ejpmr, 2021,8(11), 558-561

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

AN UNFORTUNATE OUTCOME OF ILEUM GASTROINTESTINAL STROMAL TUMOR PRESENTING WITH METASTATIC LYMPHADENOPATHY

Sheeba Bhardwaj*, Sunder Singh, Ashish Nigam, Abhishek Soni, Ashok Kumar Chauhan and Vivek Kaushal

Department of Radiation Oncology, Pandit B. D. Sharma Post Graduate Institute of Medical Sciences, Rohtak.

***Corresponding Author: Sheeba Bhardwaj**

Department of Radiation Oncology, Pandit B. D. Sharma Post Graduate Institute of Medical Sciences, Rohtak.

Article Received on 23/08/2021 **Article Revised on 13/09/2021** **Article Accepted on 03/10/2021**

ABSTRACT

Introduction: Gastrointestinal stromal tumors (GISTs), are the most common mesenchymal tumors of the gastrointestinal (GI) tract, but are rare accounting approximately 1-3% of all gastrointestinal tumors. About 50-75% of GIST originates in the stomach and about 20% in the small bowel, while less frequent sites include the colon and rectum. In this case report we present a patient with GIST of small intestine with liver metastasis and regional lymphadenopathy. **Case Presentation:** A 55-year old male presented with complaints of pain abdomen and constipation from 4-years. Contrast-enhanced computed tomography (CECT) abdomen revealed a focal, eccentric mural thickening of small intestine loop with regional lymph nodes and liver metastases. Patient received tab Imatinib mesylate 400 mg to which he showed symptomatic relief; later the patient lost to follow-up. **Conclusion:** GIST of the small Intestine with regional lymphadenopathy is a rare condition and attention should be paid to patients presenting with complaint of malena or obstruction; keeping GIST in the differential diagnosis.

INTRODUCTION

Gastrointestinal stromal tumors (GISTs), are the most common mesenchymal tumors of the gastrointestinal (GI) tract, but are rare accounting approximately 1-3% of all gastrointestinal tumors. Mazur and Clarke coined the term GIST in 1983 for a distinct set of mesenchymal tumors of the GI tract having no ultra-structural or immunohistochemical features characteristic of smooth muscle differentiation.[1] GISTs originate from the interstitial cells of Cajal (ICCs).[2] Mutations involving c-KIT and PDGFRα are known to be involved in the pathogenesis of GIST.[3] Malignant GISTs show gain-of-function mutations in c-KIT (receptor tyrosine kinase) gene, which leads to ligand independent activation of the tyrosine kinase resulting in uncontrolled proliferation. In this case report, we present a patient with GIST of the small intestine with metastatic lymphadenopathy and liver metastasis.

CASE PRESENTATION

A 55-year old male presented with complaints of pain abdomen and constipation from 4-years. Pain was insidious in onset, progressive, not associated with any aggravating factors, relieved by oral analgesics, localized in epigastrium and was non-radiating. No significant past or personal history was noted. General physical examination and systemic examination was normal. Ultra sonogram (USG) abdomen showed multiple cystic lesions in liver and a mass in pelvis measuring 7.7 × 5.2 cm. Contrast-enhanced computed tomography (CECT) of the abdomen revealed a focal, eccentric mural thickening of ileum of small intestinal stromal tumors, loop with 2.7 cm wall thickness and extending up to a length of 5.0 cm. Multiple enlarged perifocal lymph nodes were seen, largest measuring 1.8 × 1.2 cm, and multiple heterogeneous lesions with necrotic centre were also seen in both lobes of liver; largest measuring 4.8 × 2.9 cm in left lobe showing peripheral enhancement. USG guided fine needle aspiration cytology (FNAC) from the lesions in the liver revealed metastatic deposits from GIST. Patient was diagnosed as a case of GIST of the ileum part of small intestine with metastases to lymph nodes and liver. Patient was started on oral therapy with tablet Imatinib Mesylate 400 mg for 14-months and subsequently patient developed progressive disease and presented as severe pain abdomen and bleeding micturition. USG abdomen showed markedly enlarged liver with multiple cystic lesions largest measuring 8.9 × 7.9 cm along with significant fluid in the peritoneal cavity. Patient received symptomatic treatment but later lost to follow-up.

