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Case Series

Gastroduodenal gastrointestinal stromal tumour: a case series and review of literature

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ABSTRACT

Gastrointestinal stromal tumour (GIST) is the most common non-epithelial mesenchymal tumour and comprises 0.1-3% of all gastrointestinal (GI) tract tumours. They express tyrosine kinase and are potentially malignant. Therefore, early diagnosis and surgical resection is the key for good outcome. This is a retrospective analysis of medical records of five patients of gastroduodenal GIST who were managed in the department of surgery between 2014 and 2015. Demographic profile, clinical presentation, laboratory parameters, diagnostic imaging, treatment details, histopathology and long-term outcome was analysed. Patients were followed up regularly in surgery outpatient clinic. Last follow up was in December 2022. All were female; three of them presented with melena and two with lump abdomen. Patients with gastric GIST underwent sleeve resection in two and antrectomy in one patient. Patient with duodenal GIST underwent excision of tumour with primary repair of duodenum. Fifth patient had metastatic duodenal GIST; Imatinib was started in view of irresectable disease at presentation. However, there was tumour progression and she succumbed to illness seven months after treatment initiation with Imatinib. Histopathology revealed low grade GIST in two, intermediate grade in one and malignant in one. Patient with malignant GIST received Imatinib for 2 years. All four patients are well on follow up with no sign of local and distant recurrence.

Keywords: Gastroduodenal tumour, GIST, Gastric GIST, Duodenal GIST

INTRODUCTION

Gastrointestinal stromal tumour (GIST) is the most common non-epithelial mesenchymal tumour of the gastrointestinal (GI) tract. GIST originates from the intestinal cells of Cajal which are located in and around the nerve plexuses and express CD 117 (c-kit), a proto-oncogenic protein. C-kit positivity distinguishes GIST from other mesenchymal tumours of GI tract. It comprises 0.1-3% of all GI tract tumours; stomach is the commonest site (60-70%) and only 4.5% of these are located in the duodenum.[1,2]

Clinical presentation of gastroduodenal GIST is inconsistent and mainly depends upon its size and location. They may be asymptomatic and diagnosed incidentally or may be symptomatic with abdominal discomfort or pain, dyspepsia, abdominal lump, malaise, fatigue, GI bleed, gastric outlet obstruction or jaundice.[3] The most common symptom of gastroduodenal GIST is occult bleeding.[4]

Early diagnosis is important as GIST has a potential to become malignant, for that reason, complete surgical resection of resectable non-metastatic GIST is required to have a good outcome. Herein we report long term outcome of five patients of gastroduodenal GIST who were managed in a tertiary care centre in north India.

CASE SERIES

We retrospectively analysed the medical records of patients of gastroduodenal GIST who were managed in the department of surgery between January 2015 to December 2021 at Post Graduate Institute of Medical

Education and Research (PGIMER), Chandigarh. Demographic profile, clinical presentation, laboratory parameters, upper GI endoscopy (UGIE), endoscopic ultrasound (EUS), radiologic imaging, surgery details, histopathology report and long-term outcome was analysed. Tumour location and type of surgery, use of Imatinib as adjuvant or neoadjuvant treatment and its response was noted. Prognostic factors like size of tumour, mitotic index and metastasis was recorded. Patients were followed up regularly in surgery outpatient clinic three to six monthly with clinical examination and hemogram levels for two years, bi-annually for three years and annually thereafter. Contrast enhanced computed tomography (CECT) abdomen was also performed on follow up at six months for the first two years and annually subsequently for patient of intermediate and malignant GIST. UGIE was also performed on follow up. Last follow up was in December 2022.

There were five patients with age range 30-51 years; all were female. Three patients presented with melena and two patients presented with lump abdomen. Location and size of tumour is shown in Table 1. Patients with gastric GIST underwent sleeve resection in two and antrectomy in one patient (Figure 1 B). Patient with duodenal GIST underwent excision of tumour and primary repair of duodenum (Figure 1 A). Fifth patient had duodenal GIST with multiple liver metastases (Figure 2) which was confirmed on biopsy. She was put on Imatinib 400 mg twice a day. However, there was tumour progression clinically which was also confirmed on imaging. This lady expired 7 months after start of treatment with Imatinib.

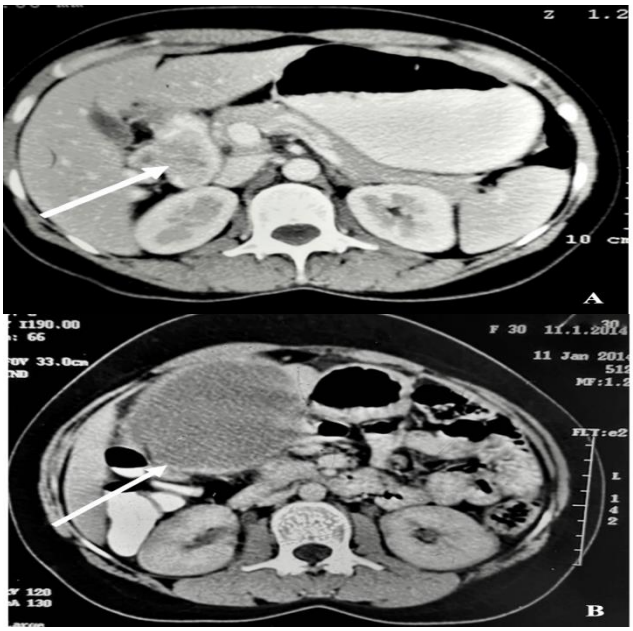

Figure 1: (A) CT of tumour originating from second part of duodenal wall (solid white arrow); (B) CT of hypodense tumour lesion Originating, from anterior wall of stomach antral region (solid white arrow).

