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CASE REPORT

Duodenal gastrointestinal stromal tumor presenting with life-threatening upper GI bleeding in a young patient: A case report and literature review

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Key Clinical Message

Duodenal GISTs are rare and challenging tumors. Acute life-threatening upper GI bleeding is a possible presentation of duodenal GISTs. Surgery is the standard treatment for localized duodenal GISTs. Imatinib is an effective adjuvant therapy for duodenal GISTs.

Abstract

GIST is the most common mesenchymal neoplasm of the gastrointestinal tract, accounting for 1%–2% of gastrointestinal tumors. They originate from the interstitial cells of Cajal and are rare in patients younger than 30 years. The stomach is the most common site, followed by the small intestine and colon. GISTs are caused by a gain-of-function mutation in the proto-oncogene receptor tyrosine kinase, with activating mutations in KIT being the most common. Most GISTs are asymptomatic. Even if gastrointestinal bleeding is the most common complication life-threatening hemorrhage is extremely uncommon. We present a case of a 31-year-old male patient presented with massive active hematemesis and melena with hemorrhagic shock. The patient presented with massive hematemesis and melena of 1 h duration. Endoscopy showed pulsating active bleeding from the third part of the duodenum which was difficult to manage via endoscopy. Histopathologic evaluation showed spindle cell type GIST. Intraoperatively, there was a nodular mass with active bleeding on the third part of the duodenum. Duodenectomy with end-to-end anastomosis was done. Discharged with no postoperative complication and was put on imatinib. There are considerable challenges that arise in the diagnosis and treatment of duodenal gastrointestinal stromal tumors (GISTs) when they present with life-threatening upper gastrointestinal hemorrhage. In order to achieve the best possible outcomes for patients,

it is crucial to have a comprehensive understanding of the clinical presentation, diagnostic methods, and treatment approaches.

KEYWORDS
duodénum, GIST, hematemesis, life-threatening, shock

1 | INTRODUCTION

Although rare, accounting for about 1%–2% of gastrointestinal tumors, gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasm of the gastrointestinal tract.[1–3] First described by Mazur and Clark in 1983, GISTS originate from the interstitial cells of Cajal.[4,5] GIST cases have been reported in all age groups; however, it is extremely rare in patients younger than 30 years with about 75 percent of the cases occurring in patients older than 50. The average age at diagnosis for GISTs is 60 years. Except for a slight predominance among males observed in some literature, there are no significant epidemiological differences concerning gender, ethnicity, or location.[6,7]

Upper GI bleeding is bleeding of the GI tract that is located above the duodenojejunal (DJ) junction (ligament of Treitz). Close to half of the cases are due to peptic ulcer disease (PUD). Gastrointestinal tumors are causes for only a small percentage of upper GI bleeding (less than 5%) with an extremely uncommon occurrence of acute life-threatening upper GI bleeding attributed to them.[8–10] Here we present a case of a young male patient who presented with acute life-threatening upper GI bleeding to the extent of hemorrhagic shock along with a review of relevant literature.

2 | CASE PRESENTATION

A 31-year-old male Ethiopian patient came to the emergency department with the sudden onset of massive persistent hematemesis and melena of 1 h duration. Up on presentation, he was conscious but with feeble pulse, hypotensive (BP was 70/50 mmHg), a temperature of 35.9°C and respiratory rate of 28. With the diagnosis of hypovolemic shock secondary to acute upper GI bleeding, He was immediately put on intravenous fluid resuscitation while he was being taken to the endoscopy room. The endoscopy showed massive pulsating active bleeding on the third part of the duodenum (Figure 1). The bleeding was too massive to apply hemostat endoscopically (Video S1).

2.1 | Methods

The patient was rushed into the operating room, and emergency laparotomy was done under general anesthesia.

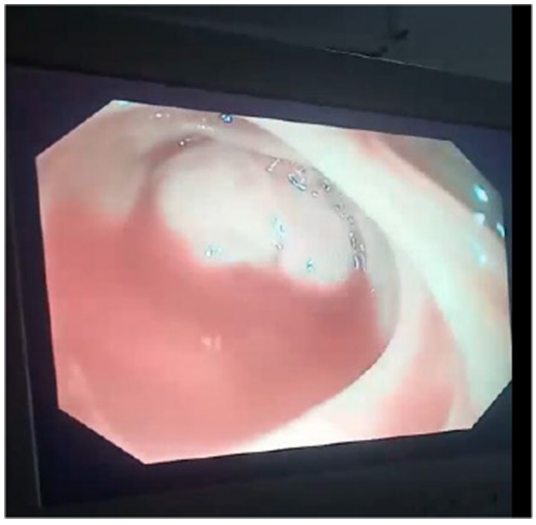

FIGURE 1 Endoscopic appearance of the actively bleeding duodenal mass.

