MGMT. OF COMPLEX CASES IN GI ONCOLOGY

Diagnostic and Therapeutic Challenges in the Management of Acute Massive Overt Bleeding of Jejunal Gastrointestinal Stromal Tumours: Case Series

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Abstract

Introduction Jejunal gastrointestinal stromal tumours (GIST) are rare mesenchymal tumours. Acute massive overt bleeding from jejunal GIST is very rare and poses both diagnostic and therapeutic challenges in emergent conditions.

Methods A case series with retrospective analysis of prospectively maintained database of patients presenting with acute massive overt bleeding secondary to histologically proven jejunal GIST was done. Clinical characteristics, endoscopic and imaging diagnostic features, histological findings, surgical procedures and outcomes in these patients were studied.

Results Three patients were included in this case series. Mean age of presentation was 49.0 years with two male and one female patient. All three patients presented with melena and hemodynamic instability, resuscitated with adequate blood transfusions. Routine endoscopic assessment were inconclusive. Multiphasic Computed Tomographic Angiography (CTA) revealed hypodense hypervascular mass in jejunum in all three patients. One patient was unresponsive to blood transfusion and underwent emergency exploratory laparotomy. One patient underwent laparoscopic resection and reconstruction. Mean length of hospital stay was 5.3 days. Histopathological examination confirmed jejunal GIST in all three patients with microscopically negative resection margins. Two patients were disease free till 18-month follow-up and the one patient lost to follow-up after 1 year.

Conclusion Multiphasic CTA is a single-step diagnostic tool for localisation of bleed and assessment of tumour characteristics in emergent conditions. Surgical resection is the mainstay of treatment for both control of bleed and to provide oncologically clear resection margins.

Keywords Gastrointestinal stromal tumour · Jejunum · Bleeding · Computed tomography · Surgery

Introduction

Gastrointestinal stromal tumours (GIST) rarely involve jejunum which constitutes 10% of all GIST and 0.04% of all small bowel (SB) neoplasm [1, 2]. The diagnosis of jejunal GIST is usually delayed due to its relative low incidence, variable non-specific symptoms, elusive by routine endoscopic techniques and wide range of radiological appearances [3]. Bleeding is the most common presenting complaint (30–40%) and accounts for less than 5% of all gastrointestinal (GI) bleed [3, 4]. Rarely jejunal GIST can present with acute massive overt GI bleed resulting in hemodynamic instability [5]. The management of these bleeding GIST without oncological compromise depends upon the patient status, volume of bleed, site of tumour, tumour characteristics and the availability of resources [6]. We are presenting a series of three cases of jejunal GIST presenting with acute massive overt GI bleed and discuss the diagnostic and therapeutic oncological goals of its management under emergent conditions.

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Methods

The study is a case series with a retrospective analysis of prospectively maintained database of non-consecutive patients presenting to emergency surgical department of Postgraduate Institute of Medical Education and Research, Chandigarh, India with acute massive overt GI bleed with hemodynamic instability secondary to histologically proven jejunal GIST during the period of July 2017 to June 2020. A total of three patients met the above said criteria and were included in the study. We describe the clinical characteristics, endoscopic and imaging diagnostic features, histological findings, surgical procedures and outcomes in these patients.

The data collected included patient demographics, symptomatology, abdominal signs, anatomical localisation, tumour characteristics, laboratory findings, surgical procedure performed, pathological findings, immunohistochemical (IHC) analysis, length of hospital stay and intraoperative and postoperative complications. Pre-operative diagnosis and evaluation of tumour characteristics were performed using upper GI (UGI) endoscopy, colonoscopy and Multiphasic Computed Tomographic Angiography (CTA) of abdomen. Patients were resuscitated with adequate blood transfusions. Hemodynamically unstable patients were subjected to emergency laparotomy and stable patients were operated electively in an early date in view of ongoing active chronic bleed. The procedure involved both open and laparoscopic techniques. Intraoperatively jejunal tumours were resected carefully with recommended adequate tumour margins (> 1 cm) and without tumour capsule breach. Pathological specimens were examined for tumour site, size, margins, serosal and mucosal breach and histologically analysed for tumour subtype, nature, mitotic rate, tumour necrosis, lymphovascular invasion and tumour grade. IHC analysis was performed using markers such as Ki67%, CD117, c-KIT, DOG1 and S-100 protein. Data were reported as nominal, ordinal, discrete and continuous variables. All the patients were followed up with length of hospital stay, routine visits initially 15 days after hospital discharge and then at intervals of 3 months up to 2 years with clinical examinations and CT.

