Radiology Case Reports 19 (2024) 1424–1431

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Malignant rectal GIST managed with chemotherapy (Imatinib Mesylate): A case report and a comprehensive review ☆

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ARTICLE INFO

Article history:
Received 1 December 2023
Revised 8 December 2023
Accepted 23 December 2023

Keywords:
Gastrointestinal stromal tumors
Rectal tumors
Metastasis
Rare
Imatinib Mesylate
Case report

ABSTRACT

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors involving the gastrointestinal tract, arising from the interstitial cells of Cajal. GIST comprises about 1% of all GI tumors. Rectal GISTs are rare and comprise of approximately 5% of all GISTs and only 0.1% of rectal tumors are found to be GISTs. Rectal GISTs may be diagnosed incidentally or present with symptoms, including defecation problems, bleeding, and/or pain. We report a case of a 46-year-old male with rectal GIST metastasized to the liver and bilateral lung parenchyma managed by Imatinib Mesylate (IM) regimen. Rectal GIST although being rare, must be considered as a differential diagnosis in a patient presenting with defecatory problems with bleeding.

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors involving the gastrointestinal tract [1].

Abbreviations: GISTs, Gastrointestinal stromal tumors; CEA, Carcinoembryonic antigen; CA-19-9, Carcinoma antigen-19-9; CT, Computed tomography; US, Ultrasound; MRI, Magnetic resonance imaging.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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https://doi.org/10.1016/j.radcr.2023.12.046

They arise from the interstitial cells of Cajal [2]. They commonly occur in the 6th and 7th decades of life [1]. GIST comprises about 1% of all gastrointestinal tumors [2]. The most common sites of GISTs include the stomach (50%-65%) followed by the small intestine (20%-30%) [1]. Rectal GISTs are rare and comprise approximately 5% of all GISTs [3]. Also, only 0.1% of rectal tumors are found to be GISTs [1]. Rectal GISTs may be diagnosed incidentally or present with symptoms, including defecation problems, bleeding, and/or pain [4].

We report a case of a 46-year-old male with rectal GIST metastasized to the liver and bilateral lung parenchyma managed by Imatinib Mesylate regimen.

Case presentation

A 46-year-old male with no prior medical co-morbidity presented to the surgical outpatient clinic with the chief complaints of intermittent constipation for 1.5 years. It was insidious in onset, and gradually progressive. According to the patient, the stool is hard in consistency with abundant mucus discharge and there is an incomplete sense of evacuation after watch defecation. The patient is a nonsmoker and nonalcoholic. He also states that his appetite had decreased and he had lost about 7 kg in the last 6 months. There was no history of bleeding per rectum, nausea or vomiting, abdominal distension, cough, chest pain, difficulty breathing, burning micturition, yellowish discoloration of eyes and skin, and fever. There was no significant past and family history of similar illness. On examination, his general condition looked fair. There were no signs of pallor, icterus, edema, dehydration, clubbing, cyanosis, and lymphadenopathy. The patient did not appear cachexic. On per-abdomen examination, the abdomen was soft, and nontender with no organomegaly. A digital rectal examination revealed a normal tone, with no mass palpable. A small bulge was felt at the anterior rectal wall 4cm above the anal verge. The examining finger was stained with stool and nonblood stained. On proctoscope examination, there was no visible bulb as it was just palpable. There was no sign of active bleeding. A routine colonoscopy was done which did not show any mass. Lab investigations were within normal limits except for raised transaminase levels in the Liver function test. Serum CEA and CA-19-9 were within normal levels. The next day a Contrast-Enhanced CT scan of the abdomen and pelvis was ordered which showed a well-circumscribed heterogeneously enhancing solid lesion of size 2.3 * 3.5 cm with nonenhancing cystic/necrotic areas within rectovesical space suggesting a rectovesical mass. It also showed multiple minimally enhancing space-occupying lesions in both lobes of liver (Fig. 1) and few enhancing soft tissue density lesions in the bilateral lung parenchyma (Fig. 2) suggesting the malignant nature of the disease. A US-guided core biopsy showed evidences suggestive of spindle cell neoplasm (Figs. 3–7). Immunohistochemistry analysis showed tumor cells with positive expression for CD117 stain, a feature suggestive of Rectal GIST (Fig. 8). The patient was determined to be a non-surgical candidate due to findings suggestive of metastasis in the liver and lungs. The patient was then referred to Oncology unit where he was planned to be kept on chemotherapy with Imatinib Mesylate. The patient was asked for 3 monthly follow-ups with contrast-enhanced CT scans of the abdomen and pelvis.

