

Presentations of Gastro-Intestinal Stromal Tumours: Experiences from a tertiary care level hospital in Eastern India

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Abstract

Eighteen patients of gastrointestinal stromal tumours (diagnosed on histopathology) were studied retrospectively. The period of study extended over sixty months. It takes into account the age, distribution, mode of presentation, diagnostic modalities, treatment including surgery and the role of Imatinib. It also analyses the recurrence pattern and risk categorization of the cases. Finally it brings to forefront the vital role of immunohistochemistry in the diagnosis and management of these lesions.

INTRODUCTION

Gastrointestinal stromal tumours are the most common non-epithelial neoplasms of the gastrointestinal tract. They are increasingly diagnosed today because of better diagnostic orientation of the clinicians, radiologists and pathologists. This prompted us to put forward our experiences in managing GIST.

AIM OF STUDY

To present the distribution, clinical presentations, diagnostic modalities, management and follow-up of our patients.

METHODOLOGY

The study is a retrospective analysis of the patients diagnosed histopathologically with stromal tumours of the gastrointestinal tract. Detailed history was taken as regards the age, sex, mode of presentation, site of the lesion, management modalities (all underwent local resection; some received adjuvant treatment) and pathology (histopathology and immunohistochemistry).

RESULTS

Eighteen cases of GIST were studied over a period of four years (2004 to 2009). Of these, fourteen were males and four females. The age of the patients ranged from 30 to 70 years. The mean age was found to be 51.5 years.

Figure 1

Table 1

| Age (in years) | Number (n) |
|----------------|------------|
| 31 – 40 | 4 |
| 41 – 50 | 5 |
| 51 – 60 | 6 |
| 61 – 70 | 3 |

All but one patients presented with some form of gastrointestinal bleeding (haematemesis, melaena, hematochezia, etc.). Three patients also had palpable lumps and three had dyspepsia; one patient presented with intestinal obstruction and one patient had complaints of difficulty in defaecation.

Figure 2

Table 2

| Presentation | Number (n) |
|---------------------------|------------|
| Gastrointestinal bleeding | 17 |
| Lump | 3 |
| Dyspepsia | 3 |
| Intestinal obstruction | 1 |
| Difficult defaecation | 1 |

The locations of the tumours in the gastrointestinal tract were as follows: seven in the stomach, four in the duodenum, one in the duodenojejunal flexure, four in jejunum/ileum, one in sigmoid colon and one in the rectum.

Figure 3

Table 3

| Location | Number |
|------------------------|--------|
| stomach | 7 |
| duodenum | 4 |
| duodenojejunal flexure | 1 |
| jejunum/ileum | 4 |
| sigmoid colon | 1 |
| rectum | 1 |

According to histopathology, the tumours were divided into three risk categories - low, intermediate and high. The total number of tumours in each category were: 9 in the low-risk group, 5 in the intermediate and four in the high-risk group.

Figure 4

Table 4

| Risk categories | Number |
|-----------------|--------|
| low | 9 |
| intermediate | 5 |
| high | 4 |

C-kit analysis (CD 117) was done in all cases. It was negative in one case and positive in seventeen cases.

Seventeen out of eighteen patients underwent surgery. Surgery could not be done in a patient with a lesion in the third part of the duodenum with liver metastasis, who was a very poor risk patient as far as surgical intervention was concerned. The diagnosis of GIST was made on gastroduodenoscopic biopsy. In all except the jejunal and ileal GISTs, the margin of resection was 2 cm. In jejunal and ileal GISTs, a 5-cm margin was taken. The rectal GIST was excised transrectally with a 1-cm margin. In duodenal GISTs a free-margin wedge resection of discrete GISTs with a favorable position on the external aspect of the duodenum was done in three patients.

Four patients out of eighteen were given imatinib mesylate.

Our indications for the use of imatinib were recurrent/high-risk tumors, positive margin, incomplete resection and metastatic disease. It was given in the dose of 400mg daily for 1 year. Three patients are doing well after imatinib therapy. This includes one patient who suffered from a recurrent duodenojejunal flexure GIST. Imatinib was started after re-excision. We lost one patient receiving imatinib in follow-up.

The follow-up period ranged from two months to five years from the time the particular patient was operated.

Recurrences occurred in three cases (at an average of eight months). Sites of recurrences were the liver in two cases (high-risk cases) and in the mesentery in one case (intermediate risk). There were two deaths. Two patients were lost in follow-up. No recurrences have been recorded in the remaining cases till date.