DISCUSSION

About 50-75% of the GISTs originates in the stomach and about 20% in the small bowel, while less frequent sites include colon and rectum.[4] Jejunum is the most common site of small intestinal stromal tumors with duodenum being the rarest. (Table-1)[5]

Table 1: Primary incidence site distribution of small intestine stromal tumors.

Site	Number of cases	%	Z value	P
Duodenum	8	10.7	14.059	< 0.001
Jejunum	43	57.3		
Ileum	24	32		

GIST occurs marginally frequent in males as compared to females, both in the fifth and sixth decades of life. There is no racial or geographical preponderance.[6] Clinical presentation varies from an incidental radiological finding, intestinal obstruction, upper or lower gastro-intestinal (GI) bleeding or melena, and also spontaneous intra-abdominal hemorrhage, some may present with a palpable abdominal lump.[7] Table -2 depicts various case reports on small intestine GIST.

Table 2: Various case reports on small intestine GIST.

S. No.	Author	Clinical presentation	Site	Lymphadeno -pathy / Mets	Treatment	Response
1	Serban et al[8]	Pain abdomen	Ileum	-	Surgery	NA
2	Mitura et al[9]	Pain abdomen	Meckel's Diverticulum	-	Surgery	NA
3	Lutz et al[10]	Painful lump	Ileum	Mandible	Imatinib	Death
4	Vassos et al[11]	Lump abdomen	Ileum	Inguinal, Axillary LN	Surgery f/b Imatinib f/b Sunitinib	NA
5	Yu CH et al[12]	Bladder symptoms, weight loss	Ileum with mesenteric invasion	-	Surgeryf/b Imatinib	Stable disease
6	Choi WH et al[13]	Pain abdomen	Duodenum	Liver	Surgery, RFA f/b Imatinib	NA
7	Mirakhor E et al[14]	Gastrointestinal bleeding	Ileum	-	-	NA
8	Matteo D et al[15]	Lump abdomen and pelvis	Ileum	-	Laparotomy	NA
9	Efremidou EI et al[16]	Pain abdomen	Ileum	-	Laparotomy f/b imatinib	NA
10	Iusco D et al[17]	Intestinal subocclusion and haemoperitoneum	Ileum	-	Laparotomy	NA
11	Pfeffel F et al[18]	Bowel obstruction	Ileum	-	Surgery	NA
12	Mijandrusić Sincić B et al[19]	Pain	Ileum	-	Segmental resection and hemicolectomy	NA
13	Furuya K et al[20]	Peritonitis	Ileum	-	Segmental resection	NA
14	Han SH et al[21]	Abdominal pain	Small bowel	-	Imatinib	Progressive disease
15	Akiyoshi T et al[22]	Abdominal pain	Small intestine	Peritoneum	Imatinib f/b surgery f/b imatinib	Complete regression
16	Tanaka J et al[23]	Tarry stools and anemia	Stomach	Liver	Surgery f/b Imatinib	Death

SIST (Small Intestinal Stromal Tumors) as a part of GIST has are biologically more aggressive. The prognosis of SIST is worse than GIST of stomach. The recurrence rate of SIST is much higher than GIST in other parts of the gastrointestinal tract (24, 25). Lymph node metastasis is rare in GIST patients in comparison to SIST patients. About 10-15% of SIST patients may present with lymph node metastasis (26, 27). GIST expresses CD117 (c-kit), which helps in differentiating GIST from other GI mesenchymal tumors.[28] KIT is negative in a minority of GISTs, especially in platelet-derived growth factor receptor alpha (PDGFRα) gene mutation harboring GISTs; in that cases mutational analyses of c-KIT and PDGFRα genes may be required for a definitive diagnosis.[29] CD34 is expressed in 70% of GISTs and indicate the probability of a lesion being malignant or not. Presence of CD44 indicates a better prognosis.[26] Peritoneal and hepatic metastases are the main routes of spread of GIST. The curative intent is operative excision with a clear R0 margin.[6] Complete resection of the tumor with negative margins is the surgical treatment of choice.[30] Adjuvant therapy should be reserved only for patients having significant prognostic indicators for disease recurrence.[31] Small intestine GISTs are treated by a segmental resection and anastomosis. Lymphadenectomy is not routinely

