Granulocytic Sarcoma of the Colon in a Child With Acute Myeloid Leukemia Presenting as Hematochezia

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Summary: Granulocytic sarcoma (GS), an extramedullary myeloid tumor composed of immature cells of the granulocytic series, can occur in patients with acute myeloid leukemia (AML), myelodysplastic syndrome, or chronic myelogenous leukemia. It can occur in any organ or tissue, but the most common involved areas are the skin, bone/spine, and lymph nodes. However, its occurrence in the gastrointestinal tract is relatively rare, and is especially rare in the colon in adults. No case of GS involving the colon in children has ever been reported. We report here an extremely rare case of GS in the colon of a 10-year-old boy with AML presenting with hematochezia. Colonic GS was diagnosed by colonofiberscopic biopsy. His hematochezia responded rapidly to induction chemotherapy and the patient remained in complete remission after 3-month follow-up. In conclusion, hematochezia may be due to colonic involvement of GS, which should be considered in the differentials in addition to thrombocytopenia, as it is usually encountered in AML patients.

Key Words: granulocytic sarcoma, hematochezia, acute myeloid leukemia, colon, children

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Granulocytic sarcoma (GS), also known as one variant of myeloid sarcoma in the World Health Organization classification, is a rare tumor resulting from extramedullary invasion of granulocyte precursor cells. It is usually found concomitantly with or after the onset of acute myeloid leukemia (AML).[1] It was previously called chloroma by King in 1853[2] because of the greenish hue noted secondary to the enzyme myeloperoxidase, but has since been renamed GS by Rappaport.[3] Its rate of occurrence varies from 2% to 8% in AML patients and most frequently occurs in patients with AML FAB M2. However, children with AML FAB M4 or M5 tend to have a higher incidence.[4–6] In rare instances, it can be an isolated event or precede the development of overt AML by a few months to a few years.[7–9] Isolated GS is frequently mistaken for lymphoma, small round cell tumor, or undifferentiated carcinoma, especially when immunohistochemistry is not used.[10]

The most common sites of GS are the skin, orbit, bone, periosteum, soft tissue, and lymph nodes. Involvement of the gastrointestinal tract is relatively rare. To the best of our knowledge, no case of GS of the colon in children has ever been reported. We describe here a case of colonic GS in a child with AML who presented with massive hematochezia.

CASE REPORT

A 10-year-old boy presented to the emergency department with a 4-day history of low-grade fever and abdominal pain. The patient had no significant medical history. On physical examination, the patient looked pale and seemed to be in severe pain. There was rebounding tenderness with hypoactive bowel sounds in the right lower quadrant of the abdomen. No hepatosplenomegaly, lymphadenopathy, gingival hypertrophy, or mucocutaneous petechiae were noted. Laboratory data revealed white cell count 3.372/μL, platelet 34000/μL, hemoglobin 6.8 g/L, hematocrit 20.9%, alanine aminotransferase 18 IU/L, aspirate aminotransferase 26 IU/L, blood urea nitrogen 4 mg/dL, creatinine 0.5 mg/dL, and lactate dehydrogenase 656 IU/L.

Computed tomography (CT) scan of the abdomen and pelvis revealed marked thickening of the cecum and proximal ascending colon, findings characteristic of acute appendicitis. Given the severity of the presenting symptoms and the CT image findings, the patient underwent emergency appendectomy. Pathologic examination confirmed a suppurative appendix. After the surgery, the patient's fever and abdominal pain abated.

Postoperative bone marrow aspiration showed hypercellularity with an excess of myeloblasts (65%) and markedly depleted hematopoietic cells. The blasts were large, with large nuclei with fine chromatin pattern, 1 or 2 nucleoli, irregular nuclear membranes with clefting, and scanty cytoplasm. Auer rod bodies were noted in some myeloblasts. In addition, mature myeloid elements were also present. Flow cytometric analysis of the bone marrow aspirate revealed CD13—73.24%, CD33—82.87%, myeloperoxidase—66.98%, CD34—42.02%, HLA-DR—58.98%, but negative for B and T-cell markers. The karyotype of the bone marrow cells was 45,X,-Y, del(2)(p21),t(8;21)(q22;q22). Acute myeloid leukemia (FAB M2) was diagnosed.

