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Acute Appendicitis Secondary to Acute Promyelocytic Leukemia

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 43
Final Diagnosis: Myeloid sarcoma appendicitis
Symptoms: Abdominal pain • chills • fever
Medication: —
Clinical Procedure: Laparoscopic appendectomy, bone marrow biopsy
Specialty: Gastroenterology and Hepatology

Objective: Rare disease

Background: The gastrointestinal tract is a rare site for extramedullary involvement in acute promyelocytic leukemia (APL).

Case Report: A 43-year-old female with no past medical history presented complaining of mild abdominal pain, fever, and chills for the past day. On examination, she was tachycardic and febrile, with mild tenderness of her right lower quadrant and without signs of peritoneal irritation. Laboratory examination revealed pancytopenia and DIC, with a fibrinogen level of 290 mg/dL. CT of the abdomen showed a thickened and hyperemic appendix without perforation or abscess, compatible with acute appendicitis.

The patient was given IV broad-spectrum antibiotics and was transfused with packed red blood cells and platelets. She underwent uncomplicated laparoscopic appendectomy and bone marrow biopsy, which revealed neoplastic cells of 90% of the total bone marrow cellularity. Flow cytometry indicated presence of 92.4% of immature myeloid cells with t (15: 17) and q (22: 12) mutations, and FISH analysis for PML-RARA demonstrated a long-form fusion transcript, positive for APL. Appendix pathology described leukemic infiltration with co-expression of myeloperoxidase and CD68, consistent with myeloid sarcoma of the appendix.

The patient completed a course of daunorubicin, cytarabine, and all trans-retinoic acid. Repeat bone marrow biopsy demonstrated complete remission. She will follow up with her primary care physician and hematologist/oncologist.

Conclusions: Myeloid sarcoma of the appendix in the setting of APL is very rare and it might play a role in the development of acute appendicitis. Urgent management, including bone marrow biopsy for definitive diagnosis and urgent surgical intervention, dramatically improve prognosis.

MeSH Keywords: Appendicitis • Leukemia, Promyelocytic, Acute • Sarcoma, Myeloid

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/892760

Background

Extramedullary involvement in acute promyelocytic leukemia (APL) is a rare condition. Some series report that about 3–5% of patients will develop this complication, mainly associated with cases of relapse of the disease.

Most of them tend to involve the central nervous system or skin and less frequently other sites [1–3]. Although leukemic and lymphomatous infiltration of the gastrointestinal tract have been well documented [4–6], the involvement of the appendix in cases of APL is very limited. We present the case of a patient with myeloid sarcoma (MS) of the appendix as the initial presentation of APL.

Case Report

A 43-year-old female patient with no past medical history came to the emergency room complaining of mild abdominal pain associated with subjective fevers and chills. Over a period of 2 hours, the pain, which was initially diffuse, localized to the right lower quadrant of the abdomen.

The patient looked pale but did not appear to be in acute distress. On examination, vital signs were significant for 115 beats/minute and temperature of 101.4 F. She had pale conjunctiva, no lymphadenopathy was identified, lungs were clear to auscultation, and her abdomen was soft and non-distended, with mild tenderness on right lower quadrant, without signs of peritoneal irritation.

Initial laboratory results were significant for a hemoglobin of 6.8 g/dL (normal value 12–16 g/dL), 2000 white blood cells/uL (3600–11 000 cells/mL) with 12% segmented, 3% bands, 40% lymphocytes, 4% monocytes, 4% metamyelocytes, 2% promyelocytes, 4% blasts, and 20% other cells. She also was thrombocytopenic with 3000 platelets (normal value 150 000–400 000 cells/uL), fibrin degradation products >20 mcg/ml (normal value: <5 mcg/ml) and D-Dimer >35.2 mg/L FEU (normal value: <0.53 mg/L FEU). CT of the abdomen showed a thickened and hyperemic appendix without perforation or abscess, compatible with acute appendicitis (Figure 1).

