

Resectable Distal Duodenal Gastrointestinal Stromal Tumour Presenting with Features of Anaemia

Abstract

Although gastrointestinal stromal tumours (GISTs) are encountered all along the gastrointestinal tract, duodenal GISTs are uncommon and account for <5% of the cases. A 45-year-old woman presented chiefly with anaemia and associated symptoms, whom on further evaluation was found to have a non-metastatic GIST in the distal duodenum sparing the pancreas and major vasculature. Patient was undertaken for segmental duodenectomy with the help of advanced bipolar energy device (tumour occupying D3–D4 with 1 cm proximal margin and 15 cm jejunum) preserving the pancreas and ampulla with end-to-end duodenojejunostomy with an uneventful postoperative course and clear margins on histopathology. Thus, the patient underwent a less morbid procedure with satisfactory oncological outcome and early resumption of activity. This highlights the need to conduct more trials to gather high level evidence in favour of conservative resection and its oncological adequacy and impact on overall survival and recurrence.

Keywords: Duodenojejunostomy, gastrointestinal stromal tumour, limited resection

Introduction

Gastrointestinal stromal tumours (GISTs) are uncommon neoplasms that arise from the intestinal pacemaker cells of Cajal. Despite the overall rarity, GISTs constitute the most common malignancy of the gastrointestinal (GI) mesenchymal tissues. The annual incidence ranges from 10 to 20/million population.^[1] The highest incidence occurs in the stomach (60%), with duodenum being the least common site (5%). However, in the context of a duodenal tumour, GISTs constitute up to 30% of primary duodenal tumours; mostly sporadic, with 5% as part of a familial syndrome.^[2] Up to 70% of the patients with GISTs are symptomatic, the rest are found either incidentally on imaging or at autopsy. Common complaints include abdominal pain, distension secondary to obstruction by the tumour mass, palpable lump, GI bleed which could be frank or occult. Patients with occult GI bleed present with anaemia and associated symptoms. Excision is the treatment of choice for localised GISTs. Earlier, pancreaticoduodenectomy was considered as the procedure of choice for duodenal GIST, but with advancement in

energy devices such as advanced bipolar device used in this case, a more limited resection can be performed thereby reducing the morbidity. However, there is a paucity of studies comparing the oncological outcome and overall survival of both the procedures.^[3]

We report a case of GIST of the distal duodenum in a patient who presented predominantly with anaemia, and treated by pancreas-sparing distal duodenectomy.

Case Report

A 45-year-old lady presented to the surgical clinic with complaints of passing tarry black stools, fatigue and dizziness for 6 months. There was history of multiple blood transfusions for the same. There was no other history suggestive of any liver pathology, peptic ulcer, menorrhagia, or drug intake. Physical examination revealed significant pallor; abdominal examination showed a 5 cm long scar of previous lower segment Caesarean section.

Upper GI endoscopy was done which revealed a large polypoidal lesion at the junction of D3 and D4 segments of the duodenum with central umbilication and superficial ulcerations associated with

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spontaneous intermittent oozing of blood with a provisional diagnosis of GIST. Biopsy was deferred in view of active bleed at the ulcer site. Positron Emission Tomography-COMPUTED TOMOGRAPHY (PET-CT) revealed a FluoroDeoxyGlucose-avid (FDG-avid), heterogeneously-enhancing, well-marginated, intraluminal polypoidal soft tissue density lesion at the junction of D3 and D4 segments of the duodenum, measuring 2.8 cm × 2.6 cm × 4.1 cm (transverse × anteroposterior × craniocaudal). The diagnosis was a likely primary mitotic lesion with no FDG-avid visible mitotic lesion elsewhere. The tumour was abutting the pancreas but had preserved fat planes with all surrounding structures and major vasculature spared [Figure 1].

