Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Gastrointestinal Stromal Tumor (GIST)-Clinical Profile & Management of Patients Admitted To a Tertiary Care Hospital in Odisha

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Received: May 2019
Accepted: June 2019

ABSTRACT

Background: Gastrointestinal stromal tumor (GIST) is the commonest mesenchymal tumor of gastrointestinal tract. Gastrointestinal bleeding, obstruction, pain and abdominal lump are the common clinical manifestations. Local or segmental resection provides satisfactory results. **Aim:** Our aim was to report our experience of gastrointestinal stromal tumors (GISTs) during the last 2 years. **Methods:** Between January 2017 and June 2019, we performed surgery for 12 cases of GIST. Metastases, recurrence and survival data were collected in relation to age, history, clinical presentation, location, size, resection margins and cellular features. **Results:** Resection was completed in 11 cases. In one case definitive surgery was abandoned due to local invasion and metastasis. Three patients with high risk GIST were treated with imatinib mesylate. **Conclusion:** Non-radical surgery in the form of local or segmental resection is the standard surgical approach for GIST management. Pathological and biological features of the neoplasm represent the most important factors predicting the prognosis.

Keywords: Gastrointestinal stromal tumor (GIST), Immuno-histochemistry (IHC), CD117.

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal neoplasm of Gastrointestinal tract. It arises from the interstitial cells of Cajal (ICC) which are part of the normal myenteric plexus of autonomic nervous system supplying the gut.[1] The estimated incidence of GISTs is approximately 10-20 per million people annually worldwide. This tumor affects men slightly more often than women and the mean age at the time of diagnosis is 60 years. GISTs can arise from any part of gastrointestinal tract but they are mostly seen in stomach and small intestine presenting commonly with gastrointestinal bleeding, anemia, mass lesion and features of intestinal obstruction. Clinical presentation is heterogeneous, even if GISTs are usually asymptomatic and are diagnosed incidentally during endoscopy, radiological imaging or abdominal exploration. Preoperative biopsy is not recommended for resectable masses, because of the fragility and predisposition. Preoperative biopsy is not recommended for resectable masses, because of the fragility and predisposition to hemorrhage of these masses, and the possibility that the biopsy needle touches a necrotic portion of the tumor. Biopsy is justified only for masses preoperatively judged unresectable, in that a definitive pathological diagnosis would allow medical treatment using imatinib to commence Understanding of the biological behaviors of GIST has been significantly changed due to identification of its molecular basis in form of mutations in KIT gene (85%), PDGFRA gene (10%) and BRAF Kinase (rare)[4] . Approximately 95% of GISTs are positive for CD 117.[4] This identification of molecular basis has excluded many undifferentiated carcinomas and malignant smooth muscle tumor from GIST.[4] Basing on its molecular characteristics and biological behaviors GISTs are now considered as malignant. Hence, all GISTs are subjected to cancer staging by the AJCC (7th edition).[5] But GISTs have different risk assessments depending on their tendency to recur and metastasize, site of origin, size and mitotic activities. In absence of specific curative therapy, surgery remains the main modality of treatment of GISTs. Recurrence occurs in high risk patients after surgery although lymph nodal metastasis is very rare. Systemic metastasis when ever present is mostly seen in liver.

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Introduction of TKIs (Tyrosire kinase Inhibitors) in the management has quite beneficial in the treatment outcome of patients with GISTs. Its dramatic response to antityrosine kinase receptor agents like imatinib mesylate and molecular aspects of this response have been the subject of published articles.[6,7] Tyrosire kinase Inhibitors like Imatinib mesylate and Sunitinib maleate has made the treatment outcome of patients with GIST quite satisfactory.[8] Surgery represents the gold standard treatment for resectable GISTs. Principles of a correct procedure include negative margins on the specimen and integrity of the pseudocapsule. GISTs do not metastasize through lymphatic spread, so systematic lymphadenectomy is not indicated. This paper provides an overview of the diagnosis and treatment of GISTs, with an emphasis on early diagnosis and management of GIST.

MATERIALS AND METHODS

In this retrospective study, we had included 12 cases of Gastrointestinal stromal tumors from January 2017 to June 2019, presenting with palpable abdominal mass (65%), gastrointestinal bleeding (46%), abdominal pain (24%) and vomiting (17%). All of them had been advised for upper GI endoscopy, endoscopic biopsy, USG Guided FNAC, Immuno-histo-chemistry (IHC), Chest X-ray in addition to routine investigations. Out of 12 cases, there were 6 males (50%) and 6 females (50%) in the age group between 35 years to 70 years. All of our cases were proved to be positive for CD 117 on IHC. All of the patients under the study had undergone open conventional laparotomy after the diagnosis of GIST was established. Adjuvant chemotherapy with Imatinib at a dose of 400 mg twice daily had been administered orally for a period of three years after surgery to patients with tumor more than 5 cm in diameter and to locally advanced tumor with metastasis to liver (1 case in this series). Metastases, recurrence and survival data were collected in relation to age, history, clinical presentation, location, size, resection margins and cellular features such as mitotic index and immunohistochemistry .

RESULTS

GISTs were infrequent before the 3 rd decade (6.5%). The peak incidence was in the 4 th and 5 th decades (49.5%). The oldest patient was 70 years old. GISTs affected men more frequently, with a M:F ratio of 1:1. In this study, mass lesion was found in all cases during operation. But their situations were found to be in stomach (53%), jejunum (13%), ileum (13%), duodenum (13%) and retroperitoneum (8%). [Table1].

