

## **Case Report**

### **Granulocytic Sarcoma of the Small Intestine: An Unusual Presentation of Acute Myelogenous Leukaemia**

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#### **Abstract**

Granulocytic sarcoma is an extramedullary tumour of primitive granulocytic cells. It can develop at any anatomic site and is often a forerunner to the development of acute myelogenous leukaemia. Granulocytic sarcoma of the small intestine presents with abdominal pain and obstruction. We report a case of a 17-years-old boy who presented with epigastric pain. His endoscopy revealed multiple polypoid lesions throughout the duodenum and small bowel. Histopathology and flowcytometry

confirmed the diagnosis of granulocytic sarcoma associated with acute myelogenous leukaemia. To our knowledge there have been only two previous case reports of multiple granulocytic sarcomas in the small intestine, both of these were adult patients. This is the first patient in the paediatric age group with multiple granulocytic sarcomas of the small intestine.

#### **Introduction**

Acute myelogenous leukaemia (AML) represents about 15% of paediatric leukaemia. Granulocytic sarcoma (GS) is an

unusual manifestation of AML and presents as a focal soft-tissue mass. GS also known as chloroma or extramedullary myeloblastoma, is an extramedullary solid tumour composed of primitive precursors of the granulocytic series of white blood cells including myeloblasts, promyelocytes, and myelocytes. It was first described by Burns in 1811.<sup>1</sup> In 1853, King initially called it 'chloroma' because of the greenish hue resulting from the large amount of myeloperoxidase present in these immature cells.<sup>2</sup> In 1966, Rappaport renamed it granulocytic sarcoma because not all of the cells are green; 30% are white, grey, or brown, depending on the state of oxidation of the pigmented enzyme or the different cellular enzyme concentrations.<sup>3</sup> Recently in 1988, Davey has proposed the term extra-medullary myeloid tumour (EMMT) to include all forms of extramedullary myeloid leukaemic infiltrates.<sup>4</sup> We report a paediatric case of multiple granulocytic sarcoma of the small intestine, a rare entity in the paediatric age group.

### Case Report

Seventeen years old boy presented in internal medicine department at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, on 8th Feb 2007 with one month history of epigastric pain. There was no history of associated nausea, vomiting, blood in stools, constipation, fever and loss of appetite or jaundice. His past medical, family and social histories were unremarkable.

On physical examination he had stable vital signs, no lymphadenopathy or jaundice. Abdominal and other systemic examination was unremarkable. Investigations showed normal complete blood counts (CBC) and biochemistry except elevated lactic dehydrogenase levels (756 U/L).

Endoscopy revealed multiple polypoid lesions throughout the duodenum and small intestine with normal stomach and colon (Figure-1). Histopathology of the polyp



Figure-1: Endoscopy at presentation; multiple granulocytic sarcomas.



Figure-2: Endoscopy at end of treatment; Normal small intestine.

was reported as consistent with lymphoblastic lymphoma. Following this report he was referred to the paediatric oncology department for further management where he was advised a staging and toxicity workup.

Repeat CBC at this stage showed increased total leukocyte count ( $29.24 \times 10^9 /L$ ) with 56% blasts, normal haemoglobin (143 g/L) and platelet count ( $200 \times 10^9/L$ ). Acute leukaemia immunophenotyping on peripheral blood showed a blast population of 72% with a single abnormal clone characterized by CD45++, CD13+++, CD33+, CD34+++, CD117++, HLA-DR++, CD11c+/- . Following the flowcytometry report, the polyp biopsy was reviewed and more immunostains were performed which were consistent with GS. Final diagnosis of acute myeloid leukaemia, favouring AML-M1 was therefore made.

His treatment was commenced on 23 Feb 2007 according to Medical Research Council (MRC)-AML-15 protocol and consisted of 2 courses of induction with ADE chemotherapy (Ara-C + Daunorubicin + Etoposide) and consolidation with MACE (Amsacrine + Cytosine + Etoposide) and MIDAC (Mitoxantrone+ high dose Cytarabine). He finished treatment on 14th July 2007.

His bone marrow aspiration (BMA) and biopsy after first chemotherapy course was in morphological remission. End of treatment BMA was also in remission. Upper gastrointestinal endoscopy repeated after end of therapy on 27th November 2007 documented resolution of all polyps and histopathology showed normal gastrointestinal mucosa (Figure-2).

