

A Gist of Gastro-Intestinal Stromal Tumors at a Tertiary Care Centre in Western India

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Abstract :

Background: Gastrointestinal stromal tumour (GIST) is the most common mesenchymal tumour of the gastrointestinal tract. We studied the different presentations of GIST at our centre and correlated the various clinical findings, investigations, operative findings and treatment outcomes with the already published data.

Materials and Methods : We analyzed the clinical presentation, endoscopic and radiological features, and operative findings in 35 adult patients with GIST (2012-2014) and compared with the available published data.

Results : Thirty five patients (M: F-2.5:1) with age ranging from 33 to 70 years (mean 50.9) were analyzed. Abdominal pain (94.3%) and lump in abdomen (60%) were the most common presenting symptoms, with mean duration of symptoms being 4.69 months. Around 25% of patients presented as acute surgical emergencies in the form of intestinal obstruction, perforative peritonitis and bleeding manifestations. The most common primary organ involved was the stomach (45.7%), followed by small intestine (37.1%). Around 25% of the patients had advanced disease in the form of adjacent organ involvement or metastatic disease. The average tumour size in this study was 7.94 cm, ranging from 2-15 cm. All patients underwent surgery except one who had extensive metastatic disease. The average duration of hospital stay was 11.08 days, ranging from 7-25 days. There were 5 post-operative deaths (14.28%). 11 patients received post-operative Imatinib (31.42%).

Conclusion : GISTs are uncommon sarcomas. Due to non-specific presentation, diagnosis may be delayed. The presentation may be an acute one. Stomach is the most common site followed by the small intestine. Complete surgical resection when possible is the best treatment.

Keywords : GIST, mesenchymal tumors, surgical resection, imatinib

I. Introduction

Gastrointestinal stromal tumors are rare neoplasms. They represent only 0.1 to 3% of all gastrointestinal malignancies.(1,2) But they account for 80% of the gastrointestinal mesenchymal tumors.(3) The term GIST was coined by Mazur and Clark to describe intra-abdominal nonepithelial tumors that lacked the ultra structural features of smooth muscle cells and the immunohistochemical characteristics of Schwann cells.(4) In the last 2 decades, the understanding of GISTs has undergone a paradigm shift due to identification of mutations in c-kit and PDGFRA (platelet derived growth factor receptor alpha) gene-encoding receptor tyrosine kinases, and the development of therapeutic agents (imatinib mesylate and sunitinib malate) that inhibit these kinases. GISTs are believed to arise from the "interstitial cells of Cajal" which are components of the intestinal autonomic nervous system the function as intestinal pacemakers.(5)

The median age at diagnosis is 60 years (40 to 80years).(2,5,6) the majority of GISTs are sporadic. However familial cases are seen in relation to von Recklinghausen's neurofibromatosis and Carney's triad. Surgery remains the standard of care and the only potentially curative therapy for patients with resectable and localised GIST. Surgery alone or in combination with traditional chemotherapy or radiation therapy largely has been ineffective in treating the majority of patients with malignant GIST.

A lot of data is available in western literature about the epidemiology, symptomatology, sites of presentation and prognostic factors of GIST. The objective of this study was to study the different presenting features and treatment outcomes of GIST at our centre in western India and correlate the findings with the published literature.

III. Materials And Methods

This retrospective study was conducted at a tertiary care referral centre. We analysed 35 patients who were diagnosed with GIST over a period of 2 years. Data regarding demographics, clinical features, treatment offered, operative findings and treatment outcomes was collected and analysed. This data was then compared and contrasted with the already published data.

IV. Results

Thirty-five patients who were analyzed included 25 males and 10 females ranging in age from 33 to 70 years (mean 50.9 and median 50 years). Mean duration of symptoms before presentation was 4.69 (range 1-24)

months.

Major presenting symptoms were abdominal pain in 33 (94.28%) patients and abdominal lump in 21 (60%) patients. Acute surgical manifestations were seen in 9 patients (25.7%) of the patients, such as obstruction (one case of intussusception with jejunal GIST as the lead point), perforative peritonitis (n=3), hemoperitoneum (n=1) and gastrointestinal bleed -- hematemesis (n=3) and per rectal bleed (n=1). One patient was diagnosed to have GIST incidentally - while undergoing a laparoscopic umbilical hernia repair. Here a 2 cm tumor was visualised on the anterior stomach surface near the greater curvature. He underwent a wedge resection and was subsequently diagnosed as having stomach GIST.

