



Jejunojejunal intussusception with chronic bleeding caused by gastrointestinal stromal tumor: a case report and literature review

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Background: Intussusception is a rare clinical condition in adults. The majority of patients present with symptoms of bowel obstruction. Intussusception is often misdiagnosed and the majority of cases are diagnosed intraoperatively. In this paper, we present a rare case of adult jejunojejunal intussusception with chronic bleeding caused by a gastrointestinal stromal tumor (GIST). We emphasize the role of contrast-enhanced computed tomography (CT) and enteroscopy in the presurgical diagnosis and the good prognosis in the high-risk GIST patient after surgery and targeted therapy.

Case Description: Herein, we present the case of a 63-year-old female patient with small bowel intussusception with chronic bleeding caused by a GIST. Her main symptoms were intermittent melena and progressive anemia. She had a 20-year history of hypertension and had never undergone previous abdominal surgery. After failure of an esophagogastroduodenoscopy and colonoscopy to locate the hemorrhagic foci in the gastrointestinal tract, contrast-enhanced CT and enteroscopy were used and a small bowel intussusception and an intraluminal mass with a bleeding ulcer was identified. The patient underwent laparoscopic partial small bowel resection, and postoperative pathological examinations showed a small intestinal GIST with a high risk of recurrence. It was suggested that the patient take imatinib regularly for at least 3 years. At the time of writing, she has remained in good health without relapse for 24 months after discharge. We also review 20 published cases of intussusception caused by small bowel GIST in the PubMed database.

Conclusions: Obscure gastrointestinal hemorrhage needs meticulous examinations to promptly determine the cause and location of bleeding. This case and literature review revealed that comprehensive surgical resection-centered treatment was the standard treatment for primary localized GISTs in patients at significant risk of relapse.

Keywords: Intussusception; gastrointestinal stromal tumor; severe anemia; case report

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Introduction

Intussusception rarely occurs in adults, with an annual incidence of approximately 2–3 per million people (1,2). Unlike pediatric intussusception cases, 90% of which are idiopathic, most adult intussusception cases are secondary to benign or malignant neoplasms such as gastrointestinal stromal tumors (GISTs) (1). However, GISTs comprise less than 0.2% of all gastrointestinal tumors and only 0.04% of small intestinal tumors (3). Gastrointestinal bleeding is a frequent symptom of GISTs (4), while only 5% of all gastrointestinal bleeding occurs in the small bowel (5). These small bowel lesions are usually difficult to find and subject to late diagnosis, leading to treatment delays. Herein, we present a rare case of adult small bowel intussusception with chronic bleeding caused by a GIST. We emphasize the role of contrast-enhanced computed tomography (CT) and enteroscopy, which allowed presurgical visualization of the lesion, and the good prognosis in the patient with high-risk GIST after surgery and targeted therapy. We present the following case in accordance with the CARE reporting checklist (6) (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-22-301/rc>). In addition, we performed a literature search and review of case reports of small bowel intussusception caused by GISTs.

Case presentation

A 63-year-old Chinese woman presented to the Department of General Surgery, Strategic Support Force Medical Center in January 2020 with intermittent melena and anemia without an obvious cause for 9 months. In early April 2019, the patient had begun to pass recurring tarry stools without mucus or pus, unaccompanied by abdominal pain, jaundice, fever, hematemesis, nausea, or vomiting. Tests at a district hospital returned a hemoglobin level (Hb) of 80.0 g/L and a mean corpuscular hemoglobin (MCH) level of 24.2 pg. Her fecal occult blood test returned positive. Esophagogastroduodenoscopy (EGD) and colonoscopy showed no gastrointestinal pathology to account for the bleeding. After pharmacological treatment, the melena improved in the short-term but later reappeared. In January 2020, the patient's blood routine was retested due to increasing fatigue and dyspnea. Her Hb at this time was 55.0 g/L, and her MCH was 17.6 pg. The patient had a 20-year history of hypertension and had never undergone previous abdominal surgery. All procedures performed in



Figure 1 CT scan showing a target sign at the jejunum. CT, computed tomography.

this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

She was admitted to Strategic Support Force Medical Center for further diagnosis and treatment. Her pulse and blood pressure were normal, but she had a deficient nutritional status with pale skin and mucous membranes. A physical examination revealed mild tenderness around the umbilicus with no abdominal muscle tension, rebound pain, or mass. Bowel sounds were slightly active, about 6–7 times per minute. Blood analysis showed an Hb of 48.2 g/L, an MCH of 17.6 pg, and normal platelet levels. Blood biochemistry and coagulation indicators were normal. Abdominal CT revealed a jejunal intussusception (*Figure 1*).

