Gastrointestinal Stromal Tumor—Single-Center Experience with Review of the Literature

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Abstract GIST or gastrointestinal stromal tumors are the most common mesenchymal tumors of the GI tract showing mostly positive c-kit (CD-117) in immuno-histochemical staining. Most of the times, early diagnosis is missed. Usually, patients present with anemia. Sometimes, the patient can present in emergency with massive GI bleed or intestinal obstruction. The aim of this paper was to make the clinicians aware about the varied presentations of GIST. Presenting herewith is our single-center experience of management of patients of GIST with review of the available literature.

Keywords GIST · Duodenal GIST · Management of GIST · GIST treatment · Imatinib in GIST management

Introduction

Gastrointestinal stromal tumors or GISTs are the most common tumors of GI tract. They mostly show positive c-kit (CD-117) on immuno-histochemical staining. They typically arise in association with the muscularis propria of the gastrointestinal tract wall [1]. They occur most frequently in the stomach (60 %), jejunum and ileum (30 %), and less frequently in the duodenum (5 %), less than 5 % colorectal, and less than 1 % in the esophagus and appendix [1]. The tumors grow mostly submucosally but can manifest as exophytic extra luminal subserosal growth [2]. Previously, these tumors were thought to have smooth muscle component and hence were classified as Leiomyomas, Leiomyosarcomas, etc. [3]. This term was first used by Mazur and Clark in 1983 [3]. GISTs are now defined as pleomorphic mesenchymal tumors of the GI tract that express

the KIT protein (CD 117—proto-oncogene that encodes the transmembrane tyrosine kinase receptor CD 117 detected by flow cytometry in most cases of acute myeloid leukemia, in small numbers of T- and B-lymphoblastic lymphomas, and in some gastrointestinal stromal tumors—stem cell factor receptor) and often also CD34 (human progenitor cell antigen) on immuno-histochemistry [4].

Clinical presentation of GIST is many times erratic, and almost 20 % of the patients are asymptomatic while 10 % are diagnosed at autopsy [3]. Bleeding is the commonest presenting feature due to erosion of the GI tract. Some of the patients present as obstruction due to the vary size of the tumor.

Material and Methods

In our hospital, we diagnosed and successfully treated 15 cases of GIST from 2007 to 2012 (Fig. 1). The age was from 23 to 70 years. Twelve out of 15 were males (Fig. 2). Two patients presented in emergency, one came as a case of intestinal obstruction while one came as massive GI bleeding. The rest of the patients presented in outpatient department for chronic complaints and eventually were diagnosed to have GIST. Four patients had duodenal GIST, five had stomach, and the other six patients had small intestinal GIST (Table 1).

Out of 15 patients, CD-117 was done for 12 patients. In ten patients, it was positive, while one was negative and one was equivocal. As CD-117 estimation facility is not locally available, patient had to get it done from higher center, and hence, three patients refused to get it done for economic reasons. In these patients, the diagnosis was made on histopathology.

Fourteen patients underwent surgery. Eleven patients had definitive procedure, while in three patients, only palliative procedures were done. One patient had only true cut biopsy.

Case no 2 came to our emergency room in shock. He was immediately admitted in ICU and received multiple transfusions

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Fig. 1 Sex distribution

as he was vomiting frank blood and was in hypotension. After correcting his hypovolemic shock, he was taken up for upper GI endoscopy. On endoscopy, there was mass in the third part of duodenum with a small crater on its surface where there was a visible arterial spurt. Glue was injected for the control of bleeding. Next day, to confirm complete control of bleeding, upper GI endoscopy was performed. It revealed complete stoppage of bleeding and a nodular mass in second part of duodenum, about 2 cm in diameter. (Endoscopy picture) His CT abdomen revealed a circumferential wall thickening with partly exophytic heterogeneously enhancing soft tissue density mass lesion involving the duodenal wall at the junction of its second and third portions. He was offered surgery. On exploration, the mass was found to be adherent to the mesocolon. The mass had to be dissected from pancreatic head. Local resection of the duodenum was done (Fig. 3).

Case no 4 presented with pain in abdomen since 3 days with history of evening rise of temperature, malena, and loss of appetite. His CT abdomen revealed large exophytic mass in left para-umbilical region abutting and displacing adjacent bowel loops with irregular wall thickening. Colonoscopy was found

to be normal. He was taken for exploration. Exophytic mass was seen arising from antimesenteric border in jejunum. Local resection with anastomosis was done (Fig. 4).

Results

In this series of 15 patients, all were given the option of surgery. Nine patients were found to be operable and underwent definitive surgical treatment. Three patients had to undergo only biopsy for confirmation by tissue diagnosis. Seven patients received Imatinib. Maximum disease-free survival was found to be 4 years.

Discussion

GISTs are common GI tract tumors involving stomach, while jejunal GIST accounts for about 20–30 % of the cases. Duodenal GISTs are least common of all [5].

GISTs are mostly benign tumors, but small intestinal GIST has high chances of malignant behavior [2].

