

## Single Case

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# Myeloid Sarcoma Presenting as Obstructive Jaundice

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## Keywords

Primary myeloid sarcoma · Gastrointestinal myeloid sarcoma · Obstructive jaundice

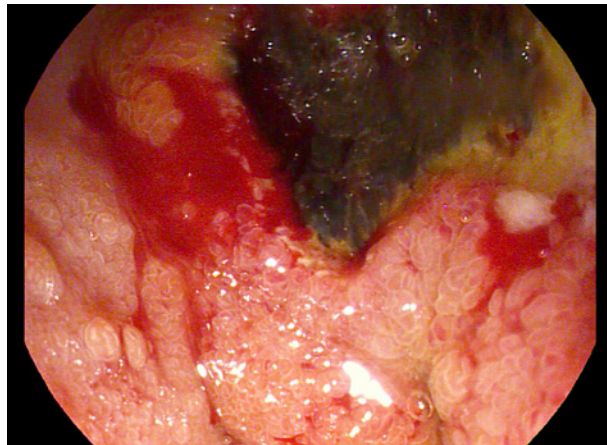
## Abstract

Myeloid sarcoma (MS) is a rare solid neoplasm that consists of extramedullary myeloid precursor cells. Generally, it is associated with underlying acute myeloid leukemia (AML) or AML yet to manifest clinically. It can present as isolated, also known as primary MS without evidence of AML or other myeloproliferative neoplasms. We present the case of a previously healthy 36-year-old male, who was admitted to hospital with new-onset painful obstructive jaundice and final diagnosis of isolated MS was made after through investigations. We are pleased to report that he had favorable response to the treatment and remains well.

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## Introduction

Myeloid sarcoma (MS) is a tumor mass composed of myeloid precursor cells that infiltrates tissues outside of the bone marrow. Typically, MS presents concurrently with acute myeloid leukemia (AML), relapse from prior AML, or as a harbinger of AML yet to come [1]. Isolated or primary MS, defined as the presence of an extramedullary myeloblastic tumor without evidence of AML on the peripheral blood smear or bone marrow biopsy, is a rare occurrence. A retrospective study of 497 AML patients found an incidence of 1.8% for isolated MS [2]. The diagnosis of MS is based on histopathology. MS has previously been known as chloroma due to the green color that is attributed to the expression of the enzyme myeloperoxidase (MPO). The most commonly expressed markers for MS are CD68/KP1, MPO, and CD117 [3]. MS is often misdiagnosed as malignant lymphoproliferative disorders, including



**Fig. 1.** Necrotic appearing ulcer with heaped up edges surrounded by the friable irregular tissue within the duodenal bulb.

