A Case of Granulocytic Sarcoma or Extramedullary Acute Myelomonocytic Leukemia of the Gallbladder

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Conflict of interest: None declared

Patient: Female, 74
Final Diagnosis: AML chloroma
Symptoms: Abdominal pain
Medication: —
Clinical Procedure: —
Specialty: Oncology

Objective: Rare disease

Background: Granulocytic sarcoma, or 'chloroma,' due to extramedullary acute myeloid leukemia (AML) or due to acute myelomonocytic leukemia (AML M5), is rare and is associated with a poor prognosis. This report is of a case of granulocytic sarcoma of the gallbladder and describes the approach to diagnosis and treatment.

Case Report: A 74-year-old Hispanic woman from Ecuador presented to the emergency department with a five-day history of fever, jaundice, and right upper quadrant abdominal pain. The right upper quadrant ultrasound showed a thickened gallbladder wall with cholelithiasis, a positive sonographic Murphy sign, and marked dilatation of the common bile duct, which was up to 17 mm in diameter. Endoscopic retrograde cholangiopancreatography (ERCP) showed purulence and a stone in the common bile duct, which was removed. She underwent laparoscopic cholecystectomy which identified gangrenous cholecystitis. Despite cholecystectomy and treatment with broad-spectrum antibiotics, she remained febrile with a leukocytosis of up to 80,000 cells/μL. Histopathology of the gallbladder showed infiltrating myeloblasts within the mucosa, submucosa, and muscularis consistent with a granulocytic sarcoma associated with gangrenous cholecystitis due to cholelithiasis. Immunohistochemistry, using a panel of antibodies to CD33, CD68, HLA-DR, and lysozyme, supported the diagnosis of granulocytic sarcoma or extramedullary acute myelomonocytic leukemia (AML M5).

Conclusions: A rare case of an extramedullary hematologic malignancy, granulocytic sarcoma of the gallbladder is presented, which highlights the importance of timely diagnosis and treatment, due to the high mortality rate associated with granulocytic sarcoma, or extramedullary AML.

MeSH Keywords: Hematologic Neoplasms • Leukemia, Myeloid, Acute • Sarcoma, Myeloid

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/911390

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Background

Granulocytic sarcoma, or extramedullary acute myeloid leukemia (AML), or chloroma, is rare and is associated with a poor prognosis. Granulocytic sarcoma is associated with a worse prognosis than AML. The French–American–British (FAB) hematologic disease classification system classifies acute myelomonocytic leukemia as AML M5 [1,2].

We present an unusually rare case of a 74-year-old woman who presented initially with hepatobiliary sepsis and who was subsequently diagnosed with a primary granulocytic sarcoma of the gallbladder.

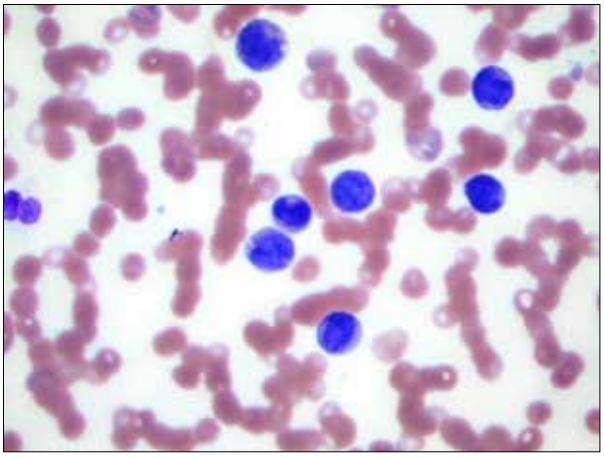

Figure 1. Photomicrograph of the light microscopy of the peripheral blood smear. Light microscopy shows immature and atypical peripheral blood monocytes. Wright-Giemsa stain. Magnification ×1,000.

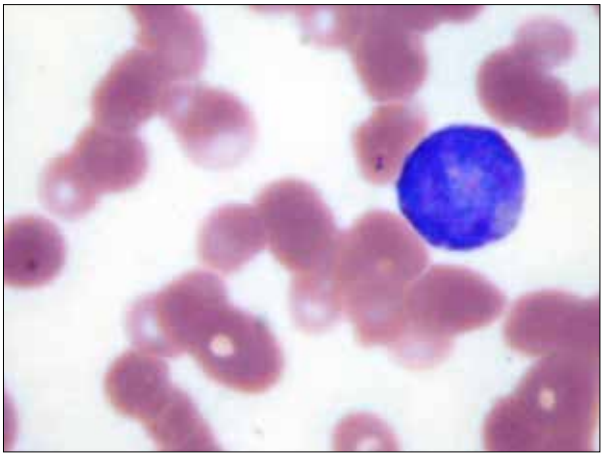

Figure 2. Photomicrograph of the light microscopy of the peripheral blood smear. Light microscopy shows immature and atypical peripheral blood monocytes. Wright-Giemsa stain. Magnification ×1,000.