Continued blood transfusion restored the patient's Hb to 94.0 g/L and provided safe conditions for further invasive examination and treatment. A small bowel enteroscopy revealed a protrusive mass of about 3.5 cm × 4.0 cm in the small intestine, 50 cm from the pylorus, with an ulcer at the top covered with white moss (*Figure 2A*). After identification of the bleeding lesion, the patient underwent an immediate laparoscopic partial small bowel resection. Intraoperative exploration revealed a palpable small intestinal mass about 50 cm from the Treitz ligament. The proximal section of the small intestine with the mass was inserted into the distal bowel, which had formed an intussusception (*Figure 2B*).

Gross examination of the surgical specimen revealed a greyish-white soft tissue mass, measuring about 3 cm × 4 cm, with a brown area of hemorrhage and a mucosal ulcer on the tumor surface (*Figure 3A*). Histopathological

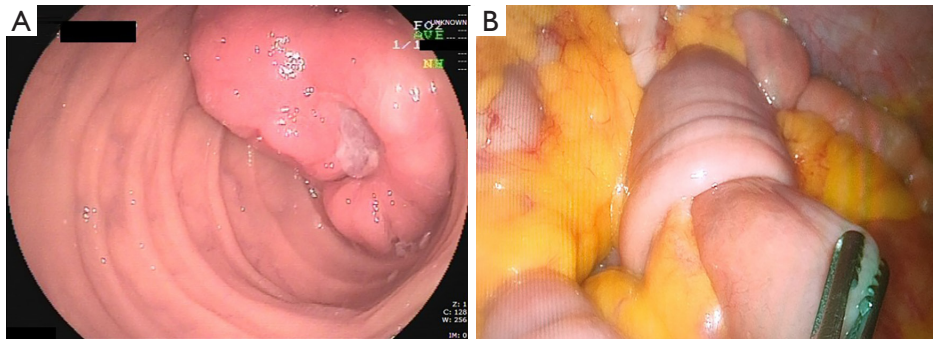


Figure 2 Enteroscopy and laparoscopic exploration. (A) Preoperative enteroscopy showing an intraluminal mass with an ulcer at the top; (B) intraoperative photograph of the jejunojejunal intussusception.

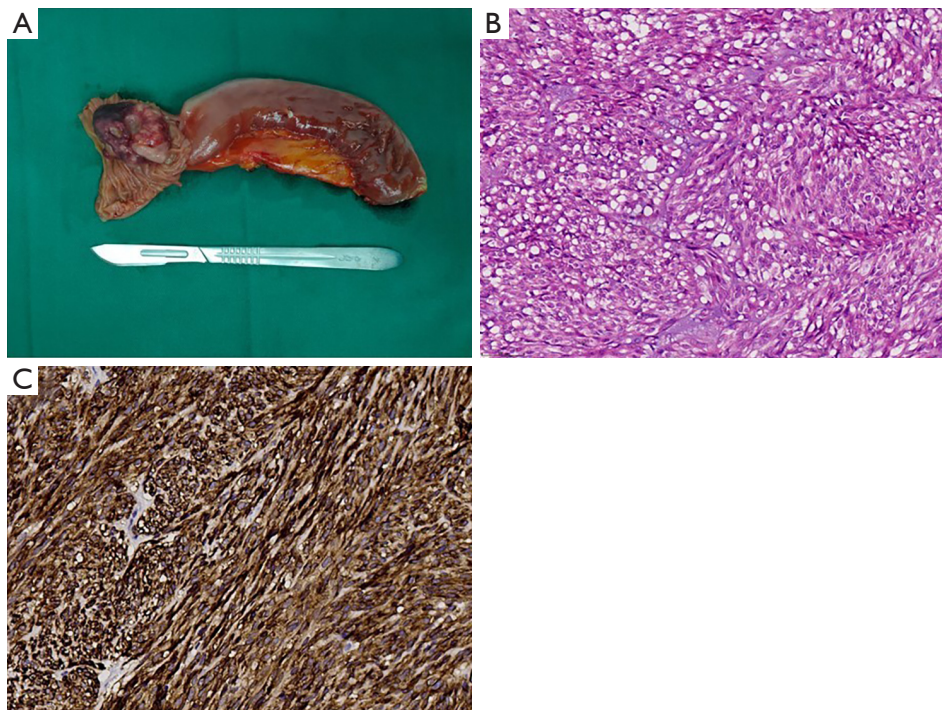


Figure 3 Gross and microscopic features of the surgical specimen. (A) Surgically resected portion of the jejunum containing an intraluminal mass; (B) H&E staining demonstrating spindle cells ($\times 200$); (C) IHC staining showing CD117 positive cells ($\times 200$). H&E, hematoxylin and eosin; IHC, immunohistochemical.

