VOLUME - 12, ISSUE - 06, JUNE - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Surgery

RECURRENT GIST – A NEW GHOST

Prof. Dr. M. Senthil Kumar M.S, Unit Chief, General Surgery, GOVT. Kilpauk Medical College

Dr. Gunasekaran M.S, Assistant Professor, General Surgery, GOVT. Kilpauk Medical College

Dr. K. Sivasankaran Postgraduate, General Surgery, GOVT. Kilpauk Medical College

KEYWORDS :

2.INTRODUCTION

Gastrointestinal stromal tumour (GISTs) are the most common mesenchymal tumour of the gastrointestinal tract and are believed to originate from the interstitial cells of Cajal. GISTs have a slight male predominance and arise most commonly from the stomach or small intestine, with a median age of 60 years at presentation. Although surgery remains the treatment of choice for localized tumour, imatinib mesylate and more recently sunitinib malate, both specific inhibitors of the KIT tyrosine kinase function, have revolutionized the management of unresectable, recurrent, and metastatic GISTs. Gastrointestinal stromal tumor (GISTs) are rare mesenchymal neoplasms of the alimentary tract accounts for 0.1 -3% . GISTs arise from interstitial cells of cajal and most commonly occurs in stomach. They are best identified by computed tomography (CT) scan and most stain positive for CD117 (C-Kit), CD34, and/or DOG

3. Case Report:(including Observations)

Case Report 1 :

45 year old male came with chief complaints of abdominal distension abdominal pain ,constipation and vomiting for 4 days and no comorbidities .Past history: He had history of abdominal pain 5 years back and radiological investigation revealed diffusion restricting mass lesion in left iliac fossa adjacent to small bowel loop -?GIST . Computered tomography guided biopsy and immunohistochemistry of the blocks showed positivity of CD117 and patient proceeded with laparotomy and en bloc resection of tumour with end to end jejunojejunal anastomosis done, post operatively patient treated with imatinib mesylate .After completion of imatinib mesylate computered tomography screening done and it revealed no residual lesion .CURRENT SCENARIO: Patient advised for x ray abdomen erect reveals - multiple dilated bowel loops with air fluid levels (figure1). Contrast enhanced computered tomography abdomen and pelvis revealed - multifocal heterodense lesion adjacent to 2 and 3 rd part of duodenum , desecending colon and sigmoid colon appears collapsed, heterodense lesion noted anterior to stomach and multiple air fluid levels with maximum dilatation of 6.5cm (figure 2).

Intraoprative Findings :

Multiple gist noted in jejunum, ileum and mesentry.(figure 3). A Mass of size approximately 10*6 cm noted about 60cm from ileocaecal valve with collapsed ileum distally.(figure 4). A mass of size 13*7 cm noted in hepatic flexure and proximal transverse colon (figure 5).

Decision Made:

RESECTION OF TUMOUR AT HEPATIC FLEXURE PROXIMAL TRANSVERSE COLON AND MESOCOLON. RESECTION OF TUMOUR AT ILEUM. MILKING OF PROXIMAL SMALL BOWEL. SIDE TO SIDE ANASTOMOSIS OF ILEUM AND TRANSVERSE COLON. MULTIPLE SMALL GISTS AT ILEUM JEJUNUM MESENTRY EXCISED (FIGURE 6). HISTOPATHOLOGY : Interlascing fascicles storiform pattern of spindle shaped cells having hyperchromatic elongated nuclei exhibiting moderate pleomorphism with >5/5 mm square mitotic figures. PATHOLOGICAL STAGE : pT4(m) according to 8 th edition AJCC. CHEMOTHERAPY : In view of recurrence of GIST along with high grade mitotic index combined with multiple in number the patient was started on imatinib mesylate high dose . Patient advised for CT SCREENING for every 6 month4

DISCUSSION :

