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CASE REPORT

# A case report of myeloid sarcoma of the gastrointestinal system

**Jing Zhou · Corrado Minimo · Manjula Balasubramanian**

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**Abstract** Myeloid sarcoma is a tumor mass of myeloblasts or immature myeloid cells occurring in an extramedullary site. The clinical presentation of myeloid sarcoma varies, and many organs or tissues can be involved. Myeloid sarcoma may be found in patients with acute myeloid leukemia (AML), myelodysplastic syndromes (MDS), myeloproliferative neoplasm (MPN), or without any history. Morphologically, these cells may appear like myeloblasts, promyelocytes, or more mature granulocytes. Cytochemical and immunohistochemical stains are extremely important to make the right diagnosis. We report here a case of myeloid sarcoma in an unusual site in an 80-year-old male, without history of AML, MDS, or MPN. The patient presented with perigastric mass and numerous tumor nodules in the liver, mesentery, and omentum. His bone marrow was reactive, without evidence of AML, MDS, or MPN. The tumor masses were proven to be myeloid sarcoma by immunohistochemical stains (positive for CD34, CD68, and lysozyme) and cytogenetic studies.

**Keywords** Myeloid sarcoma · Gastrointestinal system · Myeloblasts

J. Zhou (✉)
Department of Pathology and Laboratory Medicine,
Pennsylvania Hospital, University of Pennsylvania Health System,
800 Spruce Street,
Philadelphia, PA 19107, USA
e-mail: jing.zhou@uphs.upenn.edu

C. Minimo · M. Balasubramanian
Department of Pathology and Laboratory Medicine,
Albert Einstein Medical Center,
5501 Old York Road,
Philadelphia, PA 19141, USA

## Case report

An 80-year-old African-American man was admitted to the hospital with a recent onset of coffee colored emesis and 2 weeks of diffuse, crampy abdominal pain. His past medical history included diabetes mellitus, hypertension, and coronary artery disease. Physical examinations showed normal vital signs with a soft, nontender and distended abdomen. Laboratory tests showed WBC $15.5\times10^3/\mu L$, 86 % neutrophil, Hgb 15.0 g/dL, and Plt $494\times10^3/\mu L$. Examination of the peripheral smear revealed no blasts. Esophagogastroduodenoscopy showed a large gastric mass. A CT scan (Fig. 1) revealed a dilated stomach with significant wall thickening in the mid-body and antrum, which was almost mass-like in appearance, measuring $7.7\times4.5\times4.0$ cm; moderate amount of abdominal and pelvic ascites; peritoneal carcinomatosis; and small noncystic lesions throughout the liver. Paracentesis was performed and revealed cloudy yellow fluid. The WBC was 226/mL. A differential count showed polymorphonuclear cells 24 %, lymphocytes 24 %, monocytes 50 %, and mesothelial cells 14/mL. No blasts were seen. Ascite fluid flow cytometry and peripheral blood flow cytometry studies were negative for leukemia. Gastric brushings showed degenerated atypical cells. Biopsy of the gastric mass demonstrated a poorly differentiated malignant neoplasm (Fig. 2a), positive for CD34 (Fig. 2b) and CD68 (Fig. 2c) on immunohistochemical staining, and negative for AE1/3, CK7, Cam5.2, 34betaE12, CK20, p63, epithelial membrane antigen, CD117, myeloperoxidase (MPO), CD45/LCA, PAX5, TdT, S100, Melan-A, B72.3, HBME1, calretinin, chromogranin, synaptophysin, nonspecific esterase (NSE), muscle-specific antigen, and mucicarmine (not shown). The patient continued to deteriorate before therapy could be instituted

