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Original Research Article

GIST a rare abdominal tumor and our surgical experience

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ABSTRACT

Background: GISTs are rare abdominal tumors, encountered as the most common mesenchymal neoplasms of the gastrointestinal (GI) tract leading to GI bleeding. We report a changing trend of diagnosis and management in Indian patients.
Methods: The retrospective data was collected from medical records and 62 cases of GIST from 2003 to 2020 in General surgical unit of BHU. They were divided in three groups. In group A (36) patients only surgery, group B (14) patients surgery than adjuvant chemotherapy and in group C (12) who received neoadjuvant chemotherapy then surgery. Preoperatively, USG and CT scans of the abdomen were the main investigations, others being upper gastrointestinal endoscopy and chest x-ray confirm by histopathological and immunohistochemical evaluation.
Results: The mean age at presentation was 42.8 years (range 17-74 years) and mean duration of symptoms was of 5 months (range 10 days-2 years). It was from the stomach, (06) duodenum (14) jejunum, (06) ileum, (1) caecum and (4) from the mesentery and (4) from retroperitoneum. 44 cases had low grade benign tumors and 18 malignancies. In group A, 22 (61%) patients showed recurrence in group B, 06, (42%) patients showed recurrence and group C, 02 (33%) patient showed recurrence.
Conclusions: Most of the tumours were benign and surgical resection is the mainstay of treatment. However, the patients in which only surgery was done showed maximum recurrence and patients who received neoadjuvant chemotherapy then surgery followed adjuvant chemotherapy showed minimum recurrence.

Keywords: CD117, Gastrointestinal stromal tumours, Imatinib, Interstitial cells of Cajal (ICC)

INTRODUCTION

Although gastrointestinal stromal tumours (GIST) are the most common mesenchymal neoplasms of the gastrointestinal tract (GIT), overall, they are rare neoplasms ranking a distant third most common in prevalence after adenocarcinomas and lymphomas.[1] They can originate from the intestinal and extra-intestinal site as well such as the mesentery, the omentum and retroperitoneum. In the past, these tumours were a poorly defined pathological entity with uncertainty regarding the tumour behaviour, progression, origin and terminology often being confused with leiomyomas and leiomyosarcomas. Kindblom in 1998 first hypothesized the origin of these tumours from pluripotent mesenchymal stem cells of the gastrointestinal tract which are programmed to differentiate into the interstitial cell of Cajal (ICC).[2] These tumours have microscopic features that appears as similar as with the myenteric plexus subtype of ICC that are found in stomach and intestines, including frequent expression of CD34, embryonic smooth muscle myosin heavy chain, and the intermediate filament nestin. The observation that ICC cells can be immunohistochemically highlighted with an antibody to KIT (CD117) led to the discovery that KIT is also strongly expressed in most GISTs.[3,4] These tumours

not only substantiated the hypothesis that GISTs arise from or share a common stem cell with the ICC, but it also provided a new, more sensitive and specific marker for its diagnosis. Rapid functional mutations in exon 11 of the c-kit proto-oncogene are appeared to be associated with most GISTs.[5] Although there are multiple reported case series some larger series in the world literature, those from India are few. We present our clinical experience of management of such cases of GIST from a single teaching surgical Unit from the era of WLE to sandwich therapy and compare it with other series in view of continue evolution of managements.

METHODS

It was a retrospective analytical study and the patients were followed up both physically and telephonically for minimum 2 years. From March, 2003 to Jan, 2020, total reported 62 cases of GIST, who were recorded in medical record admitted and managed in a postgraduate training in Institute of Medical Sciences, in a General surgery unit of Sir Sundarlal Hospital, BHU. Demographic data of these patients was collected based on a retrospective study, their clinical presentation and management were analysed and we used the complete enumeration method for choosing the sample. Preoperatively, abdominal ultrasonographic examination and contrast enhanced CT scan of the abdomen were the main investigations for evaluation for anatomical diagnosis and confirmation. Results of other supporting investigations like the endoscopy, colonoscopy and blood reports were recorded. Histopathological examination with immune-histochemistry was used to confirm the all clinically diagnosed GIST. We have used the Statistical Package for Social Sciences (SPSS-25) for data analysis, and we used only descriptive statistics for describing the patient's status.

