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CASE REPORT

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Adjuvant therapy for rare rectal gastrointestinal stromal tumors: A case report

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Key Clinical Message

Anorectal gastrointestinal stromal tumors are extremely rare, constituting less than 0.1% of rectal tumors. Surgical resection using a transanal wide excision followed by adjuvant therapy with tyrosine kinase inhibitors can be a successful treatment combination to remove the mass and prevent recurrence while preserving the integrity of the anal sphincter.

Abstract

Gastrointestinal stromal tumors (GISTs) are a rare subset of neoplasms, accounting for about 1%–2% of primary gastrointestinal malignancies. The stomach is the most common site for GISTs, with anorectal GISTs being exceptionally rare, representing only 0.1% of all rectal tumors. The standard approach for managing localized GIST involves complete surgical excision to achieve negative microscopic margins (R0) while preserving the tumor capsule and maintaining anal sphincter function. Surgical resection with transanal wide excision followed by adjuvant therapy using tyrosine kinase inhibitors can successfully remove the mass, prevent recurrence, and preserve the anal sphincter's integrity. Adjuvant therapy with imatinib is the recommended treatment for all localized GISTs assessed to have an intermediate or high risk of relapse. Here, we report a case of a 63-year-old male with a rectal GIST who underwent transanal wide excision followed by adjuvant therapy with tyrosine kinase inhibitors.

KEYWORDS

gastrointestinal stromal tumors, imatinib mesylate, rectal neoplasms, recurrence, tyrosine kinase inhibitors

1 | INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are a rare subset of neoplasms, accounting for approximately 1%–2% of primary gastrointestinal malignancies.[1,2] GISTs are believed to originate from interstitial cells of Cajal or their stem cell precursors, which are recognized for their substantial influence on the modulation of autonomic nerve activities and intestinal motility. Histologically, GISTs are predominantly characterized by spindle cells, with a minority demonstrating epithelioid characteristics. Mutations in the KIT proto-oncogene or PDGFRα

have been associated with the development of GISTs. CD117, an antigen linked to the KIT protein, is considered a specific diagnostic marker of GIST. A previous case study indicated that the majority of GIST cases were positive for CD117, with CD34 being the second most frequently detected marker.[3] GISTs have the potential to develop anywhere in the gastrointestinal tract, from the esophagus to the anus, and can affect the omentum and mesentery. The stomach is the most common location for GISTs, while anorectal GISTs are significantly rare. Rectal GISTs are infrequent, representing about 5% of all GIST cases and accounting for merely 0.1% of all rectal tumors.[4] The standard approach for managing localized GIST involves complete surgical excision to achieve negative microscopic margins (R0) while preserving the tumor capsule and maintaining anal sphincter function.[5,6] Lymphadenectomy is typically deemed unnecessary due to the low incidence of lymph node involvement.[6,7] Adjuvant therapy with imatinib is the recommended treatment for all localized GISTs that are determined to have an intermediate or high risk of relapse.[6,8] Here, we report a case of a 63-year-old male with a rectal GIST who underwent transanal wide excision followed by adjuvant therapy with tyrosine kinase inhibitors.

2 | CASE HISTORY/EXAMINATION

A 63-year-old male with no significant medical history visited our outpatient department for evaluation owing to persistent tenesmus and rectal pain over the past 6 months. Furthermore, he reported experiencing rectal pain, particularly following bowel movements. During digital examination, a solid, smooth, round, immovable, palpable rectal mass with intact mucosa about 30×15 mm (approximately 5 cm from the anal verge) was found. The patient had no family history of colon cancer and had not previously undergone a colonoscopy.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS AND TREATMENT)

Following a routine colonoscopy, a submucosal mass measuring approximately 30×15 mm was found on the left side (3–6 o'clock position), approximately 5 cm from the anal verge, as shown in Figure 1. Pelvic magnetic resonance imaging (MRI) with contrast was performed to further evaluate the lesion, revealing a necrotic tumor with