Intraoperatively, there was a well delineated duodenal mucosal nodular mass on the distal part of the third part of the duodenum with active bleeding from the mass after duodenotomy (Figure 2 and Figures S5–S8). There was no hemoperitoneum, lymphadenopathy, and other abdominal organs grossly appeared normal. Therefore, duodenectomy of the third part of duodenum and end-to-end anastomosis was done.

2.2 | Outcome and follow-up

Subsequently, the patient was transferred to the surgical ICU. In the ICU, he was transfused with 4 units of additional blood and other supportive measures continued. The patient had smooth postoperative recovery while in the ICU and later in the ward. Finally, the patient was discharged from the hospital with appointment with no postoperative complications.

The resected sample was brought to the pathology department. Up on accession, there was a longitudinally opened up intestinal segment with a well circumscribed nodular mass on the mucosal aspect that measures 4.5 × 4 × 3 cm with tan white solid whorled cut surface appearance (Figure 3). The histopathology showed proliferation of monotonous spindle cells within short fascicles that occasionally followed storiform and palisading pattern

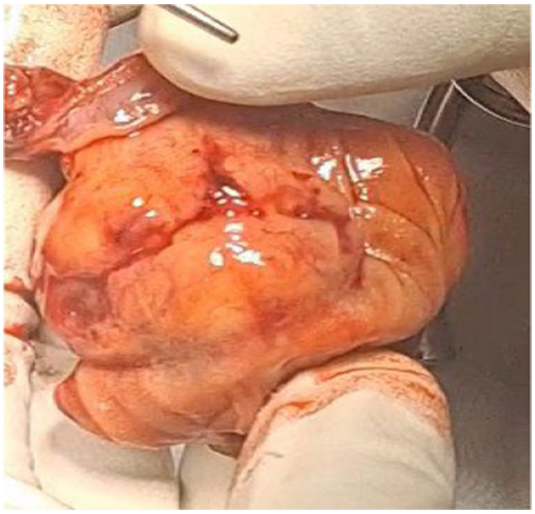

FIGURE 2 Gross appearance of the duodenal mucosal nodule with its actively bleeding focus.

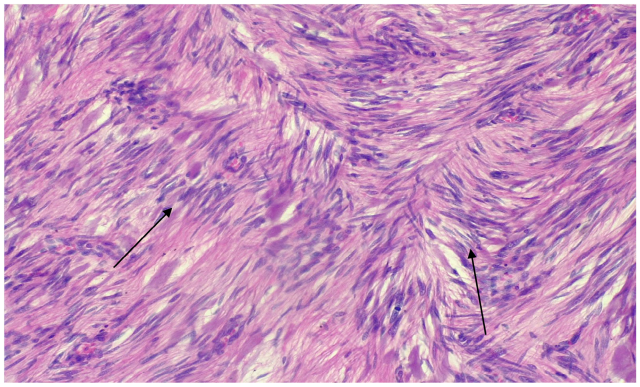

FIGURE 3 Histopathology showing a mesenchymal proliferation obliterating the muscular and submucosal layer pushing the mucosa towards the lumen.

while obliterating the muscle proper and submucosal layer and growing towards the mucosal layer of the intestine. Numerous extracellular collagen globules (Skenoid fibers) that are highly characteristic of GIST of the small intestine were evident (Figure 4 and Figures S1–S4). With the above histologic pictures, the case was signed out as low-risk GIST, spindle cell subtype.

Our patient was financially unable to have immunohistochemical (IHC) and molecular studies. Nevertheless, even though the tumor was low-risk histopathologically, due to the presentation with tumor rupture imatinib was started.

