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Journal of Surgery

Khuri S, et al. J Surg 11: 1215.

Research Article

DOI: 10.29011/2575-9760.001215

Gastrointestinal Stromal Tumor of the Small Bowel: The Forgotten Cause of Massive Obscure Gastrointestinal Hemorrhage

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Citation: Khuri S, Hallon K, Azzam A, Kluger Y (2019) Gastrointestinal Stromal Tumor of the Small Bowel: The Forgotten Cause of Massive Obscure Gastrointestinal Hemorrhage J Surg 11: 1215. DOI: 10.29011/2575-9760.001215

Received Date: 25 April, 2019; **Accepted Date:** 30 April, 2019; **Published Date:** 06 May, 2019

Abstract

Introduction: Gastrointestinal (GI) bleeding is a very common surgical emergency, with an incidence of 150 cases/100000 adults. The small bowel accounts for almost 2-10% of all causes of GI hemorrhage, with vascular abnormalities being the most common cause of small bowel bleeding, while small bowel tumors account for only 5-10%. Gastrointestinal Stromal Tumor (GIST) is the most common mesenchymal tumor of the GI tract, and represent less than 1% of all GI tumors. GIST may present as an incidental radiological/operative finding, or may even present as a surgical emergency in the form of intestinal obstruction, perforation or massive obscure GI bleeding.

Methods: A retrospective study over a period of 7 years, between January 1st, 2011 and December 31st ,2017 was performed at the general surgery department at Rambam Health Care Campus, Haifa, Israel. All patients 18 years old and older with a diagnosis of GIST were included in the study.

Results: During the aforementioned period, data on 66 patients (n=66) with a diagnosis of GIST were reported. 53% (n=35) patients had gastric GIST, 33.3% patients (n=22) involving the small bowel, 6% (n=4) affected the peritoneum, 3% (n=2) had rectal GIST, 3% (n=2) colon GIST and 1.5% (n=1) had retroperitoneal GIST.

Of patients with small bowel GIST, 50% (n=11) presented with GI hemorrhage, with 9 patients (41%) presenting with massive obscure GI bleeding. Most of these patients (7/9) presented initially with melena which evolved into cherry red rectal bleeding later. Average packed cells transfusion was 11.6 units (range 3 units- 23 units). There was no association between tumor size and risk for blood transfusion, as the smallest tumor diameter reported was 0.7 cm in a patient receiving 23 packed cells units. On the contrary, a clear correlation was observed between time from admission to diagnosis and the number of packed cells transfused, indicating the importance of high index of suspicion for such entity. 9 out of the 11 patients were diagnosed by Computed Tomographic Angiography (CTA), one was diagnosed during laparotomy and one by push enteroscopy, reflecting the important rule for CTA in diagnosing such rare entity.

Conclusion: Small bowel GIST is a rare, yet underestimated entity as a cause of massive GI bleeding, and High index of suspicion is mandatory. Abdomino-pelvic CTA is highly recommended as a first line investigation for patients with massive GI bleeding. Due to lack of studies in the English literature, multi-centric high volume studies are encouraged.

Keywords: CT Angiography; GIST; GI hemorrhage

Introduction

Gastrointestinal (GI) hemorrhage is one of the most common medical problems encountered in the acute care setting [1], being a major cause of admission to hospitals of about 300,000 patients annually [2]. The reported estimated incidence of this problem is about 150 patient/100,000 populations, with a mortality rate of 5-10% [3,4]. GI bleeding is usually classified, according to the Ligament of Treitz, into upper GI bleeding when the site of bleeding is proximal to the ligament [5], and lower GI bleeding, when the bleeding originates from a source distal to the ligament [6].

GI bleeding can also be classified, according to the bleeding rate loss, into overt, occult or obscure bleeding. Overt GI bleeding, known as acute bleeding, is usually obvious to the treating physician in the form of hematemesis, coffee ground vomiting, melena or hematochezia. While on the other hand occult bleeding, otherwise known as chronic bleeding, present as hemoccult-positive stool, with or without iron-deficiency anemia, due to slow microscopic bleeding [7,8]. Obscure GI bleeding is defined as a recurrent or persistent bleeding following negative initial upper and lower endoscopy and radiologic imaging of the small bowel, and can present as overt or occult hemorrhage [8,9]. Obscure GI bleeding represent approximately 5% of all GI hemorrhage, with the small bowel being the most common source at 41-75% [9,10]. This is mainly due to its anatomical features being inaccessible to conventional endoscopy, and thus, sometimes called "The dark continent of the GI tract" [11]. Due to the aforementioned difficulty, obscure GI bleeding due to primary small bowel pathology, usually poses a main challenge to the treating physician. Other causes of obscure GI bleeding may be missed lesions on initial endoscopy, thus repeated upper and lower endoscopy are always warranted.