Inclusion criteria

All patients with GI bleeding suspected and proven cases of GIST who underwent treatment in said duration.

Exclusion criteria

Negative for GIST, not amenable to follow up and participation.

RESULTS

The mean age at presentation was 42.8 years and the mean duration of symptoms was 5 months. Most patients presented with chief complain of intermittent abdominal pain (22%) on presentation while abdominal lump (19%) was complained of by 14 patients (Table 1). However, 16 (25%) patients in whom multiple complex of all complains such as abdominal pain, malena and weight loss were the presenting symptom. The tumor could be diagnosed by an ultrasonographic examination but CT scan was used as ideal investigation to assess for invasion, resectability and vascularity when it was added with angiography in cases of GI bleeding. Contrast CT scan was diagnostic of GIST in all 62 patients. The mean size of the tumor was 12.6 cm (4.2-21 cm). Twelve (24) patients with gastric GIST required additional upper GI endoscopic examination for biopsy and confirmation. Important findings in the CT scan included heterogeneous/homogeneous/minimally enhancing mass lesion, central necrosis, calcifications, focal thickening of pylorus and intraluminal polypoidal mass in stomach with perigastric fat stranding and enlarged lymph nodes (Figure 1).

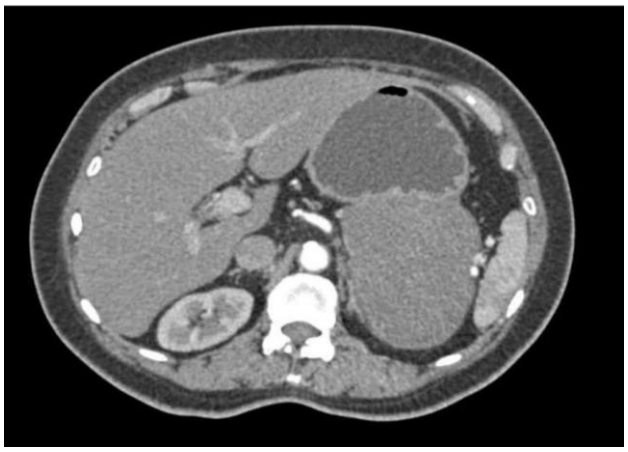

Figure 1: Axial section CT abdomen showing GIST in the stomach.

Table 1: Clinical presentation.

Mean age	**42.8 years (range 17-74 years)**
Male:female	1.7:1
Mean duration	5 months (10 days-24 months)
Abdominal pain	14 (22%)
Abdominal lump	12 (19%)
Anorexia and weight loss	08 (12.9%)
Subacute intestinal obstruction	06 (9.6%)
Upper GIT bleed	06 (9.6%)
Mixed symptoms (weight loss, pain, lump, malena)	16 (25.8%)

Table 2: Surgical management.

Gastric (24)	**Wide local resection and gastrojejunostomy (16) Billroth-I (4) Billroth-II (4)**
Jejunum (14)	Wide local excision with anastomosis (14)
Ileum (06)	Primary resection and ileo-transverse anastomosis (6)
Mesentery (4)	Wide local excision
Retroperitoneum (4)	Wide local excision

Table 3: Patient division according to NIH risk division.

Risk category	Size (cm^2)	Mitotic count (per 50 HPF)	No. of patients
Low	<2	<5	18
Intermediate	2-5 or 5-10	<5 or<5	8
High	>5	>5	36
	>10	Any mitotic rate	
	Any size	>10	

Surgeries were performed in 62 cases. In 24 (38%) cases, GIST was arising from stomach, 06 (9.6%) from duodenum, 14 (22.5%) from jejunum, 6 (9.6%) from ileum and 02 (3.2%) from caecum, 4 (6.4%) from mesentery and 4 (6.4%) from retroperitoneum. The surgical management is summarized in Table 2. Forty four (44) cases were low grade benign tumors while 18 were malignant %) (Figure 2).