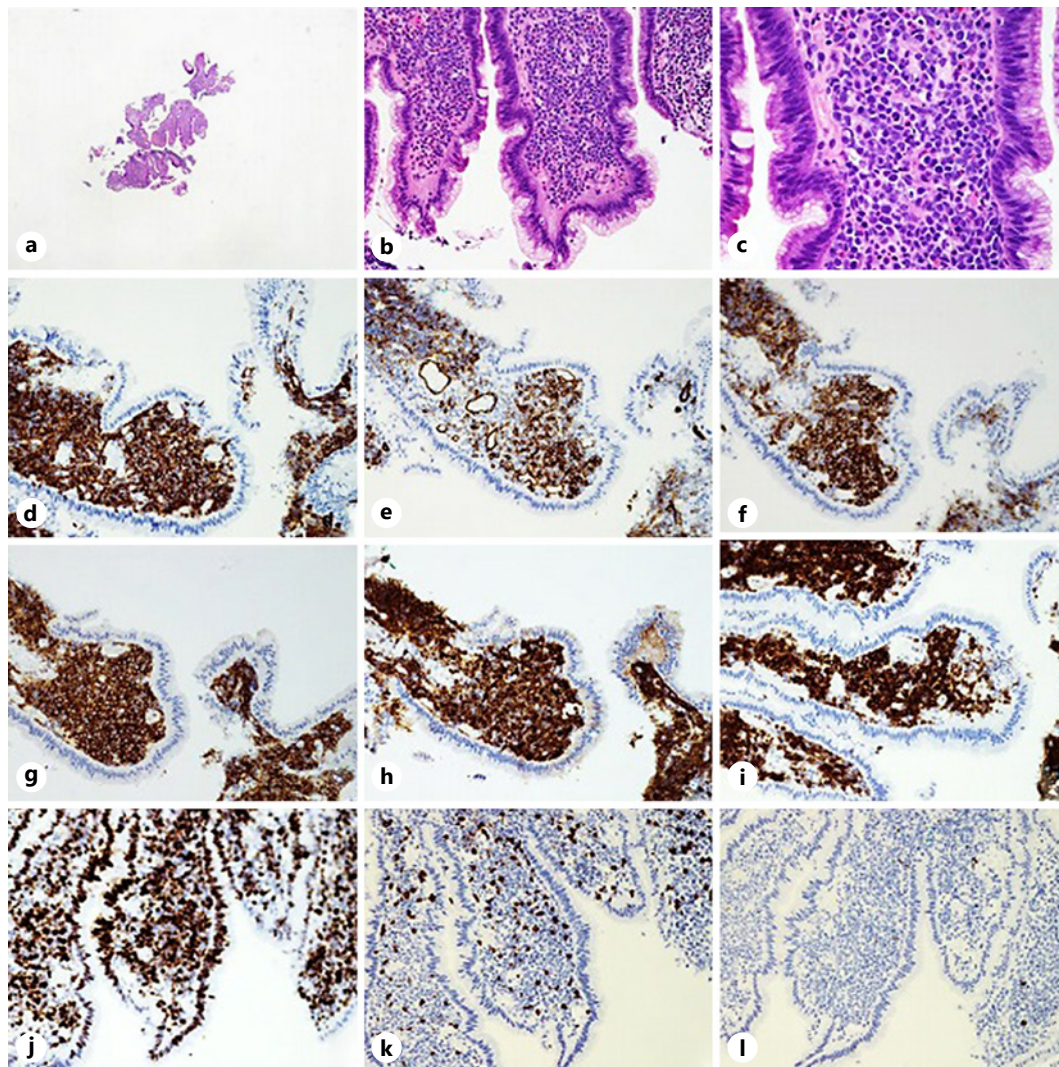
non-Hodgkin lymphomas, histiocytic lymphoma, thymoma, plasma cell myeloma, eosinophilic sarcoma, Ewing sarcoma, and carcinoma [4].

Primary MS may develop in any site of the body. It is typically reported to occur in the skin, peritoneum, bone, or lymph nodes but also infrequently develops within the gastrointestinal (GI) tract [5]. We present the case of a previously healthy 36-year-old male who presented with obstructive jaundice and later found to have primary MS isolated to the duodenum.

### Case Report

A previously healthy 36-year-old male presented with 1-month history of intermittent right upper quadrant and epigastric pain, associated with postprandial nausea and vomiting. Physical exam revealed scleral icterus and jaundice. His initial vitals were stable with a temperature of 36.9°C, heart rate of 79, blood pressure of 142/88, and O<sub>2</sub> saturation of 95% on room air. The abdomen was soft, non-tender, and negative for Murphy's sign. Initial blood work revealed normal CBC. Alkaline phosphatase was elevated at 260 U/L, alanine aminotransferase 119 U/L, aspartate aminotransferase 63 U/L, gamma glutamyltransferase 342 U/L, and a bilirubin of 167 μmol/L.

An abdominal ultrasound revealed gallbladder sludge, common bile duct dilation at 1.4 cm and 2 filling defects measuring 7 and 8 mm in size. Gastroscopy (EGD) revealed a moderate size clean-base ulcer in the duodenal bulb (Fig. 1). Furthermore, a cholangiogram revealed a distal common bile duct (CBD) structure measuring 2–2.5 cm. Sphincterotomy was performed and a 9-mm CBD stent was placed. Cytology from the CBD brushings was negative. Carcinoembryonic antigen was 3.1 μg/L (normal 0.0–5.0 μg/L) and carbohydrate antigen 19-9 was 24.0 kU/L (normal 0.0–35 kU/L). Biopsy of the duodenal ulcer showed duodenal mucosa with diffused infiltrates of medium-sized immature appearing cells and mixed with scattered few eosinophils. Immunohistochemistry demonstrated atypical cells positive for CD45, CD34, CD117, CD33, MPO, and BCL2, while negative for all the lymphoid markers, including CD163, CD68, TdT, and CD56. The immunophenotype confirmed the presence of myeloblasts. In conjunction with their high proliferation index, a diagnosis of “duodenal mucosa with proliferation of myeloblasts compatible with myeloid sarcoma versus duodenal mucosal involvement by AML” was rendered (Fig. 2). Subsequent left iliac crest bone marrow examination revealed normocellular marrow without evidence of myeloid neoplasms or acute leukemia (Fig. 3). The concurrent peripheral blood smear did not reveal any blasts. The bone marrow cytogenetics study showed normal karyotyping. The next generation sequencing study attempted

