Case Report

Small bowel bleed: The forgotten complication of chronic myeloid leukemia

Jatin Bankeylal Agrawal[1], Manjusha Yadav[2], Kartik Purohit[3], Sangeeta Vanik[4]

From [1]Consultant, Department of Gastroenterology, [2]Consultant, Department of Internal Medicine, [3]Consultant, Department of Hematology, [4]Consultant, Department of Pathology, Zydus Hospital, Vadodara, Gujarat, India

ABSTRACT

Chronic myeloid leukemia (CML) is a clonal bone marrow stem cell disorder with proliferation of granulocytes and their precursors. Gastrointestinal (GI) involvement is uncommon across all types of leukemia. It typically occurs during the blast phase or in cases of acute leukemia. However, advancements in treatment have significantly reduced the incidence of such complications. We present a unique case of a small bowel bleed in a 68-year-old patient of CML who presented with recurrent massive lower GI bleed.

Key words: BCR-ABL positive, Chronic, Leukemia, Myelogenous, Small bowel bleeding, Tyrosine kinase inhibitor

Chronic myeloid leukemia (CML) is a cancer that targets early myeloid cells in the bone marrow. It results in the building of impartially matured cells that crowd out the normal myeloid cells. This immature myeloid cell sometimes infiltrates different areas of the gastrointestinal (GI) tract. The stomach, ileum, and colon are the most common among them. In the autopsy reported series, GI infiltration was seen in 11% of cases of myeloid leukemia [1]. However, this incidence has now reduced drastically with the advent of tyrosine kinase inhibitor (TKI) therapy [2]. Usually, these patients with GI infiltration are asymptomatic even in the presence of extensive infiltration. Case reports regarding GI bleeding due to thrombocytopenia, gastroduodenal ulcers, and colonic ulcers were reported long back before the advent of TKI.

We report this unique case of acute GI bleed due to leukemic infiltration of the GI tract in a CML patient on long-term TKI therapy. Our case highlights the importance of detecting GI symptoms early in patients with leukemia to prevent life-threatening complications.

CASE REPORT

A 68-year-old male, a diagnosed case of CML on imatinib therapy, presented to the emergency department with painless hematochezia for 2 days. He was diagnosed with CML 3 years back and was doing well on imatinib, except for some vague abdominal pain and intermittent diarrhoea for the last 1 year. He was on regular follow-up with his hematologist, and his last blood parameters 2 months before presentation were suggestive of biochemical remission. He has no previous history of GI bleed.

On presentation, the vitals revealed low blood pressure with tachycardia. He was pale and ill-looking. He was managed in the intensive care unit with intravenous crystalloids, blood products, and supportive measures.

Laboratory parameters revealed hemoglobin 2 g/dL, total counts 53,010 cells/mm^3 with 70% neutrophils, 16% lymphocytes, 8% blast cells, 2% monocytes, 4% eosinophils, Platelets 150 × 10^3/mm^3 with normal kidney and liver functions. A peripheral smear revealed hypochromic anemia with blast cells and immature cells suggestive of the blast phase of CML. After resuscitation, upper GI endoscopy was done, which notably did not reveal any bleeding source. His colonoscopy showed blood clots throughout the colon and terminal ileum, which aroused the possibility of a small bowel bleed. Thus, computed tomography angiography was requested. It showed areas of bowel wall thickening in the jejunum and ileum without any active blush. Patient hemodynamics improved after spontaneous stoppage of bleeding. A hematologist was also consulted for the leukemic blast crisis. Bone marrow aspiration revealed hypercellular marrow with granulocytic hyperplasia and 8% blast cells only. Bone marrow biopsy also revealed similar findings with focal marrow fibrosis. The above findings were not typical of the blast phase of CML. A multidisciplinary team discussion was done with the patient's relatives regarding further options to find the source of the bleed, and capsule endoscopy was planned. However, before we could proceed with the capsule endoscopy, the patient again had a massive bleed with hypotension. Thus, the decision to proceed with urgent intraoperative enteroscopy was taken. Multiple blood transfusions were done before surgery. During

