

## Giant Gists

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## 1. Abstract

Gastrointestinal stromal tumours (GIST) are not uncommon in clinical practice. However giant GIST are relatively rare and present as exophytic tumors. The treatment of these giant tumours are tailored according to the size, site and resectability. When resectable, upfront surgery was done when the tumor profile precludes curative surgery, they are offered neoadjuvant Imatinib with an intention to down stage the tumor. We share our center's experience with having treated 15 giant GISTs originating from different sites of the alimentary tract with variable presentation and the different treatments offered for the same.

## 2. Introduction

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal (GI) tract [1]. They account for 0.1% to 3% of all GI malignant tumours, and 60% to 70% of them originate from the stomach [2,3]. GISTs develop from interstitial cells of Cajal due to mutation of KIT and platelet-derived growth factor receptor alpha (PDGFRA) [4,5]. Many of these tumors are asymptomatic and present to the clinician as large tumors and they are defined as giant GIST when it reaches beyond ten centimeters indimension. The presenting symptoms include abdominal mass, abdominal pain, gastrointestinal bleeding and anemia [1]. Tumor size, site and the mitotic count are the most commonly used prognostic factors to estimate the outcome and risk of recurrence of the tumour. Treatment strategy for GIST depends mainly on the site, size and presence and absence of metastasis. Small GISTs less than 2cm can be observed or if intraluminal, can also be resected endoscopically. The best treatment for GISTs is surgical resection, and neoadjuvant imatinib mesylate therapy for locally advanced GISTs contributes to long-term positive results [6,7]. Herein, we share our

centre's experience giant GISTs located at various organs in GI tract along with different presentations according to its exophytic/intraluminal presence.

## 3. Materials and Methods

Retrospective analysis of prospectively maintained database of all gastrointestinal tumour treated in the Department of Surgical Gastroenterology from January 2012 to January 2017. Those patients with tumor size more than ten centimeters were selected for the study. Patient parameters, tumor characteristics, treatment and outcome were analysed.

## 4. Results

We had 15 patients satisfying the criteria of giant GIST. The primary tumor was in the stomach in nine cases, four involving the small bowel and two cases involving the duodenum. The details are summarized in the chart.

### 4.1. Gastric GIST

Out of nine giant GIST involving the stomach, two cases were exophytic with a narrow attachment to the stomach and hence wedge resection was done. One case was exophytic involving the fundus of the stomach which warranted proximal gastrectomy. One case was had a large endophytic component involving the antrum and exophytic component involving the body and she underwent a distal subtotal gastrectomy. The remaining five giant gastric GISTs had both exophytic and infiltrating component. In this group, only one patient underwent neo-adjuvant down-sizing, followed by laparoscopic assisted resection. The remaining four cases were taken up for emergency surgery in view of severe bleeding and all underwent palliative resections, followed by adjuvant Imatinib. One patient died in the postoperative period due to pulmonary embolism which was detected pre-operatively.

**Table 1:** Type of surgery's

S.no	Age	Gender	Size	Location	Morphology Exophytic/ infiltrative	Type of surgery	CD 117+	Mitotic Index /50 HPF	Adjuvant Therapy	5 year survival	Additional Remarks
1	50	Female	15cm	Stomach (Greater curvature)	Exophytic	Wedge resection	+	>5	Imatinib	DFS	-
2	45	Female	11cm	Stomach (Lesser curvature)	Exophytic	Wedge resection	+	<5	Imatinib	DFS	-
3	40	Male	15cm	Jejunum	Exophytic- Infiltrating Right mesocolon	En bloc excision(jejunum with right colon)	+	<5	Imatinib	DFS	-
4	36	Female	12cm	Duodenum ( D2- D3 Infiltrating right colon )	Exophytic	En bloc resection(duodenum, jejunum & Right colon)	+	>5	Imatinib	DFS	Short gut syndrome-compensated
5	40	Female	16cm	Stomach	Exophytic proximally & endophytic(distally)	Subtotal Gastrectomy	+	>5	Sunitinib	DFS	(SDH positive)
6	60	Male	18cm	Stomach ( Fundus ) Infiltrating the diaphragm	Exophytic	Proximal gastrectomy with cuff of diaphragm	+	>5	Imatinib	DFS	
7	65	Male	11cm	Ileum with multiple ileal loops infiltrated	Exophytic	En bloc resection	+	<5	-	Recurrence	Defaulter on adjuvant treatment- Recurrence
8	68	Female	12cm	Stomach	Exophytic &infiltrative	Lap Wedge resection	+	<5	Imatinib	DFS	Neoadjuvant+Adjuvant
9	65	Male	19cm	Stomach – Infiltrating Bleeding	Exophytic & infiltrative, bleeding tumor	Upfront RI resection(R1 resection)	+	>5	Imatinib	-	Post Op pulmonary embolism, mortality
10	57	Male	16cm	Jejunum	Exophytic	Resection	+	>5	Imatinib	Recurrence	Recurrence after 2 years, defaulted Imatinib
11	67	Male	20cm	Stomach	Exophytic- Infiltrating bleeding type	Multiorgan resection	+	>5	Imatinib	Recurrence	Recurrence
12	57	Female	17cm	Stomach- Infiltration and perforation- R1 resection	Exophytic& infiltrative	R1 resection	+	>5	Imatinib	Recurrence	Recurrence
13	50	Male	15cm	Ileum	Exophytic	Ileal resection	+	<5	Imatinib	DFS	-
14	34	Female	11cm	Duodenum with multiple large volume liver mets	Exophytic	Palliative Imatinib	+	>5	-	Survived for 4 years	Palliative imatinib
15	62	Male	15cm	Stomach- Infiltrating	Exophytic & infiltrative	R1 resection	+	>5	Imatinib	Recurrence	Recurrence