Several variable lesions of the small bowel, such as vascular malformations, tumors and inflammatory lesions, can present as obscure GI bleeding, with the most common cause being different in different age groups [12]. In the elderly age group (older than 40 years old), the most common causes are vascular lesions and Non-Steroidal Anti-Inflammatory (NSAIDS) drugs related lesions, while tumors, Crohn's disease and Meckel's diverticulum being more common in patients younger than 40 years old [9,13]. In a study conducted by Zhang, et al. vascular anomalies were the most common cause of obscure GI bleeding in elderly patients (>65 years) and middle age group (41-65 years), while small bowel tumors were the major cause in young patients (<40 years) [13]. Primary small bowel tumors are rare tumors and account for approximately 5% of all GI tract tumors [14]. Recently, its incidence is increasing dramatically due to the increasing incidence of carcinoid tumors [15]. Although these tumors are uncommon cause of GI bleeding, they are the second most common cause of small bowel bleeding at 5-10% of cases [16].

Small bowel tumors can be classified as benign, such as adenoma, lipoma and benign stromal tumors, usually detected in autopsy series, or malignant tumors [15]. The most common malignant primary small bowel tumor is carcinoid tumor (44%), followed by adenocarcinoma (33%), stromal tumors (17%) and lymphomas (8%) [17]. Gastrointestinal Stromal Tumor (GIST) is the most common soft tissue sarcoma of the GI tract (80%), representing about 5% of all sarcomas and less than 1% of all GI tumors [18]. Although GISTs may present as multiple lesions, they are usually solitary, with an estimated frequency of 10-20 new cases/ 1 million population per year, indicating its rare incidence [19]. The most common site to be involved by GIST is the stomach (60-70%), followed by the small bowel (25-35%) [20]. Small bowel GIST usually present with nonspecific signs and symptoms, and thus, difficult to diagnose pre-operatively. The most common symptom being vague abdominal pain (70%) [20]. Although rare, these tumors can also present as a surgical emergency, such as intestinal obstruction, perforation or massive GI bleeding [21,22].

Methods

A retrospective study over a period of 7 years, between January 1, 2011 and December 31 2017 was performed at the General Surgery Department at Rambam Health Care Campus, Haifa, Israel. Rambam Health Care Campus is a referral center for 10 other hospitals that give medical cover for 2 million citizens. All patients admitted with a diagnosis of GIST, ages 18 years and over, were included in the study. Due to the retrospective nature of the study, informed consent was waived.

Aim of the study

The aim of the study was to predict the frequency of massive GI bleeding in patients with small bowel GIST and whether any association exists between tumor size/site and bleeding risk (measured by number of Packed Cells transfused). In addition, this study was aimed to identify the best method to diagnose bleeding small bowel GIST.

Results

During the study period, data on 66 patients (n=66) with a diagnosis of GIST were reported. 53% (n=35) patients had gastric GIST, 33.3% patients (n=22) had small bowel involvement, 6% (n=4) had peritoneal involvement, 3% (n=2) had rectal GIST, 3% (n=2) had colon GIST and 1.5% (n=1) had retroperitoneal GIST (Figure 1).

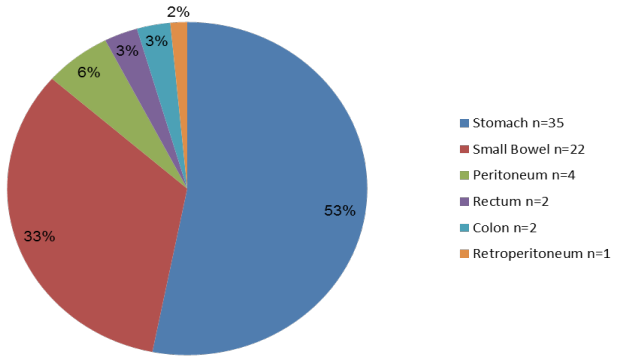

Figure 1: Demonstrates the different sites affected by GIST (shown as percentages).

Out of the patients with small bowel GIST, 13 patients (59%) were males and 9 (41%) were females (male/female ratio-1.43:1). Median age of diagnosis was 63 years old (range 23-85 years). The most common affected part of the small bowel was the jejunum (n=13), followed by the ileum (n=7) and the duodenum (n=2) (Figure 2).

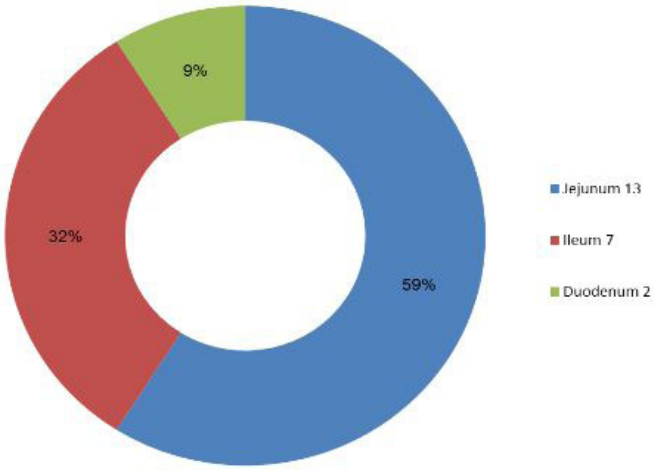

Figure 2: Shows the involved different parts of the small bowel (shown as number of patients).