Case Report

A 74-year-old Hispanic woman from Ecuador with a history of type 2 diabetes mellitus presented to the emergency department with a five-day history of fever, jaundice, and right upper quadrant abdominal pain. She traveled to America from Ecuador five days prior to hospital admission after several months of unintentional weight loss. Her abdominal pain was diffuse, but was most prominent in the right upper quadrant and epigastric region, and was associated with vomiting that did not contain blood or bile. The patient denied symptoms of chest pain, dyspnea, melena, hematochezia, dysuria, and hematuria. She had no history of cigarette, alcohol, or substance abuse, and no family history of cancer

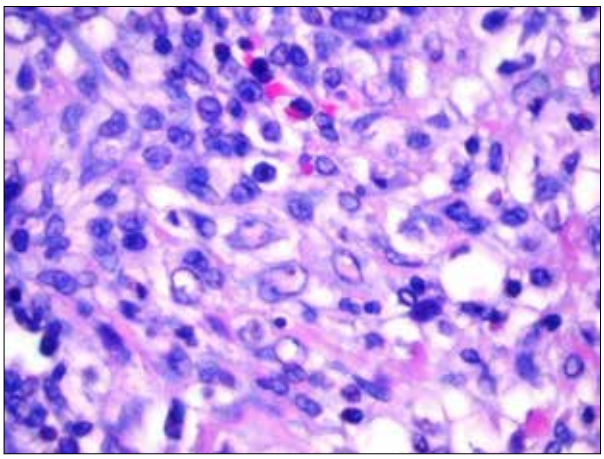

Figure 3. Photomicrograph of the light microscopy of the gallbladder. Light microscopy shows myeloblasts and monocytes in the gallbladder parenchyma. Hematoxylin and eosin (H&E) stain. Magnification ×100.

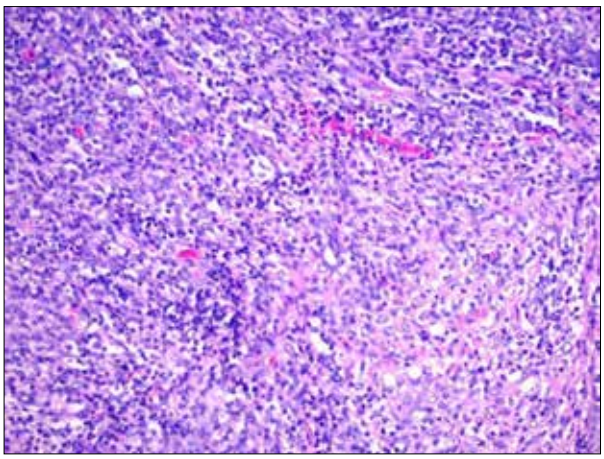

Figure 4. Photomicrograph of the light microscopy of the gallbladder. Light microscopy shows myeloblasts and monocytes in the gallbladder parenchyma. Hematoxylin and eosin (H&E) stain. Magnification ×200.

