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Therapeutic Challenges in the Management of Bleeding Duodenal Gastrointestinal Stromal Tumor: a Case Report and Review of Literature

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Abstract

Introduction Duodenum is an uncommon site for the gastrointestinal stromal tumors (GISTs). Though the principles of management are the same of that elsewhere in the gastrointestinal tract, the anatomical complexity poses challenges in deciding the most appropriate treatment. A bleeding GIST further compounds the difficulty in managing such patients.

Case Report A twenty-eight-year-old female presented with bleeding duodenal lesion secondary to mucosal ulceration. Imaging confirmed large heterogeneous lesion arising from the second part of duodenum. Surgery was planned in view of persistent blood transfusion requirement. Pancreaticoduodenectomy was done and the patient had an uneventful postoperative period.

Discussion Review of literature of duodenal GIST especially regarding the tough decisions that have to be made in the diagnosis and management of bleeding lesions has been done.

Conclusion The availability of various options in addressing bleeding duodenal GIST should make the surgeon choose the best modality for the patient weighing the pros and cons of each modality.

Keywords Gastrointestinal stromal tumor · Duodenum · Imatinib · Pancreaticoduodenectomy · Bleeding

Introduction

Gastrointestinal stromal tumor (GIST) commonly affects the stomach with rare involvement of the duodenum [1]. Bleeding is the most common presentation of these tumors [2]. The patient status, magnitude of bleed, location of tumor, tumor characteristics, and the availability of resources dictate the management in bleeding lesions [3–5]. We report a case of bleeding duodenal GIST along with the various challenges posed. Review of literature on the management options of a bleeding duodenal GIST has been discussed.

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Case Report

A 28-year-old female was referred to our surgical outpatient department with the complaints of melena and easy fatigability for 3 weeks. On evaluation elsewhere for the above complaints, she was found to have ulcerated lesion with everted margin in the medial wall of third part of duodenum. The biopsy of the lesion was suggestive of chronic inflammation. Patient was stabilized and referred on oral pantoprazole 80 mg per day. On clinical examination, she was pale with pulse rate of 90/min. A well-defined firm mass of size 5*5 cm was palpable in the right hypochondrium. Per rectal examination confirmed melena. Ultrasound showed a large heterogeneously hypoechoic mass measuring 7.9*5.6 cm seen in subhepatic region in relation to the second and third part of duodenum. On computed tomography, the lesion was arising from the pancreaticoduodenal groove with marked enhancement during the arterial phase. Tortuous vessels were seen at the periphery