Discussion

GISTs are the most common mesenchymal tumors involving the gastrointestinal tract [1]. GISTs originate from the interstitial cells of Cajal. These cells are considered the pacemaker cells of the gastrointestinal tract that are involved in the regulation of gut peristalsis [3,5]. These cells express c-KIT (CD117), which is a type III tyrosine kinase receptor. It has been proposed that mutually exclusive mutations in the KIT protooncogene or platelet-derived growth factor receptor alpha (PDGFRA), resulting in constitutive activation of KIT signaling are the reason behind the pathogenesis of these neoplasms [3,5]. The estimated annual incidence of GISTs around the world is 7-15 cases per million [6]. Because of their similar appearance on light microscopy, GISTs were previously misdiagnosed as leiomyomas, leiomyoblastomas, leiomyosarcomas, or schwannomas. But they were recognized as separate tumor entities in 1988 after the discovery of gain-of-function mutations in the c-KIT proto-oncogene [3,7]. The most common sites of GISTs include the stomach (50%-65%) followed by the small intestine (20%-30%) [1]. Rectal GISTs are rare and comprise of approximately 5% of all GISTs [3] and only 0.1% of rectal tumors are found to be GISTs [1]. GISTs commonly occur in the 6th and 7th decades of life [1]. We report a case of malignant Rectal GIST in a 46-year-old male which is rare because of the rare incidence of rectal GIST's early mode of presentation. The clinical features of GISTs varies according to the tumor site and size. They are mostly detected incidentally. However rectal GISTs may present as gastrointestinal bleeding, intestinal obstruction, abdominal pain, perforation, palpable pelvic mass, or defecation problems. In some cases, rectal GISTs may be detected incidentally as a palpable mass during a digital rectal examination [8]. Our patient presented with a defecatory problem and a small mass felt in Digital Rectal Examination but not visible on proctoscopy and colonoscopy. Diagnosis of GISTs is usually by endoscopic examination or via imaging tools like CT and MRI [9]. Endoscopic examination allows for direct visualization and can also be used for performing biopsies [9]. CT and MRI serve as the major imaging tools for diagnosing, staging, and surgical planning of rectal GISTs because of their ability to assess the size, shape, and borders of the tumor, along with the possibility of distant metastatic disease [9]. CT was also done in our case which showed findings suggestive of rectovesical space in the midline with metastatic lesions in liver and lung parenchyma. However, the definitive diagnosis depends on pathologic, cytologic, and immunohistochemical analysis of the tumor cells [2]. There are three morphological patterns of GISTs in histology: Spindle cell type (70%), epithelioid type (20%), and mixed type [10]. Other tumors like leiomyoma, leiomyosarcoma, desmoid tumor, neuroendocrine tumor, fibrous tumors, melanoma, and other sarcomas can mimic GISTs in histology. So, histology cannot differentiate between GISTs and those tumors [11]. Immunohistochemical analysis serves as the gold standard for the definitive diagnosis of GISTs. They are also useful for initiat-

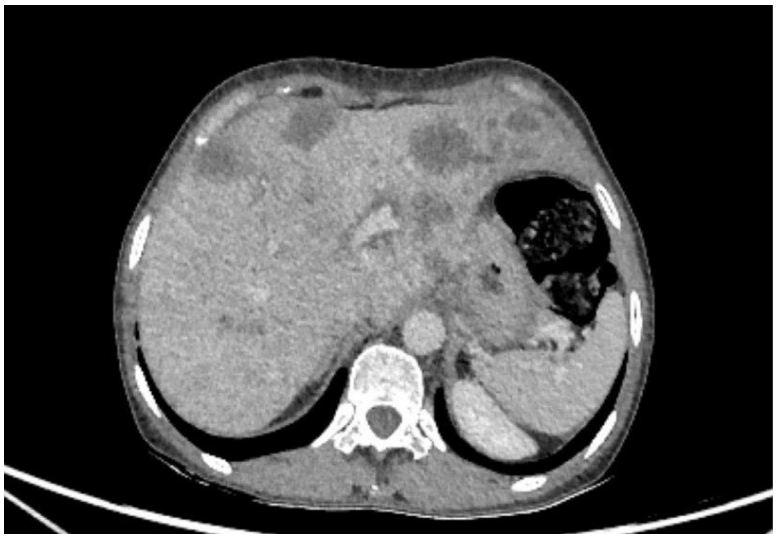

Fig. 1 – CECT showing multiple minimally enhancing space-occupying lesions in both lobes of the liver.