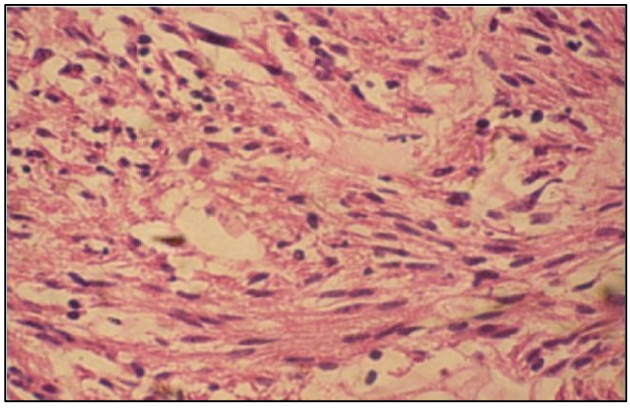

Figure 2: Microphotograph of spindle cell GIST (H and E stain × 400).

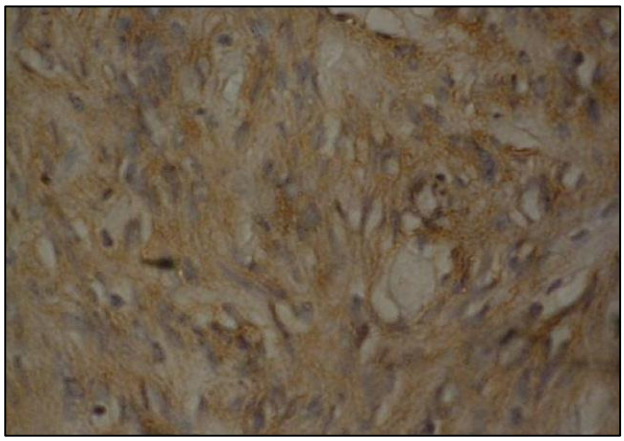

Figure 3: Immunohistochemistry of CD117.

Cut section of the tumors showed grey-white areas and microscopic examination revealed spindle cells with elongated hyperchromatic nucleus and moderate eosinophilic cytoplasm arranged in short fascicles along with areas of tumor cells showing epithelioid appearances. Mitotic counts ranged from 1-3/50 HPF (high power field) in (44/62) forty four out of sixty-two cases while the remaining eighteen showed a mitotic activity ranging from 7-8/50 HPF. Based on the size and mitotic index 36 patients had low risk tumors, 8 patients had intermediate risk tumors while 18 were in the high-risk category. All were positive for CD117 (immunohistochemistry) (Figure 3).

DISCUSSION

GISTs account for less than 1% of all gastrointestinal neoplasm. Incidence of GIST is approximately 10-20 per million people annually worldwide and it has a male preponderance, which (M:F=1.7:1) is in concordance with our series.[2] Mean age at the time of diagnosis of these tumours are usually around 60 years, which was found to present in younger population in present series (42.8 years).[6] Although the most common site of this tumour is the stomach (60%) followed by small bowel (30%) and oesophagus and rectum (10%), in the present series the stomach was most commonly involved (38%) followed by small bowel (33%) and the mesentery (6.45%).[7] Similar investigation results have been reported by Kumar et al (Table 3).[8] In our series malignancy was found in 29% of cases which is in concordance with other studies reporting a 20-30% incidence of malignancy.[4] Clinical presentation of GIST is variable and site dependent. These symptoms mostly present as abdominal lumps with pain, obstruction and pressure related symptoms, and anaemia due to GIT bleeding. Smaller GISTs are asymptomatic and diagnosed incidentally during radiological imaging or abdominal exploration or endoscopy, for other reason.[9] In the present study the most consistent symptom were abdominal pain and lump (33%) as early presentation. This is probably explained by the larger size (mean 12.6 cm) of the tumour in our patients. The diagnostic work-up is determined by the mode of presentation. Upper gastrointestinal endoscopy is done in patients having anaemia, bleeding and radiologically diagnosed lumps of the stomach. Upper GI endoscopic biopsy is usually negative due to sub mucosal location of the tumour and it increases the risk of haemorrhage. Per cutaneous biopsies are acceptable for inoperable tumours.[10] GISTs are known as immunoreactive for KIT (gene) which is a marker of ICC present in the myenteric plexus of stomach and small intestine. KIT (gene) is a part of the tyrosine kinase receptor complex which is detected to contain transmembrane receptor CD117.[11] CD117 positivity is seen in 90-100% of GIST while positivity for CD 34, the hematopoietic progenitor cell antigen, is reported in 70-80%.[12] All the tumours in our series were positive for CD 117. Recently a novel marker, discovered on GIST-1 (DOG-1) a protein of unknown function has been identified on the surface of GIST but could not use this investigation in our patients as it was not available in our institute. It has been observed that reactivity for DOG-1 may aid in the diagnosis of GIST, including PDGFRA mutants that fail to express KIT antigen.[13] Ki-67 (marker