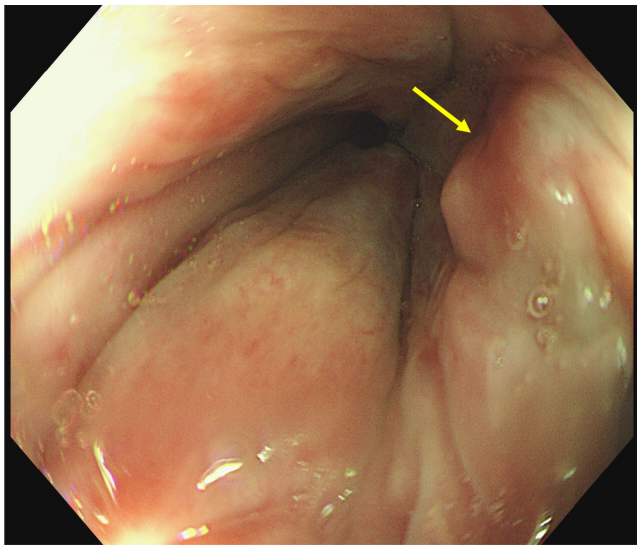

FIGURE 1 Colonoscopy reveals a submucosal rectal mass (yellow arrow) that is approximately 42×39 mm.

rim enhancement measuring 42×39 mm. Malignancy could not be ruled out, but no enlarged pelvic nodes were observed (Figure 2). Chest and abdominal computed tomography revealed no metastases. After discussion with the radiologist, a transanal approach was used to achieve negative margins and preserve the anal sphincter. Transanal wide excision was performed, and the mass was removed without breaching the capsule (Figure 3). Two 0-chromic catgut mattress sutures were subsequently placed into the incision of the rectum's muscular layer. The excised specimens were subsequently evaluated by histology. Histopathological and immunohistochemical results revealed a well-defined, encapsulated mass measuring 5×3×2.4 cm, with clear margins and positive staining for DOG 1 and CD117. The diagnosis of GIST was established. No evidence of vascular invasion existed. The mitotic index was significantly elevated with up to 21 mitoses per 50 high-power fields (HPFs) (Figure 4).

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

The patient's postoperative recovery was uneventful, and he was discharged on the second postoperative day. After extensive discussion among the multidisciplinary team and through collaborative decision-making with the patient, a treatment regimen featuring tyrosine kinase inhibitors was chosen. Adjuvant therapy with imatinib was prescribed at a dose of 400 mg/day because of a significantly elevated mitotic index, indicating a high risk of relapse.

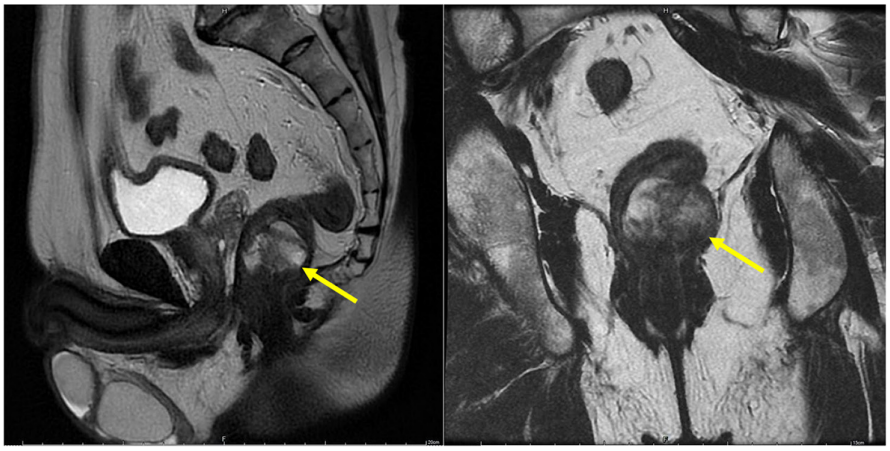

FIGURE 2 (Left: Sagittal plane; Right: Transverse plane) The results of pelvic magnetic resonance imaging reveal that the mass was in the rectum submucosa.

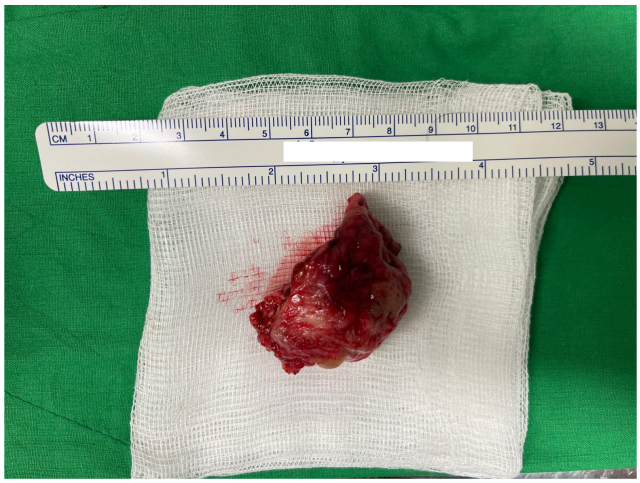

FIGURE 3 The resected mass is a complete capsule with fibrous and adipose tissue attached and tumor-free margins.

