

Original Article

Gastrointestinal Stromal Tumor - Experience From A Tertiary Care Center

Kalidas Biswas¹, Jayanta Kumar Das², Swarnabindu Banerjee³, Shibashish Bhattacharyya³, Bishan Basu⁴, Shibajyoti Ghosh⁵

¹Department of Medical Gastroenterology,

²Department of Anaesthesiology,

³Department of Medical Oncology,

⁴Department of Radiotherapy,

⁵Department of Surgery,

Calcutta National Medical College
& Hospital, Kolkata

Corresponding Author:

Dr Swarnabindu Banerjee

Email: dr.swarnabindubanerjee@gmail.com

ABSTRACT

Gastrointestinal stromal tumor(GIST) is an uncommon entity in clinical practice. Though It is the commonest mesenchymal smooth muscle tumor, it accounts for only <1% of all GI malignancies. Any part of gastrointestinal tract (GIT) may be involved . Stomach is the commonest site for this tumor. Other sites of GIT are also affected in this disease. Increasing awareness, newer diagnostic modalities and novel chemotherapeutic agents make the disease diagnosed earlier and successfully treated . Imatinib mesylate has changed the outcome of the disease .In Eastern part of India we have seen some cases over the years and expressed our observation here . Most of the patients were operated and later required Imatinib.

KEYWORDS: GIST, symptoms, surgery, imatinib.

Introduction

Gastrointestinal Stromal Tumours (GISTs) are the most common soft tissue sarcomas of the GI tract. GISTs can arise from anywhere of the GI tract, but stomach, where 60% of tumours are originated, is the common primary site followed by the small intestine, the region of origin for another 30% of cases.¹ Esophagus, colon and rectum are other uncommon sites. Symptoms range from the vague ones like early satiety, abdominal fullness to pain abdomen and abdominal swelling. Gastrointestinal or intraperitoneal haemorrhage or more grave ones like acute abdomen like condition due to tumour rupture or acute obstruction due to tumour mass may lead to an acute medical emergency.² Metastasis to liver or dissemination within the peritoneal cavity are the usual modes of distal

spread. Suspected tumour type as well as the extent of spread guides the decision to take a biopsy. If pre-operative therapy is considered, obtaining a tissue sample to confirm the diagnosis before any such intervention, is mandatory.² For obtaining such sample, endoscopic ultrasound based fine needle aspiration (FNA) is preferred over percutaneous biopsy, as the later is associated with more risks of intraperitoneal haemorrhage or tumour dissemination. Percutaneous route, though, may be more convenient route to rule out metastatic disease.³ Outcome of therapy or prognosis is related to the primary site of origin of the tumour, the size of it and the mitotic rate and the pathologic report must mention these factors. To make a proper assessment of the mitotic rate, the most

proliferative region of the tumour should be evaluated and the reporting should be done as the number of mitoses per 50 high power fields.⁴⁻⁵

Methods

A retrospective analysis was performed with respect to disease presentation, disease course and long term outcomes.

Results

In our institution we have seen 13 patients of GIST from 2010 to 2017 (**Table 1**). Age ranging from 28 to 74 years with an almost equal incidence of sexes. Pain abdomen was the predominant symptom (8/13 patient). Two patients presented with GI bleed. One patient presented with abdominal mass. Three patients had features of bowel obstruction. Stomach (6/13) was the predominant site for disease. Small intestine was seen to be affected in three patients. Two patients had retroperitoneal involvement. One patient had site of involvement at mesentery while another one had multiple sites of involvement (periampullary region and cecum). All patients were essentially diagnosed histopathologically. CD117 was

done in almost all patients. All but 1 patient underwent surgery. Most of the patients had definitive procedure and depending on the risk status chemotherapy with imatinib was initiated. Two patient was lost to follow up; while all other patients were on regular follow up. During the course of follow up, recurrence with deterioration noted in two patients. They were put on regular monitoring along with CT scan of abdomen along with escalated dosage and duration of imatinib. Two patients were lost

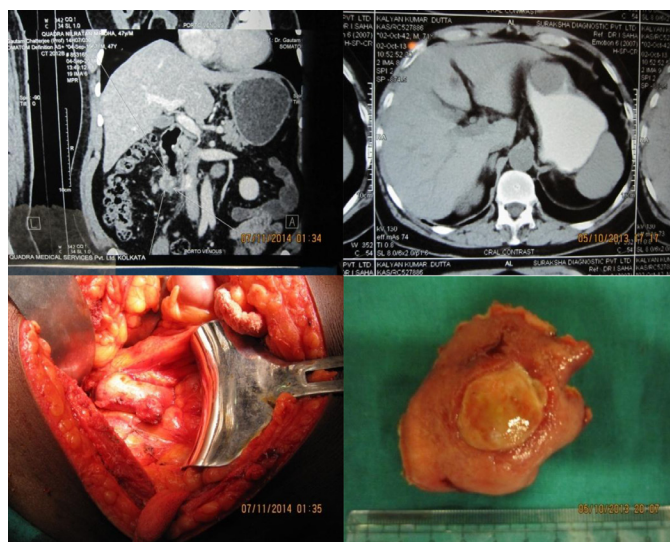


Figure 1: Photograph of duodenal GIST

Table 1: Demography of patient population.