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Correspondence to: Jatin Bankeylal Agrawal, Department of Gastroenterology, Zydus Hospital, Vadodara, Gujarat, India. E-mail: jatinagrawal1989@gmail.com

intraoperative endoscopy, the small bowel was full of blood and blood clots. After clearing blood, multiple deep ulcers could be visualized from the proximal jejunum to the distal ileum (Fig. 1). Many ulcers were associated with adherent clots predominantly in the jejunum and proximal ileum (Fig. 1). Alone endotherapy was not possible in view of diffuse and multiple bleeding ulcers, hence the intraoperative decision was taken to resect the most affected bowel segment to prevent rebleed. Around a 40 cm small bowel segment was resected (Fig. 2).

The post-operative period patient remained clinically stable. However, on the 3rd post-operative day, he again had a massive GI bleed and succumbed to death due to multiorgan failure. Surgical biopsy of resected small bowel segment revealed surface ulceration with clusters of leukemic cells infiltrating in the submucosa and muscularis propria, suggestive of leukemic cell infiltration of small bowel (Fig. 3).

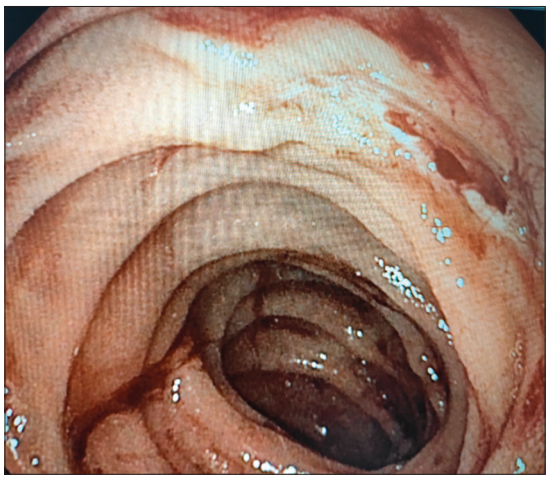

Figure 1: Enteroscopy shows deep ulcers in the jejunum with blood

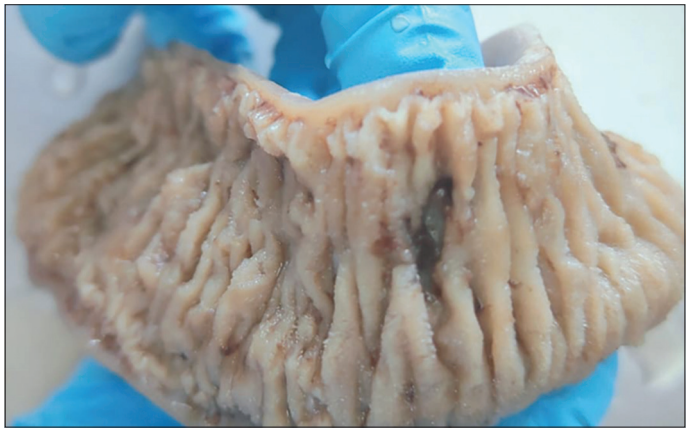

Figure 2: Resected small bowel segment shows a large deep ulcer with adherent clot

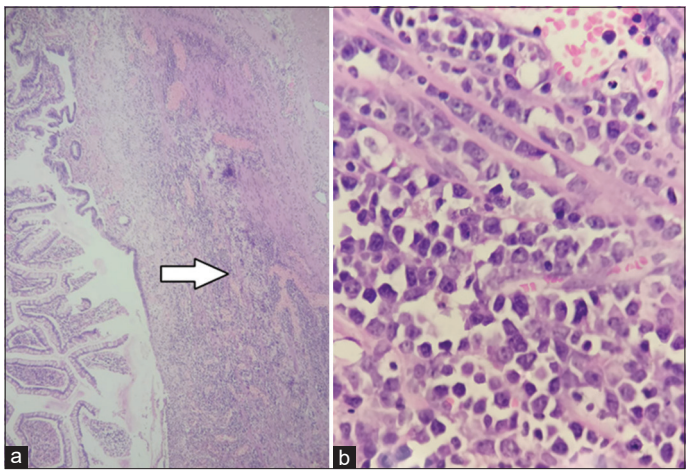

Figure 3: Clusters of leukemic cells infiltrate in the submucosa and muscularis propria of the small bowel, suggestive of leukemic cell infiltration of the small bowel