Fig. 2 Age distribution

Table 1 GIST cases from 2005–2013

Serial number	Age/sex	Surgery	HPR	CD-117/C-Kit	Chemotherapy	Status
1	52/F	Excised duodenal tumor	GIST	Positive	Imatinib 400 OD×3 years	Disease-free—1 year
2	23/M	Partial duodenectomy	GIST	Positive	Imatinib 400 OD×2 years	Disease-free—2 years
3	65/M	Trucut biopsy	GIST	Negative		Expired
4	32/M	Resection of the jejunum	GIST	Positive	Imatinib 400 OD×4 years	Disease-free since 1 year
5	55/M	Resection of the DJ flexure	GIST	Positive	Imatinib 400 OD×3 years	Disease-free since 3 years
6	56/M	Distal gastrectomy done	GIST	Not done		Expired
7	28/F	Small bowel mass resected using GI staplers	GIST	Equivocal		Disease-free since 2 months
8	70/M	Side-to-side ileoileostomy done in four layers	GIST	Positive	Imatinib 400 OD×2 years	Disease-free—3 years
9	55/M	Mass resected with midileum, side-to-side ileoileostomy	GIST	Positive	Imatinib 400 OD×1 year	Disease-free—3 years
10	63/M	Excised gastric mass with liver nodule	GIST	Positive	Imatinib 400 OD×2 years	Disease-free—3 years
11	59/M	Inoperable mass greater curvature of the stomach	GIST	Positive	Imatinib 400 OD	Disease-free—2 ½ years
12	70/M	Inoperable mass in fundic part of the stomach	GIST	Not done	Imatinib 400 OD×3 years	Disease-free—4 years
13	60/M	Second part duodenum	GIST	Positive	Imatinib 400 OD×1 year	Disease-free—1 year
14	55/M	GIST in postero-medial wall of the stomach	GIST	Positive		Lost to follow-up
15	45/F	Laparotomy with excision of the retroperitoneal tumor	GIST	Positive	Imatinib 400 OD×1 year	Disease-free—1 year 6 months

Overall, 5-year survival of completely resected GIST ranges from 30 to 80 %, while median survival of non resectable and/or metastatic GIST ranges from 2 to 20 months with mean survival being 12 months [2, 5].

Fletcher et al. have classified these tumors depending on the size and mitotic count in to very low, low, intermediate and high risk categories [6].

Even though GISTs are the most common tumors of GI tract, sometimes, these patients may present as an acute emergency case. That time, the condition of the patient needs stabilization first, followed by control of bleeding. Definitive treatment of GIST needs to be planned at latter stage. This requires multimodality approach since upper GI bleed needs good intensive care unit, endoscopic backup, and experienced surgical team. Many times GIST in female patient is confused with that of ovarian cyst and diagnosed only at laparotomy.

When GIST is diagnosed preoperatively staging is done keeping in mind the fact that most relapses affect liver and peritoneum. Contrast-enhanced CT scan is ideal for staging, while MRI and contrast-enhanced USG can also be helpful.

For rectal GISTs, MRI is more useful [7]. Routine laboratory investigations and the X-ray chest complete the list of useful investigations.

Multidisciplinary approach involving pathologist, radiologist, surgeon, and medical oncologist is needed [7]. In localized disease, surgery is the treatment of choice where R0 resection is possible. If the tumor is localized, laparoscopy can be undertaken provided that oncological principles are followed. In bulky tumors, it is better to avoid laparoscopy as there is chance of rupture of the tumor leading to local recurrence. When R0 resection is not possible, then with limited aim of reducing the tumor load, R1 resection can be undertaken with an option of second surgery if possible. In the cases where risk of relapse is high, adjuvant treatment with Imatinib is considered [7]. Imatinib has revolutionized the medical line of treatment for GIST. It is one of the first targeted molecular therapies which work by disrupting specific aspects of tumor growth [2]. It has shown good response rate and survival in advanced cases of GIST in a number of trials [2]. Response to Imatinib therapy can be assessed by imaging techniques and timing of surgery can be

Fig. 3 Duodenal GIST

Fig. 4 Jejunal GIST

planned [7]. Very less data are available about stopping of Imatinib before surgery. But consensus says that it can be stopped about 2–3 days before surgery and can be restarted once the patient recovers from surgery [7]. Imatinib treatment for 3 years has been found to be adequate in a group of patients highly prone for relapse.

In metastatic disease, the treatment can be started with Imatinib 400 mg daily and needs to be continued indefinitely as interruption is generally followed by fast tumor spread. Even though surgery is not a treatment of choice for metastatic disease, it is sometimes necessary for symptomatic relief along with Imatinib. Few patients may have to be put on 800 mg Imatinib daily indefinitely, for survival without disease progress as the statistical data has shown [7].

Conclusion

GIST is common tumor seen in GI tract but usually it is not diagnosed in early stage due to its vague clinical presentation. Clinician should have high index of suspicion to diagnose this condition at an early stage. When diagnosed early, the results of surgical treatment are good. The introduction of Imatinib has revolutionized the medical management of GIST. Imatinib can be included as neoadjuvant therapy. Metastatic GISTs need indefinite treatment with Imatinib. The treatment of cases of

GIST presenting as emergency case needs multi-specialty approach and, when treated early, shows good results.

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