examination [hematoxylin and eosin (H&E) stain, $\times 200$] showed a small intestinal spindle cell neoplasm from the mucosa to the deep muscularis (*Figure 3B*). There were more than 10 mitoses per 50 high-power fields (HPF). The surgical margin was negative, and there was no obvious intravascular tumor thrombus or nerve invasion. Immunohistochemical (IHC) staining showed that the

tumor was diffusely positive for CD117 (KIT), DOG1, and CD34 but negative for smooth muscle actin, desmin, and S100 (*Figure 3C*). Accordingly, the diagnosis of a high-risk small bowel GIST was made.

The patient recovered without complications and was discharged on the 17th postoperative day. The patient started taking imatinib besylate (400 mg per day) 1 month

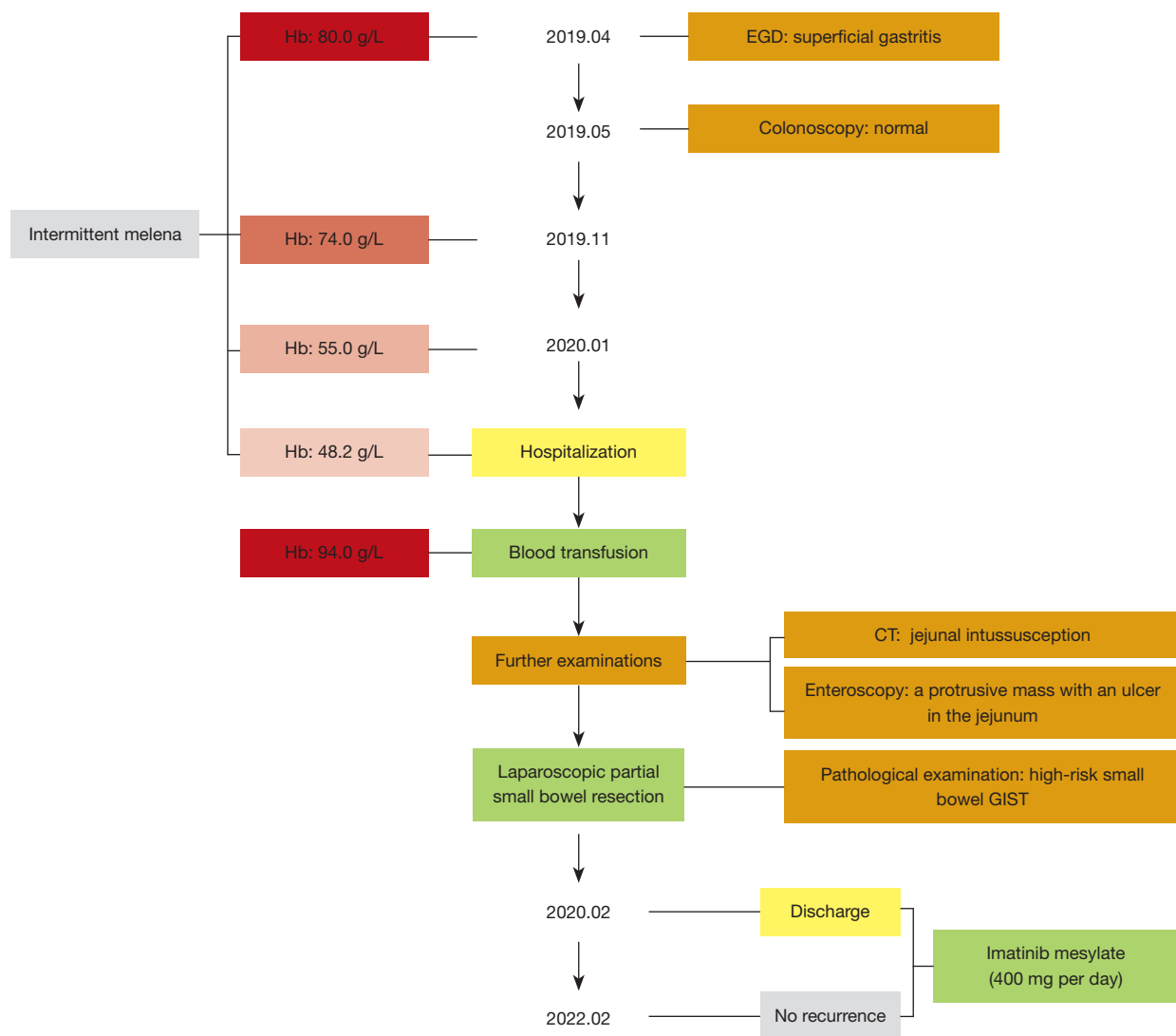


Figure 4 Disease course and treatment response. Hb, hemoglobin level, EGD, esophagogastroduodenoscopy; CT, computed tomography; GIST, gastrointestinal stromal tumor.

after surgery due to the high risk of recurrence. It was suggested that if no severe adverse reaction occurred, she should continue to use the drug for at least 3 years. Currently, we are conducting regular follow up by phone. At the time of writing, the patient is still taking imatinib regularly and has remained relapse-free for 24 months post-discharge. No adverse reactions to the targeted drug have been observed so far. She has expressed great satisfaction with the results of her surgery and targeted therapy. A timeline is shown in *Figure 4*.

Discussion

Intussusception is the telescoping or invagination of the proximal part of the gastrointestinal tract (intussusceptum) into an adjacent section (intussuscipiens). Adult intussusception is uncommon, accounting for 5% of all intussusception cases (2). The main etiologies of adult intussusception are various underlying intestinal lesions, such as inflammatory bowel disease, postoperative adhesions, Meckel's diverticulum, and benign and malignant tumors (7). Adult intussusception is an indication for surgical resection.

Intussusception caused by GISTs is rare because most GISTs are sporadic and tend to grow in an extraluminal fashion (8). The GISTs probably originate from the interstitial cells of Cajal or their cellular progenitors, which are responsible for regulating peristalsis and serve as pacemakers in the gastrointestinal tract (9). It has been reported that small bowel GISTs present less frequently than gastric GISTs, but carry a higher malignancy (10).