The most common presentation was GI bleeding 50% (n=11), in which 9 patients (41%) presented with massive obscure GI bleeding and 2 patients (9%) presented with iron deficiency anemia due to slow GI bleeding. In 4 patients (18%) GIST was detected as an incidental radiological finding (on Computed Tomography-CT- scan performed for other indications), and in 3 patients (13.6%) as an incidental operative finding. 4 patients (18%) presented as another surgical emergency (perforation and obstruction) (Figure 3).

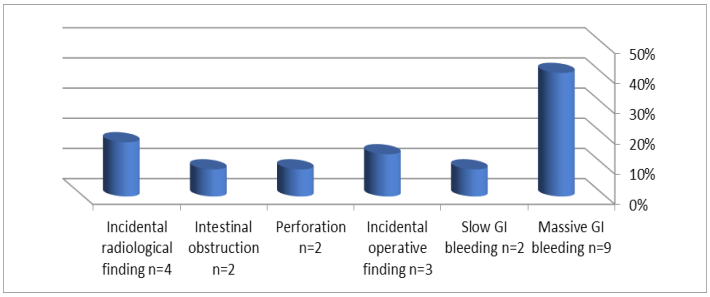

Figure 3: Presents the different clinical presentations of small bowel GIST (shown as percentages and absolute number).

Out of the patients that presented with massive GI bleeding, most of them (7/9) presented initially with melena which progressed into cherry red rectal bleeding later on. Average Packed Cells (PCs) transfusion (as a marker for bleeding risk) was 11.6 units (range 3 units- 23 units). There was no association between tumor size and risk for blood transfusion, as the smallest tumor diameter reported was 0.7 cm in a patient receiving 23 units of PCs, and the largest tumor diameter (9 cm) received only 6 units of PCs (Table 1).

	Tumor size	Tumor site	
23	**0.7 cm**	**jejunum**	**Case I**
3	1.5 cm	ileum	Case II
12	2.3 cm	jejunum	Case III
8	3.8 cm	jejunum	Case IV
19	4 cm	ileum	Case V
6	5.5 cm	jejunum	Case VI
7	7 cm	ileum	Case VII
6	9 cm	ileum	Case VIII
12	3 cm	duodenum	Case IX

Table 1: Demonstrating the number of packed cells patients received.

In relation to the site of bleeding small bowel GIST, average PCs transfusion for a bleeding jejunal GIST was 12, while it was 8 PCs for a bleeding ileal GIST. On the contrary, a clear correlation was observed between time from admission to diagnosis and the number of PCs transfused. The longer the time from admission to diagnosis, the higher the number of PCs transfused, indicating the importance of high index of suspicion for such entity (Table 2).

Number of transfused Packed Cells	Time from admission to diagnosis (Hours)	
23	356	Case I
3	6	Case II
12	168	Case III
8	40	Case IV

19	139	Case V
6	17	Case VI
7	264	Case VII
6	***4***	Case VIII
12	88	Case IX

Table 2: Showing the association between time from admission to diagnosis and the number of packed cells transfused.

Of patients presented with GI bleeding, 9 out of 11 (9 out of the total 22 patients- 41%) patients were diagnosed by CTA, one was diagnosed during laparotomy and one by push enteroscopy. These figures indicate the important rule for CTA in diagnosing such rare entity**.** Another fact worth mentioning was that the majority of patients who presented with massive GI bleeding (7 out of 9) were not treated by anti-coagulant or anti-platelet therapy, which may suggest that there is no association between treatment with the previous therapy and risk for a bleeding small bowel GIST.

Discussion

Gastrointestinal Stromal Tumor (GIST), the most common mesenchymal tumor of the GI tract, was first described in 1983 by Clark and Mazor [23]. It was termed GIST to describe a heterogenous group of non-epithelial tumors. This was later found to have C-kit mutation activation, which plays an essential role in its pathogenesis, as reported by Hirota in 1998 [24]. Althogh previously considered as a smooth muscle tumor variant, it is now well known that GISTs arise from the interstitial cells of Cajal, which are part of the autonomic nervous system of the intestine. This historical change was largely due to the immunochemistry and molecular advancement [25]. GISTs usually arise from the muscularis mucosa or muscularis propria of the GI tract wall, with a unique exophytic pattern of growth. It develops mainly in patients during the sixth decade of life [20]. Although GISTs can arise anywhere in the GI tract from the esophagus to the rectum, the most common organ to be affected is the stomach (60-70%), followed by the small bowel (25-35%) [20]. Other relatively rare GI tract sites to be involved include the colon and rectum (5%), esophagus (2-3%) and the appendix. GIST may also arise in areas outside of the GI tract, termed extra GIST, such as the greater omentum, peritoneum and retroperitoneum [26]. The same figures were documented in our study as well. The mean size of the tumor at the time of diagnosis is about 5 cm [27].