A literature review was performed for previous publications on Pub Med and Google Scholar database including terms ‘Jejunal GIST’, ‘GI bleed’, ‘Endoscopy’ and ‘Surgery’. The study has been reported in line with the PROCESS guidelines [7].

Results

The case details have been summarised in Table 1. A total of three patients, two males and one female with mean age of 49.0 years (range 38–62 years), were studied. All three patients had significant history of melena ranging from 2 days to 3 years in duration. None of the patients had hematemesis, vomiting, pain abdomen and sensation of abdominal lump. Two of these patients had similar past history of melena 1 and 2 years back with inconclusive diagnosis, treated by blood transfusions. These two patients had acute episode of melena since 2 days and 4 months and presented to surgical emergency with transient hypotension stabilised with blood transfusions. One of these patients was unresponsive to blood transfusions and was subjected to emergency laparotomy. None of these patients had significant abdominal signs and all three patients had melenic stools in digital rectal examination. The mean haemoglobin (Hb) concentration was 8.4 g/dL (range 5.4–10.7) amongst which the patient with hemodynamic instability had Hb drop to 3.9 g/dL. UGI endoscopy and colonoscopy were normal amongst all the three patients provoking a diagnostic dilemma. Multiphasic CTA revealed hypervascular hypodense mass in jejunum in all three patients with mean size of 3.8 cm in max dimension (range 3.1–5.0 cm) without any active contrast extravasation (Fig. 1). The indication for surgery in all three patients was for control of bleed and curative oncological resection. One patient underwent laparoscopic resection and intracorporeal bowel anastomosis and other two patients underwent open exploratory laparotomy with resection of jejunal mass with adequate margins (> 1 cm) and end-to-end bowel anastomosis (Fig. 2). Two patients had jejunal mass 20 cm distal to duodenojejunal (DJ) flexure and one patient with 4 cm distal to DJ flexure in which DJ flexure was mobilised to avoid anastomotic tension. Intraoperative cut section of specimen revealed mucosal ulcerations in two patients who had open exploratory laparotomy (Fig. 3). Postoperative period was uneventful in two patients. One patient who had hemodynamic instability preoperatively had postoperative ileus relieved conservatively in 3 days. The mean length of hospital stay was 5.3 days (range 4 to 8 days). One patient who underwent laparoscopic resection had the lowest length of hospital stay of 4 days. Histopathological and IHC analysis were performed according to Fletcher criteria and confirmed jejunal GIST type in all three cases (Figs. 4 and 5). The mean tumour size was 3.83 cm in maximum dimension (range 2.5–5.0 cm), which was in accordance to radiological findings. High-grade GIST, low-grade GIST and benign GIST were identified in each patient. All the lesions had microscopically negative resection margins with mucosal breach and no serosal capsular breach. Mucosal breach must have been the reason for acute massive bleed in all these submucosal GIST lesions. The high-grade GIST patient was started on oral Imatinib 400 mg daily and followed up. Two patients had 18 months of follow-up and the other was lost for follow-up after 1 year and all were disease free until then.
Jejunal GIST (60–70%) are the most common small bowel GIST followed by ileum and duodenum [1, 3]. The mean age of presentation of jejunal GIST is 56 years similar to that of our case series. Jejunal GIST are mostly symptomatic (80%–90%), which may present most commonly as an insidious slow bleed or very rarely as an acute massive haemorrhage [3, 8, 9]. In a study by Constantin et al., haemorrhagic shock was seen in 6.4% of patients of jejunal GIST [10]. Clinically, the ulcerated or necrotic component of the tumour is believed to be the source of GI bleed in jejunal GIST. Hence, it may present commonly as intraluminal bleed and rarely as intraperitoneal rupture bleed. Intraluminal bleed is usually due to the compression, ischemia or infiltration of overlying mucosa by these highly vascular sub-mucosal layer tumours [11, 12]. Intraperitoneal tumour rupture was seen in 0.11% (3/27)