The MRI scans were scheduled every 3 months for the first few months. At the one-year follow-up, the patient remained in a favorable condition, and MRI, which was conducted to assess the potential for local recurrence, showed no signs of recurrence.

5 | DISCUSSION

Anorectal GISTs are extremely rare, accounting for only 2%–8% of all anorectal mesenchymal tumors and constituting less than 0.1% of all rectal tumors.[9] These tumors can either be asymptomatic or present with symptoms, such as rectal bleeding, abdominal pain, constipation, anal discomfort, and urinary issues.[5,7]

Mitotic index, tumor size, tumor location, and tumor rupture were the four distinct independent prognostic factors for GISTs. Furthermore, the occurrence of tumor rupture should be evaluated separately to distinguish between preoperative and intraoperative events. Certain stratification systems have integrated the factors of tumor rupture, which are associated with a significantly higher risk of recurrence.[10] Surgery is the only acknowledged treatment modality capable of delivering a sustained cure for GISTs. Consequently, several risk stratification tools have been developed for prognostic assessment. For example, the 2017 American Joint Committee on Cancer guidelines for staging GISTs include tumor size categories (≤2 cm, 2–5 cm, 5–10 cm, and >10 cm) and mitotic rate (≤5 mitoses or >5 mitoses per 50 HPFs). These criteria are essential to evaluate the probability of disease progression.[11] GISTs are known for their highly aggressive nature. Tumors measuring <2 cm and exhibiting a mitotic index exceeding 5 mitoses per 50 HPFs are associated with an increased risk of recurrence and malignant potential.[12]

The standard procedure for managing a localized rectal GIST involves complete surgical removal with the goal of achieving negative microscopic margins (R0) and preserving the intact tumor capsule while maintaining the integrity of the anal sphincter.[6,13] The surgical approach for anorectal GISTs depends on multiple factors, including the size and location of the tumor (especially its distance from the dentate line) and the individual characteristics of the patient. Potential surgical options include minimally invasive techniques such as transanal, transvaginal, and transsacral excisions, as well as complete excision through low anterior or abdominoperineal resection.[14]

Thus, a sphincter-saving approach is recommended for the treatment of rectal GISTs. In cases of small lower rectal tumors (up to 3 × 3 cm) with minimal invasion beyond the rectum, the preferred surgical approach is the transanal option. Conversely, if the tumor size exceeds 5 cm or shows a significant degree of extra-rectal growth, the transrectal approach is considered nonviable.[15] In cases where abdominoperineal resection is deemed necessary to achieve a negative resection margin, preoperative administration of imatinib should be