3 | DISCUSSION

The stomach is the most common site with (59%) of those tumors occurring in the stomach followed by the small

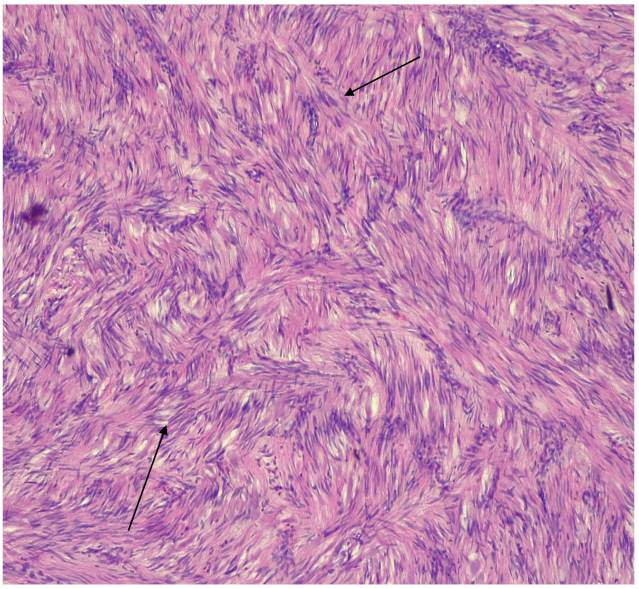

FIGURE 4 Histopathology showing monotonous spindle cells in storiform pattern (arrows).

intestine (33%) and the colon 6.5%.[11] Duodenal gastrointestinal stromal tumors (dGISTs) are extremely rare and less than 5% of all GISTs arise from the duodenum, with 30%–40% estimated frequency of malignancy.[9] The median age at diagnosis of patients with dGIST is 56 years with proportional incidence in males and females.[10] For most patients with dGIST, the tumor is located in the second portion of the duodenum.[8]

In 1998, Hirota et al. discovered GIST was due to a gain-of-function mutation in the proto-oncogene receptor tyrosine kinase within the interstitial cells of Cajal and almost all GISTs expressed activating mutations in KIT (CD117), which is now used as a diagnostic immune-histochemical marker.[12] The majority of GISTs (80%–90%) occur as a result of activating mutations in KIT and/or platelet-derived growth factor receptor-α (PDGFRA).[12,13] Other markers for GISTs include CD34 antigen (70%), smooth muscle actin (30%–40%), desmin (<5%), and S100 protein (5%).[14] KIT mutations are observed in 75% of dGISTs.[9]

Patients are often asymptomatic, especially when the tumor size is small (<2 cm), and the median size at presentation is approximately 5 cm.[15] When symptomatic, most of the clinical manifestations are nonspecific, including nausea, vomiting, early satiety, abdominal pain, obstruction, abdominal mass, anemia, and melena.[7,15] In small intestine GIST the most common symptom is GI bleeding, followed by abdominal pain, abdominal mass, and anemia.[16] Larger tumors may present with intestinal obstruction and obstructive symptoms depending on the location of the mass.[17]

Gastrointestinal bleeding, presenting with either upper or lower GI bleeding, is the most common complication of

GISTs because they are frequently associated with mucosal ulceration.[18] Factors that increase the risk of bleeding in GIST include the location of the tumor (Small intestine), tumor diameter ≥5 cm, mitotic index ≥5/50HPF, and tumor rupture.[2]

Although gastrointestinal bleeding (often with chronic anemia) is a frequent presentation of GISTs acute massive bleeding resulting in shock and requiring urgent treatment is an extremely rare presentation.[9,10] Except for a few instances of hemoperitoneum, bleeding in the majority of GIST cases is intraluminal.[18,19] GISTs arising from the small intestinal are more likely to be clinically malignant than those originating from the stomach.[20] While the liver and peritoneum are the most frequent sites of metastasis, lymph node involvement was uncommon and was documented in only six (6%) patients.[6]

Anatomical proximity of duodenal GIST to noble structures (i.e., to the head of the pancreas, biliary structures) makes the diagnosis and management of dGISTs challenging. Especially duodenal tumors that arise in the second part can be difficult to differentiate from a pancreatic tumor.[21] It is important to make an accurate diagnosis before surgery since these two tumors have different management. While surgical resection with regional lymph node dissection is done for pancreatic tumor lymph node dissection is not required for dGIST due to the low risk of lymphatic metastasis.[22]