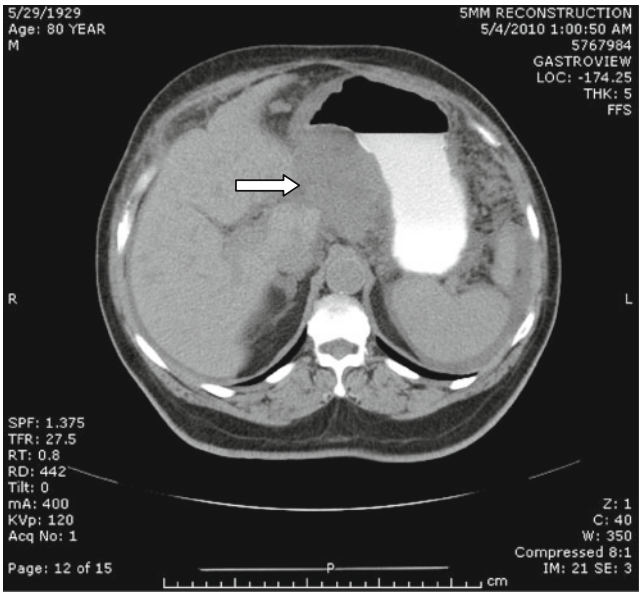


**Fig. 1** CT scan of the abdomen shows a perigastric mass (*white arrow*)

and was found unresponsive and was pronounced dead within 2 weeks of admission into hospital.

## Pathological findings

### Gross examination

At autopsy, the stomach was dilated. There was an ill-defined, tan/yellow-colored, and firm perigastric mass (10×6×3.5 cm), located behind the mid-body and antrum. The gastric mucosa adherent to the mass was dark red in color, with irregular infiltration by the mass. The liver weighed 1,440 g with innumerable 0.5- to 2-cm tan/white firm nodules throughout the entire liver. Several tan/white firm nodular lesions were also identified in the peripancreatic adipose tissue. The entire mesentery and omentum was studded with innumerable tan/white-colored firm nodular lesions. Some nodules were adherent to the serosal surface of the small and large intestines. The brain and heart did not have tumor present.

Therefore, the postmortem examination showed dramatic tumor volume, including the omentum, mesentery, liver, stomach, and diaphragm. The patient was at the terminal stage of the cancer. The wide involvement of multiple organs might alter the metabolism, which could be the possible cause of the death. The additional findings with bilateral pulmonary thrombi of secondary artery branches would also contribute to the rapid deterioration.

### Microscopic examination of the tumor

Examination of the tumor revealed a diffuse proliferation of undifferentiated single cells without any specific architectural pattern (Fig. 3a). The tumor cells were polyhedral with a high nuclear/cytoplasmic ratio. The nuclei were round, ovoid to irregular with indentation of nuclear membrane, vesicular or open chromatin pattern and prominent eosinophilic nucleoli (Fig. 3b). The cytoplasm, when visible, was slightly eosinophilic and finely granular.