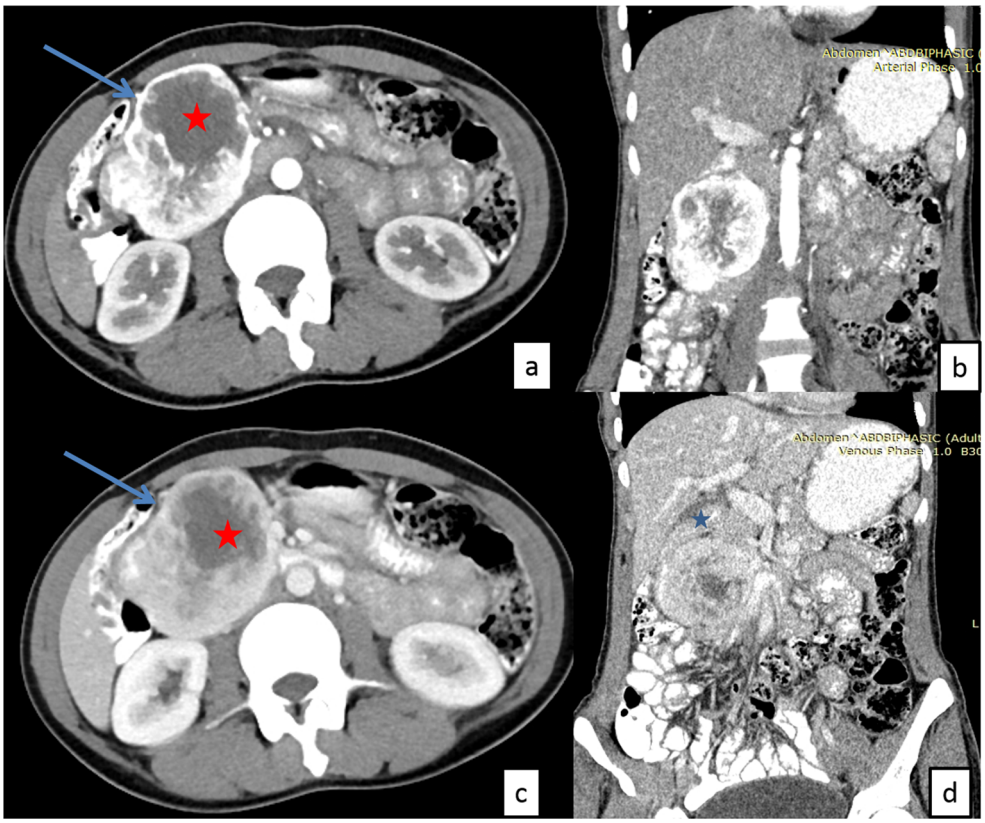

Fig. 1 a, b Axial and coronal arterial phase contrast-enhanced computed tomography image. c, d Axial and coronal contrast-enhanced computed tomography image in portal venous phase, showing ~ 8 × 8 cm hypervascular mass (blue arrow in a and c) in the pancreaticoduodenal groove closely abutting the medial wall of d2 part of duodenum with arterioportal shunting (asterik in d). Duodenum is displaced and is stretched along the periphery of this mass lesion. Central non-enhancing hypodense areas s/o necrosis seen (red asterik in a and c)

with multiple feeders arising from superior mesenteric artery and draining into the superior mesenteric vein (Fig. 1). Probable diagnosis of neuroendocrine tumor was made based on the intense arterial enhancement and elevated serum chromogranin of 208.2 ng/mL (reference value < 98.1 ng/mL). Gastrointestinal tumor was kept as a second possibility. Patient was optimized and was planned for exploratory laparotomy. Intraoperatively, a mass of size 8*5 cm was seen in the inferior pancreaticoduodenal groove splaying the duodenum laterally and displacing the pancreas superiorly (Fig. 2a). Multiple vessels were seen over the tumor draining into the superior mesenteric vein which was splayed medially. The pancreatic duct was not dilated and the parenchyma was soft. Pancreaticoduodenectomy with duct to mucosa pancreaticojejunostomy was done.

Cut section of the duodenum revealed encapsulated mass in the medial wall of the duodenum with a predominant exophytic component and ulcer in the medial wall of the third part of duodenum, 1 cm from ampulla (Fig. 2b). The lesion was predominately solid with central area of necrosis. The histological examination revealed features of submucosal GIST involving pancreas. The lesion showed 3–4 mitosis/50 hpf and was c-KIT positive (Fig. 3). As per the Fletchner grading, the tumor falls under the intermediate malignant