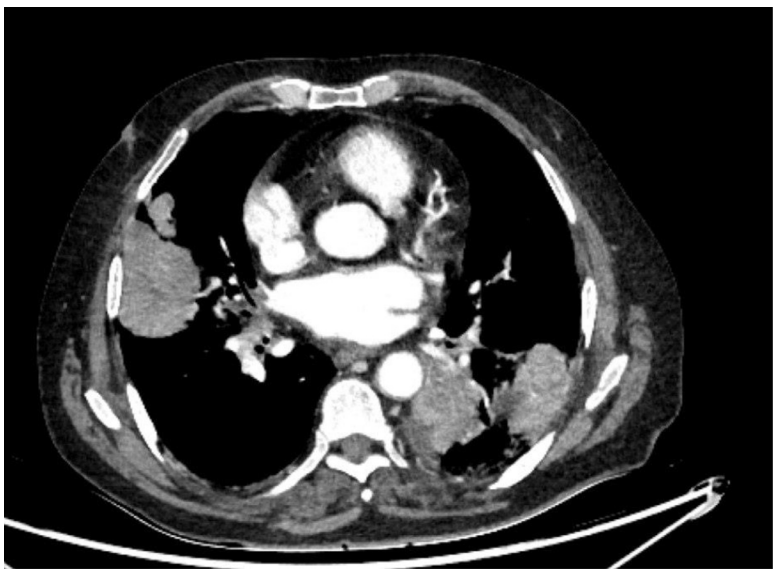

Fig. 2 – CECT showing few enhancing soft tissue density lesions in bilateral lung parenchyma.

ing neoadjuvant therapy and for surgical planning [11]. Positive expression of CD117 (c-kit) is the major diagnostic criteria with high sensitivity (95%) [10]. Rectal GISTs also show a high incidence of CD34 positivity (90%) [12]. Besides this, rectal GISTs occasionally show positive expression for PDGFRA, smooth muscle actin, S-100, and vimentin [13]. CD117, a c-kit protooncogene protein, is seen in almost all GISTs regardless of the site of origin, histologic appearance, and biologic behavior. Thus, its expression is considered to be best defining feature of GISTs [14]. Histopathology was also done in our case which showed features suggestive of spindle cell neoplasms but the definitive diagnosis was made on the basis of positive expression of the tumor cells for CD-117 on Immunohistochemistry analysis thus confirming the diagnosis of GIST. Management of rectal GISTs may be medical or surgical. Surgery is the mainstay of treatment for primary resectable GISTs. The choice of surgery depends on tumor size and location. The surgical options include local excision, anterior resection (sphincter preserving), and abdominoperineal resection [12]. Complete surgical resection with histologically negative margins is the standard curative procedure for localized tumors and is essential to prevent recurrence. Care must be taken to avoid intraoperative tumor rupture. Routine lymph node dissection is not needed because the tumors do not spread through lymphatics However, if lymph node involvement is suspected intraoperatively, routine lymph node dissection can be performed [15]. Local excision can be via transanal, trans-sacral, or transvaginal approach [3]. A preoperative chemoprophylaxis is recommended in abdominoperineal resection to obtain margin-negative resection [16]. Imatinib mesylate remains the standard therapy for advanced unresectable/metastatic GISTs. It is also recommended for tu-