Sl no	Age	Sex	Site	Presentation	Surgery	Chemotherapy	Recurrence	Date
1	55	F	Stomach	Pain abdomen	Yes	Yes	Suspected	2010
2	60	F	Stomach	Pain abd. Early satiety	Yes	Yes	Nil	2011
3	47	M	Duod 2-3	Vomiting	Yes	Yes	Nil	2014
4	50	M	Retroperitoneum	Pain abd	Nil	yes	Nil	2015
5	60	M	Stomach	UGI Bleed	Yes	nil	Lost to follow up	2015
6	52	M	Jejunum	Vomiting, Pain abd.	Yes	Yes	Nil	2016
7	38	F	Ileum	Vomiting Pain abd.	Yes	Nil		2016
8	47	M	Periampullary and colon	Pain abd.	Yes	Yes	Yes	2016
9	60	F	Stomach	Pain abd.	Yes	Nil	Lost to follow up	2016
10	28	F	Stomach	Pain abd.	Yes	Yes	Nil	2016
11	68	M	Mesentery	Pain abd.	Nil	Yes	Nil	2017
12	74	F	Stomach	UGI bleed	Yes	Yes	Nil	2017
13	50	M	Retroperitoneum	Pain abd	Yes	Yes	Nil	2017

to follow up and rest 11 patients were regularly being monitored. Two patients had experienced recurrence of the disease and 9 patients were doing well till date. Periodic endoscopies, CT scan and relevant examinations were done in all patients.

Discussion

GIST is the commonest mesenchymal tumor. Stomach is known to be affected in 60% of cases. Small intestine is the site for 20 to 30 % patients, rest are seen at esophagus, colon and rectum. Rectal GIST is the most aggressive one. Retroperitoneum is an uncommon site for this tumor. In our series stomach is the site of involvement for around 46% patients, Small intestine 25%, and retroperitoneum was involved in 15% of patients. Mesentery and multiple site involvement (8% each) is the least common variety.

Tumour size and mitotic index of more than 5 mitoses/50 High Power Field are the chief prognostic factors for a given subsite, while the subsite of origin is a separate factor affecting outcome. Gastric GISTs are relatively indolent, while rectal GISTs are very aggressive.¹ The presence of KIT and PDGFRA mutation is predictive of response to TKI therapy, while presence of SDH mutation signifies resistance to such therapies.

Imaging is useful for diagnosis, staging, restaging or for response evaluation and contrast-enhanced CT Scan is the usual choice for abdominal GISTs. MRI might be of additional help in some special circumstances like delineation of anatomic details of hepatic metastasis before surgical resection. PET/CT Scan is helpful to differentiate benign from malignant or necrotic mass from malignant tissue. In our series none of the patient undergone PET CT and all of them availed the facility of CT scan only.

However, if PET/CT Scan is planned to be used for follow up, a baseline PET/CT Scan is mandatory.² PET can give an early assessment of response to Imatinib therapy if such evaluations are needed.

RECIST, WHO or Choi criteria are used to monitor response to therapy, all using CT Scan as primary modality of imaging.¹³⁻¹⁹ While some experts did opine that Choi criteria is the better way to evaluate response to Imatinib therapy, some others think RECIST or WHO

criteria are better methods to response evaluation who are put on Sunitinib or Regorafenib after showing resistance to Imatinib therapy.¹³⁻¹⁷ EORTC has developed a separate metabolic response criteria for based upon PET/CT Scan findings.¹⁸

Surgery is the treatment of choice in tumours which are non-metastatic and resectable. In some non-metastatic tumours, to make surgical resection easier, pre-operative Imatinib may be administered. The goal of surgery is complete resection with an intact pseudocapsule and negative microscopic margin. There is no evidence to support re-resection for microscopically positive margin. Lymph node dissections are, usually, not indicated. However, grossly enlarged nodes should be removed.²⁰⁻²¹ Laparoscopic surgery is a good and acceptable alternative to the conventional laparotomic approach.^{2,22-24} A meta-analysis from 19 studies pooling data of 1060 GIST patients show that there is no difference of outcome between laparoscopic and laparotomic approach, but laparoscopic approach was associated with shorter hospital stays, less blood loss and lower complication rates.²⁵ In our patients laparoscopic approach was chosen as surgical methods. Two patients were not operated due to bad surgical risks and were directly put into imatinib therapy.