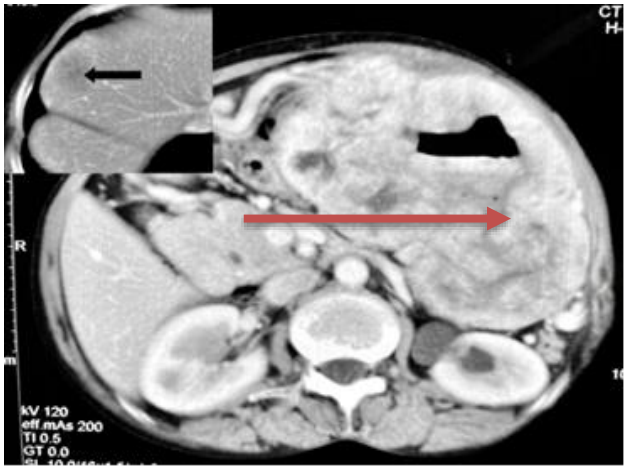

Figure 2: CT abdomen of large duodenal lesion (red arrow), with liver metastasis (black arrow)

Histopathology confirmed GIST in all patients, IHC was c-KIT positive in all (Figure 3). tumor was low grade in two patients, intermediate grade in one patient and high grade in two patients. Patient with large GIST at antrum, final histopathology of antrectomy specimen confirmed it to be malignant. This lady was put on Imatinib treatment for 2 years. She is well on follow up at 7 years. Her CECT abdomen and UGIE on follow up did not reveal local recurrence or any metastasis in the liver or peritoneum. All four patients are well on follow up with no sign of local and distant recurrence.

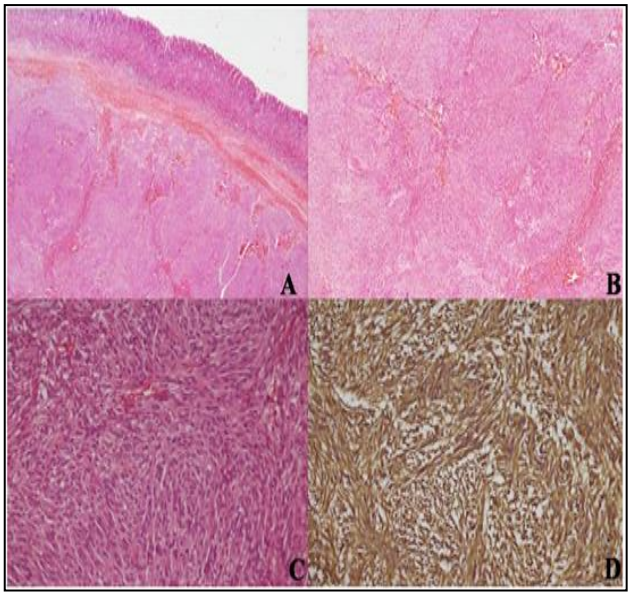

Figure 3: (A) Low power microphotograph (H and E stain, ×40) of a well demarcated tumour in the submucosa; (B) microphotograph (H and E stain, ×100) of lobules of tumour; (C) microphotograph (H and E stain, ×200) of spindle shaped tumour cells arranged in short fascicles; (D) immunohistochemistry stain for C-kit (CD117) (×200) shows diffuse membranous positivity in tumour cells.

Table 1: Comparative findings of the patients included in the study.

Age (Years)/ sex	Presentation	Location of tumour	Size (cm)	Surgery	Histopathology	Follow-up period (Years)	Imatinib
52/F	Melena	Fundus	5×5	Sleeve resection	Intermediate grade, c-KIT positive, SMA and S-100 negative	6, alive	No
35/F	Melena	Fundus	6×5	Sleeve resection	Low grade, c-KIT and CD34 positive	6, alive	No
42/F	Melena	Second part of duodenum	4×3	Duodenotomy with excision	Low grade, c-KIT positive	7, alive	No
30/F	Epigastric lump	Antrum	14×10	Antrectomy	High grade, c-KIT positive	7, alive	400 mg BD, 2 years
51/F	Epigastric lump	Third part of duodenum with liver deposits	15×10	Not done	High grade, c-KIT positive	Expired after 7 months	400 mg BD

DISCUSSION

GIST is infrequent intramural tumour of the GI tract. Majority (90-95%) of GIST have C-kit positivity which distinguishes GIST from other smooth muscle tumours (leiomyoma, leiomyoblastoma or leiomyosarcoma) or neural tumours of GI tract. They usually present in 5th to 7th decade of life and have no gender predilection. In this study, all patients were females. Stomach is the most common site (60-70%) of involvement followed by small intestine in 20-40%, colorectal in 5% and oesophagus in 4-5% of cases. Only 4.5% of small intestine GIST is located in the duodenum and less than 5% may be present in retroperitoneum, mesentery or omentum.[1,2] Duodenal involvement is commonly seen in second part, followed by third, fourth and first part.