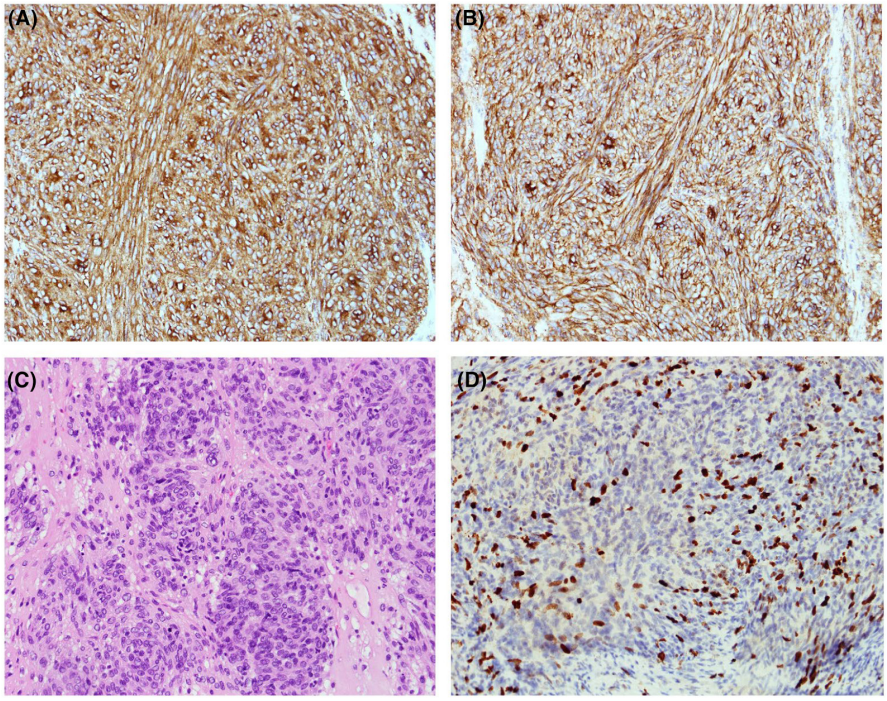

FIGURE 4 (A, B) Immunohistochemical stains show that tumor cells are positive for CD117 and DOG1 (200× magnification). (C) Histopathology: The specimen exhibits bland spindle cells with a faintly eosinophilic cytoplasm arranged in a syncytial pattern. The nuclei are elongated with inconspicuous nucleoli, and artifactual paranuclear vacuoles are frequently observed in GISTs of the stomach. These subtypes include sclerosing, palisaded, vacuolated, diffuse hypercellular, and sarcomatoid features with significant nuclear atypia and increased mitotic activity. (200× magnification). (D) Ki67 staining reveals frequent mitosis with 21 mitoses per 50 high-power fields (HPF). (200× magnification).

contemplated.[12] Administration of imatinib, both preoperatively and postoperatively, has rendered patients eligible for transrectal surgery. This is attributed to its numerous inherent therapeutic advantages, including reduction of tumor size, mitigation of mitotic activity, and a decrease in recurrence rates. Furthermore, it enhances the quality of life by preserving anal function and obviating the need for permanent colostomy. A cohort study was conducted to observe 19 patients with rectal GISTs, revealing that nine of the patients underwent a combined treatment comprising neoadjuvant imatinib followed by surgical tumor resection. None of the nine patients exhibited any indications of disease recurrence.[16] The benefits of imatinib as an adjuvant therapy for GISTs are widely acknowledged, and it has emerged as an established treatment regimen for patients deemed to be at an intermediate to high risk of recurrence.[17] In a comprehensive context, imatinib is prescribed for patients who have been diagnosed with GISTs, especially those with a tumor size exceeding 3 cm and a high mitotic rate, consisting of more than five mitoses per 50 HPFs. These observations were validated in a double-blind, placebo-controlled, randomized trial involving patients diagnosed with KIT-positive GIST and tumors with a minimum diameter of 3 cm. The trial demonstrated a notable enhancement in recurrence-free survival when imatinib was used compared with a placebo. In the case of mutational subtypes, such as KIT mutations in exons 11 and 9, and wild-type GIST, imatinib demonstrated no efficacy in delaying recurrence.[18] A systematic review conducted in August 2022 encompassing patients with rectal GISTs located throughout the gastrointestinal tract indicated that individuals who received imatinib therapy before surgical resection had improved overall survival rates compared with those who underwent surgical resection without prior chemotherapy. Nevertheless, the survival rates without disease were similar in both groups.[19]

In our case, after a multidisciplinary discussion with radiology specialists, we determined that excision of the mass with an intact capsule was feasible following a transanal wide excision. Due to the significantly elevated mitotic index, imatinib 400 mg/day was prescribed. However, the ideal duration of adjuvant imatinib treatment remains uncertain. The existing data provide support for adjuvant imatinib treatments lasting for at least 3 years. The PERSIST study demonstrated the viability of 5-year adjuvant imatinib therapy with no indication of relapse in

patients with imatinib-sensitive GIST.[20] Further clinical trials are required to determine the optimal duration of adjuvant imatinib therapy.

Rectal GISTs are infrequent, representing about 5% of all GIST cases and accounting for merely 0.1% of all rectal tumors. Low rectal GIST can be considered for transanal wide excision if achieving negative microscopic margins (R0) and preserving the intact tumor capsule while maintaining the integrity of the anal sphincter are feasible. Although the mitotic index was significantly elevated, with up to 21 mitoses per 50 high-power fields (HPFs), indicating a high recurrence rate. Transanal wide excision with negative margins, followed by adjuvant therapy with imatinib, can prevent relapse.

