Small Bowel Obstruction as a Presenting Sign of Granulocytic Sarcoma

Rotem Sivan-Hoffmann MD[1], Igor Waksman MD[3], Hector I. Cohen MD[2] and Arie Eitan MD[1]

Departments of [1]General Surgery and [2]Pathology, Western Galilee Hospital, Nahariya, Israel
[3]Department of General Surgery, Ziv Medical Center, Safed, Israel

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Granulocytic sarcomas are rare extramedullary solid tumors composed of immature myeloid cells that can involve any organ. The term "chloroma" is derived from the Greek word *chloros* (green); it describes the tumor's frequently greenish color, which is due to the presence and oxidation of the enzyme myeloperoxidase in the tumor. These tumors can arise *de novo* or can be associated with other myeloid disorders – acute myeloid leukemia or chronic myeloid leukemia – which are myeloproliferative or myelodysplastic conditions. Presentation can occur prior to, in association with, or upon relapse of the underlying myeloid disorder. The location of the tumor varies – e.g., subperiosteal bone, skull, pelvis, ribs, sternum, lung, lymph node, skin, and gums.

When it is initially found, a granulocytic sarcoma can be misdiagnosed as a malignant lymphoma. In the case presented here, the GS was a large obstructive tumor in the small bowel that caused symptoms associated with bowel obstruction.

PATIENT DESCRIPTION

A 36 year old man presented to the emergency room with abdominal pain and vomiting that he had had for the previous 10 days. His health was generally good, with no prior surgery, no history of weight loss, night sweats, anorexia, or family history of malignancy.

On physical examination the abdomen was distended and there were no signs of peritonitis. Blood tests, including complete blood count, liver enzymes, renal function and electrolytes, were normal. Abdominal X-ray revealed a few distended small bowel loops with air-fluid levels. The patient was admitted to the surgical department and a computed tomography scan was performed several hours later. The CT exam showed small bowel obstruction in the ileum but no cause could be detected. Lymph nodes were found in the root of the mesentery around the inferior mesenteric artery.

The patient underwent surgery the following day. Diagnostic laparoscopy revealed obstructing lesions of the ileum with a huge mass in the mesentery of the same segment. There was also a marked distension of the proximal small bowel. On laparotomy a segment of ileum (length 25 cm) with a mesenteric mass was resected. The frozen biopsy section taken from the mass adjacent to the intestine showed cells consistent with malignant lymphoproliferative tumor or extramedullary GS due to the greenish coloration of the mass. Consequently, no further attempts were made to resect the residual para-aortic lymph nodes.

The postoperative period was normal apart from gastric dilatation, which resolved after several days with a gastric tube.

PATHOLOGICAL EXAMINATION

The small bowel segment measured 25 cm long with a concentric annular mass in the middle. In addition, several irregularities of the mucosa without continuity with the primary mass were found. Trans-section of the specimen showed that the mass had penetrated the intestinal wall. An adjacent tumor mass with a maximal diameter of 5 cm was found in the mesentery.

Histological findings showed diffuse infiltration by malignant cells with blastic features compatible with very immature myeloid cells. No necrosis was found. Some areas of the tumor demonstrated a 'starry skies' pattern [Figure A]. Some of the cells presented fine granulation compatible with a more mature type of myeloid cell. Mature and immature eosinophils were found mixed with the tumor cells. The immunostain was typical for tumors of myeloid origin, and include CD34, myeloperoxidase, CD68, CD43 and lysozyme, which were all strongly positive [Figure B]. CD45RO and CD45RB were weakly positive. These histological and immunohistochemical results confirmed the diagnosis of granulocytic sarcoma (myeloid sarcoma).

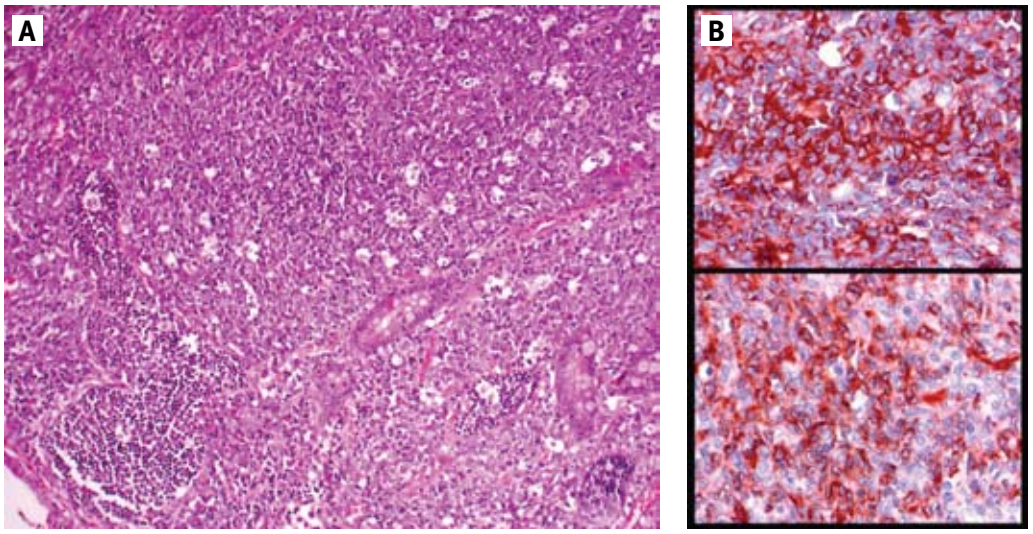
CYTOLOGICAL EXAMINATION

The bone marrow aspirate showed mildly hypocelullar marrow with erythroid and myeloid dysplastic features and 3% myeloid blasts, consistent with myelodysplastic syndrome. Cytogenetic studies showed normal karyotype 46XY. The peripheral blood cell count was normal.