The GISTs are the most common primary mesenchymal tumors of the gastrointestinal tract and possess a wide range of malignant potential (10). They occur most frequently in the stomach (55.6%) and small intestine (31.8%) (11). Most GISTs seem to be sporadic, and risk factors are poorly understood. However, some GISTs might be associated with specific tumor syndromes, such as familial GIST, Carney's triad, Carney-Stratakis syndrome, or type 1 neurofibromatosis (NF1) (9). The primary symptoms are usually nonspecific, including abdominal pain, gastrointestinal bleeding, and anemia. Other symptoms may include dyspepsia, nausea or vomiting, constipation or diarrhea, frequent urination, and fatigue (9). Sometimes, GISTs irritate and alter normal peristaltic activity, triggering an intraluminal invagination and finally causing an intussusception (12). Endoscopy is recommended as the primary diagnostic modality for symptoms such as hematochezia or melena. When a source is not found after a routine endoscopy, further diagnostic workup includes repeat testing and evaluation of the small bowel, often using enteroscopy and wireless capsule endoscopy. In addition, endoscopic ultrasound, contrast-enhanced CT, or magnetic resonance imaging (MRI), and interventional angiography can help to locate the bleeding point and primary lesion. In the abovementioned case, the primary symptoms of the patient were anemia and melena. As both the EGD and colonoscopy were negative, the possibility of a small bowel bleeding lesion was considered. Abdominal contrast-enhanced CT and enteroscopy were subsequently performed, and small bowel intussusception and a bleeding lesion were confirmed.

Surgery is the primary therapeutic option for a GIST, with the goal being complete resection for non-metastatic tumors. Lymph node metastases are rare (prevalence is about 1%) and routine removal of the lymph nodes is typically unnecessary (4). Age, comorbidity, performance status, tumor location, size, and resection margin should be considered when selecting the type of surgical resection for GISTs. A small bowel GIST is usually resected with a bowel segment.