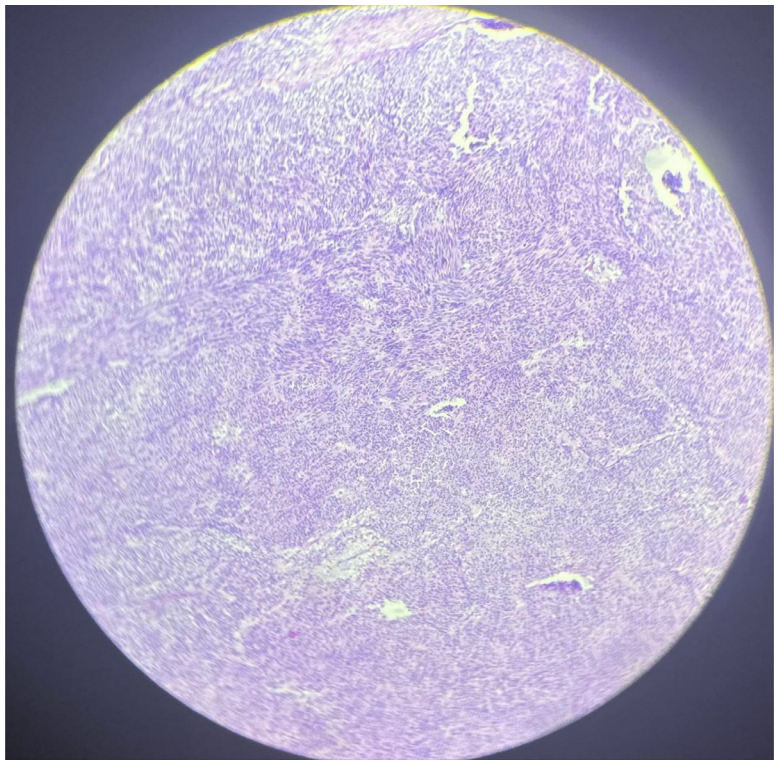

Fig. 3 – A 10 × magnification image with tumor cells arranged in fascicles and storiform pattern in H&E stain.

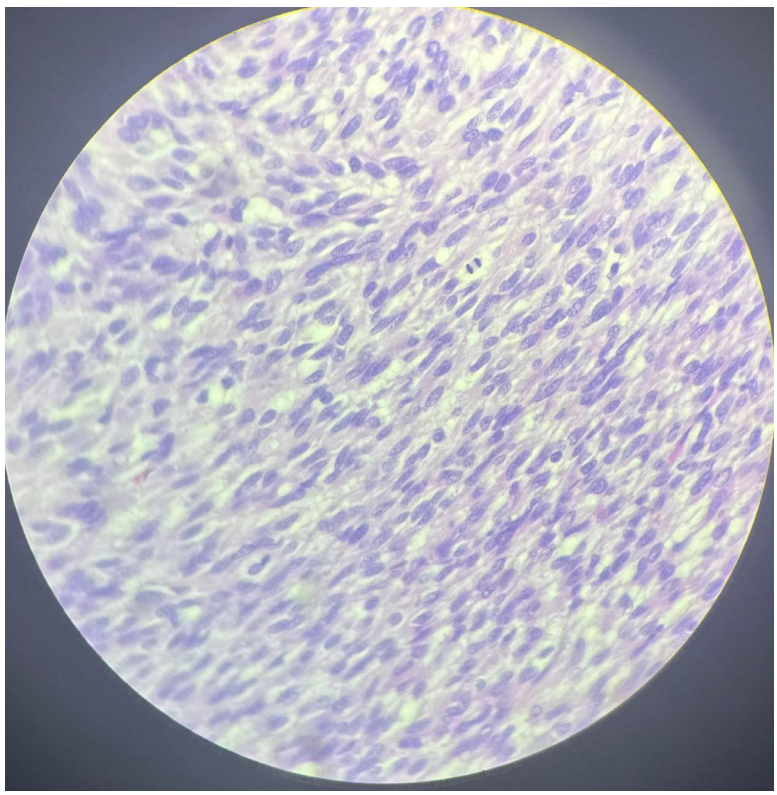

Fig. 4 – A 40 × magnification image with spindle cells showing elongated, blunt end nuclei with evenly distributed chromatin in H&E stain.