GISTs tumors are usually sporadic diseases. These tumors may also be part of other familial syndromes such as the Carney triad (paraganglioma, pulmonary chondroma and gastric stromal tumors) or Neurofibromatosis Type 1 (Von Recklinghausen's disease, an autosomal-dominant disease characterized by skin pigmentations, skeletal dysplasia, lisch nodules and plexiform neurofibromas) [28-31]. When arising as part of Neurofibromatosis Type 1, GISTs are usually multiple, affect young patients (<50 years old), and more commonly involve the small bowel with relatively uncommon malignant potential [32]. The majority of GIST tumors are benign, with 20-30% of these tumors being malignant [21]. Malignant potential depends on several factors such as tumor size, mitoses and primary tumor location. A prognostic classification, proposed by Fletcher, et al. classifies these tumors into very low, low, intermediate and high risk of malignancy (Table 3) [33].

	Size (largest dimension)	Mitotic count
Very low risk	<2 cm	<5/50 HPF
Low risk	2–5 cm	<5/50 HPF
Intermediate risk	<5 cm	6–10/50 HPF
	5–10 cm	<5/50 HPF
	>5 cm	>5/50 HPF
High risk	>10 cm	Any mitotic rate

Table 3: Fletcher, et al. prognostic classification.

Small bowel GISTs have variable clinical presentations, depending on the size of the primary tumor. Small size tumors (<2 cm) are usually asymptomatic and incidentally found on radiological studies or during operations. These tumors represent almost 30% of all small bowel GISTs [20,26]. The majority of small bowel GISTs (70%) are usually symptomatic, with vague abdominal pain being the most common symptom [20]. Other non-specific symptoms may include early satiety, nausea, vomiting and abdominal fullness.

GIST tumors can arise anywhere in the small intestine, with the jejunum being the most common site, as reported in a retrospective study about 197 patients, by Gu-sheng Xing [34]. These figures match ours. Small bowel GISTs (especially tumors > 4 cm) can present as an abdominal emergency, such as intestinal obstruction, perforation or massive GI bleeding. These surgical emergencies are more common in GISTs affecting the small bowel than any other GI tract sites. Reviewing the current English literature revealed only 25 cases of acute abdomen due to spontaneous perforation of small bowel GIST, indicating the rare incidence of such entity [35]. Small intestinal obstruction is another surgical presentation of small bowel GIST. Due to its exophytic nature of growth, intestinal obstruction develops due to compression rather than luminal obstruction. A study published by Magdy A. Sorour reported 27 cases of small bowel GIST. The majority of these patients (22 cases) presented with intestinal obstruction, while only 3 patients presented with bleeding and

2 patients with peritonitis due to perforation [35]. These figures contradict ours, as the most common presentation for small bowel GIST in our study was massive obscure GI bleeding.

GISTs also have hemorrhagic potential and can present as a GI bleeding, due to ulceration of the overlying bowel mucosa [36]. They may present as a life threatening massive obscure GI bleeding, with the incidence of this presentation being variable in different studies. In contrast to the results of our study, with bleeding being the most common presentation of small bowel GIST, the previously mentioned study by Gu-sheng Xing, reports bleeding being the most common presentation of small bowel GIST originating in the duodenum, while those originating from the jejunum and ileum present mainly with epigastric discomfort, abdominal mass or as an incidental finding (34). Another study by Vij, et al. showed that GI bleeding was the most common clinical presentation of GIST (69%) at all levels of the small bowel [37].

Recently, it was revealed that GI bleeding may be considered as an independent risk factor for tumor recurrence, according to several researchers [38,39]. Despite the previously mentioned risk of recurrence, until now, there has been no study conducted to detect whether any association between tumor size and bleeding risk exists. According to our study, there is no association between tumor size and risk of bleeding and blood transfusion, as the patient with the smallest tumor diameter (0.7 cm) received more units of PCs than any other patient, while patients with the largest tumor diameter received only 6 units of PCs. On the other hand, a clear correlation was noted between time from admission to diagnosis and the number of packed cells transfused, indicating that high index of suspicion is always warranted, especially in patients with a massive form of GI bleeding.