Owing to the localised nature of the mass and no evidence of any distant metastatic disease, the patient was prepared for surgical resection. The patient's nutrition and haemoglobin were built up pre-operatively and informed consent obtained. The abdomen was explored through a transverse "roof-top" incision. After excluding evidence of

metastasis, the entire duodenum was exposed with generous Kocher's and Cattell-Braasch manoeuvres, exposing a single growth of 4cm at the junction of D3 and D4 segments of the duodenum just below the uncinate process of the pancreas with no infiltration in the surrounding structures. A pancreas-preserving distal duodenectomy taking 3cm of proximal margin and 15cm of jejunum distally, in view of the preserved dissection planes with the large vessels. The ampulla was also well away from the transected D2 end. A retrocolic hand-sewn end-to-end duodenojejunostomy (extramucosal all-knots-outside interrupted with 4-0 polydioxanone) was performed to maintain bowel continuity [Figure 2]. The postoperative course was unremarkable; the patient was orally allowed on post operative day 5 and discharged on post operative day 8. On macroscopic examination, a nodular growth was identified measuring 4.1 cm × 3 cm × 2.4 cm about 2.5 cm from viable bowel margin. Cut-section revealed a solid homogenous grey-white mass reaching up to serosa with mucosal congestion. Histopathological examination

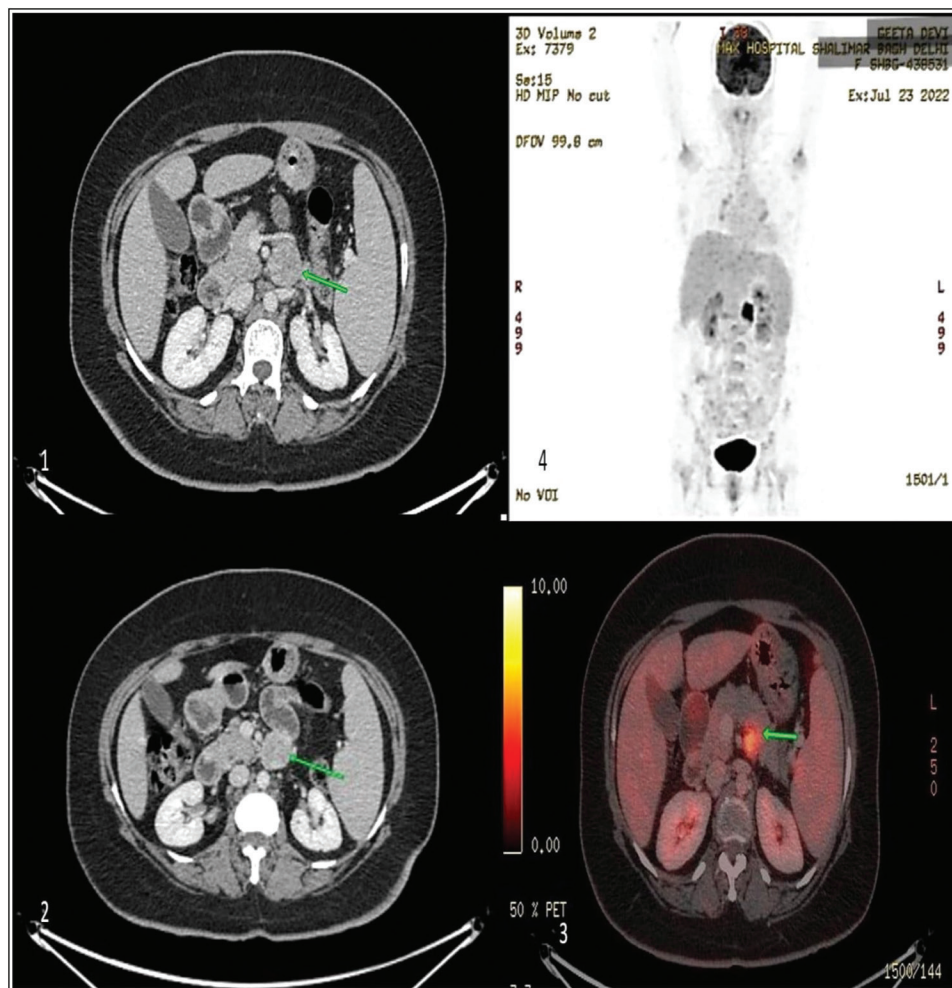


Figure 1: (Anticlockwise from top left) (1, 2): Cross-sectional image of contrast-enhanced CT scan showing a mass (*thin green arrow*) arising from D3 to D4 abutting the pancreas but with preserved fat planes with surrounding major vasculature. (3): PET-CT in axial plane showing the same mass with florid fluorodeoxyglucose uptake (standard uptake value = 10). (4): Fluorodeoxyglucose-PET image in coronal section showing area of increased uptake at the tumour site, with brain and bladder acting as reservoir organs