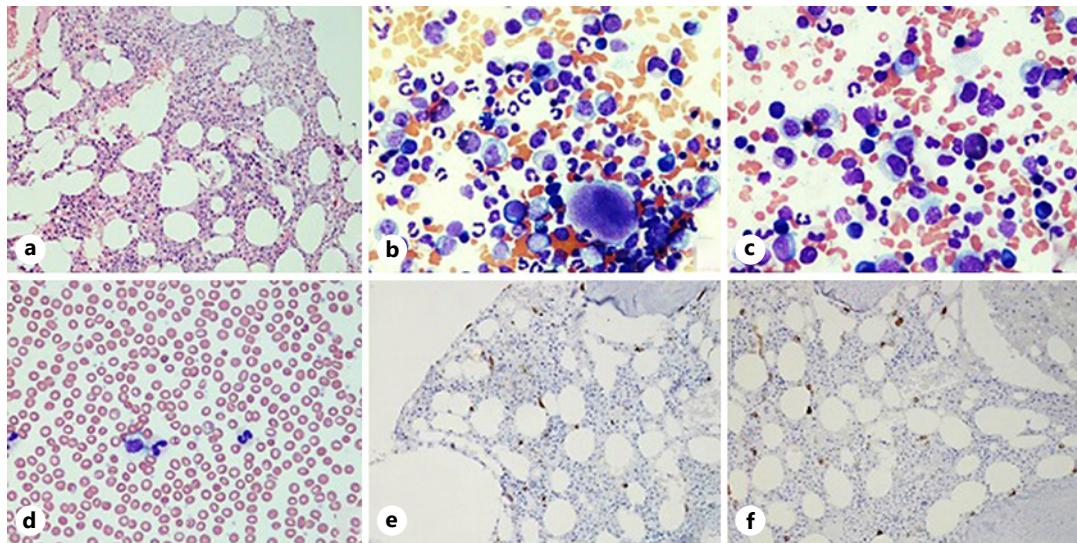


**Fig. 2.** Biopsy of the duodenal ulcer demonstrates duodenal mucosa with proliferation of many myeloblasts, consistent with either myeloid sarcoma or involvement by AML. **a–c** H and E images show proliferation of monotonous immature appearing neoplastic cells consistent with blasts (amplification at  $\times 20$ ,  $\times 100$ , and  $\times 200$ , respectively). The immunostains show blasts positive for CD45 (**d**), variably positive for CD34 (**e**), positive for CD117 (**f**), positive for CD33, MPO, and BCL2 (**g–i**); negative for CD3 (**k**), and CD20 (**l**). The blasts show a high proliferation index Ki67 (**j**). AML, acute myeloid leukemia; MPO, myeloperoxidase.

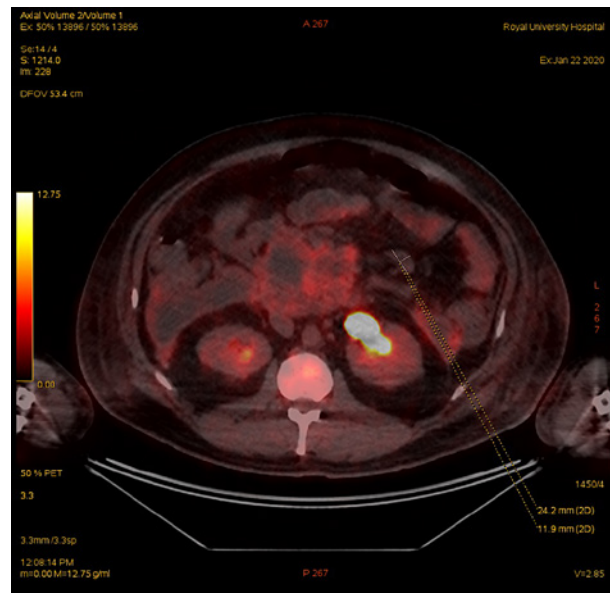
on the paraffin block of duodenal mucosa specimen did not reveal any recurrent somatic cytogenetic abnormalities or hotspot mutations. Thus, the final diagnosis was primary or de novo MS. PET scan illustrated diffuse heterogenous activity within the abdominal ascites (SUV 6), and moderate heterogenous diffuse activity throughout the pancreas (SUV 6) suggestive of either inflammatory versus neoplastic involvement (Fig. 4). Additionally, a large mesenteric lymph node was present, measuring  $2.4 \times 1.2$  cm.