### Table 1  Case details

|                          | Patient 1          | Patient 2          | Patient 3          |
|--------------------------|--------------------|--------------------|--------------------|
| Age                      | 62 years           | 47 years           | 38 years           |
| Sex                      | Female             | Male               | Male               |
| Melena                   | Yes                | Yes                | Yes                |
| Duration                 | 2 days             | 4 months           | 3 years            |
| Hematemesis              | No                 | No                 | No                 |
| Pain abdomen             | No                 | No                 | No                 |
| Previous history         | 1 year back        | 2 years back       | No                 |
| Tenderness               | No                 | No                 | No                 |
| Lump per abdomen         | No                 | No                 | No                 |
| Hemodynamic stability    | No                 | Yes                | Yes                |
| Blood (PRBC) transfusions| Yes                | Yes                | Yes                |
| Number of blood transfusion| 4 units           | 2 units            | 2 units            |
| Hb at admission          | 5.6 to 3.9 g/dL    | 10.7 g/dL          | 8.9 g/dL           |
| UGI endoscopy            | Normal             | Normal             | Normal             |
| Colonoscopy              | Normal             | Normal             | Normal             |
| Multiphasic CTA location | Mid-jejunal mass   | Distal to DJ flexure| Mid-jejunal mass   |
|                          | 5 × 4 × 3.5 cm     | 3.4 × 2.3 × 1.6 cm | 3.5 × 2.6 cm       |
| Surgery type             | Open exploratory laparotomy | Open exploratory laparotomy | Laparoscopic        |
| Elective/emergency       | Emergency          | Elective           | Elective           |
| Indication for surgery   | Unstable           | Ongoing bleed      | Ongoing bleed      |
| Procedure                | Jejunal segmental resection | Jejunal segmental resection | Laparoscopic segmental resection |
| Intraoperative findings  | 5 × 5 cm jejunal mass | 3 × 2 cm jejunal mass | 5 × 5 cm jejunal mass |
|                          | Extra and intramural | Extra and Intramural | Extra and intramural |
| Distance from DJ flexure  | 20 cm from DJ flexure | 5 cm from DJ flexure | 20 cm from DJ flexure |
| Postoperative complications| Postoperative ileus | None               | None               |
| Length of hospital stay  | 8 days             | 5 days             | 4 days             |
| Tumour type              | Jejunal GIST       | Jejunal GIST       | Jejunal GIST       |
| Tumour size              | 4 × 3 × 3 cm       | 2.5 × 2.5 × 2 cm   | 3 × 3 × 5 cm       |
| Nature                   | Spindle cell       | Spindle cell       | Spindle cell       |
| Mitotic rate             | < 5/50 hpf         | No                 | > 5/50 hpf         |
| Tumour grade             | Low risk           | Benign             | High risk          |
| Margins                  | Free of tumour     | Free of tumour     | Free of tumour     |
| Mucosal breach           | Yes                | Yes                | Yes                |
| Serosal breach           | No                 | No                 | No                 |
| CD 117/c-KIT             | Positive           | Positive           | Positive           |
| DOG1                     | Positive           | Positive           | Positive           |
| S-100                    | Negative           | Negative           | Negative           |
| Ki 67                    | < 15%              | > 15%              |                    |
| Follow-up                | 12 months lost to follow-up | 15 months, asymptomatic | 18 months, asymptomatic |