Commonly GIST is single, well-circumscribed with a pseudo capsule and has variable clinical presentation which invariably is related to its size and location. They may be asymptomatic and diagnosed incidentally or may present with non-specific symptoms. A large GIST can produce symptoms secondary to mass effect like gastric or duodenal obstruction or jaundice. A large GIST also outgrows its blood supply causing either intra-luminal or extra-luminal bleeding secondary to central necrosis. In this study, all patients were symptomatic at diagnosis and bleeding was the commonest symptom.

GIST may grow expansively without being invasive with a low incidence of lymph node and distant metastasis. GIST is potentially malignant (10-30%) and can have metastasis to liver and peritoneum.[6,7] Gastric GIST can also have aggressive behaviour in 20-25% of cases.[6] Diagnosis of malignancy is based upon biopsy and presence of metastasis. GISTs are classified as very low, low, intermediate, or high risk of malignancy by their clinical behaviour and biopsy report. In this study, out of five patients one patient was of intermediate grade and two were malignant.

Diagnosis is mainly established by UGIE and EUS. Immunohistochemical staining confirms GIST and differentiates it from other intramural tumours. EUS-guided fine needle biopsy also helps to confirm GIST preoperatively. Preoperative laboratory diagnosis research is still underway for specific biomarkers. Cross section imaging of abdomen helps to determine the exact location and its relationship with adjacent organs. Duodenal GIST which is in third and fourth part of duodenum requires Push enteroscopy for the diagnosis.

For GIST, en bloc resection without capsular breech is the gold standard treatment. It can be performed endoscopically, surgically or using hybrid technique using both endoscope and laparoscope.[8-10] Formal lymph node dissection is not required as GIST rarely metastasise to lymph nodes. Early surgery is indicated for the prevention of bleeding or obstructive symptoms. Gastric GIST can be dealt with sleeve resection and formal gastric resection is only required when tumour is near to pylorus or gastroesophageal junction. Similarly, majority of duodenal GIST can be resected locally, and duodenum can be closed primarily without lumen compromise. Large duodenal GIST may require segmental duodenal resection or pancreaticoduodenectomy when tumour is located near ampulla of vater. Therefore, aim should be to have wedge /sleeve / segmental, R0 resection preserving the organ function.

Adjuvant treatment with tyrosine kinase inhibitor (Imatinib) should be considered when tumour is >10 cm in size and have high mitotic index of >10/50 HPF; and if there was intra-operative tumour rupture. For malignant lesion, neoadjuvant treatment with Imatinib should be considered. If there is reduction in the size of tumour after Imatinib therapy, surgery can be considered at later

date. Response of Imatinib treatment should be assessed at 8 weeks; and 80% of patients respond to imatinib treatment and tumour may become operable. However, 13% of patients may have disease progression on imatinib.[11] In this series, two patients had malignant GIST. En boc resection with postoperative Imatinib helped to achieve disease free survival at seven years of follow up. Patient who had duodenal GIST with liver metastasis did not respond to Imatinib treatment with disease progression and succumb at seven months of treatment. Role of Imatinib for intermediate risk tumour is controversial. In this study we had one patient with intermediate risk gastric GIST who did not receive Imatinib postoperatively and she is doing well on follow up at six years. GIST is resistant to both chemotherapy and radiotherapy.

Local recurrence can be there even in benign lesion despite of complete resection. Local recurrence and metastasis depends mainly upon tumour size >5 cm and mitotic rate >5/50 HPF; other factors are R0 resection, age and location of tumour.[6] Post operative local recurrence as well as metastasis can occur in about 50% of patients with GIST.[6,12] Therefore, these patients should be kept on regular follow up despite of having R0 resection. Postoperative follow up should be done by CECT abdomen 6 monthly to annually for low to moderate grade GIST and 4-6 monthly for high grade and high risk GIST.[12] Reported 5-year survival after complete surgical resection is 35-65% and median survival for unresectable disease is10-20 months.[12,13] Recurrences has been reported even after 10 years of follow up, therefore these patients should be followed up even after 10 years of curative surgery.[13]

CONCLUSION

Gastroduodenal GIST is a rare tumour but has a good survival prospects after en bloc surgical resection. Patients with intermediate and high risk tumour should receive Imatinib. Imatinib can also be given to downstage malignant or locally aggressive GIST to make it operable with negative margins.

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