of tissue proliferation) presents a significant prognostic factor for GIST recurrence which could be of great importance in evaluating malignant potential of disease.[14] Recently it has been reported and shown that PET has a valuable potential in diagnostic work-up of GIST and follow up.[15] Direct and haematogenous spreads are common. Surgery is the gold standard of curative treatment in which the resected specimen should have negative margins and integrity of the pseudo capsule.[16] Laparoscopic treatment of GIST can be performed taking strict oncological precaution to avoid rupture of the pseudo capsule. However laparoscopic surgery is discouraged in large tumour because of risk of tumour rupture and subsequent high relapse rate. International guidelines recommend laparoscopic surgery only for tumours smaller than 5 cm.[16] Five year overall survival following R0 resection is satisfactory (88%) while it can reach 0% following palliative surgery.[17] The postoperative treatment of palliated patients includes targeted therapy with Imatinib mesylate (400 mg per day), which is a tyrosine kinase inhibitor. The current data demonstrate a response in 50% of these cases and a continued response in 75%.[11] Imatinib has also been used to downstage the disease.[12] Recent clinical practice guidelines recommend adjuvant chemotherapy for all patients being categorized as intermediate and high risk groups and in incomplete resections/unresectable tumours and the treatment should continue indefinitely.[18] However mutational analysis is essential before adjuvant therapy is started. It is believed that PDGFRA D842V-mutated GISTs should not be treated with any adjuvant therapy, as this genotype confers resistance to chemotherapy.[18] In metastatic disease adjuvant imatinib therapy is the standard practice, although surgery as a primary mode of therapy is not indicated. There is reliable data to show the effectiveness of a higher dose of imatinib (800 mg per day) in patients with KIT exon 9 mutation.[19] In case of progressive disease with Imatinib therapy or in rare cases of imatinib intolerance, sunitinib is the standard second-line therapy.[20] It is difficult to predict the biological behaviour and outcome of these tumours however the most reliable prognostic factors are the site, size and mitotic index for management point of view.[17] On the basis of these factors two risk classifications have been proposed.[4] The biological features of these tumours represent important prognostic factors predicting outcome.[21]

Table 4: Comparison of previous data of GIST with the present series.

Parameters	Historical data	Indian data past series	Present series
Mean age of presentation	Middle age (58-60 years)	46.2 years	42.8 years
Gender	No difference	More common in males	More common in males
Presentation	Bleeding (50%) pain (20%)	Abdominal lump and pain (69%)	Abdominal lump (19%) pain (22%)
Site	Stomach (60%	Stomach (31%)	Stomach (38%)
	Small bowel (30%)	Small bowel (54%)	Small bowel (jejunum+ileum) (33%)
Location	Subserosal (30%)	Subserosal (69%)	Subserosal (88%)

However, this study being a small retrospective study, a bigger cohort and randomizations is needed for validation of such management.

CONCLUSION

GISTs in our series presented at an earlier mean age of 42.8 years (17-74 years) with a male preponderance (1.7:1). Patients had subacute to chronic presentation with mean duration of symptoms of 5 months (10 days-24 months). Pain and lump in the abdomen were the most common clinical symptoms and was associated with vomiting, upper GI bleed and weight loss. Most of the tumors were benign (70%). Gastric involvement was most common (38%). Twenty nine percent of these tumors were malignant and mortality rate was 8.3%. Surgical resection remains the mainstay of treatment. Immunohistochemistry (CD117 staining) was positive in all (100%) and thus is an important tool for diagnostic confirmation.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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