However, the patient started to suffer from massive hematochezia after the bone marrow aspiration. His abdomen was soft without tenderness and abdominal sonography

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revealed inflammation of the bowel without ascites. Stool cultures were negative for *Salmonella*, *Shigella*, *Vibrio*, and *Clostridium*. Platelet transfusions were administered to maintain a platelet count greater than 100,000/μL but the hematochezia persisted. Colonfiberscopy showed 2 actively bleeding ulcerative tumors located 32 and 55 cm from the anal verge, respectively (Fig. 1). Biopsy specimens of the masses showed infiltration of large atypical myeloid cells with fine chromatin and abundant granular cytoplasm admixed with eosinophils and lymphoplasma cells, findings consistent with GS (Fig. 2). Immunohistochemical studies showed that the infiltrating cells were immunoreactive for myeloperoxidase and CD34, but not for CD3 and CD20. No microorganisms were detected by acid fast, P-aminosalicylic acid, or Grocott's methenamine silver stains.

The patient received chemotherapy according to the Taiwan Pediatric Oncology Group (TPOG)-AML-97A protocol.[11] Induction treatment consisted of ara-C (100 mg/m^2, continuous infusion, days 1 to 7) along with idarubicin [9 mg/m^2, intravenous push, days 1 to 3]. Intrathecal methotrexate (15 mg) was administered on day 1. Three days after induction chemotherapy, the amount of bloody stool gradually decreased. No bloody stool was noted 5 days after beginning induction chemotherapy.

Bone marrow examination at 1-month follow-up revealed no blast cells. Postremission therapy consisted of 4 monthly courses of ara-C (1 g/m^2/12 h on days 1 to 4) and etoposide (100 mg/m^2/d on days 1 to 5) alternating with ara-C (1 g/m^2/12 h on days 1 to 4) and mitoxantrone (10 mg/m^2/d on days 2 to 5). At 3-month follow-up, the patient was tolerating the chemotherapy and remained in complete remission.

DISCUSSION

GS is a localized solid tumor composed of immature cells of the granulocytic series infiltrating an extramedullary site. It usually manifests in the late stage of AML, or as a primary symptom when AML is diagnosed.[1]

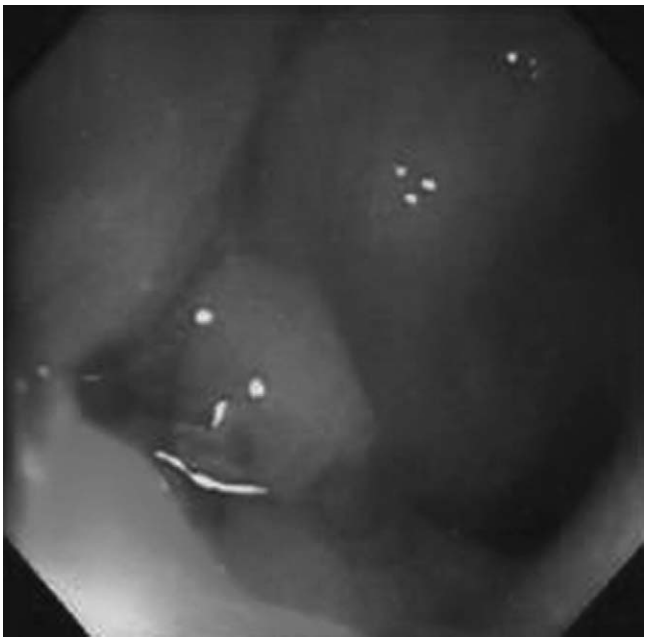

FIGURE 1. Colonofiberscopy showed an ulcerative mass, 2.0 cm × 2.0 cm, with patchy hyperemic areas in the colonic mucosa in the 32-cm segment from the anal verge.

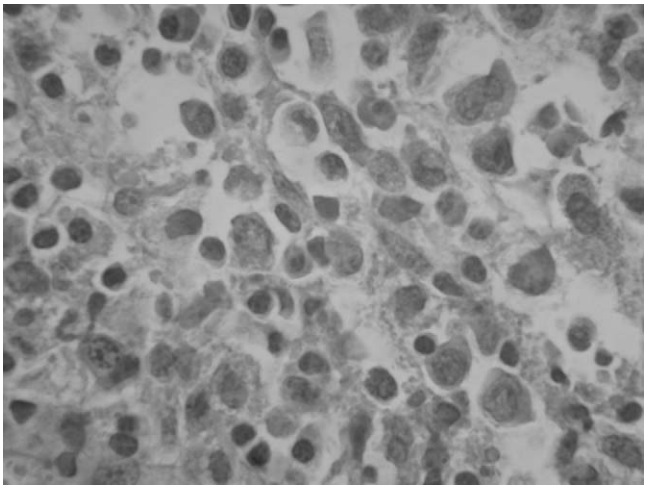

FIGURE 2. Blastic, hyperchromatic, and pleomorphic cells of the granulocytic series infiltrating the lamina propria of the colonic mucosa (hematoxylin and eosin 600 ×).