English literature also lacks studies concerning an association between anticoagulant/antiplatelet management and risk for bleeding small bowel GIST. According to figures from our study, there is no clear correlation as only two patients (out of nine) were treated by these medications. Regarding mode of diagnosis, none of the diagnostic procedures used nowadays, including ultrasound, barium examination, CT scan, angiography and magnetic resonance imaging, has a 100% certainty for diagnosis of small bowel GIST [35]. Recently, multi detector CTA has become one of the most commonly used method for the diagnosis of acute GI bleeding, due to its wide rapid availability. CTA has the ability to diagnose GI arterial and venous bleeding, delineate the underlying cause and direct specific treatment [40]. Its disadvantages include high radiation dose, need for intravenous contrast material, decreased sensitivity relative to other diagnostic modalities, such as radionuclide studies and the inability to perform therapeutic procedures [41]. Multiple studies evaluate the rate of bleeding that can be detected by mutidetector CTA. A study by Dobritz, et al. showed that rates of bleeding above 0.25 ml per minute can be detected by the previously mentioned modality, with a sensitivity of 97% and specificity of 100% [42]. CT Angiography (CTA) was the most sensitive tool in our study, as 41% of our patients were diagnosed by this modality.

A retrospective study by Lei Zhou revealed that the detection rate of small bowel GIST by CTA was about 71%, preceded only by double balloon enteroscopy at a rate of 89% [43].

The following are brief descriptions of some of our patients that presented with massive GI bleeding in our study:

Case 1

A 70-year-old male patient presented with dark tarry stools of 3 days' duration that progressed into dark red stool in a few hours prior to admission. On his admission, his vital signs revealed tachycardia of 126/min and blood pressure of 100/60. CTA showed a lobular mass of 8 cm diameter, with calcification at the pelvis, attached to the terminal ileum, with an intraluminal blush of contrast material (Figure 4). At surgery, a hypervascular mass of 8 cm diameter at the right pelvis was found. The mass was partly calcified and seemed to arise from the distal ileum (Figure 5). En bloc resection of the mass along with a 20 cm of ileum and primary side-to-side anastomosis was performed. The histopathological exam revealed an epithelioid type GIST, of 9 cm diameter, arising in the muscularis propria and extending to the pericolonic adventitia, reaching the serosa.

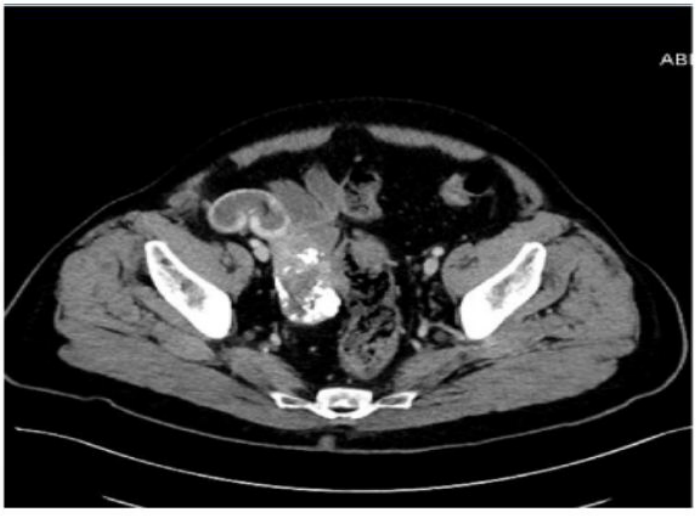

Figure 4: Axial CTA of the abdomen showing a calcified mass at the right pelvis, attached to the distal ileum with intraluminal contrast blush.

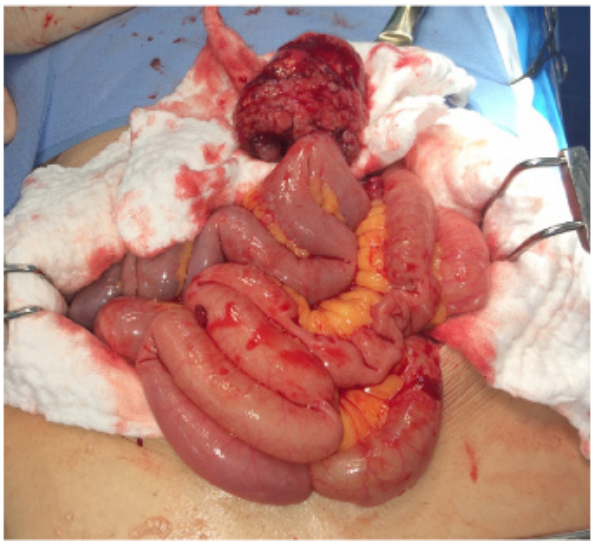

Figure 5: At exploratory laparotomy, a hyper vascular calcified mass of 8 cm arising from the distal ileum, with ongoing intraluminal bleeding was shown.

Case 2

An 85-year-old male patient presented to our department with melena and syncope of one-day duration. Vital signs on his admission were within normal limits. An upper endoscopy showed a suspected Diulafoy's lesion in the 4th part of duodenum. Endoscopic management by clips failed and thus the patient underwent CTA which revealed a space occupying lesion of 4*3.5 cm at the upper jejunum with intra-luminal contrast blush. On exploration of the abdomen, an exophytic mass of 4 cm diameter at the upper jejnum (10 cm distal to the treitz) ligament was demonstrated (Figure 6). En bloc resection with primary hand-sewn anastomosis was completed. Histopathological findings were consistent with low risk GIST.