performed because of less frequent involvement. Unresectable tumors are treated with imatinib.[26] For completely resected primary GISTs, mitotic rate, tumor size and tumor location are important risk factors for recurrence. However, molecular markers for recurrence are still lacking.[32] GIST often recurs within first year post surgery, or sometimes it may take upto 10 years post surgery. The recurrence rate is 40-50% post surgery and the most common sites are liver and peritoneum. The 5 – year survival rate in patients with liver metastasis is 24%.[33]

Therefore, a careful long-term following-up after surgery is advised (34). With the advent of imatinib mesylate since 2000, targeted molecular therapy has made successful inroads in the management of patients with operated GIST having no clear margins, tumors which are unresectable, or those with recurrences. The drug was approved by the FDA for use against metastatic GIST in 2001 and for prevention of recurrences in operated GIST, for intermediate and high risk groups in year 2008.[6] Response to imatinib in patients with GIST mainly depends on the mutational status of KIT or PDGFRα. Imatinib targets both of these mutated genes and block cellular communications that result in tumor growth.[35] Sunitinib treatment may be one of the most important therapeutic options for unresectable imatinib-resistant GIST.[36] Better understanding of the cell of origin and immunohistochemical markers has made timely targeted therapy possible in GIST.[34] Table -3 depicts the 5 year survival rate of GIST as per SEER analysis.[37] Further improvements in GIST treatment may require targeting GIST stem cell populations and/or additional genomic events.[3]

Table 3: 5-Year Relative Survival Rate as per SEER analysis.

SEER Stage	5-Year Relative Survival Rate
Localized	93%
Regional	80%
Distant	55%
All SEER stages combined	83

SEER= Surveillance, Epidemiology, and End Results

CONCLUSION

GIST of small intestine is a rare condition and attention should be paid to patients presenting with complaint of malena or obstruction; keeping GIST in the differential diagnosis. Small intestine being a rare site for GIST; emphasis should be given to investigate its pathogenesis and potentially more specific treatment. Lymphadenopathy and liver metastasis at presentation makes the prognosis worse; thus, multiagent chemotherapy and/or targeted therapy in combination with surgery may be investigated in further trials. More detailed research papers should be published for in depth understanding of the disease.

