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Case Report

Chronic Myeloid Leukemia (CML) as Surgical Emergency

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ABSTRACT

Ileal perforation peritonitis is a critical surgical emergency often encountered in developing countries, commonly associated with typhoid fever, tuberculosis, trauma, and non-specific enteritis. This case report presents a unique instance of nonspecific enteritis associated with chronic myeloid leukemia (CML). A 16-year-old girl with a history of pulmonary tuberculosis presented with symptoms, leading to the diagnosis of ileal perforations and CML. Surgical intervention involved ileal resection and double barrel ileostomy. The postoperative course included complications and chemotherapy with imatinib, demonstrating the challenges and management strategies in such cases. The discussion emphasizes the varied aetiologies of non-traumatic ileal perforation in different regions and sheds light on the rare gastrointestinal manifestations of CML. Notably, this report underscores the significance of prompt imatinib therapy in controlling CML while highlighting the need for vigilant monitoring and dose adjustments due to chemotherapy-related adverse effects.

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Introduction

Ileal perforation peritonitis is a frequently encountered surgical emergency, especially in developing countries [1]. Typhoid fever, tuberculosis, trauma, and non-specific enteritis are common aetiology associated with ileal perforation peritonitis. The incidence of perforation in typhoid fever ranges from 0.8% to 18% [2]. In India, tuberculosis is responsible for 5-9% of all small intestinal perforations, making it the second most common cause after typhoid fever [3]. The incidence of non-specific enteritis ranges from 26-56% in various studies [4-6]. In such cases, ileostomy is often required as a life-saving intervention [6]. Individuals with chronic myeloid leukemia (CML) may experience gastrointestinal symptoms like abdominal pain, bloody diarrhoea, and pancreatitis as the disease progresses. These manifestations can be attributed to the leukemia or its treatment. Notably, small bowel complications in CML are exceptionally uncommon, with only two documented cases [7]. We present a first ever case of nonspecific enteritis associated with CML managed successfully in our centre.

Case Presentation

A 16 years girl with past history of pulmonary tuberculosis treated with anti-tubercular treatment (ATT) 2 years ago presented to surgical emergency with complaints of low-grade fever on and off for last 5-6 days followed by generalised abdominal pain, vomiting, abdominal distension and inability to pass faeces and flatus for last 3 days. There was no history of weight loss or decreased appetite. On clinical examination patient revealed pallor and tachycardia of 140 beats per min with a blood pressure (BP) of 112/78 mmHg, without any lymphadenopathy. Abdominal examination revealed generalised tenderness, guarding and rigidity with absent bowel sounds.

Her blood profile showed a haemoglobin (Hb) of 8.7 g per Dl, a platelet counts of 240,000 per mm^3 and an unusually high total leukocyte count (TLC) of 167,000 per mm^3. Other laboratory workup was unremarkable. Her chest X ray showed air under diaphragm suggestive of intestinal perforation. Patient underwent emergency exploratory laparotomy

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which revealed 3 litres of pyo-peritoneum mixed with intestinal content, and 2 ileal perforations (90 cm from the ileocecal junction) with 1 intestinal ulcer (85 cm from the ileocecal junction). Splenomegaly was also confirmed intra-operatively. Ileal resection with double barrel ileostomy was performed in view of oedematous bowel.