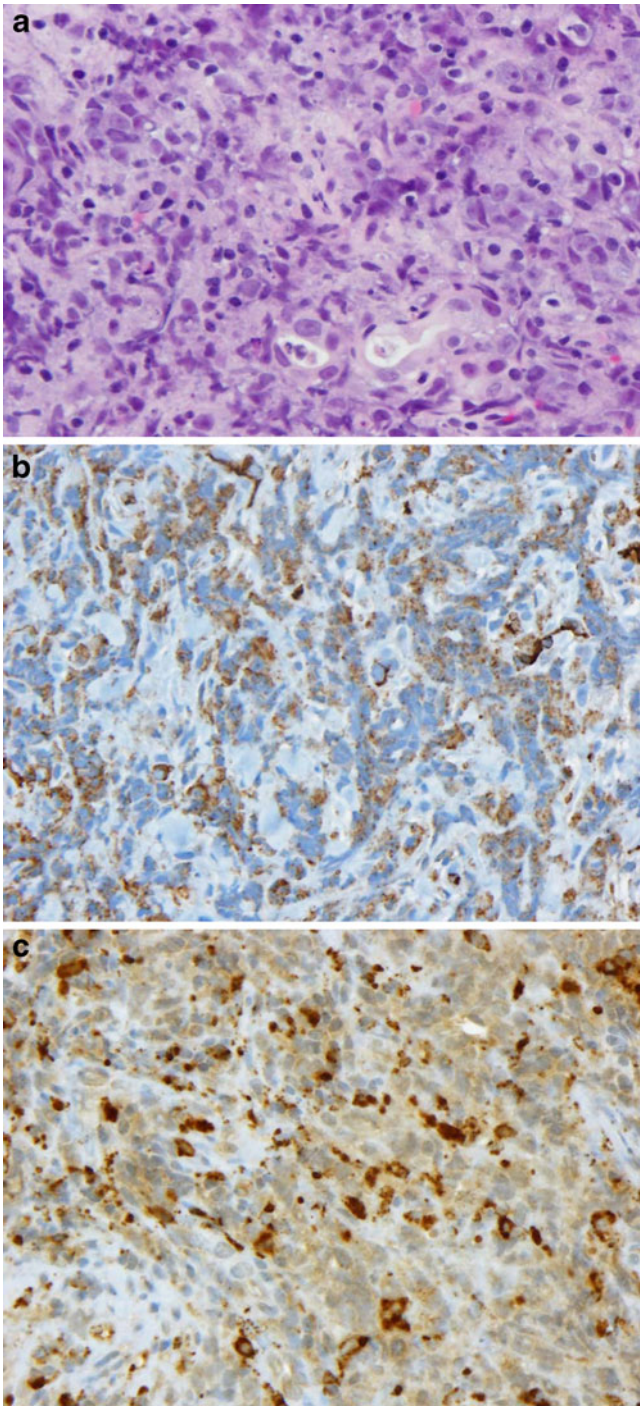


**Fig. 2** Gastric biopsy. **a** H&E (×400). **b** CD34 (×400) immunostain is positive. **c** CD68 (×400) immunostain is positive

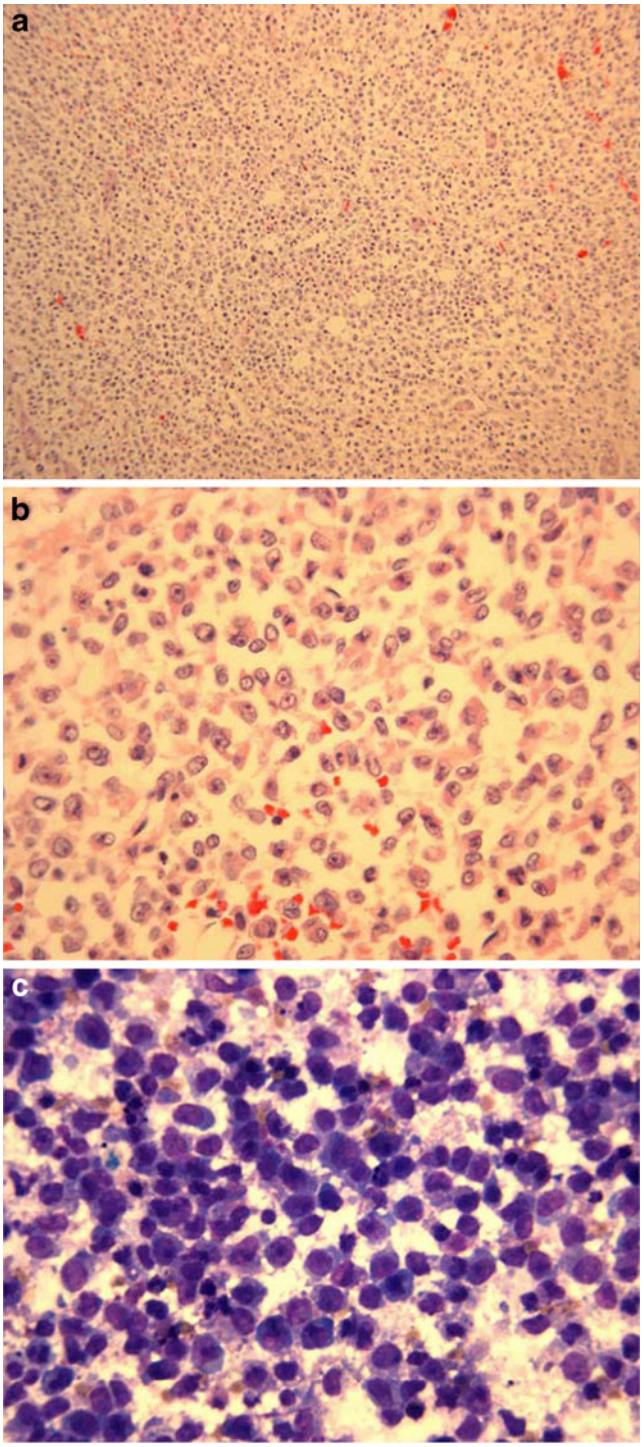


**Fig. 3** Myeloid sarcoma involving the liver. **a** Sheets of tumor cells and no architecture identified (H&E, ×200). **b** Intermediate to large cells with high nuclear/cytoplasmic ratio, ovoid to irregular indentation of nuclear membrane, vesicular or open chromatin pattern, and prominent eosinophilic nucleoli (H&E, ×400). **c** Touch preparation cytology of tumor cells showing sheets of medium to large cells with round to oval nuclei with some nuclear folding and prominent nucleoli (×400)

A touch preparation performed during autopsy showed sheets of very discohesive cells, medium to large in size, with high nuclear/cytoplasmic ratio. The nuclei were round to oval with some nuclear folding and prominent nucleoli. Some cells showed a perinuclear hof (Fig. 3c).