Patient is 25 months post treatment now and is on regular follow up in paediatric oncology clinic and remains clinically well with no evidence of disease recurrence.

### Discussion

Granulocytic sarcoma may occur as a manifestation of

AML, chronic myelogenous leukaemia (CML) or other myeloproliferative syndromes in blastic transformation. It can also occur in association with myelodysplastic syndromes such as refractory anaemia with excess of blasts (RAEB) or RAEB in transformation (RAEB-T).<sup>5</sup> GS usually occurs concomitantly with or after the onset of AML in 2.5-9.1% of patients with AML and occurs five times less frequently in patients with CML. However, the true incidence depends on the post-mortem examinations because about 50% of GS are asymptomatic. The incidence is equal in both sexes and 60% of patients are younger than 15 years of age.<sup>3</sup> Although GS most frequently occurs in acute myeloblastic leukaemia with maturation that is AML-M2 according to FAB classification, yet it has been described in all the other subtypes except M6. Rarely, GS may precede the onset of AML by several months, or even years. Isolated GS has also been reported in patients without haematological disorders.<sup>5</sup>

GS occurs in bone marrow and spreads via Haversian canals to penetrate periosteum and form a soft-tissue mass. Though this would account for the typical location near bony structures, but GS has been described in almost every location. The presentation depends upon the size and location of the tumour, ranging from indolent or painful swellings, neurologic compression signs, obstructive jaundice, hydrocephalus, ileus or GIT bleeding to right ventricular failure due to cardiac muscle infiltration. It may present either as an isolated or multiple lesions involving one or more organ systems, and lesions may be synchronous or metachronous. In patients with multiple lesions, up to four organ systems involved at one time have been described.<sup>5,6</sup>

Gastrointestinal GS represent approximately 6.5% of cases of GS with the ileum being the most common site of involvement. Clinical symptoms include acute or intermittent abdominal pain, symptoms of partial to complete small bowel obstruction, nausea, vomiting, weight loss, fever, anaemia, gastrointestinal bleeding and perforation.<sup>6,7</sup> The present case had epigastric pain and no symptoms of intestinal obstruction or blood loss. He had multiple lesions present throughout the small intestine, which to our knowledge has only been described previously in two reported cases of GS of the small intestine in adults. One was reported by Corpechot et al<sup>7</sup> and the 2nd was reported by Kohl et al.<sup>6</sup>

The diagnosis of GS can be challenging especially in the absence of a known haematological disorder. GS needs to be distinguished from Hodgkin lymphoma, Burkitt's lymphoma, large cell lymphomas, and small round blue cell tumours. The morphologic features of the tumours vary from well differentiated to poorly differentiated or blastic with little or no evidence of myeloid differentiation. Poorly differentiated GS, in particular, may resemble large cell non-Hodgkin lymphoma.<sup>8</sup> A significant

proportion of tumours (47%-56%) are initially misdiagnosed as malignant lymphoproliferative disorders, Ewing sarcoma, rhabdomyosarcoma, neuroblastoma, medulloblastoma, or poorly differentiated carcinomas.<sup>5,6</sup> Immunophenotypic features of GS also remain poorly recognized and frequently are confused with other malignant neoplasms.<sup>8</sup> The present case was also initially misdiagnosed as lymphoblastic lymphoma and then after the diagnosis of AML on flowcytometry, the histopathology was reviewed and reported as GS.

No controlled study has been reported regarding the treatment of isolated GS which has been managed with surgical resection, radiation therapy, systemic chemotherapy and stem cell transplantation.<sup>6,9</sup> Isolated GS if left untreated almost always progressed to AML. In this setting, the majority (88%) of untreated patients progress to AML within 11 months.<sup>5</sup> Whereas, a much longer disease free interval is noted in such patients if they receive upfront treatment with AML chemotherapy.<sup>5,6,10</sup> The prognosis of GS is variable but seems to be somewhat similar to that of AML.

In summary, gastrointestinal GS most commonly involves the small intestine and can present as abdominal pain without any other symptoms and often precedes the development of AML. Pathologists must consider GS in any mass with a diffuse infiltrating population of tumour cells, as the diagnosis is often initially unrecognized, especially in non-leukaemic patients. All GS, even those cured by resection or irradiation should be treated with intensive systemic chemotherapy as for AML because initial correct diagnosis of GS and early start of anti-leukaemic therapy would promise a longer survival for these patients who are mostly young.

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