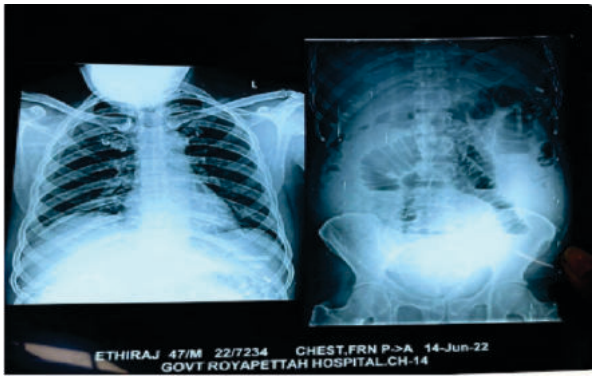
GISTs represent more than 80% of all mesenchymal tumour found in the gastrointestinal tract, though they account for only approximately 3% of all gastrointestinal malignancies. In the case of primary GIST, surgery remains the definitive therapy for patients with low- and intermediate-risk disease . For patients with high-risk disease (defined by the NIH Consensus Criteria as [1] size >10 cm, [2] mitotic rate > 10/50 hpf or [3] mitotic rate > 5/50 hpf and tumor size > 5 cm, or [4] tumor rupture spontaneously or at surgery), adjuvant TKI therapy has been shown to add significant survival benefit. Imatinib mesylate (STI 571), a phenylaminopyrimidine derivative, is a small molecule that selectively inhibits the enzymatic activity of several tyrosine kinases, including ABL; the BCR–ABL fusion protein of chronic myeloid leukemia and Philadelphia chromosome-positive acute lymphoblastic leukemia; PDGFR; and the product of the KIT gene . Recently, several clinical trials have demonstrated that imatinib was effective for metastatic and recurrent GIST. On the other hand, some GISTs are resistant to imatinib from the beginning (primary resistance), or they acquire resistance after the initial response or disease stabilization (acquired resistance).

The efficiency of and resistance to imatinib treatment for GIST depend on where the mutation is located. In GISTs with the exon 11 mutation in c-kit, imatinib treatment is effective. However, the therapeutic effect of imatinib may not be as good if exon 17 is mutated Several mechanisms for biological imatinib resistance have been suggested (A) acquisition of a new c-kit or PDGFRA point mutation, coexpressed with pre-imatinib mutations in the same genes, with the resultant strong phosphorylation of KIT or PDGFRA; (B) KIT genomic amplification with overexpression of the KIT oncoprotein, without a new point mutation (C) activation of other types of tyrosine kinase receptor. The Scandinavian Sarcoma Group (SSG) trial, comparing 1 and 3 years of imatinib therapy, showed improved 5-year recurrence-free survival of 47.9% and 65.6%, respectively. GIST recurrence in the Imatinib era is largely considered incurable, and treatment strategies are aimed at delaying progression . Despite response to TKI therapy, many patients with high-risk GIST eventually develop recurrent disease. In the SSG study, 65.6% of those who completed 3 years of adjuvant imatinib were alive without recurrence 5 years after study entry. However, 34.4% of those treated experienced recurrence requiring further management. Treatment options are to initially escalate TKI

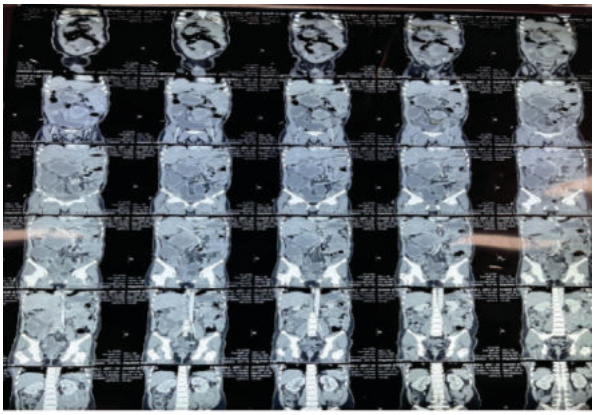
dose or switch to a second-line drug, typically sunitinib malate. A key principle in treatment of recurrent and/or metastatic GIST is to continue imatinib or second-line therapy indefinitely, as it has been shown that patients who discontinue therapy have higher rates of disease progression. surgery remains an important consideration in the management of recurrent GIST upfront surgery for GIST recurrence regardless of response to adjuvant TKI therapy, while also highlighting the combinatory effect of these two treatment strategies. In patients with resectable, recurrent disease, complete resection of recurrent GIST may eliminate possible mutant strains, avoiding the need for escalation of TKI dosage. Winer and Raut recommend that imatinib therapy commence prior to surgery, and surgeons should wait a minimum of six months before proceeding with resection. surgery reduces tumor burden, this may delay time to development of secondary resistance, and offers a survival benefit when imatinib therapy is initiated prior to surgery. The quality of resection for GIST recurrence has been found to play a pivotal role in survival. A survival benefit from curative resection but reduced 5-year overall survival for R2 resection as compared to TKI therapy. The surgical intervention should be reserved only for patients with possibility of achieving R0/R1 resection, 6–12 months after initiation of imatinib therapy. surgical intervention should be reserved only for patients with possibility of achieving R0/R1 resection, 6–12 months after initiation of imatinib therapy. Importantly, R0/R1 resection of residual disease had a benefit when the number of metastatic lesions was less than 4, total tumor size was less than 100 cm, and disease remained stable or responsive to TKI therapy.