Morphologically, these cells showed features compatible with hematopoietic tumor, stromal tumor, or melanoma. The mode of presentation and spread was not characteristic for stromal tumor. Melanoma markers were negative (see "Immunohistochemistry").

### Immunohistochemistry

Immunohistochemical studies were performed on the liver nodule, mesentery nodule, and bone marrow sections, with adequate positive and negative controls. The tumor cells were positive for CD34 (Fig. 4a), CD68/KP1 (Fig. 4b), and lysozyme (Fig. 4c) and negative for AE1/3, S100, CD45/LCA, CD117, DOG1, MPO, CD99, CD3, CD4, TdT, and Leder (naphthol-AS-D-chloracetate-esterase, CAE) stain (not shown).

The immunohistochemical results were not specific for myeloid lineage. Nonreactivity for MPO and CD117 does not allow a definitive identification of these cells as of myeloid lineage; however, the positivity for CD34 and CD68 along with the morphologic impression indicated that these cells may be very immature forms of a myelomonocytic lineage. CD117 and DOG1 were negative indicating that the tumor was not a gastrointestinal stromal tumor. Melanoma markers were negative.

Sections of the bone marrow showed a markedly hypercellular bone marrow with trilineage hematopoiesis. In the bone marrow, the MPO stain highlighted myeloid lineage, negative for CD34 and CD68.

### Genetic studies

Fluorescent in situ hybridization studies of the lesion revealed monosomy 5, monosomy 7, monosomy 11, and deletion of chromosome 17p; these alterations have been reported in acute myeloid leukemia and related precursor neoplasms.

## Discussion

Myeloid sarcoma, also known as chloroma, extramedullary myeloid tumor, or granulocytic sarcoma, is a tumor mass consisting of myeloid blasts with or without maturation occurring at an anatomical site other than bone marrow [1]. Myeloid sarcomas were initially termed "chloroma" in the early nineteenth century. The name chloroma came from the green hue of the lesion because of high levels of myeloperoxidase in the myeloid cells. The green color disappears when the tumor is exposed to air. The name later was changed to granulocytic sarcoma, since not all chloromas