Chemotherapy in the form of doxorubicin, vinblastine, and gemcitabine (AVG protocol) was initiated 11 days after his initial presentation. Cytarabine was deferred to avoid pancreatitis given patient's recent post-ERCP pancreatitis. Repeat examination to assess response to treatment was undertaken 7 weeks post initial chemotherapy. EGD and repeat biopsy of duodenal ulcer showed gastric metaplasia without evidence of dysplasia or neoplasia.





**Fig. 3.** Staging bone marrow examination shows maturing trilineage hematopoiesis and absence of myeloid neoplasms or AML in the bone marrow. **a** Bone marrow core biopsy H and E slide ( $\times 200$  amplification). **b, c** Bone marrow aspirate smears show slightly left-shifted myeloid cells, maturing erythroid cells, and adequate megakaryocytes ( $\times 500$  amplification). **d** Concurrent peripheral blood smear shows neutrophils with some toxic changes, and absence of blasts. **e** CD34 immunostain does not show increased blasts. **f** CD117 immunostain shows a few scattered mast cells only and does not show increased blasts. AML, acute myeloid leukemia.



**Fig. 4.** PET/CT showing mesenteric lymph node measuring  $2.4 \times 1.2$  cm.

The repeat bone marrow examination revealed no evidence of myeloid neoplasm or acute leukemia. Therefore, the patient received only 1 round of chemotherapy. He was discharged home upon completion of treatment and remains in remission without progression to AML.

Four weeks after discharge, the patient was readmitted with a perforated duodenum at the ulcer site. He was taken to the operating room where he received appropriate medical and surgical treatment with an omental patch. After 2 months post-op, he underwent repeat EGD

which did not reveal any pathology except Brunner's gland hyperplasia that was extensively biopsied. Flow cytometry analysis was performed on the specimen which was negative for the blast cells. Biopsies rather showed mild chronic inflammatory changes and, most importantly, negative for MS.

## Discussion & Conclusions

In WHO classification, MS is extramedullary malignant neoplasm and of myeloid origin [6]. While MS is most often associated with AML; it is seen to a lesser extent with chronic myeloid leukemia, myelodysplastic syndrome, and other myeloproliferative neoplasms but even rarer as a de novo occurrence [1, 2]. The most common sites associated with isolated MS are the skin (28–36%), lymph nodes (13–16%), testis (2.9–6.5%), intestine (6.5–8.9%), bone (3.3–4.9%), and central nervous system (3.2%) [3, 7]. Case reports have been published showing primary MS involving GI tract and associated organs that include the stomach [8–11], gallbladder [12], pancreas [13], small intestine [14–19], colon [20], and mesentery [21]. These articles have been summarized in Table 1. These cases include MS only affecting the GI organs with no progression to AML at least by the time of their publication.

The diagnosis of primary MS is difficult with a rate of misdiagnosis ranging from 25 to 75% [22–24]. The most common misdiagnoses are malignant lymphoproliferative disorders, including non-Hodgkin lymphoma, histiocytic lymphoma, thymoma, plasma cell myeloma, eosinophilic sarcoma, Ewing sarcoma, and carcinoma [4]. The tissue biopsy of primary MS reveals infiltration of blasts of myeloid lineages and immunohistochemistry staining shows the blasts positive for the stem cell markers (CD34 and CD117) and myeloid cell lineage markers (CD33, MPO, CD68, CD163, etc.). A bone marrow biopsy and peripheral blood smear should be completed to rule out the underlying AML and other hematological malignancies [6].