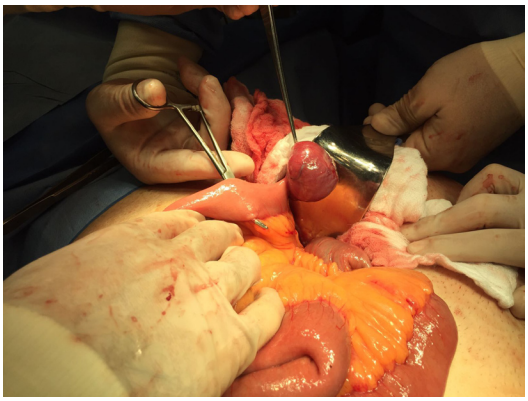

Figure 6: On exploration of the abdomin, an exophytic 4 cm mass originating from the upper jejunum was seen.

Case 3

A 68-year-old female patient, known to have oral cavity squamous cell carcinoma with percutaneous endoscopic gastrostomy for feeding purposes, presented with melena and coffee ground secretion per gastrostomy of 2 days' duration. Initial upper endoscopy revealed an ulcer in the third part of the duodenum, who was treated by adrenaline injection and clip placement. During the next day the patient continued to pass cherry red stool. CTA showed a 2 cm mass at the 4th duodenal/ 1st jejunal part with contrast blush (Figure 7). On exploratory laparotomy, an exophytic small tumor at the Treitz Ligament level was demonstrated (Figure 8). Resection with primary anastomosis was completed. Histopathology revealed low-risk GIST.

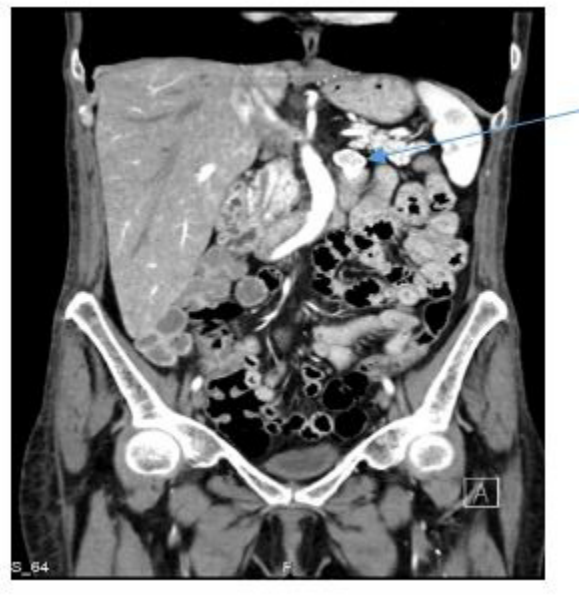

Figure 7: Coronal CTA of the abdomin showing a hyperdense, lobular 2 cm mass (arrow) at the treitz ligament level.

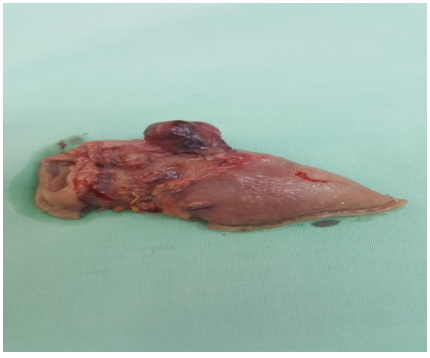

Figure 8: The resected small bowel segment along with the exophytic lobular mass.

Case 4

A 75-year-old male patient was referred to our hospital from a tertiary hospital due to melena of 6 days' duration. Two upper endoscopies led to the high suspicion of bleeding originating from the 3rd part of the duodenum with no definite lesion. CTA revealed a hyperdense mass during the arterial phase in the 3rd part of the duodenum with active bleeding (Figure 9). On surgery, a 3 cm exophytic mass in the 3rd part of the duodenum was demonstrated. Resection of the 3rd and 4th part of the duodenum and 1st part of the jejunum along with hand sewn anastomosis of the 2nd part of the duodenum and jejunum was completed. Histopathological report was consistent with low risk GIST.

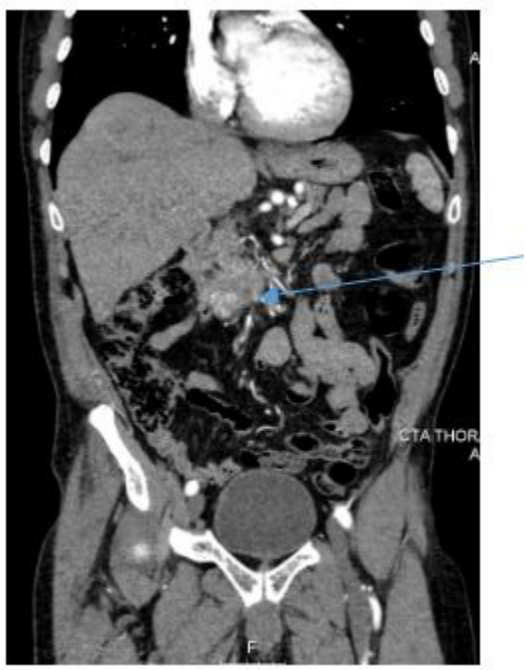

Figure 9: Coronal CTA of the abdomin and pelvis showing a hyperdense mass at the 3rd part (arrow) of the duodenum during the arterial phase of the CTA.