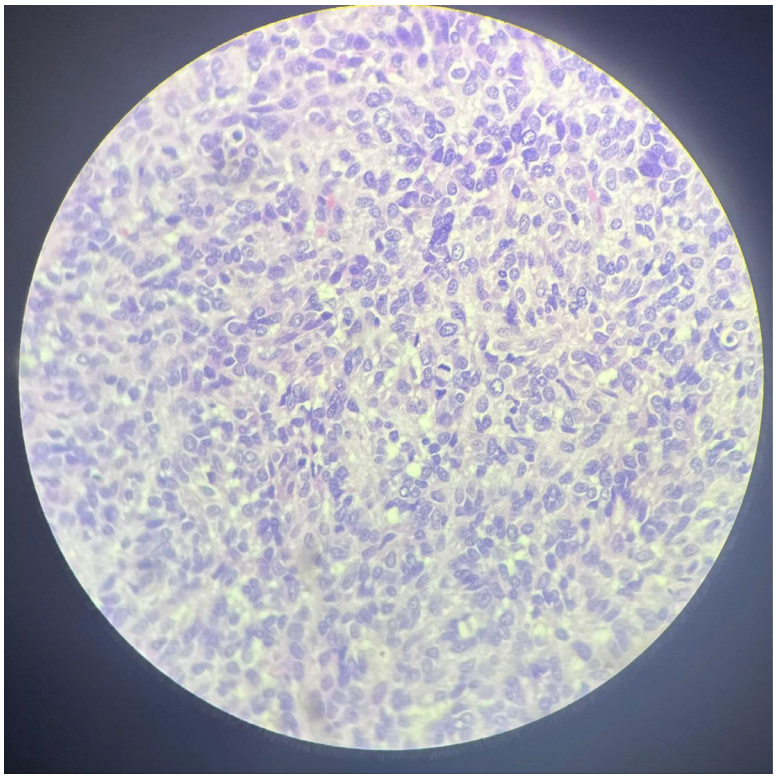

Fig. 5 – A 40 x magnification image showing epithelioid cells that are round with vesicular chromatin, visible nucleoli with abundant eosinophilia and clear cytoplasm in H&E stain.

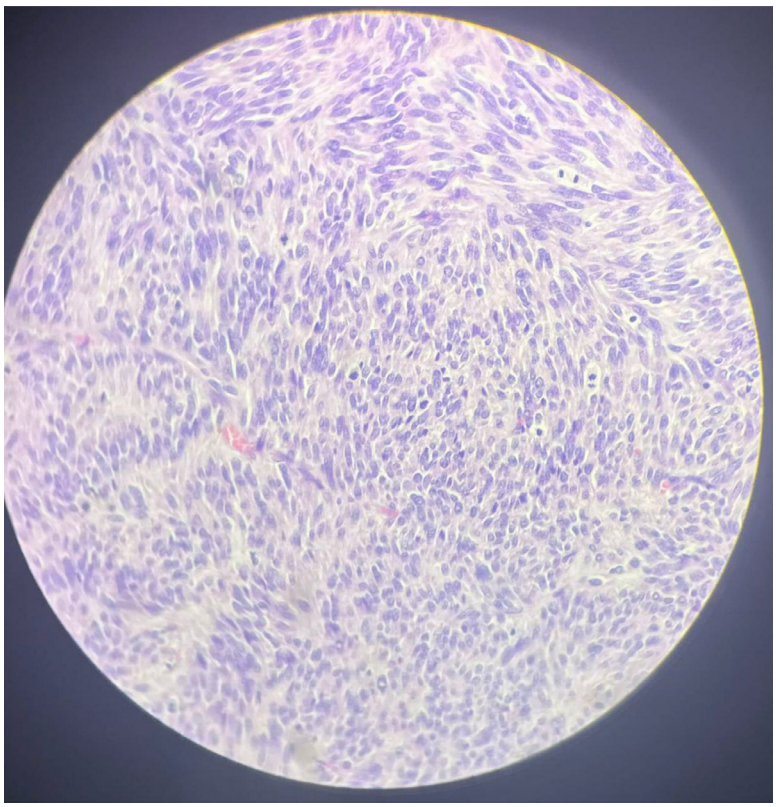

Fig. 6 – A 40 x magnification image showing frequent mitotic figures including atypical ones in H&E stain.