DISCUSSION

Managing small bowel bleed is challenging due to the inaccessibility of the endoscopist and the long length. Multiple modalities, including push enteroscopy, single or double enteroscopy, capsule endoscopy, and small bowel imaging, are required to establish a diagnosis and treatment of GI bleed [3]. In complex and emergency cases, intraoperative endoscopy is required. Our patient had a massive GI bleed with unstable hemodynamics, which warranted an emergency laparotomy and intraoperative endoscopy.

CML is a myeloproliferative neoplasm characterized by overproduction of mature granulocytes. Treatment of CML was revolutionized by the introduction of a BCR-ABL TKI. Several TKI pathways may be selected for the first-line CML treatment, including first-generation imatinib or second-generation TKIs, such as bosutinib, nilotinib, and dasatinib [4]. However, TKI use is associated with various adverse effects (AEs), including hematological and non-hematological AEs, including GI disturbances, cardiotoxicity, liver toxicity, pleural effusion, edema, and muscle cramps. Monitoring and management of these AEs are crucial for the success of CML treatment [5]. GI manifestations such as abdominal pain, diarrhea, bleeding, and pancreatitis are seen during the disease course [2]. Some of these manifestations are due to leukemia itself, while others are related to CML treatment.

In the current era, GI bleeding in CML patients is commonly due to long-term adverse events of TKI or superadded GI infection. TKI has documented the risk of GI bleeding [6]. Hemorrhagic colitis has been reported in a CML patient on dasatinib treatment [7]. Meta-analysis has reported that imatinib and other TKIs cause GI bleeding in 3–11% of cases [8,9]. However, most of these bleeds are mild and rarely cause unstable hemodynamic as these are generally diffuse mucosal bleeds. As our patient had a massive GI bleed, the possibility of a drug-related bleed was dismissed. Decades before the invention of TKI, cases of such bleeding were reported in CML patients. Old case series have shown GI involvement of leukemia [2,10].

The lesions vary according to the type of leukemia and the phase of leukemia. Four types of intestinal lesions are described in the literature – plague-like lesion, nodular lesion, diffuse infiltration, and polyp-like lesion. Among these, the plague and diffuse infiltration type involves the submucosa and muscle coat and is associated with ulceration and intestinal perforation. While nodular and polyp lesions affect more of the mucosa and

submucosa, thereby associated with intestinal obstruction and intussusception [10]. Our patient had a diffuse involvement pattern involving almost the whole small bowel, resulting in deep ulceration and bleeding. Leukemic blast cells infiltrate into the wall of the intestine, resulting such ulcerated lesions. However, after the advent of TKI, such pathologies have not been reported over the last 2 decades. To our knowledge, diffuse small bowel bleeding ulcers due to myeloid cell infiltration have not been reported in the last 2 decades, especially after the introduction of TKI for the treatment of CML.

Patients with leukemic infiltrates are usually asymptomatic or have vague GI symptoms for a long time before they complicate. If these vague symptoms are identified in the early stages, complications can be prevented. Such patients should be evaluated for GI studies using endoscopies or imaging modalities. Our patient had vague GI symptoms in the form of abdominal pain for the past 1 year. However, his biochemical profile was suggestive of the remission stage, which delayed his evaluation and ultimately led to GI complications. Such complications are seen only in untreated or relapse cases. Hence, early detection of symptoms is important to improve treatment outcomes and quality of life care.

CONCLUSION

Our case underscores a rare but significant adverse event in patients with CML who are receiving highly effective targeted therapy in today's clinical landscape. This highlights the need for ongoing vigilance and individualized patient monitoring to ensure optimal outcomes and to prevent life-threatening complications.

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