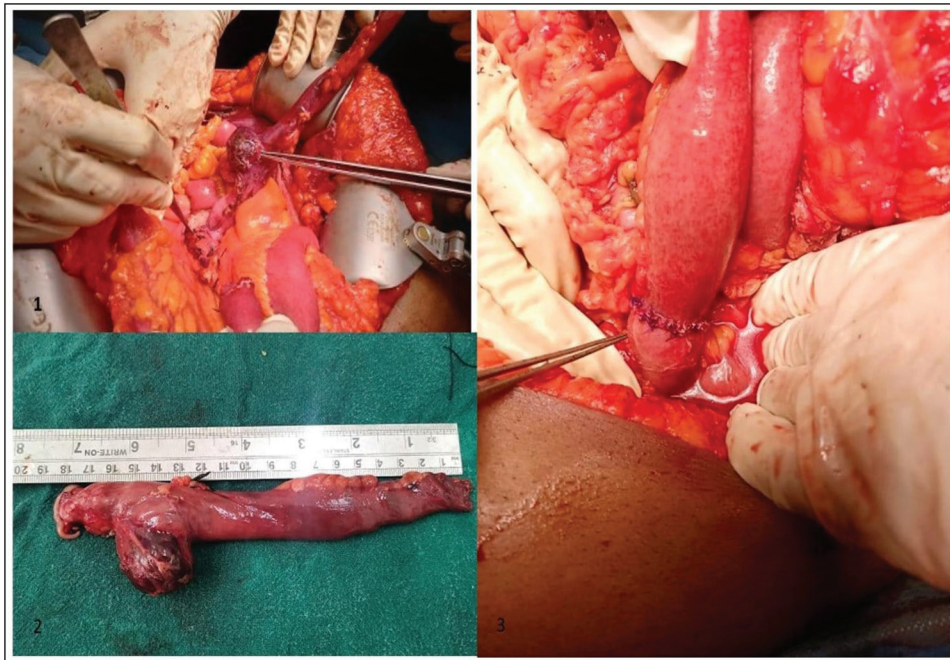


Figure 2: (Anticlockwise from top left) (1) A 4 cm growth was seen at the junction of D3–D4 (mainly exophytic and partly occluding the duodenal lumen) just below the uncinate process, sparing the ampulla with no local spread to surrounding structures. (2) Resected specimen including growth with a 3 cm proximal margin and 12 cm distal margin. (3) End-to-end extramucosal all-knots-outside interrupted duodenojejunostomy done with 4-0 polydioxanone