DISCUSSION

Traditionally, GISTs were thought to be of stromal cell origin, showing an undifferentiated pattern. [1] However, recent views suggest the cell of origin to come from the interstitial nerve cells of Cajal [2] which are the pacemaker cells of the gastrointestinal tract. The age distribution in our study shows the most common affection in the fourth and fifth decades of life. This series shows a predominant male affection with a ratio of 3.5:1 for males:females. The literature review shows a male:female ratio of 1:1 [3]. Nearly all the patients had presented predominantly with gastrointestinal hemorrhage. GISTs can arise anywhere along the GI tract but are most common in the stomach (50%) and small bowel (25%). [4] GISTs often project from the stomach or intestine and tend to displace adjacent structures.

Essential elements of the workup include history and physical examination, abdominopelvic CT scan with contrast and/or MRI, chest imaging, endoscopic ultrasound, endoscopy as indicated (if not previously done) and surgical assessment.

CT scan could detect but not characterize the lesions except for one case where it was able to characterize the lesion. However, we feel that preoperative radiological characterization was in no way important for the further management of the patients. CT-guided FNAC has the advantage of diagnosing metastatic lesions though the treatment plan remains unaltered, considering the fact that palliative resection was indicated anyway.

Gastroduodenoscopy and double balloon enteroscopy were the other modalities which helped in making the preoperative presumptive diagnosis of GIST affecting stomach and small bowel.

Most of the literature reviews do not recommend radical organ removal and en-bloc soft tissue dissection [5]. However, we believe that en-bloc removal of the mesentery maybe helpful especially in small bowel GISTs as one of our

patients had recurrence in the mesenteric lymph nodes (8.33%). However, there is not enough literature available showing good evidence in favour of any surgery above wide local excision in terms of overall survival or disease-free survival.

GISTs should be handled with care to avoid tumour rupture. The aim is to achieve complete gross resection with an intact pseudo-capsule. Since the tumour does not show an infiltrative pattern of spread, a margin of 1cm is considered sufficient. [6]

It is important to send an intact specimen, as macroscopic size of the lesion and presence of necrosis are major prognostic factors determining the risk categories of the lesions. In this series, all cases of recurrences had primary lesions of a size more than 5cm. Histopathologically, the number of mitoses per high-power field (HPF) is the most important marker of risk categorization.

Figure 5

Table 5 []

| Risk categories | Size of lesion | Mitotic count/50 HPF |
|-----------------|----------------|----------------------|
| Low | Up to 5cm | <5 |
| Intermediate | < 5cm | 6 – 10 |
| | 5 – 10cm | < 5 |
| High | > 5cm | > 5 |
| | > 10cm | Any |
| | Any | >10 |

Most GISTs (85-95%) are KIT positive. A few GISTs (about 5%) may be CD117 (KIT) negative; therefore, the diagnosis of GIST for a tumour that is otherwise morphologically typical is not precluded by an absence of KIT staining.[8] . In this series we had one patient in whom IHC for PDGF Ag could not be done because of unavailability of the kit. However, in this particular patient, the tumour was negative for desmin and S-100, indirectly favouring the diagnosis of GIST.

Following surgery, imatinib mesylate, a selective tyrosine kinase inhibitor of c-KIT [9], may be used. It is a specifically targeted molecular therapy for GIST. Initial results suggest that 54% of the GISTs respond to imatinib and there is no benefit of doses over 400mg/day. There is no consensus about the optimal duration of treatment with imatinib. This

series only comprised four patients in whom imatinib was used, three of them did not show any adverse effect, the fourth patient was lost in follow-up after 8 months of surgery and hence the drug's effect on him is not known.

CONCLUSION

This series is based on only eighteen patients, focusing on our initial experiences with GIST. The age distribution coincides with the international literature but there is a marked preponderance of male sex affection. The study could conclude that lesions >5cm definitely have a higher chance of recurrence, irrespective of the risk categorization.

We firmly believe local resection with 1-2cm margin with the aim of organ preservation should be the principle of surgical treatment. Local recurrences can be notorious and at times elusive. IHC should be done routinely while assessing specimens of GIST, not only because it is the hallmark of diagnosis but also an important predictive factor. Though the study period was short, our study recommends the use of imatinib in the adjuvant setting in high-risk, recurrent and metastatic settings.

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