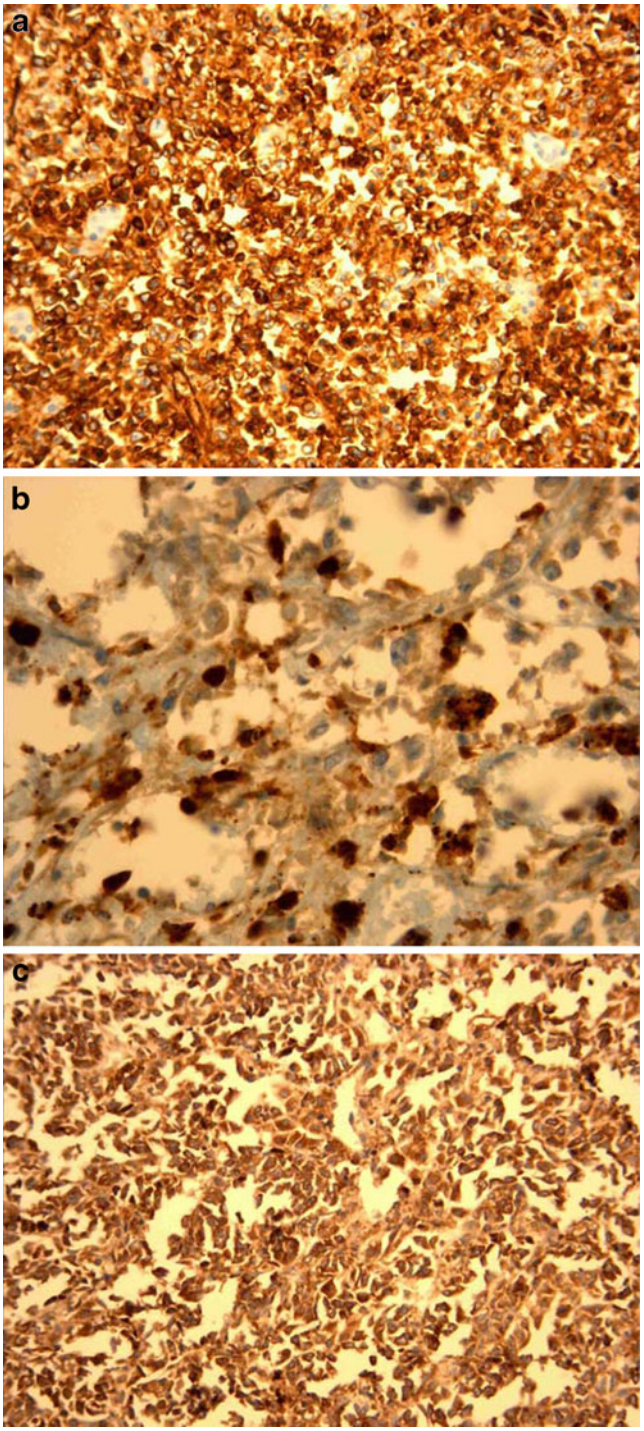


**Fig. 4** Immunohistochemistry. **a** CD34 immunostain is positive (CD34, ×200). **b** CD68 immunostain is positive (CD68, ×400). **c** Lysozyme immunostain is positive (lysozyme, ×200)

were green or had the gross features of a sarcoma. The current WHO term is myeloid sarcoma, since not all myeloid leukemias are derived from granulocytes. The median age is 56 years (range from 1 month to 89 years) with male-to-female ratio of 1.2:1, and it presents in 2–8 % of acute myeloid leukemia (AML) cases [1].

The clinical presentation of myeloid sarcoma varies and is dependent on the site of involvement. Any body site can be involved, including the skin, lymph nodes, gastrointestinal tract, bone, soft tissue, testis, and paranasal sinuses with the skin being the most common site [1]. A single tumor or sometimes multiple nodular masses of various sizes may occur. The gastrointestinal tract is a relatively common location for myeloid sarcoma [2]. Symptoms include abdominal pain, nausea, vomiting, weight loss, fever, and gastrointestinal bleeding. The most frequently involved region of the gastrointestinal tract is the small intestine (10–11 %) [2]. Other regions of the gastrointestinal tract that have been reported to be involved are the stomach and the large intestine, including two cases involving adenomatous polyps. Only four cases involving the appendix have been identified.

Myeloid sarcomas can be seen in four settings: (1) with concurrent myeloid disease (including AML, myelodysplastic syndromes (MDS), myeloproliferative neoplasm (MPN), or MDS/MPN), (2) with prior history of myeloid neoplasm, (3) relapse after induction or transplantation, and (4) de novo in healthy subjects, in whom a typical form of AML may occur after an interval of weeks, months, or even years, or rarely no leukemia develops. The presence of myeloid sarcoma is diagnostic of AML, regardless of the bone marrow or blood status [1]. It is more common in pediatric AML, with approximately 10 % of cases [3].

Grossly the neoplastic tissue appears firm with a fish-flesh cut surface. Larger tumors may contain necrotic and hemorrhagic areas [4, 5]. Microscopically, there is a diffuse monotonous infiltrate that usually destroy underlying normal structures. The blast cells are usually medium to large sized, pleomorphic, with irregular nuclear membranes, and medium-sized or large centrally located nucleoli and finely dispersed chromatin. The cytoplasm is scant to moderate and variably eosinophilic. The mitotic count may be high. There may be apoptotic bodies phagocytosed by histiocytes (tingible body macrophages) that might show a starry sky appearance.

The best way to see the morphology of the blasts is by using Giemsa or Wright/Giemsa stains on imprints. Cytochemical stains including NSE stains can be performed to identify the monocytic differentiation. MPO and CAE are helpful to identify the myeloid lineage. CAE (Leder) stain can be performed on paraffin-embedded tissue sections to show granulocytic differentiation.