5 CONCLUSION

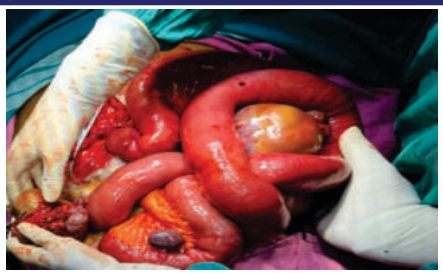
Paucity of high level evidence investigating the management of recurrent gist calls for prospective randomized controlled studies to evaluate and to design appropriate treatment protocols. Molecular profiling might help in deciding the number and dosage of tyrosine kinase inhibitors therapy in GIST recurrence.



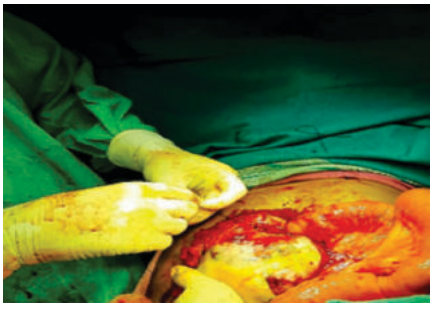
13.1 Figures Figure 1 Xray Abdomen Erect



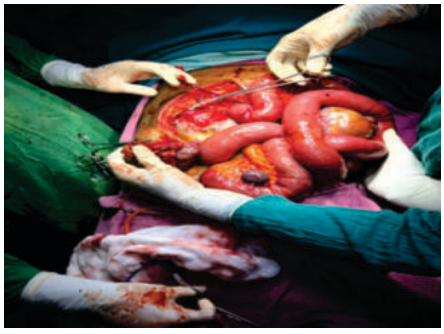
13.2 Figures Figure 2 Cect Abdomen And Pelvis



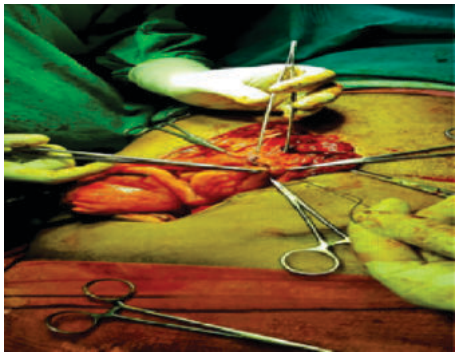
13.3 Figures Figure 3 :multiple Gist Noted In Jejunum Ileum Mesentry



13.4 Figures Figure 4 : Mass Noted From 60cm Ileocaecal Valve



13.5 Figures Figure 5: A Mass Of Size 13*7 Cm Noted In Hepatic Flexure And Proximal Transverse Colon With Collapsed Rest Of Colon



13.6 Side To Side Anastomosis Of Ileum And Transverse Colon

6 REFERENCES

1. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg. 2000;231:51–58.
2. Nishida T, Hirota S. Biological and clinical review of stromal tumors in the gastrointestinal tract. Histol Histopathol. 2000;15:1293–1301.
3. Raut CP, Posner M, Desai J, Morgan JA, George S, et al. Surgical management of advanced gastrointestinal stromal tumors after treatment with targeted systemic therapy using kinase inhibitors. J Clin Oncol. 2006;24:2325–2331.
4. Antonioli DA. Gastrointestinal autonomic nerve tumors. Expanding the spectrum of gastrointestinal stromal tumors. Arch Pathol Lab Med. 1989;113:831–833.
5. Appelman HD. Smooth muscle tumors of the gastrointestinal tract. What we know now that Stout didn't know. Am J Surg Pathol. 1986;10(suppl 1):83–99.
6. Graadt van Roggen JF, van Velthuysen ML, Hogendoorn PC. The histopathological differential diagnosis of gastrointestinal stromal tumours. J Clin Pathol. 2001;54:96–102

7. Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. Am J Pathol. 1998;152:1259–1269
8. Huizinga JD, Berezin I, Chorneyko K, Thuneberg L, Sircar K, et al. Interstitial cells of Cajal: pacemaker cells? Am J Pathol. 1998;153:2008–2011.
9. Rumessen JJ, Mikkelsen HB, Qvortrup K, Thuneberg L. Ultrastructure of interstitial cells of Cajal in circular muscle of human small intestine. Gastroenterology. 1993;104:343–350.
10. Sircar K, Hewlett BR, Huizinga JD, Chorneyko K, Berezin I, Riddell RH. Interstitial cells of Cajal as precursors of gastrointestinal stromal tumors. Am J Surg Pathol. 1999;23:377–389.
11. Hirota S, Isozaki K. Pathology of gastrointestinal stromal tumors. Pathol Int. 2006;56:1–9.