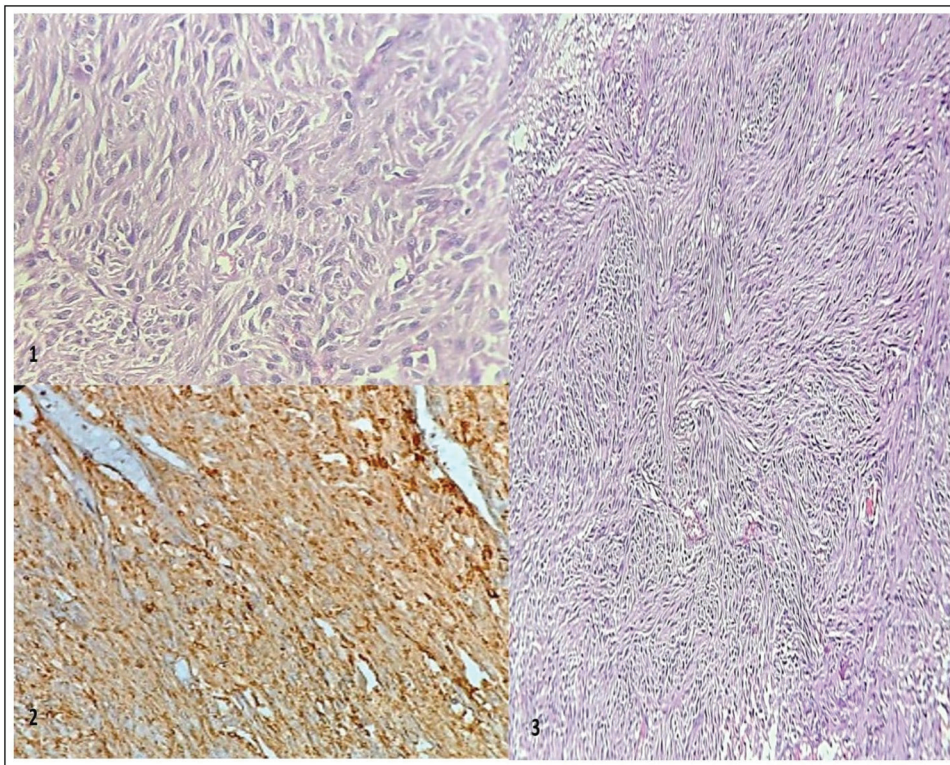


Figure 3: (Anticlockwise from top left) Histopathological sections (1) Haematoxylin and Eosin stain in high power field with 40× magnification showing spindle cells with oval to elongated nuclei, vesicular chromatin, inconspicuous nucleoli with moderate amount of eosinophilic cytoplasm, Mitoses 2/high power field. (2) Immunohistochemistry in 40× magnification showing cytoplasmic and membranous positivity for discovered on gist-1. (3) Haematoxylin and Eosin stain in low power field with 10× magnification showing a storiform tumour arranged in fascicles and composed of spindle cells

confirmed the diagnosis of a GIST, mixed (predominantly spindle-cell type with low mitotic rate (<5/5 mm²) with both proximal and distal margin free of tumour cells [Figure 3].

Tumour cells stained strongly positive for discovered on gist-1 and focally positive for cluster of differentiation 117. There were no signs of metastasis in locoregional

lymph nodes (single lymph node examined only). Tumour was classified as probable benign according to Miettinen classification and adjuvant therapy with tyrosine kinase inhibitor Imatinib 400 mg orally daily was started owing to tumour size of >3 cm. The patient has done well 6 months after follow-up. No complications were observed up to the time of case reporting.

Discussion

The term GISTs were initially used to describe intra-abdominal non-epithelial neoplasm which were frequently misclassified as leiomyomas, leiomyoblastoma/sarcoma or other soft tissue histology. In 1998, Hirota *et al.*,^[4] two crucial findings—(1) near universal expression of receptor tyrosine kinase in GIST. (2) Gain of function mutation in c-kit proto-oncogene. With improved recognition of this tumour and improvement in radiology, there is a rise in the incidence of GISTs in the past few years. They can be recognised by their morphology or they are found positive for cluster of differentiation 117, cluster of differentiation 34, discovered on gist-1 on immunohistochemistry. GISTs show an extensive range of biological appearance, from tumours found incidentally which appear benign on the one hand, to aggressive disease with metastasis. Even such benign appearing GISTs harbour a risk of malignancy and metastasis, thereby mandating treatment for all GISTs. Surgery is the treatment of choice for all tumours without local invasion into vascular structure or any distant metastasis^[5] and may be considered curative.

Owing to the retroperitoneal location of duodenum, common blood supply with the pancreas, difficult access and rarity of the tumours, the optimum procedure for a localised GIST remains controversial. The options include pancreaticoduodenectomy (PD) or limited resections for tumours in the distal duodenum sparing the ampulla of Vater. The latter may be tumour enucleation, pancreas-preserving duodenectomy, distal duodenectomy, segmental resection or wedge resection with maintenance of intestinal continuity.^[6] GISTs are mesenchymal tumours that have similar behaviour to a sarcoma and they will not follow the same oncological principles as a duodenal adenocarcinoma. They rarely metastasise via lymphatic route, have a capsule which prevents local invasion even in tumour with high risk features, and a small margin of clearance is effective,^[7] making limited resection a feasible option and avoids lymphadenectomy unless there are enlarged lymph nodes intraoperatively or on imaging.^[8] Limited resection is superior in terms of a lower morbidity and a better quality of life for the patient, as it prevent the symptoms of endocrine and exocrine insufficiency post pancreatic resection, less trauma to the organs, with a less demanding reconstruction to maintain the alimentary continuity, which contributes to decreased postoperative complications associated with anastomotic leak and stenosis.^[9] A recent meta-analysis by Shen *et al.*^[10] involving 623 cases showed