REFERENCES

1. Mazur MT, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. Am J Surg Pathol [Internet]. 1983 [cited 2021 Mar 18]; 7(6): 507–19. Available from: https://pubmed.ncbi.nlm.nih.gov/6625048/
2. Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, et al. Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science (80-). 1998; 279(5350): 577–80.
3. Corless CL, Barnett CM, Heinrich MC. Gastrointestinal stromal tumours: Origin and molecular oncology. Nat Rev Cancer [Internet], 2011; 11(12): 865–78. Available from: http://dx.doi.org/10.1038/nrc3143
4. Gokhale U, Rajasekharan Pillai G. Large brunner's gland hamartoma: A case report. Oman Med J., 2009; 24(1): 6–8.
5. Lifang Zhao, Zhigang Zhao, Weidong Wang, Weiwei Zhao**1**, Shengjun Tuo**1**, Yupeng Shi et al. Current characteristics on small intestinal stromal tumor- a case control study. *Ann Palliat Med,* 2020; 9(1): 98-107
6. Sashidharan P, Matele A, Matele U, Al Felahi N, Kassem KF. Gastrointestinal stromal tumors: A case report. Oman Med J [Internet]. 2014 [cited 2021 Mar 18]; 29(2): 138–41. Available from: /pmc/articles/PMC3976734/
7. Lasota J, Miettinen M. KIT and PDGFRA mutations in gastrointestinal stromal tumors (GISTs). Semin Diagn Pathol, 2006; 23(2): 91–102.
8. Serban C, Constantin GB, Firescu D, Rebegea L, Manole CP, Truş C et al. Perforated Ileal GIST Associated with Meckel Diverticulum - A Rare Pathological Entity of Surgical Acute Abdomen. Chirurgia (Bucur). 2020; 115(3): 404-9.
9. Mitura K, Blicharz P, Romańczuk M. Perforated gist of Meckel's diverticulum. Pol Przegl Chir, 2012; 84(5): 258-61.
10. Lutz JC, El-Bouihi M, Vidal N, Fricain JC, Robert M, Deminière C et al. Mandibular metastases from an ileum stromal tumor. Rev Stomatol Chir Maxillofac, 2008; 109(6): 399-402.
11. Vassos N, Agaimy A, Hohenberger W, Croner RS. Extraabdominal lymph node metastasis in gastrointestinal stromal tumors (GIST). J Gastrointest Surg, 2011; 15(7): 1232-6.
12. Yu CH, Ting HK, Kao CC, Tsai WC, Wu ST, Yu DS et al. A rare case of extraluminal gastrointestinal stromal tumor of the ileum presenting with lower urinary tract symptoms: A case report. Medicine (Baltimore), 2019; 98(49): e18103.
13. Choi WH, Kim S, Hyung WJ, Yu JS, Park CI, Choi SH et al. Long-surviving patients with recurrent