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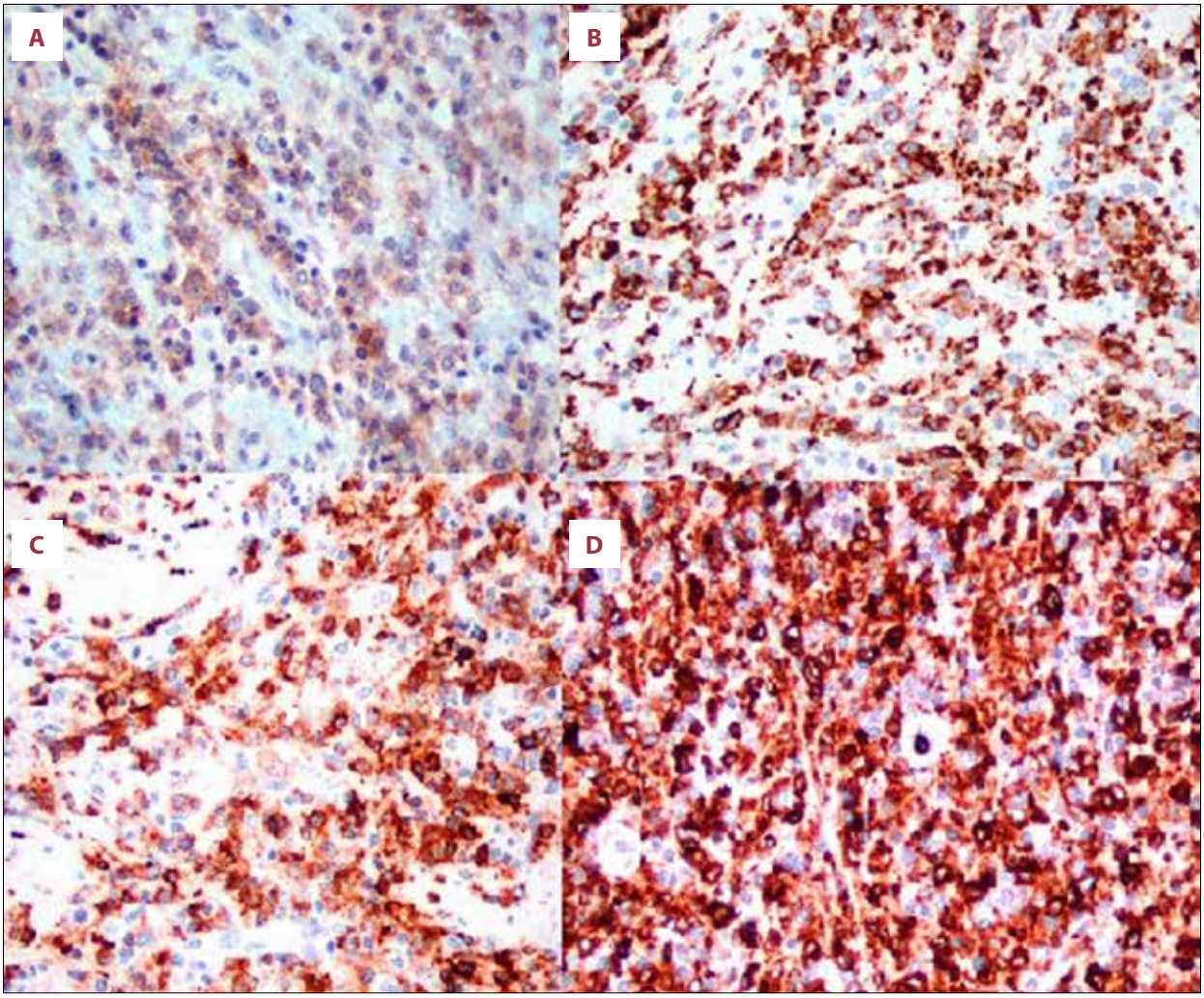

Figure 5. Photomicrograph of the light microscopy of the immunohistochemistry staining of the gallbladder. (**A**) Immunohistochemistry shows cells expressing CD33 (brown). Magnification ×200. (**B**) Immunohistochemistry shows cells expressing CD68 (brown). Magnification ×200. (**C**) Immunohistochemistry shows cells expressing HLA-DR (brown). Magnification ×200. (**D**) Immunohistochemistry shows cells expressing lysozyme (brown). Magnification ×200.

In the emergency department, she was found to have a markedly an elevated serum alkaline phosphatase (ALP) of 800 IU/L, serum creatinine of 3.83 mg/dL, an international normalized ratio (INR) of 1.4, and serum lactate dehydrogenase (LDH) of 471 U/L. A complete blood count (CBC) showed leukocytosis with a predominant monocytosis (17,300 cells/µL), marked thrombocytopenia (10,000/µL), and macrocytic anemia that included hemoglobin (Hb) 9 g/dL, and a mean corpuscular volume (MCV) of 102.4 fL, and no blasts were identified. Because a diagnosis of sepsis was made, she was admitted to the intensive care unit (ICU) and treated with broad-spectrum antibiotics.

Ultrasound imaging of the right upper quadrant showed cholelithiasis and a thickened gallbladder wall with a positive sonographic Murphy sign, or abdominal tenderness during pressure from the ultrasound probe. The common bile duct was dilated, measuring up to 17 mm in diameter. Endoscopic retrograde cholangiopancreatography (ERCP) showed purulence and a stone in the common bile duct, which was removed. A sphincterotomy was not performed due to the presence of thrombocytopenia. However, a plastic stent was placed in the common bile duct.