that pancreaticoduodenectomy had a higher long-term morbidity and postoperative complication rate and limited resection is recommended to obtain negative margins in carefully selected patients.

Alimentary continuity post-segmental resection can be maintained via an end-end, end-side or side-side duodenojejunal anastomosis. Limited number of small series compared the superiority of one procedure over the other, like Dorcaratto *et al.*,^[11] showed increased complications and postoperative stay in end-to-side anastomoses over end-to-end in 11 patients. Side-to-side duodenojejunostomy is a technically easier procedure, owing to wide stoma and sparing of mesenteric side.^[12] Lastly, it was left to determine the oncological adequacy in terms of short- and long-term survival, recurrence and metastasis.

Blanco-Fernández *et al.*,^[9] performed a retrospective analysis of 12 patients, considered pancreas-preserving duodenectomy a safe procedure with adequate oncological results and side-to-side anastomosis was considered to be an easier procedure, with a good functional outcome in infraampullary duodenal lesions. Goh *et al.*,^[6] retrospectively included 22 patients with suspected duodenal GIST who underwent surgery and reported similar mean disease-specific survival and recurrence rates, similar morbidity rate between limited resection and PD; however limited resection had a significantly shorter operative time. Beham *et al.*,^[13] in their single centre experience with 13 patients, concluded that the type of operative procedure did not affect the long-term survival and the choice of procedure should depend on resectability and patients' performance status. Similar results were published by Buchs,^[3] showing segmental duodenectomy to be a curative option with comparable disease-free survival for most duodenal GISTs.

Metastatic, unresectable and recurrent tumours carried a grave prognosis in the past and showed resistant to chemotherapy. However, with the advent of tyrosine kinase inhibitors like Imatinib, there is a paradigm shift in the management of GISTs. In a multicentre randomised controlled trial by Demetri *et al.*,^[14] imatinib mesylate showed a response in over 50% of the test patients with advanced or metastatic disease, was well absorbed and safe to use and has with reference to Kelly *et al.*^[15] has become the first line treatment for metastatic GIST. This has also expanded the use to this drug in the neoadjuvant setting to shrink the tumour mass and make it resectable, or in the adjuvant setting as a mode to prevent recurrence and distant metastasis. The Z9001 randomised trial by the American College of Surgeons Oncology Group, selected patients with who underwent resection of 3 cm or larger duodenal GISTs to receive Imatinib 400 mg daily or placebo for up to 1 year and showed higher recurrence free survival; however, overall survival was deemed to be similar.^[16]

In our study the lesion was <5 cm, free from ampulla and surrounding structures, with no evidence of metastasis, and

therefore underwent a pancreas-preserving duodenectomy with end-to-end duodenojejunal anastomosis. The post-op histopathological report classified the tumour as probably benign according to the Miettinen classification.^[17] Owing to tumour size >3 cm, patient was started on Imatinib.

Conclusion

GISTs are rare but the most common GI mesenchymal malignancy. Up to 70% of the patients with GISTs are symptomatic, the rest are found either incidentally. Treatment of choice for duodenal GISTs remains surgery, but owing to complex anatomy and shared blood supply of the duodenum, the choice of surgery remains controversial. In this case report, a localised duodenal GIST with a limited resection (pancreas-sparing distal duodenectomy) which has been shown to confer a lower morbidity and a comparable overall survival to pancreaticoduodenectomy and can offer the patient with a better quality of life and can be considered a curative option.

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Conflicts of interest

There are no conflicts of interest.

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