GIST after receiving cytoreductive surgery with imatinib therapy. Yonsei Med J., 2009; 50(3): 437-40.
14. Mirakhor E, Wong MT, Jamil LH. Gastrointestinal stromal tumour masquerading as a diverticular bleed. BMJ Case Rep., 2019; 12(11): e232169.
15. Matteo D, Dandolu V, Lembert L, Thomas RM, Chatwani AJ. Unusually large extraintestinal GIST presenting as an abdomino-pelvic tumor. Arch Gynecol Obstet, 2008; 278(1): 89-92.
16. Efremidou EI, Liratzopoulos N, Papageorgiou MS, Romanidis K. Perforated GIST of the small intestine as a rare cause of acute abdomen: Surgical treatment and adjuvant therapy. Case report. J Gastrointestin Liver Dis., 2006; 15(3): 297-9.
17. Iusco D, Jannaci M, Grassi A, Bonomi S, Ismail I, Navarra G et al. Giant ileal gastrointestinal stromal tumour presenting as an intestinal subocclusion and subsequent haemoperitoneum: a case report and a review of the literature. Updates Surg, 2010; 62(3-4): 189-93.
18. Pfeffel F, Stiglbauer W, Depisch D, Oberhuber G, Raderer M, Scheithauer W et al. Coincidence of Crohn's disease and a high-risk gastrointestinal stromal tumor of the terminal ileum. Digestion, 1999; 60(4): 363-6.
19. Mijandrusić Sincić B, Kovac D, Jasić M, Grbas H, Uravić M, Depolo A et al. Crohn's disease and a gastrointestinal stromal tumor in an 81-year-old man--a rare coincidence. Zentralbl Chir, 2005; 130(6): 597-9.
20. Furuya K, Hada M, Sugai H, Miyasaka Y, Nakagomi H, Oyama T et al. Gastrointestinal stromal tumor arising in an ileal duplication: report of a case. Surg Today, 2012; 42(12): 1234-9.
21. Han SH, Park SH, Cho GH, Kim NR, Oh JH, Nam E et al. Malignant gastrointestinal stromal tumor in a patient with neurofibromatosis type 1. Korean J Intern Med., 2007; 22(1): 21-3.
22. Akiyoshi T, Oya M, Fujimoto Y, Kuroyanagi H, Ueno M, Yamaguchi T. Complete resection after imatinib treatment of a gastrointestinal stromal tumor of the ileum with peritoneal metastases: report of a case. Surg Today, 2010; 40(3): 272-6.
23. Tanaka J, Oshima T, Hori K, Tomita T, Kim Y, Watari J et al. Small gastrointestinal stromal tumor of the stomach showing rapid growth and early metastasis to the liver. Dig Endosc, 2010; 22(4): 354-6.
24. Burkill GJ, Badran M, Al-Muderis O, et al. Malignant gastrointestinal stromal tumor: distribution, imaging features, and pattern of metastatic spread. Radiology, 2003; 226: 527-32.
25. Grover S, Ashley SW, Raut CP. Small intestine gastrointestinal stromal tumors. Curr Opin Gastroenterol, 2012; 28: 113-23.
26. Sridharan S, Kumar R, Dinesh KB, Sundaravadanan BS, Kirouchenaradj V, Balamurali S. Small Intestine Gastrointestinal Stromal Tumour—A Case Report. Case Reports Clin Med., 2020; 09(01): 7–14.
27. Lifang Zhao, Zhigang Zhao, Weidong Wang, Weiwei Zhao**1**, Shengjun Tuo**1**, Yupeng Shi et al. Current characteristics on small intestinal stromal tumor- a case control study. *Ann Palliat Med*, 2020; 9(1): 98-107.
28. Piessen G, Lefèvre JH, Cabau M, Duhamel A, Behal H, Perniceni T, et al. Laparoscopic versus open surgery for gastric gastrointestinal stromal tumors: What is the impact on postoperative outcome and oncologic results? Ann Surg, 2015; 262(5): 831–40.
29. Hirota S, Isozaki K. Pathology of gastrointestinal stromal tumors. Pathol Int., 2006; 56(1): 1–9.
30. Demetri GD, van Oosterom AT, Garrett CR, Blackstein ME, Shah MH, Verweij J, et al. Efficacy and safety of sunitinib in patients with advanced gastrointestinal stromal tumour after failure of imatinib: a randomised controlled trial. Lancet, 2006; 368(9544): 1329–38.
31. Hohenberger P, Ronellenfitsch U, Oladeji O, Pink D, Ströbel P, Wardelmann E, et al. Pattern of recurrence in patients with ruptured primary gastrointestinal stromal tumour. Br J Surg, 2010; 97(12): 1854–9.
32. Manxhuka-Kerliu S, Sahatciu-Meka V, Kerliu I, Juniku-Shkololli A, Kerliu L, Kastrati M, et al. Small intestinal gastrointestinal stromal tumor in a young adult woman: A case report and review of the literature. J Med Case Rep., 2014; 8(1): 1–7.
33. Yi-Nan Shi, Yong Li, Li-ping Wang, Zhen-Hua Wang, Xiao-Bo Liang, Han Liang et al. Gastrointestinal stromal tumor (GIST) with liver metastasis: An 18 year experience from the GIST cooperation group in north China. Medicine, 2017; 96: 46.
34. Arcía de Polavieja Carrasco M, de Juan Ferré A, Mayorga Fernández M. Gastrointestinal stromal tumours at present: an approach to burning questions. Clin Transl Oncol, 2010; 12: 100-12.
35. Dhull AK, Kaushal V, Dhankhar R, Atri R, Singh H, Marwah N. The inside mystery of jejunal Gastrointestinal Stromal Tumor: A Rare Case Report and Review of the Literature. Case Rep Oncol Med., 2011; 2011: 985242. doi:10.1155/2011/985242.
36. Casali PG. Successes and limitations of targeted cancer therapy in gastrointestinal stromal tumors. Prog tumor Res., 2014; 41: 51–61.
37. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2017, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2017/, based on November 2019 SEER data submission, posted to the SEER web site, April 2020.