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Our experience with gastrointestinal stromal tumors at tertiary care hospital in central India: A retrospective observational study

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Abstract

Gastrointestinal stromal tumors (GISTs) are the commonest mesenchymal tumor of gastrointestinal tract. Commonly found in Stomach and Small intestine, may present as E GIST. A case series of 30 patients over a period of 3 years managed at Government medical college and hospital. A Retrospective study of the GIST cases. Around 30 patients who were diagnosed having GIST, their records were compiled. Data analysis of all patients in terms of demographics, clinical presentation, location of the tumor, management has been done. Presented with varied complaints such as pain in abdomen, lump in abdomen, upper/lower GI bleeding, weight loss, obstruction perforation, hematuria and retention of urine depending upon the site involved. Sites involved were small bowel (16), Stomach (10), Colon (1), Rectosigmoid (1), retroperitoneum (1) and omentum (1). Half the cases took imatinib including neoadjuvant and post operative cases and rest lost to follow up. Surgery being the main stay of treatment.

Keywords: Gastrointestinal stromal tumor, Imatinib, EGIST.

Introduction

Gastrointestinal stromal tumors (GISTs) are rare but, the most common mesenchymal tumor of the gastrointestinal (GI) tract^[1]. They are benign mostly but can be malignant. The diagnosis of GISTs is mainly based on the morphology and immunohistochemical (IHC) findings. The discovery of the mutation in tyrosine kinase receptors such as KIT and PDGFRA genes and clinical application of their tyrosine kinase inhibitors such as imatinib have dramatically changed our understanding of clinical features, diagnosis and treatment of GISTs. GISTs are supposed to be arising from the interstitial cells of Cajal, which is positive for CD34, and have tyrosine receptor which are positive for CD117 and DOG1.

Although rare it has a incidence of around 1-1.5 in 100 000 per year. 2 GISTs can be found anywhere in the GI tract with stomach (56%) being the most common location, followed by small intestine (32%), colon and rectum (6%), Oesophagus (<1%). 3 The remaining less common locations like mesentery, pelvis, pancreas, omentum, retroperitoneum, liver and genitourinary tract and are described as extra gastrointestinal GIST (E-GISTs), where KIT positive mesenchymal cells are found.

Clinically, GIST are often asymptomatic and discovered only as incidental findings on imaging studies or endoscopies performed for other indications, as it is sub mucosal in location. GIST as often highly vascular, soft, friable, therefore bleeding is common complaint. Other symptoms may include abdominal pain, palpable lump in abdomen, distention due to obstruction. GIST may cause life threatening hemorrhage if it ruptures into bowel lumen or may cause intraperitoneal hemorrhage and dissemination as peritoneal seedlings. Between 15% and 47% of patients with GISTs have metastatic disease at diagnosis.⁴ Common sites of metastasis include liver, Peritoneum and omentum; lymph node metastasis are rare^[5].

In this case series, we present 30 cases of Gastrointestinal Stromal Tumors managed at tertiary care hospital attached with the medical college over a period of 3 years.

Material and Methods

This is Retrospective study of the GIST cases. Around 30 patients who were diagnosed having

GIST, there records were compiled. Data analysis of all patients in terms of demographics, clinical presentation, location of the tumor, management has been done.

Results

Out of 30 Patients, almost equal number of male and female (Slight preponderance) were there i.e. 13 and 17 respectively. Age ranging from 24 to 74 years, with mean age 51 years. Patients presented with symptoms ranging from Abdominal Pain (80%), Lump (43.3%), Upper/Lower GI bleeding (30%), weight loss (53.3%), Small and Large bowel obstruction and Peritonitis, Retention of urine and hematuria in a case of pelvic GIST. Stomach (n=10, 33.3%), small bowel (n=16, 53.3%), Colon (n=1, 3.3%), Retroperitoneal (n=1, 3.3%), Rectosigmoid (n=1, 3.3%), Omentum (n=1, 3.3%) involvement was seen with metastasis seen in 5 cases at presentation.

9 cases were inoperable, Small bowel resection and anastomosis done in 10 patients, Whipple's procedure in 2 cases, Left Hemicolectomy in 1 case, Anterior resection in 1 case, Billroth's II resection in 5 cases, Sleeve gastrectomy in 1 case of GIST and omentectomy of E-GIST case. 16 cases received Post-Operative Chemotherapy with Imatinib, while rest were lost to follow up. 3 Cases received Pre-operative Neoadjuvant Chemotherapy with Imatinib and one them is operated 2 patients still on Chemotherapy.

Discussion

GISTs are the most common mesenchymal tumors of the gastrointestinal tract. We found out that GIST has almost equal prevalence in males and females with median age of around 51 years, while study by Casali *et al.* found out that it has slight male preponderance with median age around 60-65 years. Another study states that GIST in children and young adults is rare but distinct subsets of pediatric GIST, and syndromic GISTs may be found in children and individual in early middle age. Although As per AJCC, stomach (60%) has the highest incidence of GIST, followed by small intestine (30%), then rectum, colon, oesophagus and rarely mesentery, omentum, pelvis, but in our study small intestine have higher incidence then stomach. A trend of the disease in the population can't be predicted as the small size in our study is relatively small.

The presenting complaints of the patient were variable according to the site of tumor, with maximum patients complained of having vague pain in abdomen, Lump in abdomen, epigastric discomfort, upper and lower gastrointestinal bleeding and weight loss. Some small bowel GIST presented with obstruction and perforation peritonitis. Colonic GIST presented with rectal bleeding, while Rectal GIST with Obstruction and Retroperitoneal GIST with urinary retention and hematuria.