### Discussion

Jejunal GIST (60–70%) are the most common small bowel GIST followed by ileum and duodenum [1, 3]. The mean age of presentation of jejunal GIST is 56 years similar to that of our case series. Jejunal GIST are mostly symptomatic (80%–90%), which may present most commonly as an insidious slow bleed or very rarely as an acute massive haemorrhage [3, 8, 9]. In a study by Constantin et al., haemorrhagic shock was seen in 6.4% of patients of jejunal GIST [10]. Clinically, the ulcerated or necrotic component of the tumour is believed to be the source of GI bleed in jejunal GIST. Hence, it may present commonly as intraluminal bleed and rarely as intraperitoneal rupture bleed. Intraluminal bleed is usually due to the compression, ischemia or infiltration of overlying mucosa by these highly vascular sub-mucosal layer tumours [11, 12]. Intraperitoneal tumour rupture was seen in 0.11% (3/27)
patients of SB GIST in a study by Sorour et al. [12]. In our study all three patients presented with intraluminal bleed, amongst which the patient with hemodynamic instability had tumour arising from mesenteric border. Retrospectively, we realised and assumed that the magnitude of bleed may depend upon the location along mesenteric border with direct mesenteric feeding vessels. Most of the GIST have deficient stromal collagen and prominent, delicate thin-walled vessels, making stromal haemorrhage a striking feature of these tumours [13].

Diagnostic Challenges

The diagnosis of a lesion in small bowel is determined by its location, assessment of its characteristic features and confirmation of diagnosis together by clinico-radiological, endoscopic and pathological studies. However, a massively bleeding GIST does not provide adequate time for a complete evaluation and optimised treatment plan. Usually the surgeon encounters a dilemma of whether to locate and control the source of bleed non-operatively or to proceed with upfront surgery. This dictates a dynamic multidisciplinary approach that prioritises diagnostic and therapeutic options promptly. Diagnostic modalities are wisely chosen for the
field of interest to provide the most probable diagnosis in short duration of time.

**Endoscopy**

Jejunal GIST are termed as ‘dark continent’ of small bowel by routine UGI endoscopy and colonoscopy due to its intraperitoneal location, high mobility and long length [3]. Recent advances in endoscopy such as Video Capsule Endoscopy (VCE), single balloon (SBE), double balloon (DBE) and spiral enteroscopy (SE) have made jejunal lesions accessible for both diagnostic and therapeutic indications. However, its use is recommended in chronic stable or mild to moderate suspected bleeding lesions [4]. Hence, its use in acute massive overt bleeding is doubtful. Nonetheless, these recent advances can be used as bridging procedure by temporary bleeding control with techniques like haemoclip, laser therapy and argon plasma coagulation [4]. These techniques, though available, were not used in view of acute massive overt bleeding of patients in our study.

**Radiographic Studies**

Recent advancements in multiphasic CTA have brought substantial changes in the management of acute GI bleed. Multiphasic CTA is strongly recommended by recent guidelines as the investigation of choice in acute massive overt GI bleed in hemodynamically stable patients [4, 13]. It has an accuracy of 100% in localisation of bleed at a sensitivity of 85% to detect bleeding at rates of 0.3 mL/min. Furthermore, the multiphasic enhancement panel guides in synchronous assessment of the tumour characteristics, level of exophytic component and relation to adjacent structures with faster acquisition time for early surgical planning [9, 13]. Multiphasic CTA has been used as the first-line investigation in our series. The importance

![Fig. 5](image-url)

**Fig. 5** a and b Histopathological section showing circumscribed tumour comprised of monomorphic spindle-shaped cells (inset shows necrosis) (200X, 400X haematoxylin and eosin). c IHC staining of the tumour is diffusely positive for c-KIT (CD117), 400X DAAB chromogen. d IHC staining with low Ki67 index, 400X DAAB chromogen.
of the use of multiphasic CTA in acute massively bleeding jejunal GIST has been clearly documented in a study by Daldoul et al. [13]. However, the main impediment of CTA is that the patient must be actively bleeding at the time of scan to localize the bleed and has increased risk of renal complication [4, 9].

Conventional angiography (CA) has been recommended strongly to be performed in hemodynamically unstable patients with acute massive overt GI bleed requiring more than five blood transfusions [4]. An additional advantage of CA is the ability to perform super selective trans-arterial embolisation as a therapeutic intervention at the time of diagnosis with the bleeding rates of 0.5–1.0 mL/min. Studies have shown an overall clinical success rate of more than 95% with CA in active bleed [4, 14]. It can be used as an interim procedure before surgery in achieving haemostasis and facilitates limited resection in metastatic GIST by tumour size reduction. The potential detrimental effects of this procedure include bowel infarction (4%) and procedure-related complications such as arterial dissection, non-target embolisation, renal failure and catheter site infection and hematoma up to 10% [15, 16].