#### 4.2. Small Bowel Giant GISTS

In small bowel giant GISTS, we have 4 cases, two of which were predominantly exophytic and underwent segmental R-0 resection. One of the tumours was located in jejunum (15cm) which was infiltrating the right mesocolon hence the patient underwent en bloc right hemicolectomy with jejunal resection. One Ileal giant GIST (11cm) presented with intestinal obstruction and was involving multiple loops of small bowel, warranted segmental resection two areas of the bowel.

#### 4.3. Duodenal Giant GISTS

Two cases of exophytic giant duodenal GISTS were also treated at our centre. One case was an exophytic GIST (12cm) which was infiltrating the nearby right colon, patient underwent en bloc Right hemicolectomy with segmental duodenectomy. Another was an inoperable duodenal gist (11cm) with massive liver metastasis, treated with palliative imatinib, and she survived for four years

#### 5. Discussion

GIST tumours are well defined, not encapsulated, firm in consistency and whitish in colour. Small lesions have a homogeneous aspect on overall section surface, while large lesions may present with zones of necrosis, haemorrhage and cystic degeneration. Grossly, they appear fleshy pink or tan- white cut surface with

haemorrhagic foci. Microscopically, they can have a moderate or high cellularity, and can be divided into spindle cell, epithelioid, signet ring cell, pleomorphic, oncocytic variants or those with myxoid stroma variant [8]. They have variable symptoms depending on the location and size of the tumour, those related to the tumour mass effect (abdominal pain, discomfort, distension and a palpable mass), or others presenting with anaemia and GI haemorrhage [9, 10]. Contrast- enhanced abdominal is the investigation of choice for staging and follow- up. MRI may be an alternative such as for rectal GISTS. Chest CT scan and routine laboratory testing complement the staging work up. Evaluation of fluorodeoxyglucose (FDG) uptake using an FDG- positron emission tomography (PET) scan, or FDG- PET- CT/MRI, is useful for early detection of tumour response to molecular- targeted therapy or neoadjuvant therapy [11,12] Mutational analysis can play a role in GIST, as mutations involving KIT and PDGFRA can confirm the diagnosis of GIST. Surgery is the standard treatment for localised GISTS. The tumour should be removed en- bloc with its pseudocapsule to yield an adequate resection margin. The presence of metastasis does not contraindicate surgery of the primary tumour, while neoadjuvant imatinib should be considered for those large gastric or rectal primaries where immediate resection is likely to be morbid, for example total gastrectomy or abdomino- perineal resection. The

standard therapy for imatinib is 400 mg daily for 3 years, and randomised clinical studies are ongoing to test longer durations of adjuvant therapy [12] Patients who progress despite imatinib dose escalation or are intolerant to imatinib are candidates for dose escalation or a trial of other tyrosine kinase inhibitors such as sunitinib, a standard second line treatment.

Herein we share the experience of 15 cases of Giant GIST from our centre which is the first giant gist case series published until now. Stomach was the common site followed by small intestine. When dealing with giant GISTs, there are two options in front of the clinician, upfront surgery and neo-adjuvant Imatinib followed by surgery. Size alone is not a criteria for preoperative down-staging with Imatinib. Morphology of the tumor, whether, exophytic, endophytic or infiltrative, would determine the approach. The clinician should determine whether R-0 resection can be achieved comfortably. In our series two cases, despite the massive size the tumor had a very narrow attachment to the stomach, and hence R-0 resection was achieved with simple wedge resection. In two cases upfront surgery in the form of proximal gastrectomy and subtotal gastrectomy could achieve R-0 resection. When the imaging is suggestive of infiltrative type of growth, it is preferable to down-stage the tumour and follow it with resection and this approach was followed in one case, with significant down-sizing we could do a lap assisted sleeve resection. Four other cases were not suitable for Imatinib down-staging as these patients presented with severe bleeding and hence offered palliative resections as a semi-emergency procedure. Giant GIST of the small bowel tend to involve adjacent bowel loop or derive parasitic supply. In this series two cases were treated with segmental resections and two more cases required enbloc resection of adjacent bowel, right colon in one case and small bowel in one case. The one duodenal GIST with massive liver secondaries received palliative Imatinib, she showed excellent response for the secondary deposits than the primary tumor and survived for four years after diagnosis. All the patients received Imatinib for three years and patients undergoing palliative resections were put on Imatinib for five years and beyond. There was one mortality due to pulmonary embolism. Nine patients who underwent R-0 resection are disease free at the end of five years. Three patients with R-1 resection continued to be on Imatinib to control the recurrence. Two patients defaulted Imatinib, recurred and restarted on therapy.

## 6. Conclusion

Giant GIST forms a subset of tumours having heterogenous patterns. Exophytic tumors, Gastric GIST and R-0 resections have favourable results in terms of disease free survival at five years. Infiltrative tumors, palliative resections and defaulters ended up in recurrence and are on imatinib to control the disease

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