Pre-operative cross sectional imaging was done in 30/35 patients (85.7%). Of the rest, 3 were diagnosed as perforative peritonitis and one as intestinal obstruction on plain abdominal X-ray films and based on these as well as clinical features they proceeded directly to surgery while one was incidentally diagnosed during laparoscopic surgery for some other purpose. Preoperative endoscopy was done in 17 patients (48.57%). These included 12 for stomach growths, 3 for duodenal growths, and one each in case of GE junction and ascending colon masses. 34.29% patients had a preoperative histopathological diagnosis, as a biopsy was done in 12 of the 17 patients who underwent endoscopy.

The most common organ of origin was the stomach (n=16; 45.71%) followed by small intestine (37.14%; n=10 for jejunum; n=3 for ileum). There were 4 cases (11.42%) of duodenal involvement with one of these at the DJ flexure. There was only one case involving the large intestine, an ascending colon GIST, and one case involving the gastroesophageal junction.

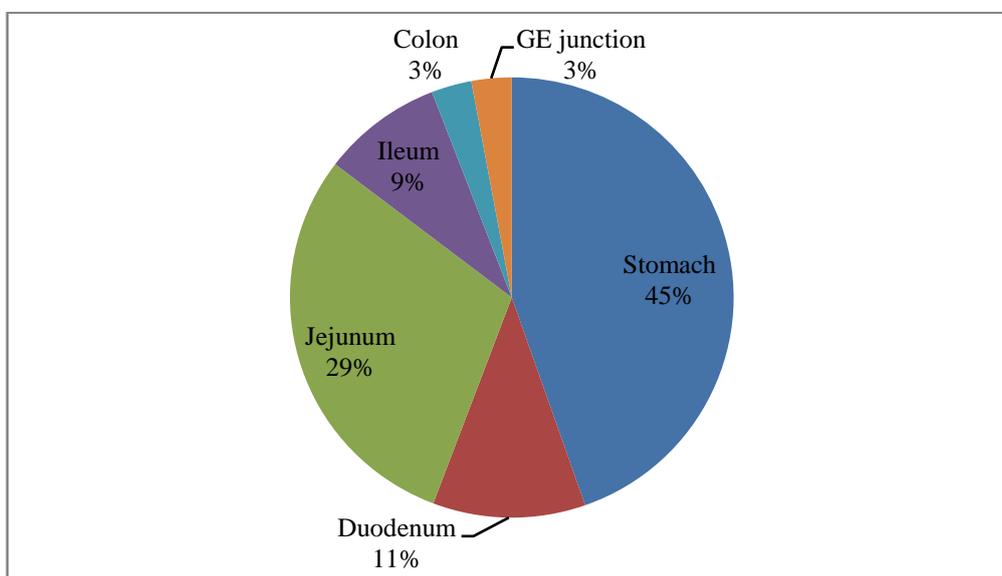


Figure 1. Organ-wise distribution

The mean size of the tumors in this study was 7.94 cm, with a range of 2-15 cm.

The risk stratification of the patients in this study was as follows :

- 23(65.7%) were low risk (up to 5 mitoses per hpf)
- 9(25.7%) were intermediate risk (6 to 10 mitoses per hpf)
- 3 (8.57%) were high risk (more than 10 mitoses per hpf).

25.71% patients presented with advanced disease in the form of either adjacent organ involvement (n=7) or metastatic disease (n=2). The most common primary sites in case of advanced disease were stomach (n=4) and duodenum (n=2). The locally advanced stomach GISTs involved the spleen (n=2) or the pancreas (n=2), while one case of locally stomach GIST also had liver metastases. One locally advanced duodenal tumor also involved the gall bladder while the DJ flexure GIST had transverse colon involvement. Another case of metastatic disease to the liver was from a jejunal primary, while one locally advanced ileal primary involved the adjacent mesentery. The ascending colon GIST was also locally advanced involving adjacent mesocolon.