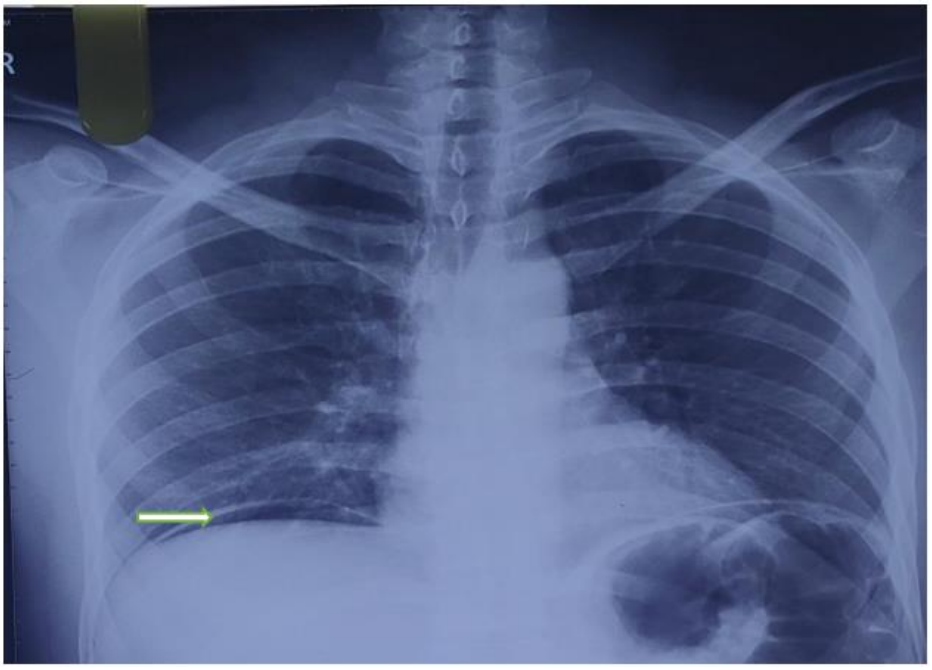

Figure 1: Chest X Ray PA view showing air under diaphragm (white arrow).

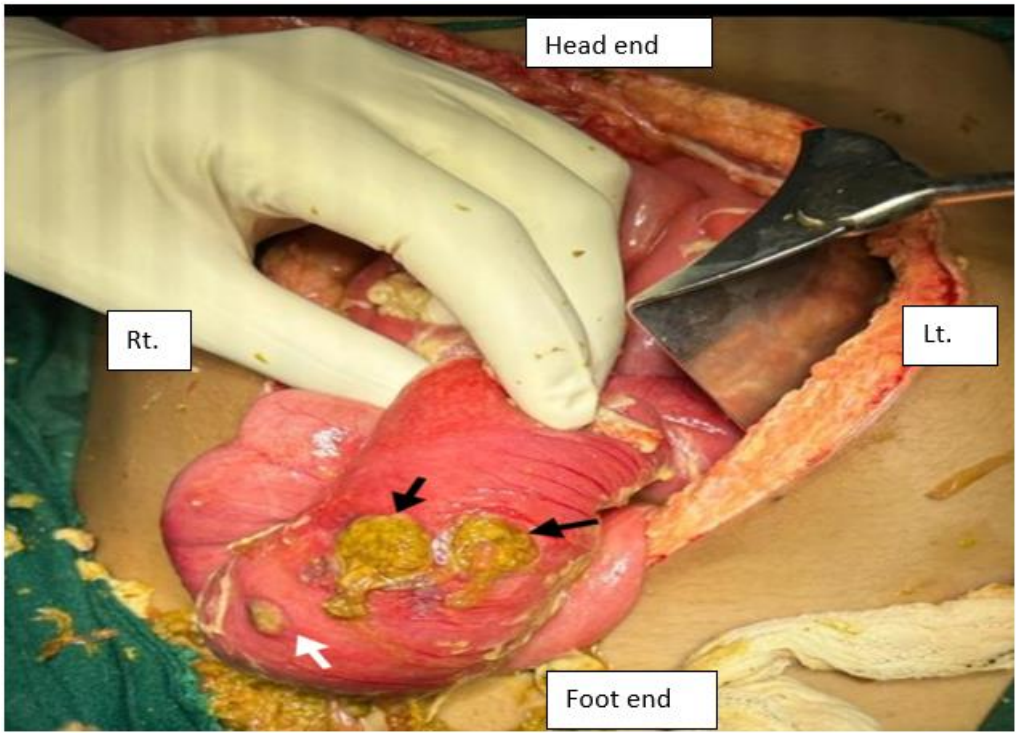

Figure 2: Showing perforations in distal ileum (black arrow) and an impending perforation (white arrow) with faecal output from perforation.