In a multicenter study of 1832 children with AML,[5] the most common sites of GS in children were skin (54.8%), the orbit (either unilateral or bilateral), head and neck (19%), and the central nervous system (19%). GS involving the gastrointestinal tract is relatively rare and occurs most in the small bowel, specifically the ileum.[1,6,7,12–15] GS involvement of the colon and rectum is exceedingly rare in adults and has never been reported in children with AML.

Symptoms of GS are nonspecific, and can include pain, tumor nodules, and motor disturbance.[4] Muss and Moloney[16] reported that the majority of GS in their series of 478 patients with granulocytic leukemia were clinically silent, indicating that these tumors may be unreported in leukemic patients. For AML patients, gastrointestinal involvement of GS often presents as abdominal pain or small bowel obstruction, but less commonly as diarrhea or massive hemorrhage. When leukemic patients with GS involvement of the gastrointestinal tract have gastrointestinal bleeding, this may be confused with complications of thrombocytopenia or coagulopathy caused by leukemia. Therefore, infiltration of the gastrointestinal tract by GS may be an underestimated event in leukemic patients. In our patient, massive hematochezia was the presenting symptom. If colonofiberscopy was not performed, the hematochezia might have been mistaken for a complication of thrombocytopenia and the colonic GS might not have been found. Early diagnosis of colonic GS can, therefore, guide management decisions and warn of risk of perforation with treatment response.

The CT features of GS of the bowel are variable, and can include an intraluminal or exophytic polypoid mass, bowel wall thickening, or a combination of these manifestations.[12] Thus, it is difficult to differentiate bowel GS from lymphoma or other neoplastic conditions, or

from inflammatory bowel disease by CT imaging studies. GS of the bowel also has a high predilection for mesenteric and peritoneal spread, making it difficult to clarify the precise location and shape. The CT images in our patient showed marked thickening of the cecum and proximal ascending colon without evidence of tumor in the bowel. This was because the tumor masses were too small to be seen using this modality. Colonofiberscopy is a better diagnostic method for GS of the colon because it can identify small lesions and used to obtain biopsy specimens for pathologic study. Colonofiberscopy in our patient revealed 2 small tumors located 32 and 55 cm, respectively, from the anal verge. The pathology of the biopsy specimen confirmed the diagnosis of GS.

A pathologic diagnosis of isolated GS may be difficult because the morphology varies from well-differentiated to poorly differentiated cells. In as many as 40% of cases, isolated GS is misdiagnosed as lymphoma or small round cell tumors.[8,9] Immunohistochemical study or immunophenotyping by flow cytometry can increase the accuracy of the diagnosis.[10] Immunohistochemistry for expression of myelomonocytic antigens (CD34) and myeloid-associated enzymes (myeloperoxidase) can help differentiate GS from malignant lymphoma and acute lymphocytic leukemia, and can help recognize early myeloid cells. In our patient, B-cell and T-cell lymphomas were excluded by negative stains for CD20 and CD3. In addition, tumor cells were immunohistochemically positive for CD34 and myeloperoxidase. The chromosome rearrangement in our patient was t(8; 21), which has been reported to be associated with GS and the FAB M2 subtype of AML.[5,17]

AML regimens are recommended for patients with GS because 80% to 90% of cases progress to AML within a year (mean, 11 mo) after the diagnosis.[1,7–9] Nonetheless, most patients will achieve complete remission with aggressive systemic AML-type combination chemotherapy.[1] There is no proof that localized radiation therapy is beneficial, and its late side effects in children are of real concern.[5] In this patient, the gastrointestinal bleeding improved soon after chemotherapy without radiation therapy. Without treatment, most patients will die within 8 to 12 months after disease onset.[9] Factors associated with poor prognosis include higher initial white blood cell counts, younger age at diagnosis, presence of the FAB M4 or M5 subtypes, and central nervous system blasts at diagnosis.[5]

In conclusion, in addition to thrombocytopenia and coagulopathy, colonic involvement of GS should be considered in patients with AML who present with lower gastrointestinal bleeding. For patients not (yet) diagnosed as AML, GS also needs to be considered in the differential diagnoses of colonic lesions causing lower gastrointestinal bleeding, such as primary colonic lymphoma. Colonofiberscopy and biopsy can establish the diagnosis. Immediate chemotherapy without radiation therapy can stop the gastrointestinal bleeding due to the colonic GS.

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