Due to progressive leukocytosis and continued fevers, she underwent laparoscopic cholecystectomy with the insertion of a Jackson-Pratt drain, which was done without complications. Intraoperatively, the gallbladder appeared gangrenous. She was given 1.8 liters of crystalloid fluid, two units of platelets, and one unit of irradiated packed red blood cells (PRBCs) during surgery. Despite cholecystectomy and the use of broad-spectrum antibiotics, she continued to have a fever and progressive leukocytosis of up to 80,000 cells/µL. Her condition

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deteriorated, with a clinical appearance of sepsis. At the request of her family, active treatment was discontinued, and she was made as comfortable as possible.

Histopathology of the gallbladder showed myeloblasts, promyelocytes, and myelocytes within the mucosa, submucosa, and muscularis, consistent with a granulocytic sarcoma (Figures 1–4). Immunohistochemistry showed that the neoplastic cells were positive for the expression of lysozyme, CD68, CD33, and HLA-DR (Figure 5). Subsets of the malignant cells were also positive for the expression of CD117, myeloperoxidase, and CD56, but negative for CD34, consistent with acute myelomonocytic leukemia (AML M5)

Discussion

Granulocytic sarcoma, or chloroma, are both terms used to describe an extramedullary tumor occurring in soft tissue or bone with the presence of atypical myeloid or monocytic blast cells [1,2]. Granulocytic sarcomas are extramedullary manifestations of acute myeloid leukemia (AML). The term 'chloroma' was first used in 1853 and refers to the sometimes green coloration of the tumor [2]. The t(8;21) karyotype is associated with AML solid tumors [3], but was not identified in this case. Granulocytic sarcoma may present as a sign of leukemic relapse in patients who have been previously diagnosed with AML, or who may not have received prior therapy, or as a *de novo* diagnosis in the absence of any previous pathology [4].

Granulocytic sarcoma at any site is a rare occurrence, with a reported incidence of between 2.5–9.1% in patients with preexisting AML [5]. Granulocytic sarcoma usually occurs in the bone, skin, and lymph nodes [6]. The gastrointestinal (GI) tract is an extremely rare anatomical site for the involvement of granulocytic sarcoma. Due to this rarity, the exact frequency of involvement of the GI tract is relatively unknown, as there have been few previously reported cases of GI granulocytic sarcoma. One of these cases involved the small intestine, mesentery, and mesenteric lymph nodes in a 25-year-old man [7]. Another case report was that of a 64-year-old woman with known AML who was diagnosed with a granulocytic sarcoma of the gallbladder, 20 days after receiving chemotherapy [8]. These previous case reports highlight the two distinctive features of the present case report, the rare anatomical location in the gallbladder, and the *de novo* diagnosis.

Patient symptomatology in any GI-based granulocytic sarcoma may vary and is based on location. In this case report, the patient presented with acute cholecystitis and cholangitis. A temporal and causal relationship between the patient's clinical presentation and granulocytic sarcoma could only be established once histopathology and immunohistochemistry confirmed the presence of atypical myelomonocytic blasts in the gallbladder. In the French–American–British (FAB) classification system of hematologic disease, the presence of monocytic blasts demonstrated by immunohistochemistry in the cell infiltrates of the gallbladder wall confirmed the diagnosis of granulocytic sarcoma or extramedullary acute myelomonocytic leukemia (AML M5) [8]. Further clinical studies are required to determine the optimal treatment modalities specifically for GI-based granulocytic sarcoma.

Conclusions

This report is of a case of an exceedingly rare presentation of a hematologic malignancy, granulocytic sarcoma, or extramedullary acute myeloid leukemia (AML), also known as chloroma, in the gallbladder. A combined diagnostic strategy, including imaging, endoscopic retrograde cholangiopancreatography (ERCP), histopathology, immunohistochemistry, and laboratory investigations were required to confirm the diagnosis of granulocytic sarcoma of the gallbladder. Timely diagnosis is essential, so that appropriate treatment with chemotherapy can begin as soon as possible, as granulocytic sarcoma has a high mortality rate.

Acknowledgments

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Department and Institution where work was done

The Department of Medicine, UMass Memorial Medical Center, the Department of Pathology, Milford Regional Medical Center, and the Department of Pulmonary Critical Care Medicine, Milford Regional Medical Center.

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