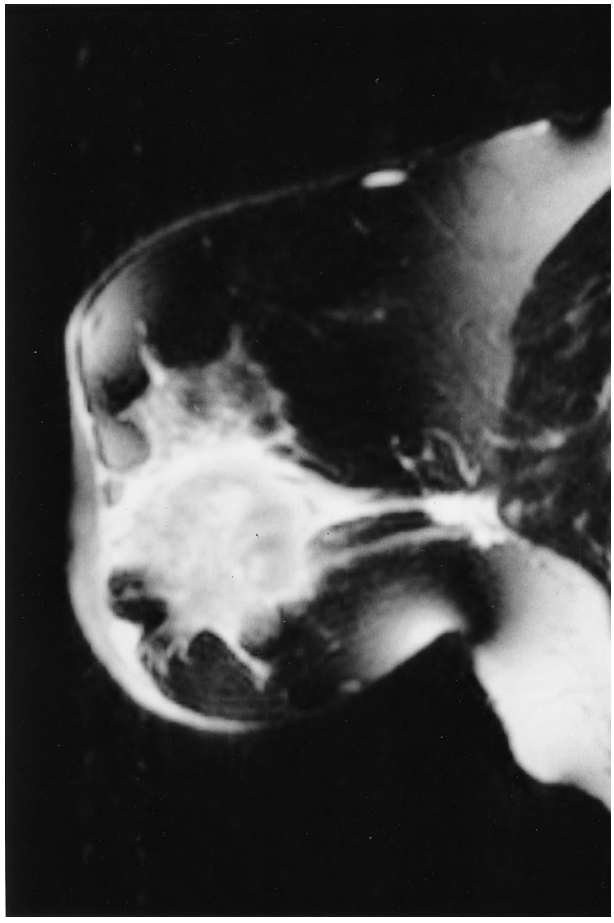

Fig. 2

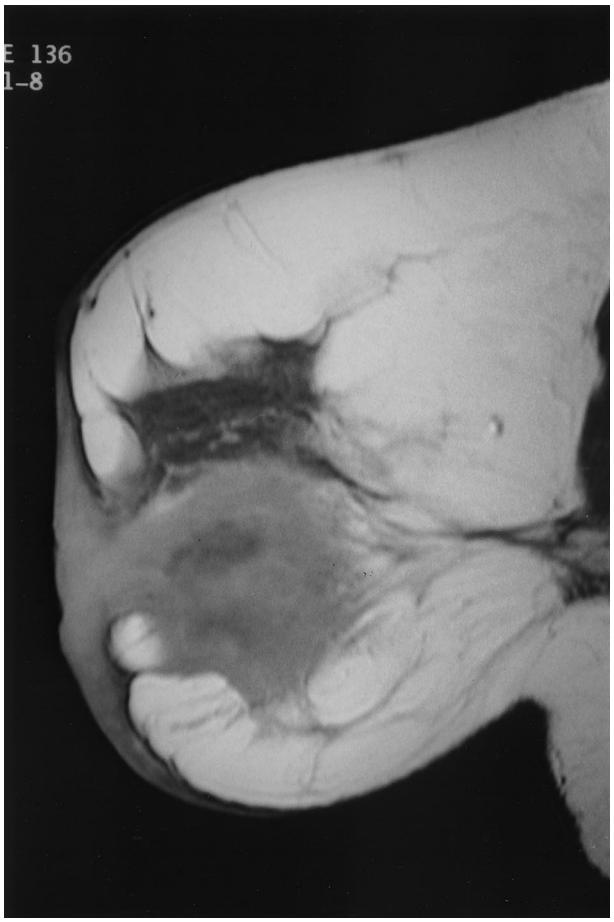

Fig. 3

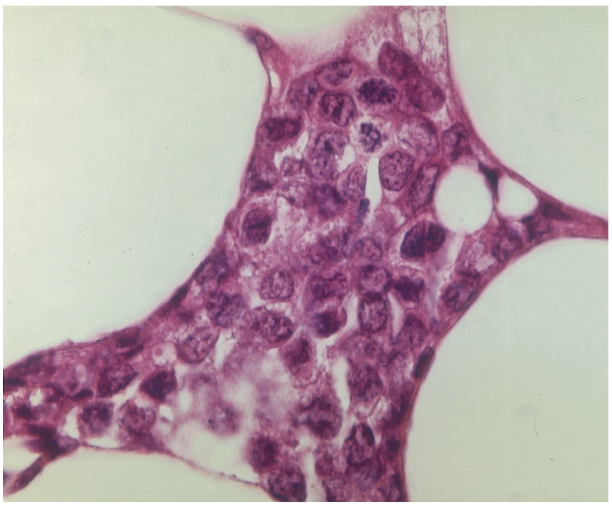

Fig. 4

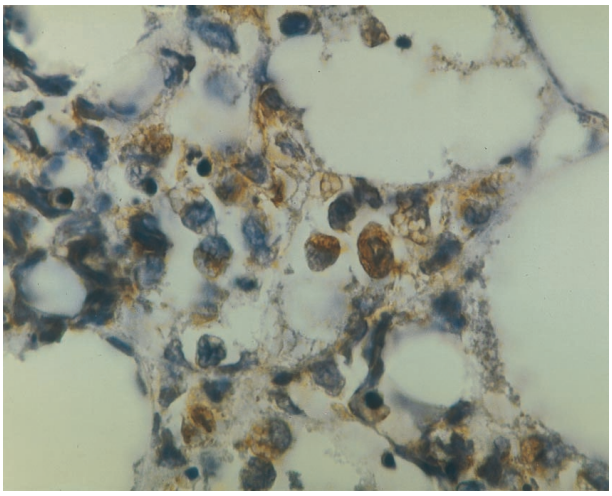

Fig. 5

(MRI), the mass was inhomogeneous and hyperintense on T2-weighted images (Fig 2), hypointense on T1-weighted images, and enhanced strongly but quite inhomogeneously after gadolinium administration (Fig 3). The mass spiculation and skin thickening were also visible. The MRI findings were those of a malignant breast lesion. The fine-needle breast biopsy showed an infiltration of blast cells. The blasts were relatively uniform in appearance, with round or oval nuclei and a moderate amount of cytoplasm (hematoxylin and eosin stain, ×1,000; Fig 4). Myeloperoxidase reaction revealed intracytoplasmic granules (×1,000 magnification; Fig 5). The tumoral cells were also positive for CD45 but negative for the cytokeratins CD20 and CD3. These immature myeloid cells were positively stained with the CBF-beta/MYH11 probe in fluorescence in situ hybridization. The differential WBC count and the results of the bone marrow aspiration were normal, although polymerase chain reaction analysis for the CBF-beta/MYH11 transcript was positive in bone marrow. The peripheral-blood cells were 100% donor. The patient received two courses of high-dose cytarabine (3 g/m^2 every 12 hours on days 1, 3, and 5). Five weeks later, the mass was no longer clinically palpable. A postcontrast T1-weighted MRI scan showed a marked reduction of the tumor size and contrast enhancement (Fig 6).

Chloroma, also called extramedullary myeloblastoma or granulocytic sarcoma, mainly associated with myeloblastic leukemia, is an uncommon malignant tumor that rarely involves the breast.[1] It is essentially a solid tumor composed of granulocyte precursor cells.[2] Chloroma can occur during either leukemia relapse or remission and may be the only presentation of the disease.[3] It may also occasionally occur as a complication in the course of chronic myeloid leukemia or