COMMENT

Granulocytic sarcoma is an extramedullary tumor of immature myeloid cells (leukemic cells) that was first

GS = granulocytic sarcoma



[A] Hematoxylin & eosin stain showing the 'starry skies' pattern of the specimen (medium-power magnification)

[B] Immunohistochemistry showing positive staining of the tumor cells for myeloperoxidase (top) and for CD34 (bottom).

described in 1811 by Burns in his book *Observations of Surgical Anatomy*. GS can be isolated or it may be encountered during the course of acute myeloid leukemia, chronic myeloid leukemia, in myelodysplastic syndrome or myeloproliferative disorders. It may be detected coexistently with the initial diagnosis of these diseases or it may be seen in the relapse or as the first sign of the disease relapse [1]. Less commonly, it may also occur as an isolated mass in non-leukemic patients (primary GS). In this latter setting, the majority (88%) of untreated patients progress to AML within 11 months [2,3]. The true incidence of GS is not known and is generally underestimated. Clinically the incidence of GS in AML is 2%–8% [3].

Granulocytic sarcoma has been reported to occur in almost every anatomic location imaginable. The most common sites are the skin (13%–22%), bone/spine (9%–25%), and lymph nodes (15–25%) (2,3). It has even been found as an isolated central nervous system and meningeal disease, as reported previously in this journal [4]. Gastrointestinal system involvement is not frequent but in a review of 74 non-leukemic GS patients, the prevalence of small bowel involvement was found to be 15% [2]. This is undoubtedly a rare presentation of a rare disease. Most of these cases underwent surgery due to gastrointestinal bleeding or obstruction. In a review of 20 cases of GS in the small intestine the age of presentation ranged from 8 to 69 years (mean 43 years), with the majority occurring in male patients (17/20 cases). In 65%, ileal involvement was identified. Most of the cases occurred in non-leukemic patients. The gross features were described as a variety of appearances including polypoid or exophytic masses, regions of wall thickening, and/or ulcerations. The lesions are typically pink to gray-white, and greenish discoloration has been described in only one case involving the stomach and regional lymph nodes [5]. A significant proportion of tumors (47–56%) are initially misdiagnosed as malignant lymphoproliferative disorders, Ewing sarcoma, rhabdomyosarcoma, neuroblastoma, medulloblastoma, or poorly differentiated carcinomas [5]. In one large series the majority of misdiagnoses were associated with lesions categorized as "blastic" (62%) [3].

The correct diagnosis can be derived with the aid of histochemical and immunoperoxidase stains such as naphthol-ASD-chloroacetate esterase, lysozyme, CD34, CD117, and myeloperoxidase. The majority of lesions stain for either naphthol-ASD-chloroacetate esterase (75–80%) or lysozyme (89–90%) [5].

We present a rare occurrence of GS expressed as small bowel obstruction, which was the first and solitary manifestation of the disease, in a young patient who was subsequently diagnosed with low-grade myelodysplastic syndrome (IPSS score 0). In such cases of primary GS (in which a previous diagnosis of leukemia or myelodysplastic syndrome had not been made), the correct diagnosis is of major importance since there is a significantly longer non-leukemic period in patients receiving systemic chemotherapy [5].

There is no consensus regarding the treatment of granulocytic sarcoma. Generally, these patients are considered as having high-risk AML with a poor outcome, and early and intensive therapy according to AML protocols is strongly suggested [2].

Our patient received standard induction of remission chemotherapy with daunorubicin and cytarabine, as for AML patients. He later received two consolidation therapies, first with high dose cytosar and then with etoposide + mitoxantrone. After 26 months, without any therapy, he was in complete remission.

This case emphasizes the major role of surgical biopsy in the search for the cor-

AML = acute myeloid leukemia

rect diagnosis and treatment. Pathologists should consider GS when confronted with any mass that has a diffuse infiltrating population of tumor cells, and attention should be paid to three phenomena: the 'starry skies' appearance, the absence of necrosis (usually seen in other tumors), and the presence of eosinophils. The initial correct diagnosis of GS and early start of anti-leukemic therapy should promise a longer survival for these patients, who are mostly young.

In conclusion, the diagnosis of granulocytic sarcoma can be difficult. As in this case, the disease is often not suspected on clinical grounds and a high index of suspicion is needed. Full investigations into the morphology, immunohistochemistry, immunophenotyping, and perhaps even cytogenetics are essential.

Corresponding author:
Dr. R. Sivan-Hoffmann
P.O. Box 2, Kiryat Bialik 27100, Israel
email: rotemsivan3@gmail.com

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