Around 21 patients were operated and 9 were inoperable. Study by Joensuu H, shows 20 to 25% of gastric and 40 to 50% of small gut GIST exhibit aggressive behavior^[9]. Metastasis was seen in 14.2% cases as compared to the study by DeMatteo RP *et al.*, Metastatic GIST is found in 10% to 25% of patients^[10].

Histologically, GISTs can occur in three different types: spindle cell type (70%), epithelioid cell type (20%), and mixed type (10%)^[11]. Rarely, GISTs may have myxoid stroma, neuroendocrine feature, signet ring variant or marked lymphocytic infiltrate. Important molecular marker that is useful in the diagnosis of GISTs is the presence of mutations in either KIT or PDGFRA; nearly 80 % and 10 % of GISTs, respectively, are positive for these mutations. 4 GISTs are identified on immunohistochemical staining for the CD117 antigen, part of KIT receptor. CD117 expression is characteristic of most GISTs.

95% of GISTs are positive for KIT (CD117) and DOG1, and 70% are found to be positive for CD 34 by IHC^[11]. When KIT is negative in a morphology suggestive of GIST as found in approximately 5% of cases. DOG1 staining, followed by CD34 staining, is considered diagnostic. KIT positivity is not only sufficient for diagnosis (Fig.1). Colonic GIST presented with complaint of hematochezia and on colonoscopy polypoidal growth was seen, Left Hemicolectomy was done. Histological finding of the specimen was suggesting GIST but on immunohistochemistry CD117 and DOG1 were negative. So CD34 was done, which came positive, which is also suggestive of GIST.

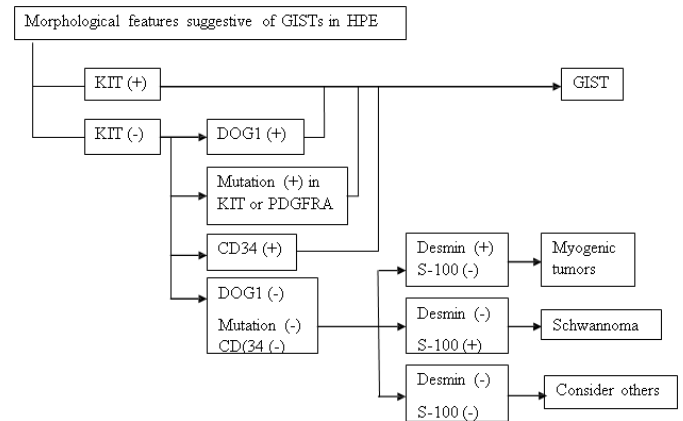


Fig 1: Pathological diagnosis of gastrointestinal stromal tumor (GIST) by immunohistochemistry and genotyping. The algorithm for the pathological diagnosis of GIST is shown. The number sign means solitary fibrous tumors should be ruled out. DOG1 discovered on GIST-1.11

Studies shows when gastric GISTs have no mutations in KIT or PDGFRA, immunostaining for succinate dehydrogenase (SDH) iron-sulfur subunit (Subunit B) (SDHB) is recommended^[4, 7].

Half of the cases took imatinib and other were lost to follow up. Imatinib mesylate is a tyrosine kinase inhibitor. ACOSOG Z9001 placebo-control trial of 1 year of imatinib treatment after complete resection of GISTs ≥ 3 but less than 10cm. The patient who received imatinib has significantly improved relapse free survival (RFS), which maintained on long-term followup^[12].

Imatinib has also shown improvement in the survival of the unresectable and metastatic GISTs with response rate up to 70%, with a median of progression free survival of nearly 2 years and overall survival of up to 57 months^[13, 14].

9 cases were inoperable, 2 of them were explored and because of the difficult situation and planes, and ease of dissection was not there, so biopsy was taken and tumor was not resected and cases were advised to take chemotherapy. The 7 other cases were inoperable on radiological findings. Large tumor size, involvement of adjacent organs, difficult position of tumor and metastasis at presentation were the reasons for inoperability and were advised for chemotherapy and serial radiological imaging, so that in future if the tumor regress or become operable, then definitive management may be planned^[1]. Such case in our study, who was in operable at presentation, after receiving neoadjuvant Imatinib became operable later and was operated for the same. In a study in patients with locally advanced, non metastatic GISTs who received neoadjuvant imatinib, tumor response was seen in 80% and 83% were undergone R0 resection^[15]. The duration of preoperative therapy in such patient is usually from 4 to 12 months and response is monitored with serial imaging studies. Surgery should be carefully planned,

when maximum response to imatinib has occurred. After surgery Imatinib therapy is to be continued for 1-2 years to reduce recurrence rates.

GIST present anywhere other than gastrointestinal tract is termed as E-GIST. These are rare entities and are found in mesentery, omentum, pelvis or retroperitoneum or pancreas. 1 of our case presented with lump in abdomen, on exploration the lump was seen arising from the omentum. ON histopathology and IHC it was suggestive on GIST. E GIST have been reported in case reports.

Conclusion

GISTs, a mesenchymal tumor of commonly found in gastrointestinal tract mainly in stomach and small intestine. Wide spectrum of clinical presentation as per the site of tumor. Surgery and chemotherapy with imatinib being options for the management. Surgery being the mainstay of treatment for resectable tumor. Complete en bloc resection followed by Imatinib, shown long- term survival with less recurrence. Neoadjuvant imatinib for the initially unresectable tumor for downsizing, so subsequently resection may become possible. Immunohistochemical markers have added into the diagnosis and management of this tumors. E-GIST and there different clinical presentation. Metastatic tumor or recurrent GIST, primary treatment is Imatinib. Other Tyrosine kinase receptor inhibitors are also being considered for patients resistant to imatinib.

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