There is a substantial dispute in the use of ⁹⁹ᵐTc-labelled RBC scintigraphy for acute overt GI bleed. It has been recommended in ambiguity of active bleed and to guide timing of angiography [4].

**Therapeutic Challenges**

Surgical resection remains the linchpin in treatment of non-metastatic GIST [3, 8, 17]. The two main goals in surgical management of acute massive jejunal GIST bleed are the control of bleed and to provide an oncologically clear resection margins. Control of bleed initially begins with adequate resuscitation. Volume replacement is the key element of resuscitation, but off-targeted combative fluid resuscitation must be desisted to allow clot formation and to prevent massive bleeding. Coagulopathy must be corrected and hypothermia obviated. Any medications such as antiplatelet and anticoagulants are immediately stopped [18]. In our study all three patients had hemorrhagic shock at presentation and two patients responded to resuscitation.

The oncological principle precepts R0 resection with wide margins of 1–2 cm without tumour capsular breach [17, 19]. Surgical procedure may include local excision and segmental resection based on the size of tumour [8]. En bloc resection along with the tumour mass should be attempted with adjacent organ involvement, in order to avoid tumour capsule rupture and intraabdominal spillage, whenever feasible [20]. A study by Wu et al. showed that complete tumour resection is an important predictor for patient survival with a significantly increased median survival of 123.3 months compared with 12.0 months for those who had inadequate surgical resection. Jejunal GIST has a serious risk of early recurrence after curative resection. In the same study, 51.8% patients had recurrence within a median time of 20.5 months after curative resection [8]. In a study by Liu et al., GI bleeding caused by GIST was identified as an independent risk factor for recurrence and death (p = 0.039). This study also showed that both disease-free survival (p = 0.0002) and overall survival (p = 0.023) were shorter for patients with GIST bleed [21]. As jejunal GIST rarely metastasise to local or regional lymph nodes, lymphadenectomy is not routinely required [17, 19]. All our patients had complete R0 segmental resection without tumour capsule breach.

Surgical techniques include open and laparoscopic resection. One patient in our study underwent laparoscopic resection and other two patients had open exploratory laparotomy. Laparoscopic surgical approach is clearly discouraged in large GIST due to increased risk of intraabdominal seeding [22]. A favourable short-term postoperative outcome without oncological compromise was reported by Ihn et al. by laparoscopic resection of SB GIST < 10 cm in diameter, when compared with open surgery [23]. This study has several limitations such as being a case series of three cases, single centre, retrospective study and potential confounding factors were not studied. Proper management mandates recommendation guidelines from large-scale randomised control trials and meta-analysis.

**Conclusion**

Acute massive overt bleed of jejunal GIST is very rare entity. High suspicion and anticipation is mandated for treating surgeons. Multiphasic CTA should be considered as single-step diagnostic aid for localisation of bleed and assessment of tumour characteristics in emergent conditions. Surgical resection is the mainstay of treatment for both control of bleed and to provide oncologically clear resection margins. Jejunal GIST has a high propensity for recurrence. GIST bleed is an independent risk factor for poor prognosis. Regular close follow-up is recommended for jejunal GIST bleed [19, 20, 22].

**Author Contribution** Satish Subbiah Nagaraj and Hemanth Kumar contributed to the study conception and design. Material preparation, data collection, analysis and first draft of the manuscript were written by Satish Subbiah Nagaraj, Sriram Deivasigamani, Amresh Aruni and Anurag Sachan. Manuscript review, editing, supervision and final approval was done by Satish Subbiah Nagaraj, Hemanth Kumar, Jayanta Samata and Amanjit Bal.
Declarations

Ethical Approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent Written informed consent for the paper to be published (including images, case history and data) was obtained from the patient/guardian for publication of this paper, including accompanying images.

Conflicts of Interest The authors declare no competing interests.

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