A combination of endoscopic and radiological techniques (CT and/or MRI) is usually utilized for accurate diagnosis of GIST. This is followed by tissue histology and immunohistochemistry for definitive diagnosis.[16] Since preoperative percutaneous biopsy carries the theoretical risk of peritoneal seeding or tumor rupture it is not usually recommended.[15] In addition to tissue sampling capability endoscopy has the added advantage of securing hemostasis in case of acute bleeding. GISTs are visualized as a bulging mass covered by the mucosa on endoscopy.[23] Contrast-enhanced CT scan is the choice of imaging often used for diagnosing, surgical planning, and follow-up in patients with GIST.[16,24]

CT scan evaluation fundamentally shows GISTs as submucosal tumors of the gastrointestinal tract with various degrees of enhancement, including hypo-enhancing, iso-enhancing, and hyper-enhancing neoplasms.[23,25] However, small bowel GISTs exhibit different pattern of enhancement from gastric GISTs. Small bowel GISTs show a washout pattern with marked enhancement during arterial phase, whereas gastric GISTs show a plateau pattern with intermediate enhancement.[23,26]

Since GISTs arise from the outer muscular layer they have a predilection of exophytic growth. However in about half of the cases there is some growth towards the lumen resulting mucosal ulceration and hence gastrointestinal bleeding. In large tumors, this results in cavitation/fistula, rupture, and perforation.[23,27] On sectional imaging, ulceration is seen as a recess on the surface of the tumor and cavitation/fistula is seen as tract continuing to the lumen that contains gas or fluid.[23]

Almost any GIST requiring treatment has the potential to become malignant making it difficult to label these tumors benign. Thus Fletcher and his associates suggested a classification based on size and mitotic count as very low, low, intermediate, and high risk. They suggested that tumors >5 cm in diameter plus a mitotic count higher than 5/50 high power fields (HPF) and tumors >10 cm with any mitotic rate have a higher risk of recurrence, subsequently requiring adjuvant drug therapy.[28]

Grossly GISTs are well-circumscribed gray-white to red-brown masses in the bowel wall that can be submucosal, intramural, or subserosal in location. They are generally unencapsulated but may have pseudocapsules.[29]

Histologically, 60%–70% of GISTs have a spindle cell pattern while 30%–40% of the tumors occur in epithelioid pattern.[23] The spindle cell GISTs are typically highly cellular tumors, often having a basophilic appearance. Other common histological features include nuclear palisading and bundling of tumor cells in fascicles separated by myxoid stroma. The epithelioid GISTs most commonly occur in the stomach. They are typically composed of polygonal cells with ample, amphophilic cytoplasm, and round nuclei.[30]

Similar to other small intestine GISTs, dGISTs are mostly spindle cell tumors. Epithelioid morphologic pattern is also observed in small intestine. However, unlike epithelioid gastric GISTs, small intestinal epithelioid GISTs probably represents morphologic manifestation of tumor progression rather than a distinct histologic subtype.[20]

Radical surgical resection is the standard treatment for localized primary GISTs, which is the potentially curative.[31] Indications for surgery include nongastric location, tumor size larger than or equal to 2 cm, or symptoms like gastrointestinal bleeding.[32] Lymphadenectomy is usually not required, since GISTs rarely metastasize to local or regional lymph nodes.[6,15]

The available operative approaches to manage duodenal GIST consist of open surgery, endoscopy, laparoscopy, and hybrid surgery such as endo–laparoscopic cooperative procedure. The choice of surgical procedure is particularly difficult to dGISTs because of their anatomic proximity to other biliary and pancreatic structures. Open surgery is applicable in most cases, especially in cases involving Ampulla of Vater and pancreas.[33]

There is a range of operative techniques described for resecting duodenal gastrointestinal stromal tumors (dGISTs) in medical literature, varying in invasiveness and

complexities. Limited resection (LR) of dGISTs involves local excision or wedge resection (WR) and segmental resection. Local excision involves excising the tumor with primary closure, without transecting or anastomosing the duodenum.[34,35] WR is a local excision with primary closure without duodenal transection or anastomoses. Segmental resection involves transecting the duodenum and reconstructing it. Reconstruction options include Billroth I gastroduodenostomy, Billroth II or Roux-en-Y gastrojejunostomy, end-to-end duodenoduodenostomy, and end-to-end or end-to-side duodenojejunostomy (DJ) anastomosis.[36] Pancreaticoduodenectomy (PD), also known as Whipple's procedure, is a more extensive resection technique. It involves resecting the duodenum, head of the pancreas, common bile duct, gallbladder, and sometimes the pylorus. This procedure also requires creating three anastomoses: gastrojejunostomy, choledochojejunostomy, and pancreaticojejunostomy. Another effective procedure is pylorus-preserving pancreaticoduodenectomy, which leaves the pyloric remnant intact. This procedure is equally effective as PD but preserves the pylorus.[37] In the case of this patient, a well-defined duodenal mucosal nodular mass measuring 4*4 cm was identified in the distal segment of the third part of the duodenum. During duodenotomy, active bleeding was observed from the mass. Consequently, a segmental resection was performed, followed by an end-to-end duodenoduodenostomy, considering the location of the mass in the third part and the adequate distance from the Ampulla of Vater.