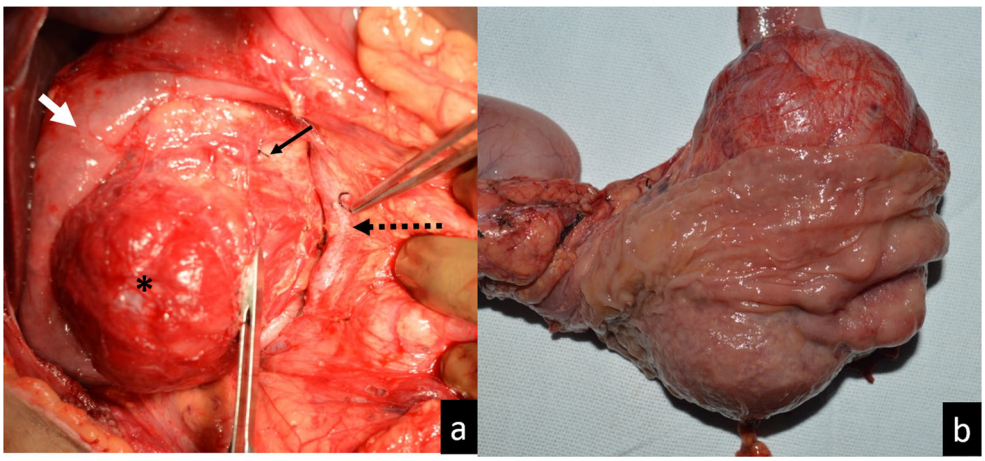

Fig. 2 a Intraoperative image showing the tumor (*) arising from the inferior pancreaticoduodenal groove splaying the duodenum (white arrow) laterally, superior mesenteric vein (dashed black arrow) medially, and the pancreas (solid black arrow) superomedially. 2 Cut section of the tumor showing the ulceration at D3 and a predominant exophytic component

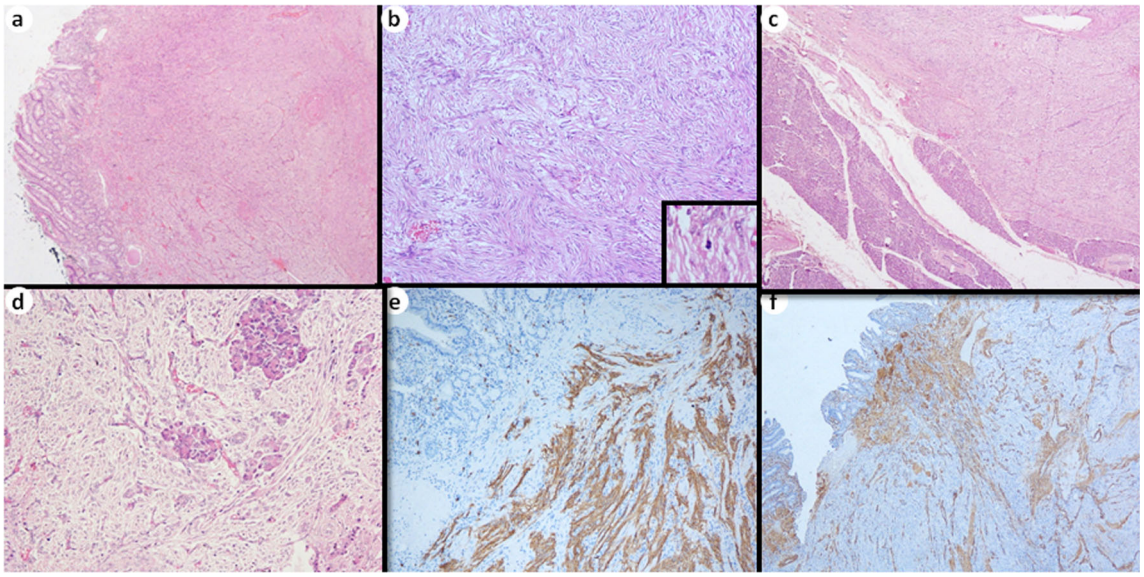

Fig. 3 a Photomicrograph showing a tumor in the submucosa focally infiltrating the mucosa (Hematoxylin and Eosin, 40×). b Photomicrograph showing whorling and short fascicular pattern with spindle cell morphology of the tumor cells (Hematoxylin and Eosin, 200×); Inset showing a mitotic figure (Hematoxylin and Eosin, 400×). c The tumor abutting the pancreas with focal tongue like infiltration (Hematoxylin and Eosin, 40×). d The tumor replacing the pancreatic parenchyma completely at places with few interspersed islands of pancreatic acini preserved within the tumor nodule (Hematoxylin and Eosin, 400×). e, f Immunohistochemistry for CD117 showing diffuse strong membranous positivity in the tumor cells (100×) (e) and immunohistochemistry for SMA (smooth muscle actin) showing negativity in the tumor cells (40×) (f)

potential [6]. The resected stomach showed features of chronic atrophic gastritis. Patient was started on Tab. Imatinib 400 mg once daily. She is doing well after 8 months.