To identity the cause of perforation following investigations were done, Typhi-dot Ig M & Ig G were negative and blood culture showed no growth ruling out typhoid as the cause and biopsy of the resected small bowel segment revealed acute on chronic trans mural inflammation with serositis, suggestive of non-specific enteritis. For her unusually high leucocytosis peripheral smear was sent which showed 2% band forms, 12% myelocytes, 13% metamyelocytes, and 5% blast forms. Further investigations indicated a NAP score: of 56 with a positive BCR-ABL gene, clinching the diagnosis of CML in chronic phase.

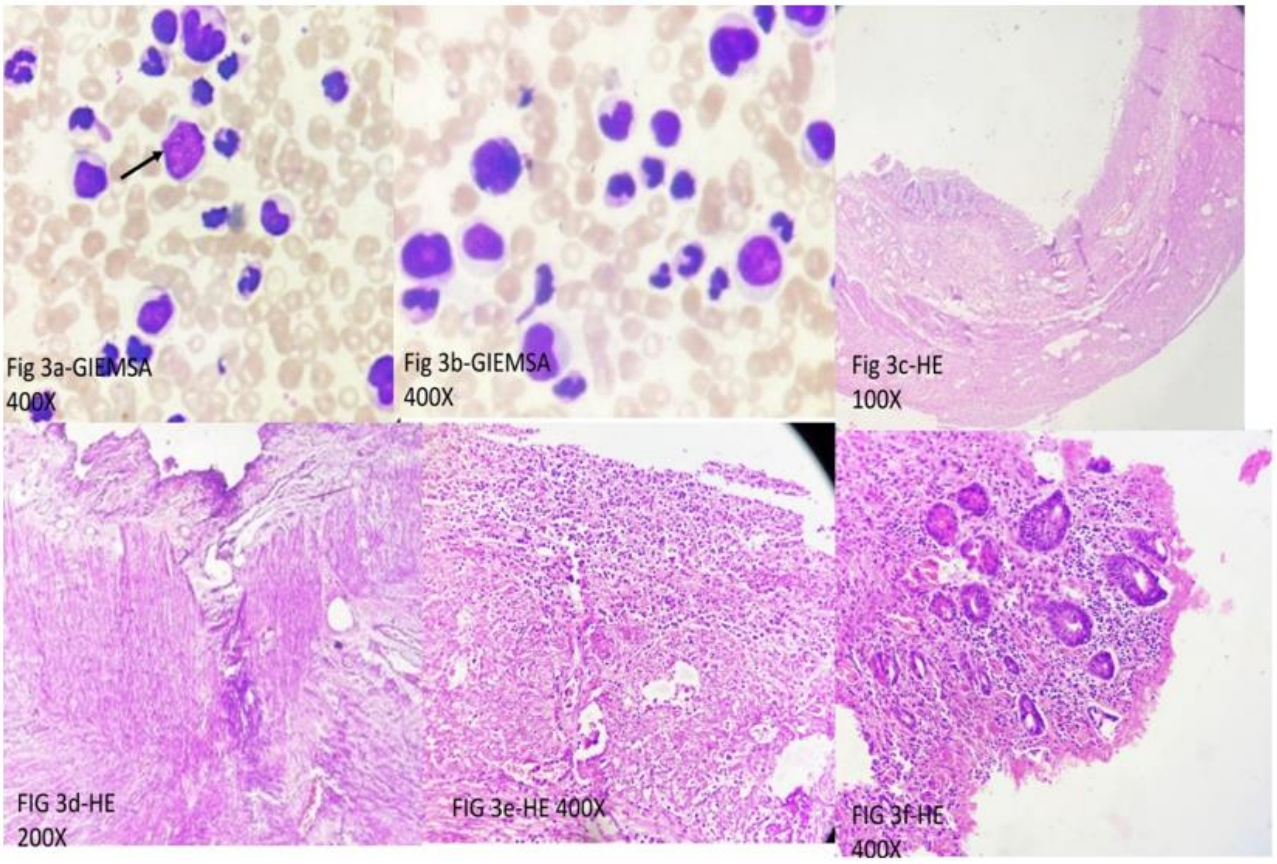

Figure 3: a) GIEMSA 400X- Smears show leukocytosis with present of immature precursors of myeloid series along with neutrophils and a blast (arrow). **b)** GIEMSA 400X- Smears show presence of myelocytes, metamyelocytes, stab and neutrophils in a case of CML. **c)** HE 100X- Sections from the small intestine in the same patient showing junction of normal and ulcerated mucosa. **d)** HE 200X- Sections show muscle splaying in area of perforation. **e)** HE 400X- Sections show presence of exudate with transmural inflammation at the site of perforation. **f)** HE 400X- Sections show partly distorted crypt architecture with evidence of cryptitis.

Post Operative Course

On POD 3 oral feeding was initiated with a gradual increase in food intake. Abdominal drains were removed on post operative day 3 and 6 (subhepatic and pelvic drain respectively). By the 14th postoperative day, complications emerged as the patient developed a burst abdomen with pus discharge from the midline and drain site. An intra-abdominal collection in the pelvis necessitated the reinsertion of pelvic drain, which was subsequently removed after 7 days. In weeks 2 to 3 post-surgery, chemotherapy with Imatinib was initiated on postoperative day 14, resulting in a reduction of total leukocyte counts from 1,60,000 to 18,000 within the following 10-14 days. However, the patient experienced severe vomiting and musculoskeletal pain following chemotherapy, necessitating dose adjustments. In the fourth week, the only midline skin was closed secondarily due to dense adhesion of bowel with the rectus muscle rectus sheath was not closed. Currently, the patient is in the follow-up phase for stoma closure.