All patients except one underwent exploratory laparotomy, the exception being a case of stomach GIST with extensive metastatic disease and poor general condition. All the remaining patients with stomach GIST underwent either wedge resection (n=6) or distal gastrectomy (n=10), with 2 of the latter group also undergoing distal pancreatectomy with splenectomy. All jejunal and ileal GISTs underwent resection followed by primary anastomoses including the jejunal GIST with liver metastases as that patient had presented with perforative peritonitis. The duodenal GISTs underwent wide excisions, including also a cholecystectomy and a transverse colon resection anastomoses in two cases of locally advanced disease. The ascending colon tumor was treated

with a right hemicolectomy, while the GE junction growth was resected following which a primary anastomoses between esophagus and stomach was performed.

The average duration of hospital stay was 11.08 days, ranging from 7-25 days.

There were 5 deaths in this case series (14.29%), of which one was a locally advanced and high-risk tumor, two were locally advanced but low risk and two presented with perforative peritonitis.

11 patients received imatinib mesylate, of which 2 were high-risk and locally advanced (the third high risk patient expired in post-operative period), one was a case of perforative peritonitis, one was a stomach GIST with liver metastases (not operated) and the last three had intra-operative tumor spillage and all from intermediate risk group.

V. Discussion

The median age at diagnosis in this study was 50 years which is lower than the median age mentioned in literature – 60 years.(1,2) Also, in literature the incidence of the disease in males and females is the same. However, in our study, the male : female ratio was 2.5 : 1.

Only 70% of the patients with GIST are symptomatic; 20% are asymptomatic and diagnosed incidentally while the remaining 10% of GISTs are found only in autopsies. Symptoms may vary greatly and depends on the size and location of the tumor.(3,7,8) In our study, 94% of the patients presented with abdominal pain while 60% presented with a lump in abdomen. Such non-specific presentation may delay the diagnosis. GISTs are often highly vascular, soft and friable and they may cause life threatening hemorrhage by erosion into the bowel lumen. Alternatively, tumor rupture can cause intraperitoneal bleeding or perforative peritonitis as seen in a few of our patients. Between 15 and 47% of patients with GISTs have metastatic disease at diagnosis.(2,9) Common sites of metastasis include liver, peritoneum and omentum. Lymph nodes metastasis are rare.

GISTs can develop anywhere in the gastrointestinal tract. But the most common locations are the stomach (50 to 70%) and the small intestine (25 to 35%). Other sites include the colon and rectum (5 to 10 %), mesentery or omentum(7%) and esophagus (<5%).(3,10) Rare locations include duodenal ampulla, appendix and gall bladder.(11–13) In our case series, 45% of the cases were in the stomach while the small intestine accounted for 38% of the cases. GISTs can vary in size from a few millimetres to around 30 cm but their median size is between 5 and 8 cm.(3,14) The median size in our study was 8cm.

The initial imaging study for a suspected or confirmed GIST is a contrast enhanced CT scan of the abdomen and the pelvis.(15) It can also be used to monitor response to therapy and for surveillance for recurrence.(16) On endoscopy they are often indistinguishable from other GI tumors of smooth muscle origin such as leiomyomas. A preoperative biopsy is not routinely necessary for a primary resectable neoplasm suspected to be a GIST. However, if neoadjuvant therapy is under consideration, then biopsy is appropriate. The three established prognostic factors are tumor size, mitotic index and tumor site of origin.(17)

Surgical removal is the primary treatment of choice in localized or potentially resectable GIST. These tumors are considered to be very fragile, so they must be handled with care in order to avoid tumor rupture, and achieve complete tumor resection with their pseudocapsule intact. Lymphadenectomy is not required as GISTs have a low incidence of nodal metastases.(15,16) For moderate and high risk patients, adjuvant imatinib is indicated. Imatinib is also the primary therapy in recurrent and unresectable GISTs and also in GISTs with metastasis at presentation.(15) Sunitinib may be used in cases of resistance to imatinib. During follow up, 50% of patients with GIST will develop recurrence of their disease or metastasis following complete surgical resection.(14,18,19) The NCCN consensus panel recommends that patients who have had resection of a primary GIST should undergo physical examination and an abdominal CT scan every 3-6 months during the first 3 to 5 years and then annually thereafter.(20)

VI. Conclusion

GISTs are the most common mesenchymal tumors of the GI system. Improved knowledge of the oncogenic mutation and its targeted therapy has acted as a foundation for the general understanding of the role of targeted therapies in human cancers. Surgery is the primary treatment of choice in localized or potentially resectable GIST. Surgery and imatinib form the first-line therapy and their effectiveness for the majority of patients has been revolutionary.

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