Table 1: Demographic and clinical characteristics

Sl. No	Sex	Age	Site	Presentation	Finding	Meta stasis	Operation	Recur rance
1	M	62	Stomach	Bleeding, Palpable mass	8X8cm mass in fundus		Wedge Resection	No
2	F	36	Stomach	Bleeding	4x4 cm mass in body		Wedge Resection	No
3	M	57	Jejunum	Palpable mass	10x10cm mass near DJ flexure with local invasion	Yes	Exploratory laparotomy	Yes
4	F	42	Duodenum	Bleeding	7x7cm mass near ampula	No	Sleeve Resection	No
5	F	55	Stomach	Bleeding	6x5 cm mass in fundus	No	Wedge Resection	No
6	F	56	Retro peritoneum	Pain, Palpable mass	20x20cm mass in retroperitoneum	No	Resection	Yes
7	M	32	Duodenum	Bleeding	5x5cm mass near ampula	No	segmental Resection	No
8	M	37	Ileum	Bleeding, Palpable mass	15x15 cm mass in mid ileum	No	Segmental Resection	Yes
9	M	44	Ileum	Bleeding	10x10cm mass in ileum	No	Segmental resection	No
10	M	35	Stomach	Pain	8x8cm mass in antrum	No	Wedge Resection	No
11	F	55	Stomach	Pain	7x10cm mass below GE junction	No	Wedge Resection	No
12	F	72	Jejunum	Vomiting	Annular mass 25cm distal to DJ FLEXURE	No	Segmental resection	No

Resectional procedures were performed (varying from wedge resection to segmental resection) depending on the situation of the tumor. Proper attention was given for adequate resection to achieve Ro clearance except in one case where the disease was locally advanced by infiltrating to surrounding structures with hepatic metastasis. GISTs ranged in size from 1.5 to 30 cm. The smallest was found in

the gastric fundus synchronously with a carcinoid tumor. Majority of the GISTs (40%) ranged in size from 5 to 10 cm and slightly fewer (34%) were >10 cm, which categorized the latter as definitely malignant and in the high-risk group. Majority of the GISTs (53%) grossly presented as mass lesions and the next most frequent presentation (25%) was polypoid lesions. The cut-surfaces were mainly firm to soft to fleshy and dark variegated, with 60% showing hemorrhage, 25% showing additional necrosis and 23% showing cystic change. In tumors <5 cm in size, these secondary changes were uncommon. All the patients remained symptom free following surgery without any complications. There was no side effects among patients receiving Imatinib following surgery as per our criteria mentioned herein. During follow up, three patients developed local recurrence.

DISCUSSION

During the last decade , since the GIST has been recognized as a well-defined pathological entity with its own characteristics, the surgical management of GISTs has changed. The lack of lymphatic spread of this kind of tumor makes lymphadenectomy unnecessary, so the only oncological criteria is to maintain the integrity of the capsule and to perform an R0 resection. Wedge resection is a correct procedure from an oncological point of view, but if technically unfeasible, as for esophageal or rectal GISTs, a segmental resection becomes necessary. [9] Clinical presentation is extremely heterogeneous in the literature as in our series: a recent Swedish study demonstrated that 70% of GISTs had associated symptoms, 20% had none and 10% were detected at autopsy. Symptoms were generally non specific: nausea, vomiting, abdominal pain or discomfort; sometimes GISTs caused gastrointestinal bleeding, because of the erosion of gastric or small bowel mucosa; dysphagia occurred rarely, and was associated with a tumor located in the esophagus; biliary obstruction could occur if the tumor was located in the duodenum; and intussusception, could occur if the tumor was located in the small bowel.From the above results, it is seen that Gastrointestinal stromal tumor (GIST) is more prevalent in females than males affecting between fourth and fifth decades of life. It is more common in stomach and small intestine. Commonest presenting feature of these patients is gastrointestinal bleeding followed by abdominal mass. Surgery in the form of local or segmental resection is the treatment of choice in all the cases. [10]Adjuvant Imatinib therapy for larger (more than 5cm) and locally advanced tumors gives long term tumor free survival in most of the cases. [11] Larger numbers of patients with high-risk GIST need to be followed-up after adjuvant imatinib therapy for meaningful conclusions to be drawn from our patients.

Molecular studies of KIT and PDGFRA gene mutations also need to be correlated with these treatment protocols and outcomes as it has been recently shown that changing patterns of KIT expression and morphological differentiation can occur in GISTs treated with imatinib that develop resistance to therapy[12].

Surgical treatment remains the gold standard therapy for resectable GISTs.[13] Surgical strategies are different and heterogeneous, as the only oncologic criteria imposes the preservation of the integrity of the capsule and the avoidance of infiltration of the resection margins.[14] The laparoscopic approach is considered safe and effective for masses not exceeding 5 cm, in centers experienced in advanced laparoscopic surgery.[15] In the presence of resectable and non metastatic masses, correctly removed by the surgeon, pathological and biological features of the tumor, expressed by Fletcher's classification, remain the most important factors for predicting the prognosis.[16] For high risk or metastatic tumors as for non resectable masses, molecular therapy with the tyrosine kinase inhibitor imatinib mesylate has improved survival.

CONCLUSION

The use of the laparoscopic technique in combination with molecular therapy will permit the development of a minimally invasive treatment for this type of neoplasm, improving patients' survival and quality of life.Surgery followed by Imatinib therapy in selected cases is the standard of care in patients of GIST.

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How to cite this article: Sarangi CR, Jayasing SC. Gastrointestinal Stromal Tumor (GIST)-Clinical Profile & Management of Patients Admitted To a Tertiary Care Hospital in Odisha. Ann. Int. Med. Den. Res. 2019; 5(3):SG47-SG50.

Source of Support: Nil, **Conflict of Interest:** None declared