Discussion

In developing nations, infection, especially typhoid, tuberculosis, and non-specific enteritis rank among the most common aetiologies, while in industrialized nations, closed-loop small bowel obstruction and tumor have been found to be the most common causes in various studies which have excluded trauma [8-10]. The most common aetiology of non-traumatic bowel perforation in third world countries is infective and inflict a younger population as compared to western world [10, 11]. In contrast, the western world often encounters ileal perforations due to conditions such as Crohn's disease, foreign body ingestion, perforated diverticula, and radiation enteritis. The perforation of the terminal ileum poses a challenging diagnostic situation for surgeons. In cases of trauma, management is typically straightforward because the tissues are healthy, and patients typically present in a stable clinical condition [5]. While non-specific enteritis may share operative characteristics with typhoid fever, laboratory evidence helps distinguish between the two. Various surgical procedures have been devised for addressing distal ileal perforations [5].

CML is a myeloproliferative neoplasm characterized by the presence of the Philadelphia chromosome (translocation t (9;22) (q34; q11.2)), leading to the BCR-ABL1 fusion oncoprotein. It predominantly involves proliferating granulocytes and affects both peripheral blood and bone marrow [12]. Chronic myeloid leukemia (CML) exhibits a global annual incidence rate of 0.87% per 100,000 individuals, with this rate rising to 1.52% in patients aged 70 and older. It also shows a slight male predominance, and the median age for diagnosis is 56 years [12].

I Chronic Phase: Peripheral Blood Smear

Leucocytosis with mature neutrophils and myelocytes. Blast cells are <2%, increased basophils and eosinophils. Bone marrow: Hyper cellularity, granulocytic proliferation, increased myeloid-to-erythroid ratio, <5% blasts, reduced erythroid precursors, variable megakaryocytes, and increased reticulin fibrosis.