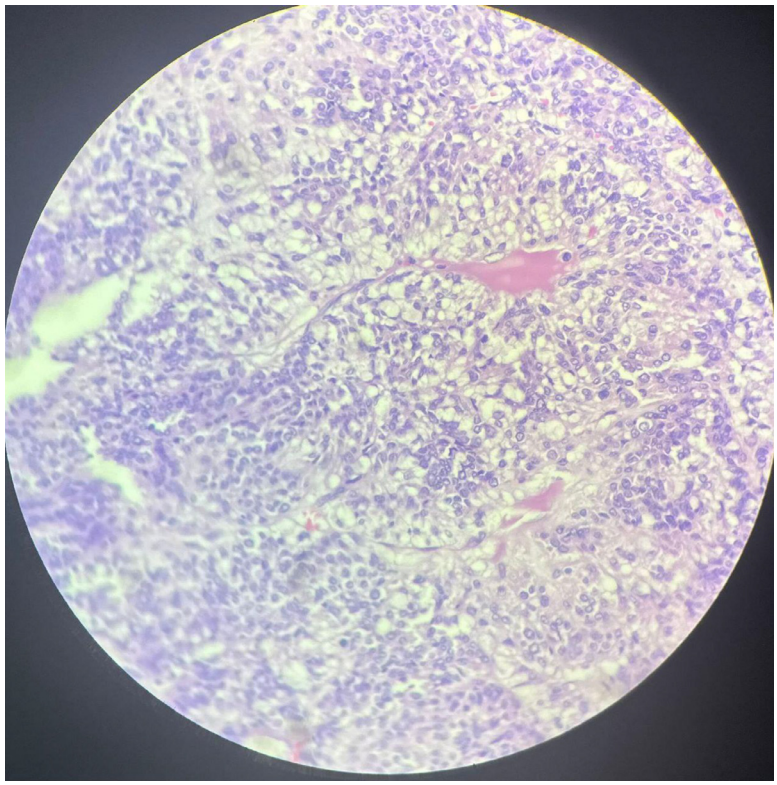

Fig. 7 – A 40 x magnification image showing some of the cells exhibiting cytoplasmic vacuoles pushing nucleus to the periphery imparting signet ring like appearance in H&E stains.

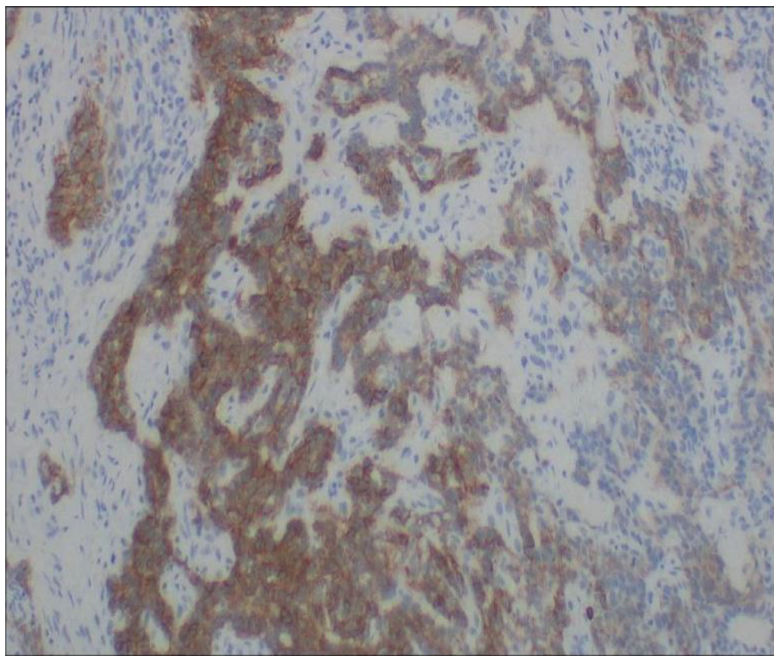

Fig. 8 – A 40 x magnification image with tumor cells showing positive expression for CD117 stain.

mors larger than 5 cm, in order to get a negative resection margin, which is an important factor for survival in rectal GISTs [17]. Imatinib Mesylate is a selective inhibitor of transmembrane receptor KIT protein tyrosine kinases which acts by inhibiting the proliferation of GIST cells that are stimulated by activated KIT receptors [3]. Because of the presence of metastatic lesions as observed in contrast-enhanced CT of our patient, he was planned to be treated with IM. The prognosis of the patients with GISTs depends upon the primary tumor site, tumor size, and mitotic count [5]. GISTs arising from the rectum are found to have a very high recurrence rate [3]. Also, tumors of size greater than 5 cm and with greater than 10 mitoses per high power field typically have a high rate of recurrence [5]. Therefore, long-term follow-up is needed for patients with rectal GISTs after treatment. CT or MRI should be performed every 3-6 months for the first 3-5 years after treatment, followed by annual imaging [18]. Because of the presence of metastasis of the tumor in our patient, he was kept under high suspicion for recurrence and was arranged a follow-up on a 3 monthly basis with reports of a contrast-enhanced CT scans of the abdomen and pelvis.

Conclusion

Rectal GIST although being rare, must be considered as a differential diagnosis in a patient presenting with defecatory problems with bleeding. Early suspicion and diagnosis using imaging, histopathological, and immunochemical analysis is needed for early recognition of the tumor. Management with Imatinib Mesylate is recommended for unresectable and metastatic tumors of rectal GISTs. Because of the high recurrence of the rectal GISTs, patients under chemotherapy must be kept under regular follow-up.

Ethical approval

The study is exempt from ethical approval in our institution.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Role of generative AI

None.

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