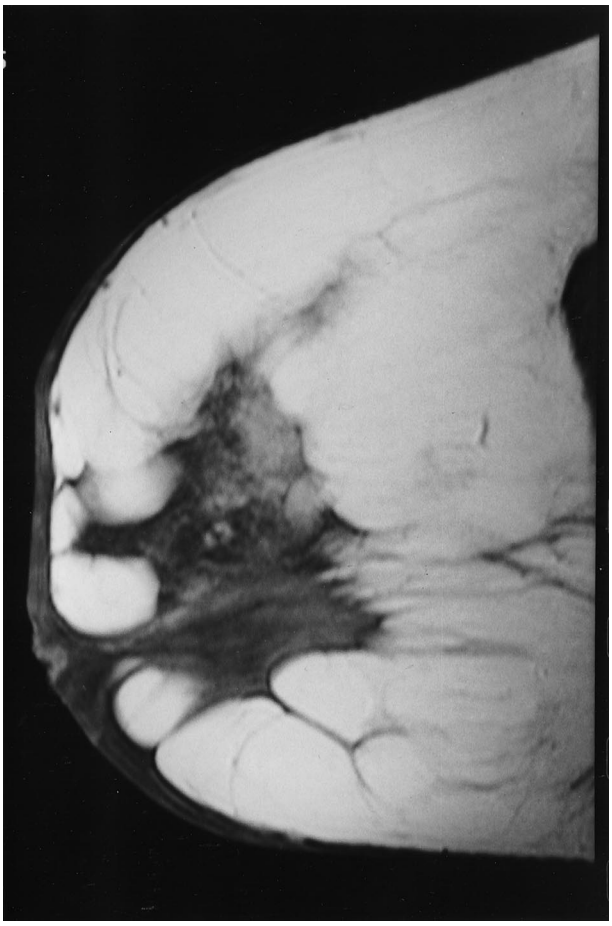

Fig. 6

other myeloproliferative disorders.[4] This lesion has a predilection for the CNS, bones, soft tissues of the head and neck, and skin.[5] However, its presentation in the breast is uncommon and may be misdiagnosed, mainly as a lymphoma or carcinoma, especially in the absence of bone marrow involvement.[4,6] Special stains are necessary for diagnosis.[6] Most cases of breast granulocytic sarcoma are reported in adults and clinically mimic primary breast tumors. Only one case was reported in an adolescent patient.[1] Mammographically, breast chloromas are noncalcified, irregular masses with poorly defined "feathery" margins.[7] Ultrasound shows a large mass, including spiculation, angular margins, and areas of marked low attenuation.[1] In our study, MRI was shown to be an accurate study for detecting and monitoring this lesion after treatment.

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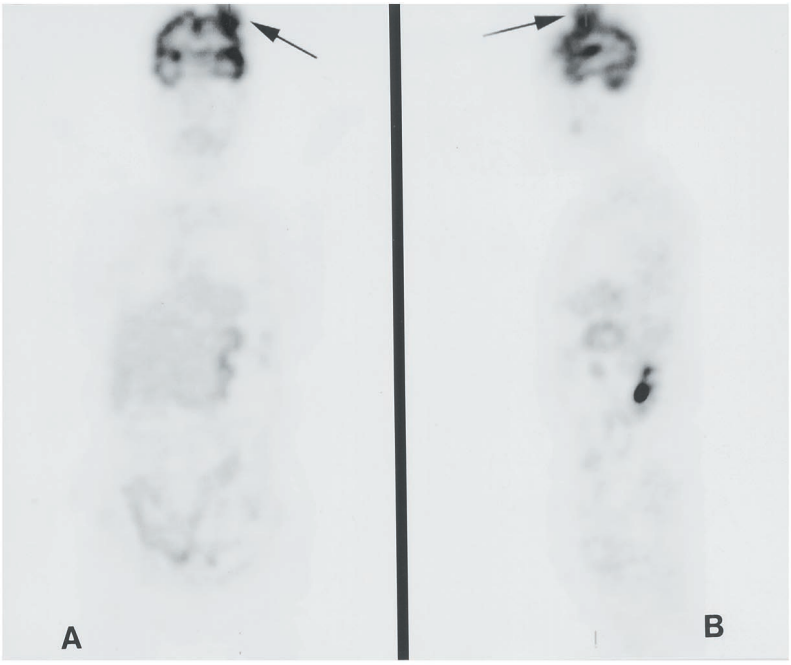
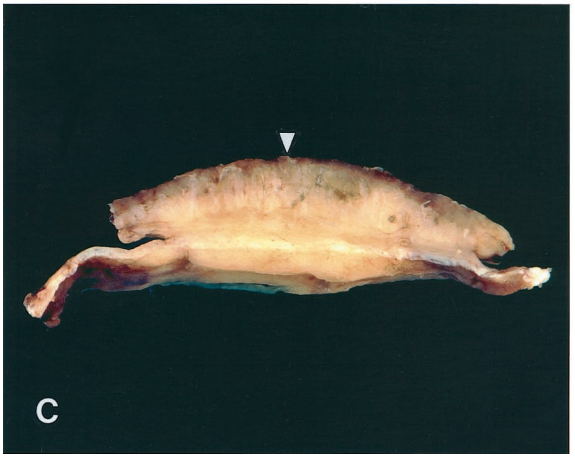
CASE 2. MENINGEAL GRANULOCYTIC SARCOMA (CHLOROMA) IN ESSENTIAL THROMBOCYTHEMIA