Initial treatment consisted in transfusion of 5 units of packed red blood cells and 5 units of platelets, as well as initiation of broad-spectrum antibiotics. Once the patient was stabilized, she underwent bone marrow biopsy and by the fifth day of hospitalization, an uncomplicated laparoscopic appendectomy. Bone marrow biopsy revealed neoplastic cells accounting for greater than 90% of the overall bone marrow cellularity, and flow cytometry indicated presence of 92.4% of immature myeloid cells with t (15: 17) and q (22: 12) mutations. In addition,

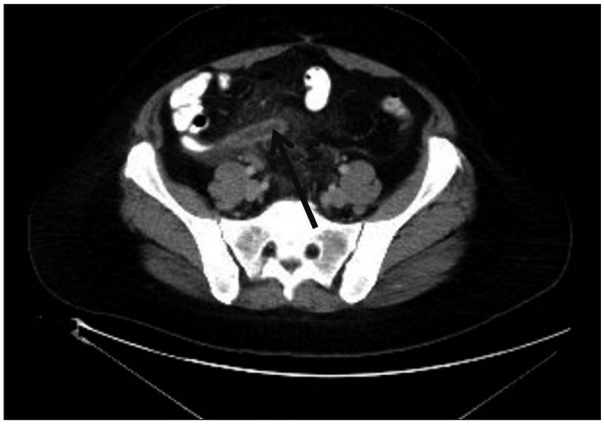

Figure 1. CT of the abdomen showing acute appendicitis.

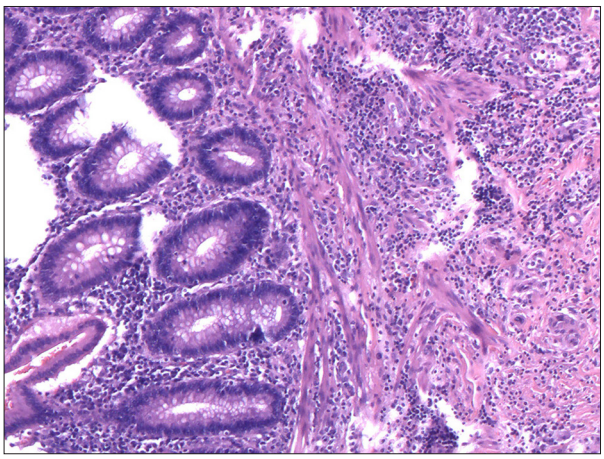

Figure 2. Leukemic cells infiltrating the mucosa of the appendix.

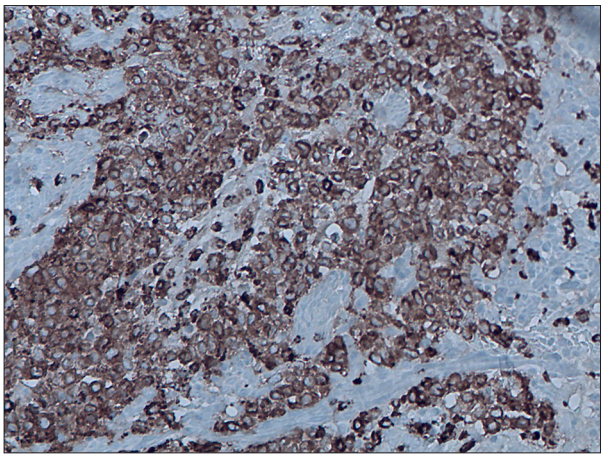

Figure 3. Leukemic cells immunoreactive with myeloperoxidase.

FISH analysis for PML-RARA demonstrated a long-form fusion transcript, positive for APL (AML M3 subtype according to WHO classification). The appendix was macroscopically described as hemorrhagic and pathology reported infiltration by leukemic blasts, that co-expressed myeloperoxidase (MPO) and CD68, consistent with myeloid sarcoma of the appendix (Figures 2–4).

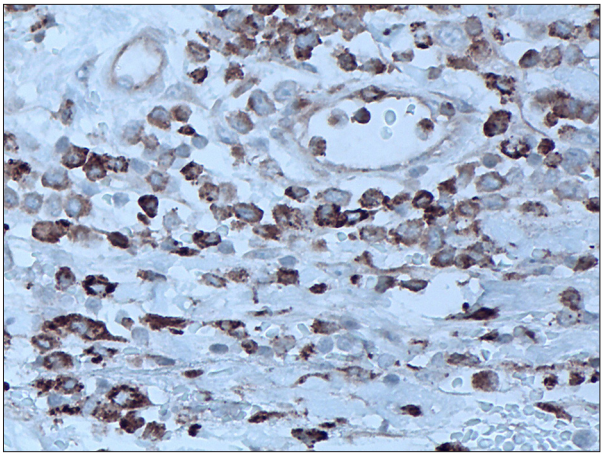

Figure 4. Leukemic cells immunoreactive with CD68.