Currently, the definitive diagnosis for myeloid sarcoma is based on immunohistochemistry [1]. CK68/KP1 is regarded as the most common marker [6]. The other immunohistochemical stains include MPO and lysozyme. MPO immunostain is positive in most myeloblastic and some myelomonocytic variants. Lysozyme is frequently expressed in monoblastic variants, as seen in our case. CD68/PGM1 is

more specific for the monocytic variants. CD45 expression demonstrates the leukocytic origin of the neoplastic cells; however, it is often not expressed. Megakaryoblastic cells are characterized by the expression of factor VIII, CD61, and CD31. Undifferentiated blasts may be positive for CD13, CD33, CD34, CD117 (c-Kit), or CD99. TdT is usually negative. Sometimes expression of aberrant markers such as B cell-, T cell-, or natural killer (NK)-associated antigens including CD30 may be seen [6, 7]. Expression with CD43 and without coexpression of CD3 should always prompt consideration of a myeloid tumor, instead of being interpreted as a neoplasm of T cell origin. The use of only four antibodies (MPO, CD68, lysozyme, and CD34) has been proposed to distinguish the more common variants of myeloid sarcomas [8]. A study of 92 cases showed CD68/KP1 reactivity in 100 %; CD117, 80.4 %; MPO, 83.6 %; CD99, 54.3 %; and CD34, 43.4 % [6]. A very recent study demonstrated that lysozyme, CD68, and CD43 have the highest sensitivity yet are nonspecific; use of more specific markers of myeloid disease, such as CD33, myeloperoxidase, CD34, and CD117, is necessary to establish the diagnosis [9].

Myeloid sarcoma has been found to occur in association with a variety of chromosomal abnormalities, including *MLL* rearrangement and t(8;21). The most frequent chromosomal abnormality associated with myeloid sarcomas is t(8;21)(q22;q22), an abnormality that it shares with some AMLs, especially in pediatric cases. Other abnormalities include monosomy 7, trisomy 8, monosomy 16, 16q-, 5q-, 20q-, and trisomy11 [6, 9]. About 15 % of cases carry nucleophosmin (NPM) mutations, as shown by aberrant cytoplasmic NPM expression [10].

The diagnosis of myeloid sarcoma may be difficult especially in patients without previous history of AML, MDS, or MPN and is dependent on cytochemical and/or immunophenotypic analysis [5, 9]. The differential diagnosis includes non-Hodgkin lymphoma (including precursor B or T cell, Burkitt, some peripheral NK/T cell, and diffuse large B cell lymphomas), small round cell tumors (including neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, peripheral neuroectodermal tumor, and medulloblastoma), undifferentiated carcinoma or melanoma, histiocytic sarcoma, and malignant mastocytosis with atypical mast cells. Extramedullary localizations of chronic myeloproliferative diseases without blast crisis should also be differentiated from myeloid sarcoma. Histiocytic sarcoma is a tumor comprising a diffuse noncohesive proliferation of large cells. The tumor cells are large and round to oval in shape, with abundant and vacuolated cytoplasm. Immunohistochemical stainings show positivity for CD163, CD68, and lysozyme, with negativity for myeloid markers. Histiocytic sarcoma rarely shows antigen receptor gene rearrangements. The other rare cytogenetic finding is isochromosome 12p in histiocytic sarcoma arising in mediastinal germ cell tumor.

The current treatment for myeloid sarcoma is similar to that for AML, including isolated tumors with no blood or bone marrow involvement. Radiotherapy and chemotherapy for patients with massive tumors or for patients with spinal cord compression have been used. Unfortunately, according to ClinicalTrials.gov, there are no active trials for myeloid sarcoma therapy at present, which is likely due to the rare incidence of this disease.

The progression of myeloid sarcoma in patients with AML has the same prognosis as the underlying leukemia. Patients with an AML associated with a t(8;21) and presenting with myeloid sarcoma have a low rate of complete remission, and overall survival is poor [11, 12], in contrast to the better prognosis generally seen in AML with t(8; 21). It was also reported that myeloid sarcoma with monoblastic/myelomonocytic differentiation, distinctive phenotypic profile, and chromosomal aberrations other than t(8;21) requires supramaximal therapy [6, 12]. The clinical behavior and response to therapy seem not to be influenced by any of the following factors: age, sex, anatomic site, de novo presentation or clinical history, histotype, phenotype, or cytogenetic findings. Patients who have allogenic or autologous bone marrow transplantation seem to have a higher probability of prolonged survival or cure [6, 12].

In summary, the case we present here is an unusual presentation of de novo myeloid sarcoma in an uncommon location, with monoblastic/myelomonocytic differentiation, and a unique immunophenotype.

**Conflict of interest** The authors declare that they have no conflict of interest.

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