Conclusion

Massive obscure GI bleeding can be due to several small bowel etiologies. Small bowel GIST, a rare underestimated tumor can be the cause in several cases, and a high index of suspicion is always warranted. Due to its high sensitivity, abdomino-pelvic CTA is a highly recommended radiological modality as a first line investigation for massive GI bleeding, especially when the cause is due to a bleeding small bowel GIST. Due to lack of studies in the English literature, multi-centric high volume studies are encouraged.

Limitations of the study

The limitations of our study include a retrospective, small size and single center study.

Conflicts of interest

The authors do not have any conflicts of interest.

Worth mentioning, this study was partly presented as an abstract at the "International Conference on Surgery and Anesthesia" in Rome, November 2018.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Cutler JA, Mendeloff AI (1981) Upper gastrointestinal bleeding. Nature and magnitude of the problem in the U.S. Dig Dis Sci 26: 90S-96S.
2. Manning-Dimmitt LL, Dimmitt SG, Wilson GR (2005) Diagnosis of gastrointestinal bleeding in adults. Am Fam Physician 71: 1339-1346.
3. Hilsden RJ, Shaffer EA (1936) Management of gastrointestinal hemorrhage. Can Fam Physician 41: 1939-1941.
4. Blatchford O, Davidson LA, Murray WR, Blatchford M, Pell J (1997) Acute upper gastrointestinal haemorrhage in west of Scotland: case ascertainment study. BMJ 315: 510-514.
5. Longstreth GF (1995) Epidemiology of hospitalization for acute upper gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol 90: 206-210.
6. Davila RE, Rajan E, Adler DG, Egan J, Hirota WK, et al. (2005) ASGE Guideline: the role of endoscopy in the patient with lower-GI bleeding. Gastrointest Endosc 62: 656-660.
7. British Society of Gastroenterology Endoscopy Committee (2002) Non-variceal upper gastrointestinal haemorrhage: guidelines. Gut 4: 1-6.
8. Bull-Henry K, Al-Kawas FH (2013) Evaluation of occult gastrointestinal bleeding. Am Fam Physician 87: 430-436.
9. Raju GS, Gerson L, Das A, Lewis B (2007) American Gastroenterological Association (AGA) Institute medical position statement on obscure gastrointestinal bleeding. Gastroenterology 133: 1694-1696.
10. Szold A, Katz LB, Lewis BS (1992) Surgical approach to occult gastrointestinal bleeding. Am J Surg 163: 90-92.
11. Katz LB (1999) The role of surgery in occult gastrointestinal bleeding. Semin Gastrointest Dis 10: 78-81.
12. Gunjan D, Sharma V, Rana SS, Bhasin DK (2014) Small bowel bleeding: a comprehensive review. Gastroenterology Report 2: 262-275.
13. Zhang BL, Chen CX, Li YM (2012) Capsule endoscopy examination. Identifies different leading causes of obscure gastrointestinal. Bleeding in patients of different ages. Turk J Gastroenterol 23: 220-225.

14. Schwartz GD, Barkin JS (2006) Small bowel tumours. Gastrointest Endosc Clin N Am 16: 267-275.

15. Bilimoria KY, Bentrem DJ, Wayne JD, Ko CY, Bennet CL, et al. (2009) Small bowel cancer in the United States: changes in epidemiology, treatment, and survival over the last 20 years. Ann Surg 249: 63-71.

16. Lewis BS, Kornbluth A and Waye JD (1991) Small bowel tumours: yield of enteroscopy. Gut 32: 763-765.

17. Weiss NS, Yang CP (1987) Incidence of histologic types of cancer of the small intestine. J Nat Cancer Inst 78: 653-656.

18. Joensuu H, Fletcher C, Dimitrijevic S, Silberman S, Roberts P, et al. (2002) Management of malignant gastrointestinal stromal tumours. Lancet Oncol 3: 655-664.

19. Nilsson B, Bumming P, Meis-Kindblom JM, Odén A, Dortok A, et al. (2005) Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era - a population-based study in western Sweden. Cancer 103: 821-829.

20. Connolly EM, Gaffney E, Reynolds JV (2003) "Gastrointestinal stromal tumours," British Journal of Surgery 90: 1178-1186.

21. Efremidou EI, Liratzopoulos N, Papageorgiou MS, Romanidis K (2006) "Perforated GIST of the small intestine as a rare cause of acute abdomen: surgical treatment and adjuvant therapy. Case report," Journal of gastrointestinal and Liver Diseases 15: 297-299.