The pathologic diagnosis of a GIST mainly depends on IHC characteristics. More than 95% of GISTs are positive

for CD117 (KIT) and/or DOG1 (13). If the tumor cells are negative for CD117 and DOG1 in highly suspicious cases, mutational analysis for the KIT or platelet-derived growth factor receptor alpha (PDGFRA) gain-of-function mutations may help to confirm the diagnosis of a GIST. Moreover, mutation detection has important significance in guiding targeted therapy and prognostic assessment for patients with this type of tumor. The European Society for Medical Oncology, European Reference Network for Rare Adult Solid Cancers, and European Reference Network for Genetic Tumor Risk Syndromes Clinical Practice Guidelines (ESMO-EURACAN-GENTURIS CPGs) recommend that mutational analysis be considered as a routine examination in the diagnostic workup of all GISTs (4). However, 10–15% of GISTs do not have a detectable KIT or PDGFRA mutation. These are called wild-type GISTs and include GISTs in NF1, Carney-Stratakis syndrome, Carney's triad, BRAF mutation, succinate dehydrogenase (SDH) subunit mutations (SDHA, SDHB, SDHC, SDHD), and RAS-family mutations (HRAS, NRAS, KRAS) (9). The immunoreactivity of SDHB can be used to identify SDH-deficient GISTs (14). In GISTs, the mitotic index has more important prognostic significance than Ki-67 analysis. The tumor in our case exhibited diffuse CD117 and DOG1 positivity. The mitotic index indicated that the patient was at high risk of early recurrence. Imatinib mesylate, an oral tyrosine kinase inhibitor, has been taken by the patient for 24 months to date to prevent recurrence after surgery, and she remains in good health without relapse at the time of writing.

We searched PubMed with the search terms "intussusception", "small bowel" and "gastrointestinal stromal tumor" to identify relevant studies. Only 20 cases of intussusception caused by small bowel GISTs have been reported (*Table 1*). Of the 21 patients (including our case), 12 were female, and 9 were male. The age of the patients ranged from 6 to 91 years, with a median age of 55 years. The median size of the maximum tumor diameter was 4 cm (1.5–15 cm). A total of 13 patients (62%) presented with melena or hematochezia on admission. The data showed that 95% (n=20) were CD117-positive, and 5% (n=1) were CD117-negative. All patients underwent curative surgery, and 6 patients were treated with imatinib after surgery. A 79-year-old woman with an ileoileal intussusception secondary to a terminal ileum GIST underwent resection of the neoplastic segment and a wide mesenteric lymphadenectomy (16). The pathology report showed all identified mesenteric lymph nodes were

Table 1 General characteristics of 20 cases of intussusception due to small bowel GIST reported in the literature