Isolated MS can occur following, concurrently, or preceding a diagnosis AML. MS always progresses to AML within 3–6 months but this period is noted to be longer in those receiving chemotherapy [22]. Many studies have shown that isolated MS responds to AML chemotherapy protocols [25–28]. The typical AML chemotherapy regimens include combinations of idarubicin, cytarabine, fludarabine, daunorubicin, granulocyte colony-stimulating factor, and cyclophosphamide [26]. One study has shown that chemotherapy alone was less successful than chemotherapy plus hematopoietic stem cell transplant; however, the study was small with only 12 patients from a single center [23]. Radiotherapy and debulking surgery can be used as adjuncts but should never take the place of systemic chemotherapy [27–29]. Furthermore, the primary tumor sites have implications on patient outcomes including mortality. MS isolated to the pelvis/GU organs had the highest 12 month survival at 81% compared to the soft tissue involvement at 26% and GI involvement having intermediate survival at 61% [7].

Of the cases listed in Table 1, individuals with primary MS of the GI tract were on an average 47 years old at diagnosis, and 58% male. 58% of the individuals were still alive by the time the case was published. Of those that died, 66% had gastric involvement. The most common treatment for primary GI MS that did not progress to AML was the standard chemotherapy for AML alone which includes cytarabine, daunorubicin, and etoposide. Complications of primary GI MS include small bowel obstruction, ascites, and perforated viscus [30–32]. Comparing the literature to the case we presented here illustrates some notable differences. First, our patient was 36 years old at the time of diagnosis compared to the average age of 47. Second, of the cases listed in Table 1 most patients with GI involvement presented with either abdominal pain or bowel obstruction whereas our patient's presenting concern was obstructive jaundice. Last, our patient went into remission despite cytarabine being excluded from the standard AML treatment due to the increased risk of pancreatitis, given his post-ERCP pancreatitis [33].

**Table 1.** Summary of adult cases published with de novo MS involving the GI tract

|                        |      |                       |   |  |
|------------------------|------|-----------------------|---|--|
| Derenzini et al. [11]  | 40/M | Stomach and duodenum  | Standard AML Chemotherapy   | Alive at publication                     |
| Kwan et al. [14]       | 39/F | Terminal ileum        | Ileal resection and standard AML chemotherapy                         | Alive and no recurrence of disease       |
| Narayan et al. [15]    | 48/M | Duodenum              | Standard AML chemotherapy and radiation therapy                       | Alive and no recurrence of disease       |
| Vachhani and Bose [10] | 52/F | Stomach               | Standard AML chemotherapy and radiation therapy                       | Died to metastatic disease               |
| Ohanian et al. [21]    | 54/M | Mesentery             | Standard AML chemotherapy   | Alive and no recurrence of disease       |
| Yu et al. [8]          | 31/F | Stomach and duodenum  | Standard AML chemotherapy and radiation therapy                       | Died to metastatic disease               |
| Huang et al. [9]       | 38/M | Stomach               | Standard AML chemotherapy   | Alive and no recurrence of disease       |
| Ocak et al. [16]       | 37/M | Jejunum and mesentery | Jejunum and descending colon resection, and standard AML chemotherapy | Alive and no recurrence of disease       |
| Holzwanger et al. [12] | 74/F | Gall bladder          | Cholecystectomy   | Died at presentation secondary to sepsis |
| Yoshida et al. [17]    | 47/M | Ileum and appendix    | Ileal and appendiceal resection, and unstated type of chemotherapy    | Unknown                                  |
| Aslan et al. [18]      | 57/F | Ileum                 | Ileal resection   | Unknown                                  |
| Mizumoto et al. [19]   | 54/M | Jejunum               | Jejunal resection and standard AML chemotherapy                       | Alive and no recurrence of disease       |

Reports with preceding, concurrent or subsequent AML were excluded. Standard chemotherapy for AML refers to cytarabine, daunorubicin, and etoposide.

MS, myeloid sarcoma; GI tract, gastrointestinal tract; AML, acute myeloid leukemia.

Finally, our case highlights complications and morbidity of primary MS. Not only did our patient developed pancreatitis but experienced perforated viscus. While primary MS involving the GI tract does not have the highest mortality of all the potential organ involvements, it is significant with a 12-month mortality of 39% [7].

### Acknowledgements

We thank our patient for providing consent for publication of this case for the purpose of learning and advancing medicine.

### Statement of Ethics

The following research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient provided informed written consent to publish their case including the publication of the images.

## Conflict of Interest Statement

The authors have no conflict of interests to declare.

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## Author Contributions

Matthew Patterson was involved in drafting the manuscript. Yue Wu was involved in interpreting the pathology and revision of the manuscript. Mina Niazi was involved in revision and approval of the final version of the manuscript.

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