A 55-year-old woman presented in 1988 with high platelet counts (hemoglobin level of 16.5 g/dL, WBC count of 16.5 $\times$ 10^9/L, and platelet count of 1,210 $\times$ 10^9/L). A bone marrow biopsy showed features consistent with essential thrombocythemia (ET). Melphalan (4 mg weekly) was given for 7 years, after which it was substituted with hydroxyurea at 0.5 g daily. In 2000, she was admitted with persistent fever, weight loss, and night sweats. Her blood counts showed a hemoglobin level of 9.6 g/dL, WBC count of 6.3 $\times$ 10^9/L, and platelet count of 344 $\times$ 10^9/L. Extensive investigations for





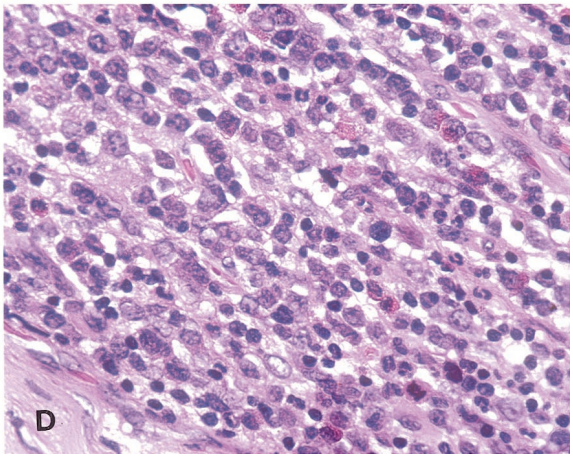


Fig. 1

infections, autoimmune diseases, and malignancies were negative. Because of unremitting fever, a total-body positron emission tomography scan with fluorine-18–labeled glucose was performed, showing a 4-cm hypermetabolic mass in the left parietal bone (Fig 1, A and B). At operation, a greenish tumor (4 cm × 5 cm) straddling the dura and skull bone but sparing the underlying brain tissue was found (Fig 1C). Histologic examination showed a myeloblastoma, also called a chloroma or granulocytic sarcoma (GS), characterized by sheets of leukemic cells intermingled with fibrotic tissue (Fig 1D). The blasts and immature myeloid cells were positive for myeloperoxidase, CD31, and CD34. Cytogenetic analysis showed 47,XX,+der(1;7)(q10;p10),−7,+8[3]/47,XX,+der(1;7)(q10;p10),−7,+12[3]. Molecular testing for *BCR/ABL* was negative. Iliac crest bone marrow examination did not show leukemic infiltration.

ET is a trilineage myeloproliferative disorder characterized by high platelet counts and megakaryocytic hyperplasia. Other reactive or malignant causes, including chronic myelogenous leukemia, must be excluded.[1] Our case was unique in being a GS presenting as persistent fever. Leukemic transformation of ET is rare and mostly therapy-related, with alkylating agents mainly incriminated.[1] Characteristically, alkylating agent–related acute myeloid leukemia (AML)/myelodysplasia is associated karyotypically with –5/5q− and/or –7/7q−.[2] The unbalanced t(1;7)(q10;p10) resulting in monosomy 7q in this case has also been reported in alkylating agent–related myelodysplasia /AML.[3,4] Therefore, our case was most likely a therapy-related AML secondary to melphalan therapy, instead of a transformation de novo. GS is an exceedingly rare complication of ET and, to our knowledge, has only been reported once.[5] Localization of GS may be difficult in clinically occult sites (eg, intracranial and retroperitoneal sites). Our case demonstrated the usefulness of a positron emission tomography scan in localizing extramedullary blastic transformation in myeloproliferative disorder.

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EDITOR'S NOTE

Myeloblastomas are extramedullary tumors of myeloblasts and other immature myeloid cells appearing either green in color (chloroma) or nonpigmented. The green color is related to cytoplasmic myeloperoxidase (verdoperoxidase) and porphyrins, possibly destined originally in a common stem cell for erythroblastic precursors (Muss HB, Moloney WE: Chloroma and other myeloblastic tumors. Blood 42:721-728, 1973). Of note, chloromas are rapidly oxidized to white tumors with exposure to light and air.