Discussion

Gastrointestinal stromal tumor is a mesenchymal tumor which can involve any part of the alimentary tract. The stomach is the most common site, followed by rectum with duodenal GIST constituting for 12–18% of small intestine GIST and 1–4% of all the stromal tumors [1]. Gastrointestinal stromal tumors are of wide spectrum ranging from benign small lesions to malignant large lesions.

Clinico-pathological Features of Duodenal GIST

With regard to the clinical features, our index case differed from the general nature of duodenal GISTs in many ways. Table 1 compares the clinico-pathological characters of duodenal GIST reported in literature with our case. The median age group of duodenal GIST is above 50 years in comparison to the young age (28 years) in our patient [8–10]. The third part of the duodenum is the third common site among the duodenal segments to be involved by the stromal tumor [11]. Though the common presentation of duodenal GIST is gastrointestinal bleeding, like in our case, the size of 8 cm is large for a duodenal GIST which usually measure around 4 cm [2, 8].

Diagnostic Dilemma in Duodenal GIST

Hyper-enhancement of the lesion and raised chromogranin led us to consider the possibility of neuroendocrine tumor. In a study of 34 duodenal GISTs, Cai et al. [11] found that all were hyper-enhancing during the arterial phase secondary to arterioportal shunting. In the same study, all the five lesions that were arising from the third part of duodenum had superior mesenteric artery as the feeding vessel and superior mesenteric vein as the draining vessel similar to our patient [11]. Retrospectively, we realized that the prolonged and persistent usage of proton pump inhibitor together with chronic atrophic gastritis could have resulted in elevated serum chromogranin A levels. The patient was prescribed proton pump inhibitor for more than 4 weeks and was taking them during serum chromogranin A estimation [12].

Bleeding Duodenal GIST

The most common presentation of duodenal GIST is gastrointestinal bleeding. However, the magnitude of bleed and presentation can be variable ranging from insidious slow bleed to acute massive bleed [3]. The source of the bleed can be mucosal ulceration or peritumoral submucosal large vessels [4]. Our patient had the GIST ulcerating into the duodenal mucosa causing slow but persistent bleed resulting in fall in hemoglobin. The means of tackling stromal tumor bleed include endoscopic, interventional radiology, surgical, and imatinib therapy.

Table 1 Comparison of clinicopathological characteristics of index case and literature review

Character	Duodenal GIST	Index case
Age	> 50 years [7–10]	28 years
Part of duodenum	2 > 1 > 3 > 4 [7, 10]	3rd part
Size	4–5 cm [2, 7]	8 cm
Clinical presentation	Gastrointestinal bleeding [2, 10]	Gastrointestinal bleeding
	Epigastric pain	Abdominal discomfort
	Obstructive jaundice	Palpable mass
	Palpable mass	
	Obstruction	
Computed tomography findings	Small tumors - homogenous soft tissue masses with moderate contrast enhancement	Hyper-enhancing lesion on early arterial phase
	Large tumors - central necrosis and cavitation with heterogeneous enhancement [2]	
Mitosis	< 5/50 HPF [2, 10]	3–4/50HPF

Endoscopic Management

Endoscopic management of bleeding gastric stromal tumors is common [5, 13]. They help in converting a surgical emergency to an elective surgical procedure [5, 13]. The choice of technique will be based on the tumor morphology and the endoscopists preference. Techniques like hemoclip, endoloop, laser therapy, and argon plasma coagulation can be used for temporary bleeding control followed by definitive surgery. However, techniques like loop-and-let-go would be a single-step management option [14]. Most of these techniques have been described for gastric GISTs with a prominent intraluminal component. The most vital technical point in the abovementioned techniques is complete visualization [14]. The bent and narrow anatomy of the duodenum makes application of these hemostatic techniques very challenging and sometimes visualization of the duodenal GIST is difficult. In our case, the lack of endophytic component and predominate ulcer bleed makes it a difficult lesion to tackle endoscopically.