Table 1. Table showing hospital course of the patient.

Day	Event
1	Admission. Bone marrow biopsy
5	Laparoscopic appendectomy
6	Biopsy result back
7	Daunorubicin, cytarabine, ATRA strarted
11	Daunorobucin stopped
14	Cytarabine stopped
40	Repeat bone marrow biopsy
41	Discharge
48	Remission. ATRA stopped

The patient completed course of daunorubicin and cytarabine. Underwent repeat bone marrow biopsy and was discharged home. When results came back showing remission, the patient was contacted and told to stop ATRA (Table 1). She is scheduled to follow up with her primary care physician and hematology/oncology (Table 1).

Discussion

The association of acute appendicitis in the setting of acute leukemia has been previously described [4–6], but documented cases of appendiceal involvement in APL are not common. Karachiwala et al. [7] and Papageorgiou et al. [8] each described 1 case of a patient that developed acute appendicitis while receiving chemotherapy. Both case reports described clinical presentation of acute appendicitis by the eleventh day of chemotherapy. We believe ours is the first documented case of a patient with MS of the appendix mimicking acute appendicitis as first presentation of APL, who underwent chemotherapy and was discharged with remission of the disease.

Upon admission, there was a high degree of suspicion that the patient had APL because apart of being pancytopenic and neutropenic, she also had DIC, which has been well described in these cases of leukemia (M3).

Antibiotics were given upon presentation because the patient met SIRS criteria and had acute right abdominal pain, so sepsis secondary to acute appendicitis was very likely.

The patient benefited from the prompt treatment with uncomplicated laparoscopic appendectomy and early initiation of chemotherapy. Patients with acute abdomen such as appendicitis need early surgery [9]. In the past, surgical management was delayed because of the high rate of surgical mortality. A high degree of suspicion for possible surgical causes should always be considered in pancytopenic and neutropenic patients.

The pathology report described the appendix as infiltrated by leukemic blasts and that co-expressed MPO and CD68, consistent with MS. This is an extramedullary malignancy composed of immature myeloid cells. Other names used to describe it include granulocytic sarcoma, monocytic sarcoma, extramedullary myeloid cell tumor, myelosarcoma, myeloblastoma, and chloroma [10]. Leukemic infiltrate might have caused the inflammation of the appendix that ultimately led to the presentation of acute appendicitis.

Another cause of acute right lower quadrant abdominal pain in patients with leukemia is necrotizing enterocolitis (NEC). Its risk has been directly related to the degree of neutropenia of the patient. Typhlitis is the localized presentation of NEC and usually presents with dilatation of the ascending colon, fluid accumulation around the cecum, and a thickened appendix [10]. Clinically, the 3 entities can present similarly, with nausea, vomiting, abdominal distention, fever, and sometimes gastrointestinal bleeding [11–13].

MS are twice as common in children as in adults, without any significant sex predominance [14–16]. They can arise concurrently with, following, or preceding the diagnosis of intramedullary acute myelogenous leukemia. Isolated cases, meaning no blood or marrow involvement, tend to have a better prognosis; however, treatment is the same for both, largely based on observations of high relapse and poor overall survival when treatment is limited to surgical or radiation techniques [17–19]. Although isolated cases of MS can be sensitive to radiation therapy, this is typically not employed as a first-line strategy as it may potentially delay the receipt of systemic chemotherapy due to excess toxicity [20].

Conclusions

Myeloid sarcoma of the appendix in acute promyelocytic leukemia is very rare. It is not known with certainty if it was the actual leukemic infiltrate that triggered the acute appendicitis. Urgent management, including bone marrow biopsy and initiation of appropriate chemotherapy, as well as surgical intervention if needed, should be carried out as soon as possible.

Statement

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