Within the gastrointestinal tract, segmental resection of the intestine and stomach is commonly accepted, avoiding excessive removal of unaffected tissue. Radiological criteria for unresectability include infiltration of the celiac trunk, superior mesenteric artery, or mesenteric artery-to-portal vein. En bloc resection may be considered in specific cases, but multivisceral resection should be avoided. Multidisciplinary consultation with GIST experts is highly recommended.[38]

R1 resection of a GIST tumor does not increase the risk of recurrence or worsen survival, while macroscopic incomplete resection (R2) is associated with poorer outcomes. Re-excision after R1 surgery is not well-defined but may be offered if it does not pose significant risks or functional consequences.[39] Laparoscopic resection should adhere to the principles of open surgery, aiming for an R0 resection. However, laparoscopic resection is not recommended for tumors >10 cm due to the high risk of tumor rupture. It may be considered for GIST <5 cm in favorable anatomical locations, such as the greater curvature, fundus, and anterior gastric aspect. The extraction of the surgical specimen must be performed in a bag to prevent locoregional dissemination. The decision for laparoscopic resection should be made on a case-by-case basis, following multidisciplinary evaluation by experienced laparoscopic surgery teams.[40,41]

Even though surgery can be potentially curative, the high rate of recurrence emphasize the need for adjuvant therapy. Imatinib mesylate is a potent tyrosine kinase inhibitor that can be utilized preoperatively to reduce the tumor and/or as adjuvant therapy to prevent recurrence. Many develop resistance to this drug due to secondary KIT mutations.[13]

Endoscopic is commonly utilized to secure hemostasis in cases GISTs presenting with upper gastrointestinal.[23] However failure to identify and/or stop active source of bleeding through upper-GI endoscopy led to urgent surgical intervention in other case reports,[42] which is also the case in our patient.

In a study conducted by Ronald P. DeMatteo et al. involving 200 patients with GISTs the overall survival rate was 35% at 5 years and with a median follow-up of 24 months, recurrence occurred in 40% patients. Some patients may develop late recurrences and metastases, 10 years after excision of the primary tumor.[10]

Prognostic factors in patients with GISTs are the mitotic index, tumor size, tumor location (small bowel GISTs have unfavorable prognosis than gastric GISTs), and tumor rupture. It is observed that prognosis of GIST patients with gastrointestinal bleeding and patients with tumors containing KIT exon 9 mutations or KIT exon 11 deletions was significantly worse.[43]

4 | CONCLUSION

Even if GISTs usually present with chronic GI bleeding, acute GI bleeding to the extent of life-threatening hemorrhagic shock is also a possibility, and GIST has to be considered as a differential diagnosis for patients who present with acute upper GI bleeding.

AUTHOR CONTRIBUTIONS

Samuel Addisu Abera: Writing – original draft; writing – review and editing. **Amanuel Kassa Tadesse:** Supervision; writing – original draft. **Kirubel Addisu Abera:** Supervision; writing – review and editing. **Kassa Berie Zegeye:** Resources; supervision. **Mohammed Alemu Ibrahim:** Resources; supervision. **Ashenafi Amsalu Feleke:** Writing – original draft; writing – review and editing. **Cheru lilay Gebrehiwet:** Supervision; writing – original draft. **Segenet Bizuneh Mengistu:** Writing – original draft; writing – review and editing. **Hirut Tesfahun Alemu:** Conceptualization; writing – original draft. **Yohannis Derbew Molla:** Writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest in this work.

DATA AVAILABILITY STATEMENT

The authors of this manuscript are willing to provide information regarding the case report. All the data can be provided by the corresponding author.

ETHICS STATEMENT

After being reviewed by an ethics board, this case report was found to be morally sound.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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