Targeted therapy aiming at KIT inhibition has emerged as the primary modality of therapy, along with surgery, in KIT positive GISTs.²⁶ Long term follow-up data from B-2222 study confirmed that Imatinib mesylate produces durable disease response in patients with advanced GIST.²⁷ Data from EORTC 62005 study and S0033/CALGB 150105 study have established that 400mg/day is an acceptable starting dose for Imatinib. For patients who had progressive disease following the above-mentioned dose of Imatinib, dose escalation to 800mg/day is an acceptable option (EORTC 62005 study).²⁸⁻³¹ Most of our patients were on 400mg imatinib therapy.

RTOG0132/ACCRIN6665 was the first prospective study to establish the efficacy of imatinib in preoperative setting.³³ Since then, numerous studies have been conducted, all showing dependable results. Maximal response may require more than six months of therapy and preoperative imatinib should only be used when there is

a definite possibility of surgical risk reduction with usage of such therapy.³⁴⁻³⁷ None of our patients had received preoperative imatinib therapy.

Based on the encouraging results shown in ACOSOG Z9001 as well as in SSGXVIII/AIO, postoperative imatinib is recommended for all patients who are higher risk (high or intermediate risk groups) of recurrence. Risk of recurrence is determined by the primary tumour size, the mitotic index, non-gastric location and tumour rupture. Recommended duration of therapy is 36 months. Risk assessment for patients who did receive preoperative imatinib is difficult. So, they should receive adjuvant imatinib for at least 2 years. All of our patients received imatinib therapy and depending on the risk status, they had prolonged imatinib therapy in some patients. Patients who had residual disease after surgery should undergo repeat surgery and should receive imatinib irrespective of second surgical status. The decision of surgery in patients with resectable, but metastatic disease is a controversial one, while patients with unresectable disease should receive preoperative imatinib. Evaluation for resectability is done by contrast-enhanced CT scan or MRI every 8-12 weeks. Patients with metastatic GIST should receive imatinib till progression of disease.³⁸⁻⁴² None of our patients was operated for second time.

Progression of disease is defined as increase in tumour size and/or appearance of new lesions in CT scan or MRI, while PET/CT scans can help to clarify ambiguous lesions. Patients progressing on standard dose imatinib (400mg/day) can be shifted to higher dose protocol or switching to sunitinib. Patients progressing on high dose imatinib or sunitinib can be treated with regorafenib. In our series because of certain reasons and financial constraints we opted for imatinib therapy.

Indian Data

Indian data on GIST is limited. From this part of India we have no available data on GIST as noted with Pubmed search. Gupta et al presented their experience from SRMS-IMS of treating four cases of GIST of diverse stages.⁴³ While in our study we encountered recurrence, Gupta et al had experienced recurrence free disease in their study. Suresh Babu et al presented their experience

of treating 44 patients with metastatic GIST with imatinib. They reported a median PFS of 26 months, while their estimated median survival was 48 months.⁴⁴ In our study we had metastatic disease in 2/13 patients and they were on imatinib therapy. Zanwar et al shared their experience of treating 23 cases of rectal GIST and concluded that neoadjuvant imatinib helps to spare the sphincter without any adverse effects on the overall outcome.⁴⁵ Pai et al in their retrospective evaluation of 13 patients with rectal GISTs, out of which 11 were non-metastatic, revealed that sphincter preservation may not be feasible in spite of treatment with imatinib.⁴⁶ However, we did not encounter any rectal GIST. Sahu et al reported their experience of treating 15 patients of GIST, who had developed imatinib resistance, with sunitinib.⁴⁷ Yacob et al reviewed their experience of treating 150 patients of GIST at their centre⁴⁸, while Borgaonkar et al shared their experience of successfully treating 15 such patients.⁴⁹ We experienced a good response to surgery followed by imatinib therapy in most of our patients.

Conclusion

GIST in an uncommon tumor with protean manifestations. Our study with a small number of patients enlightened us with its variations. Surgery and chemotherapy with imatinib are acceptable modalities of treatment. In our experience overall prognosis is satisfactory unless metastasized. Multimodality and multispeciality treatment approach are essential to treat the disease.

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