II Accelerated Phase: Peripheral Smear

10-19% blasts possible. Bone marrow: Resembles chronic phase with increased blasts, possible granulocyte dysplasia, and increased fibrosis.

III Blast Phase: Peripheral Smear or Bone Marrow

>20% blasts or extra-medullary blast proliferation (may include different lineages). Common extra-medullary sites: skin, lymph nodes, bone, and CNS [12].

IV Presentation

Many patients are asymptomatic and diagnosed during routine blood tests. As CML progresses, it can cause symptoms related to anaemia, splenomegaly, thrombocytopenia, basophilia, and other complications [13].

Gastrointestinal manifestations in individuals with chronic myeloid leukemic may manifest as the initial signs of leukemia, emerge during the course of CML, or result from treatment complications. Interestingly, most reported cases involve patients with CML and encompass conditions like pancreatitis, esophagitis, reactivation of viral hepatitis, and gastrointestinal malignancies. In CML, leukemic infiltration can lead to malignant tumors in the gastrointestinal tract, and there is also a heightened risk of developing non-haematological malignancies, including colonic neoplasms. Notably, documented cases of enteric perforation in CML patients are limited, often occurring after treatment initiation during follow-up assessments. It's worth mentioning the absence of reported incidents where a CML patient presented with perforation peritonitis [7]. A limited number of instances involving enteric perforation in patients with CML have been documented, typically occurring subsequent to the initiation of treatment during follow up assessments. Noteworthy is the absence of any reported incidents wherein a CML patient has presented with a perforation peritonitis.

The prompt initiation of imatinib therapy, a tyrosine kinase inhibitor targeting BCR-ABL1, played a crucial role in controlling the patient's CML[14]. However, the chemotherapy led to adverse effects, including severe mouth ulcers and musculoskeletal pain, as in our highlighting the importance of vigilant monitoring and dose adjustments during treatment [13].

Table 1: [7]

Age	Mean age at presentation 49.6 years, range (18-85)	
Gender	44 Female	85 Male
Phase of CML	n= 10 blast phase n= 114 chronic phase	n=5 accelerated phase
Gastroesophageal	n= 2 gastritis n= 1 GAVE	
Small bowel	n= 1 perforation n= 1 Appendicitis	
Small and large bowel cancer	14 total n= 3 gastric adenocarcinoma n= 11 colorectal cancer : 5 had colon cancer before CML	
Pancreas	n= 3 Pancreatic adenocarcinoma All known CML	n= 16 Pancreatitis * All were known CML , after start of treatment n= 14 TKI related (mainly nilotinib) n= 2 interferon related
Colon	n= 2 colonic Ulcer n= 1 colonic polyp	n= 21 colitis* (20/21 TKI related) CMV colitis in 7 patients
hepatobiliary	n= 4 UC n= 2 CD n= 3 HCC (all known CML) n= 1 PBC	Hepatitis* 20/24 (TKI related) HB reactivation* 28/28 (TKI related)

- The table shows the characteristics of patients with chronic myeloid leukemia who developed gastrointestinal manifestations.
- HCC: hepatocellular carcinoma, PBC: primary biliary Cirrhosis(cholangitis), CD: Crohn's disease , UC: ulcerative colitis, GAVE: gastric antral vascular ectasia
- Mostly TKI related *

Conclusion

The absence of reported cases depicting chronic myeloid leukemia (CML) manifesting with small bowel perforation peritonitis is noteworthy. This case report underscores the importance of considering atypical presentations of haematological disorders such as CML, especially in young patients. The patient's unique clinical course, including the initial presentation with gastrointestinal perforation, highlights the significance of timely diagnosis, multidisciplinary care, and the management of chemotherapy-related side effects in complex cases of CML. Early recognition and intervention are crucial to achieving optimal outcomes for patients with CML and its complications.

This case also serves as a reminder to healthcare providers to maintain a high index of suspicion and remain open to diverse diagnostic possibilities when confronted with patients with unusual clinical presentations.

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