Interventional Radiology Management

Interventional radiology includes procedures to selectively cannulate the feeding vessel of the tumor and injection of hemostatic agents [15, 16]. Beddy et al. [15] used embolization in treating bleeding duodenal GIST in a surgically unfit patient and Kurihara et al. [16] used it as a bridge to surgery in achieving hemostasis and size reduction facilitating limited resection. Multiple feeders and complex anatomy will make it challenging to apply this technique in the duodenal GIST. The possible adverse effects of the procedure include pancreatitis, duodenal ischemia, and other procedure-related complication such as arterial dissection, non-target embolization, and access site hematoma [17].

Neoadjuvant Imatinib

Imatinib, as a neoadjuvant agent, reduces the tumor size and need for multi-organ resection [18]. The current guidelines recommend the administration of preoperative imatinib to reduce the radicality of the surgery [2]. Emergency pancreaticoduodenectomy done for massive bleed secondary to tumor regression from a duodenal GIST on preoperative imatinib therapy has been reported [19]. Given the location of the tumor, we felt patient would require pancreaticoduodenectomy even if the tumor responded to imatinib therapy. In addition, the stable clinical condition and intention to avoid the possibility of emergency pancreaticoduodenectomy made us decide in favor of upfront surgery.

Surgical Management

Surgery remains the mainstay treatment of duodenal GIST [1]. GISTs mandate the achievement of R0 resection and the radicality of the surgery is not of consequence if this principle is maintained [7, 8]. However, the complex anatomy of the duodenal region poses various challenges. Factors that dictate the type of surgery include the segment of duodenum involved, wall of the duodenum, distance from papilla, and the involvement of pancreas. Hoeppner et al. [8] analyzed the outcomes after conservative surgery of duodenal GIST in selected patients and found no impact on overall survival. Types of conservative surgery include duodenal sleeve or wedge resection and segmental resection with reconstruction to maintain gastrointestinal continuity [2]. Pancreas preserving total duodenectomy and segmental resection of duodenum in bleeding duodenal GIST have also been described [2]. In our case, the location along the pancreaticoduodenal groove with pancreatic involvement necessitated pancreaticoduodenectomy to confine to the surgical principles of R0 resection and avoidance of tumor spillage.

The management of remnant pancreatic stump in these cases forms the crux given the soft texture and non-dilated main pancreatic duct. Variations of the pancreatico-enteric anastomosis following pancreaticoduodenectomy primarily involve the stomach or the jejunum. Within pancreatico-jejunostomy modifications include the type of anastomosis (duct to mucosa, invagination, dunking), type of jejunal loop (conventional, isolated roux loop), type of suturing (continuous, interrupted), and use of adjuncts (omental wrapping, stenting, octreotide usage) [20]. The verdict is still controversial regarding the ideal reconstruction. Initially, we contemplated performing pancreatico-gastrostomy or dunking type of pancreaticojejunostomy since pancreatic duct could not be identified. However, on freshening the pancreatic stump, the duct could be identified and we proceeded with our preferred duct to mucosa pancreaticojejunostomy with internal stenting and omental wrapping.

Conclusion

Duodenal GISTs pose a variety of challenges in their management. Given their low incidence, no standard guidelines exist. Emphasize is made on the diagnostic dilemma in our case, though uncommon, to create awareness. The availability of various options in addressing bleeding duodenal GIST should make the surgeon choose the best modality for the patient weighing the pros and cons of each modality. Choice of surgery may be subjected to change after intraoperative assessment in an effort to avoid radical surgery. However, if required, surgical expertise is needed to tackle the inherent problems of soft pancreas and non-dilated duct following pancreaticoduodenectomy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Informed Consent Was obtained from the patient regarding the usage of his information for the purpose of publication.

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