22. Ludwig DJ, Traverso LW (1997) "Gut stromal tumors and their clinical behavior," The American Journal of Surgery 173: 390-394.

23. Mazur MT, Clark HB (1983) "Gastric stromal tumors. Reappraisal of histogenesis," The American Journal of Surgical Pathology 7: 507-519.

24. Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, et al. (1998) Gain-of-function Mutations of C-kit in Human Gastrointestinal Stromal Tumors. Science 279: 577-580.

25. De Vogelaere K, Aerts M, Haentjens P, Grève J, Delvaux G, et al (2013) Gastrointestinal Stromal Tumor of The stomach; progesses in diagnosis and treatment. Acta Gastro-Enterologica Belgica 76: 403-406.

26. Miettinen M, Majidi M, Lasota J (2002) Pathology and diagnostic criteria of gastrointestinal stromal tumors (GISTs): A review. Eur J Cancer 38: S39-51.

27. Poveda A, García Del Muro X, López-Guerrero JA, et al. (2017) GEIS guidelines for gastrointestinal sarcomas (GIST) Cancer Treat Rev 55: 107-119.

28. Carney JA (1999) Gastric stromal sarcoma, pulmonary chondroma, and extra-adrenal paraganglioma (Carney Triad): natural history, adrenocortical component, and possible familial occurrence. Mayo Clin Proc 74: 543-552.

29. Takazawa Y, Sakurai S, Sakuma Y, Ikeda T, Yamaguchi J, et al. (2005) Gastrointestinal stromal tumors of neurofibromatosis type I (von Recklinghausen's disease) Am J Surg Pathol 29: 755-763.

30. Han SH, Park SH, Cho GH, Kim NR, Oh JH, et al. (2007) Malignant gastrointestinal stromal tumor in a patient with neurofibromatosis type 1. Korean J Intern Med 22: 21-23.

31. BajorJ (2009) Gastrointestinal stromal tumors in patients with type 1 neurofibromatosis. ClinExp med J 3: 247-254

32. Na Jo G, Lee KH, Ahn BK (2015) Acute Gastrointestinal Bleeding with Hypovolemic Shock Induced by Gastrointestinal Stromal Tumor Coincident with Neurofibromatosis Type 1: A Case Report. J Gastrointest Dig Syst 5: 299.

33. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, et al. (2002) "Diagnosis of gastrointestinal stromal tumors: a consensus approach," Human Pathology 33: 459-465.

34. Xing G-s, Wang S, Sun Y-M, Yuan Z, Zhao, X-M, Zhou C-w (2015) Small Bowel Stromal Tumors: Different Clinicopathologic and Computed Tomography Features in Various Anatomic Sites. PLoS ONE 10: e0144277.

35. Khuri S, Gilshtein H, Darawshy A, Bahouth H, Kluger Y (2017) Primary Small Bowel GIST Presenting as a Life-Threatening Emergency: A Report of Two Cases. Case Reports in Surgery 2017.

36. Sorour MA, Kassem MI, Ghazal AA, El-Riwini MT, Nasr AA (2014) Gastrointestinal stromal tumors (GIST) related emergencies. International Journal of Surgery 12: 269- 280.

37. Vij M, Agrawal V, Kumar A, Pandey R (2010) Gastrointestinal stromal tumours: a clinicopathological and immunohistochemical study of 121 cases. Indian J Gastroenterol 29: 231-36.

38. Lv A, Li Z, Tian X, Guan X, Zhao M, et al. (2013) SKP2 high expression, KIT exon 11 deletions, and gastrointestinal bleeding as predictors of poor prognosis in primary gastrointestinal stromal tumors. PLoS One 8: e62951.

39. Liu Q, Li Y, Dong M, Kong F, Dong Q (2017) Gastrointestinal bleeding is an independent risk factor for poor prognosis in GIST patients. Biomed Res Int 2017: 7152406.

40. Foley PT, Ganeshan A, Anthony S, Uberoi R (2010) Multi-detector CT angiography for lower gastrointestinal bleeding: can it select patients for endovascular intervention? J Med Imaging Radiat Oncol 54: 9-16.

41. Schenker MP, Majdalany BS, Funaki BS, Yucel EK, Baum RA, et al. (2010) ACR appropriateness criteria® on upper gastrointestinal bleeding. J Am Coll Radiol 7: 845-853.

42. Dobritz M, Engels HP, Schneider A, Bauer J, Rummeny EJ (2009) Detection of intestinal bleeding with multi-detector row CT in an experimental setup. How many acquisitions are necessary? Eur Radiol 19: 2862-2869.

43. Zhou L, Liao Y, Wu J, Yang J, Zhang H, et al. (2018) Small bowel gastrointestinal stromal tumor: a retrospective study of 32 cases at a single center and review of the literature. Dove press 14: 1467-1481.