AUTHOR CONTRIBUTIONS

Ting-Yi Chu: Visualization; writing – original draft; writing – review and editing. **Ta-Wei Pu:** Conceptualization; methodology; project administration; supervision. **Chao-Yang Chen:** Conceptualization; methodology; project administration; resources; supervision.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

1. Miettinen M, Lasota J. Gastrointestinal stromal tumors – definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. *Virchows Arch*. 2001;438(1):1-12. doi:10.1007/s004280000338
2. Beltran MA, Cruces KS. Primary tumors of jejunum and ileum as a cause of intestinal obstruction: a case control study. *Int J Surg*. 2007;5(3):183-191. doi:10.1016/j.ijsu.2006.05.006
3. Sarlomo-Rikala M, Kovatich AJ, Barusevicius A, Miettinen M. CD117: a sensitive marker for gastrointestinal stromal tumors that is more specific than CD34. *Mod Pathol*. 1998;11(8):728-734.
4. Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. *Arch Pathol Lab Med*. 2006;130(10):1466-1478. doi:10.5858/2006-130-1466-gstrom
5. Kelley KA, Byrne R, Lu KC. Gastrointestinal stromal tumors of the distal gastrointestinal tract. *Clin Colon Rectal Surg*. 2018;31(5):295-300. doi:10.1055/s-0038-1642053
6. Zhou Z, Chen Z, Chen M, Wang R, Yin Y, Yao Y. Clinicopathologic factors predicting outcomes in patients with gastrointestinal stromal tumors of the rectum and colon. *Tumour Biol*. 2014;35(5):4357-4362. doi:10.1007/s13277-013-1572-7
7. Centonze D, Pulvirenti E, Pulvirenti D'Urso A, Franco S, Cinardi N, Giannone G. Local excision with adjuvant imatinib therapy for anorectal gastrointestinal stromal tumors. *Tech Coloproctol*. 2013;17(5):571-574. doi:10.1007/s10151-013-0976-0
8. Karthikeyan M, Kolandasamy C, Naganath Babu OL. Malignant gastrointestinal stromal tumor of rectum: a case report and review of literature. *Surg J (N Y)*. 2022;8(1):e60-e64. doi:10.1055/s-0042-1742778
9. Grassi N, Cipolla C, Torcivia A, et al. Gastrointestinal stromal tumour of the rectum: report of a case and review of literature. *World J Gastroenterol*. 2008;14(8):1302-1304. doi:10.3748/wjg.14.1302
10. Nishida T, Cho H, Hirota S, Masuzawa T, Chiguchi G, Tsujinaka T. Clinicopathological features and prognosis of primary GISTs with tumor rupture in the real world. *Ann Surg Oncol*. 2018;25(7):1961-1969. doi:10.1245/s10434-018-6505-7
11. Edge SB, Compton CC. The American joint committee on cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol*. 2010;17(6):1471-1474. doi:10.1245/s10434-010-0985-4
12. Network NCC. NCCN Guidelines Version 1.2023: gastrointestinal stromal tumors.
13. Corless CL, Barnett CM, Heinrich MC. Gastrointestinal stromal tumours: origin and molecular oncology. *Nat Rev Cancer*. 2011;11(12):865-878. doi:10.1038/nrc3143
14. Brucchi F, Lauricella S, Bottero L, Faillace GG. Anal canal gastrointestinal stromal tumour (GIST). *BMJ Case Rep*. 2023;16(4):e255040. doi:10.1136/bcr-2023-255040
15. Gervaz P, Huber O, Morel P. Surgical management of gastrointestinal stromal tumours. *Br J Surg*. 2009;96(6):567-578. doi:10.1002/bjs.6601
16. Wilkinson MJ, Fitzgerald JE, Strauss DC, et al. Surgical treatment of gastrointestinal stromal tumour of the rectum in the era of imatinib. *Br J Surg*. 2015;102(8):965-971. doi:10.1002/bjs.9818
17. Laurent M, Brahmi M, Dufresne A, et al. Adjuvant therapy with imatinib in gastrointestinal stromal tumors (GISTs)-review and perspectives. *Transl Gastroenterol Hepatol*. 2019;4:24. doi:10.21037/tgh.2019.03.07
18. Dematteo RP, Ballman KV, Antonescu CR, et al. Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double-blind, placebo-controlled trial. *Lancet*. 2009;373(9669):1097-1104. doi:10.1016/s0140-6736(09)60500-6
19. Liu Z, Zhang Z, Sun J, et al. Comparison of prognosis between neoadjuvant imatinib and upfront surgery for GIST:

a systematic review and meta-analysis. *Front Pharmacol*. 2022;13:966486. doi:10.3389/fphar.2022.966486

20. Raut CP, Espat NJ, Maki RG, et al. Efficacy and tolerability of 5-year adjuvant imatinib treatment for patients with resected intermediate- or high-risk primary gastrointestinal stromal tumor: the PERSIST-5 clinical trial. *JAMA Oncologia*. 2018;4(12):e184060. doi:10.1001/jamaoncol.2018.4060

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