Author	Country/region	Year	Patient age (years)	Gender	Presentation	Surgical approach	Tumor size (cm)	c-Kit/CD117, mitotic index (mitosis/50 HPF)	Adjuvant therapy	Follow-up (months), recurrence
Hoshino et al. (15)	Japan	2000	42	F	Anemia, massive melena, abdominal pain	Partial small bowel resection	3	Positive, 5-8	No	11, no recurrence
Vasiladis et al. (16)	Greece	2008	79	F	Lower abdominal colicky pain, abdominal distension, nausea, vomiting, constipation	Partial small bowel resection, wide mesenteric lymphadenectomy	2.2	Positive, 7-8	No	7, no recurrence
Menendez-Sanchez et al. (17)	Spain	2009	55	F	Abdominal pain, rectal bleeding	Partial small bowel resection	5	Positive, NR	No	NR, no recurrence
Theodoropoulos et al. (8)	Greece	2009	45	M	Abdominal pain, vomiting, obstipation, abdominal distention	Partial small bowel resection	6	Positive, NR	NR	14, no recurrence
Rabbani et al. (18)	Morocco	2010	59	F	Abdominal distension and pain, obstipation, vomiting	Partial small bowel resection	NR	Positive, NR	NR	NR
Wall et al. (19)	UK	2010	36	F	Collapse, melena,	Pancreaticoduodenectomy	15	Positive, NR	No	NR, no recurrence
Ku et al. (20)	Taiwan	2011	39	F	Melena, anemia	Partial small bowel resection	1.5	Positive, NR	NR	NR
Dhull et al. (21)	India	2011	38	M	Abdominal pain	Partial small bowel resection	15	Positive, 6	Yes	6, no recurrence
Sam et al. (22)	Canada	2011	50	M	Intermittent melena, mild cramping abdominal pain, anemia	Partial small bowel resection	2.5	Positive, 0	No	6, no recurrence
Gupta et al. (23)	India	2011	59	M	Abdominal pain, distension, vomiting, constipation	Partial small bowel resection	NR	Positive, NR	Yes	NR
Bhanvadia et al. (24)	India	2012	75	F	Abdominal pain, vomiting, abdominal distention, constipation	Partial small bowel resection	4.5	Negative, >5	NR	NR
Gunaydin et al. (25)	Turkey	2012	6	F	Abdominal pain, vomiting	Partial small bowel resection	2.5	Positive, 2-3	No	14, no recurrence
Basu et al. (26)	India	2014	46	F	Abdominal pain, abdominal distension, anorexia, vomiting, constipation	Partial small bowel resection	4	Positive, 6	Yes	24, no recurrence
Chen et al. (27)	China	2014	34	F	Abdominal pain, melena	Partial small bowel resection	2.5	Positive, NR	NR	NR
Sadeghi et al. (5)	UK	2015	68	M	Melena, anemia, abdominal pain and distension, vomiting and constipation	Partial small bowel resection	4	Positive, 0-1	Yes	NR, no recurrence
Sankey et al. (28)	UK	2015	70	M	Abdominal pain, nausea, vomiting, constipation, melena, anemia	Partial small bowel resection	4	Positive, NR	Yes	3, no recurrence
Rahimi et al. (29)	USA	2016	77	M	Abdominal discomfort, vomiting, melena, syncope, anemia	Laparoscopic small bowel resection	3	Positive, 1-2	NR	NR
Fujimoto et al. (30)	Japan	2019	91	F	Vomiting, anorexia, anemia, hypoproteinemia	Palliative segmental duodenectomy	4	Positive, 20	NR	6, no recurrence
Kim et al. (3)	South Korea	2019	51	M	Massive hematochezia, hypotension, abdominal pain, anemia	Partial small bowel resection	3.5	Positive, <5	NR	2, no recurrence
Burch et al. (31)	India	2021	76	M	Melena	Laparoscopic small bowel resection	NR	Positive, NR	NR	NR
Our case	China	2022	63	F	Melena, anemia	Partial small bowel resection	4	Positive, >10	Yes	24, no recurrence

GIST, gastrointestinal stromal tumor; F, female; M, male; NR, not reported; HPF, high-power field; USA, United States of America; UK, United Kingdom.

negative for malignancy. Wall *et al.* (19) reported the case of a 36-year-old woman with a 15-cm GIST in the second part of the duodenum who underwent pylorus-preserving pancreaticoduodenectomy due to the large size of the tumor and inseparable adhesion to the head of the pancreas. A 91-year-old Japanese woman with a GIST in the third portion of the duodenum received a segmental duodenectomy without reduction of the intussusception but did not undergo a pancreaticoduodenectomy due to her age and performance status (30). All other patients (including our patient) underwent a curative partial small bowel resection. The median follow-up period of all patients was 7 months (2–24 months), and no tumor recurrences were reported.

The strengths of our case were listed as follows. Firstly, among the various gastrointestinal bleeding pathologies, small intestinal bleeding is uncommon, and adult jejunojejunal intussusception with gastrointestinal bleeding caused by a small intestinal GIST is extremely rare. Secondly, timely diagnoses of small bowel intussusception and bleeding tumor were made after contrast-enhanced CT and enteroscopy. After surgical resection and adjuvant targeted therapy, the high-risk GIST patient got a favorable prognosis. Among 20 cases of intussusception caused by small bowel GISTs reported, only one had a disease-free survival time of 24 months (22), and our case had a higher mitotic index (>10 *vs.* 6 mitosis/50 HPF). There are several limitations of this study: this is a case report, so the findings cannot be generalized. Besides, genetic analysis was not performed to further clarify the specific classification. More cases should be collected, and deeper studies should be done.

In summary, adult jejunojejunal intussusception with chronic gastrointestinal bleeding caused by a small intestinal GIST is very rare. If both EGD and colonoscopy fail to find the hemorrhage foci in the gastrointestinal tract, contrast-enhanced CT and enteroscopy can be performed to identify the small bowel lesion. Comprehensive surgical resection-centered treatment is the standard treatment for primary localized GISTs in patients at significant risk of relapse.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://jgo.amegroups.com/article/view/10.21037/jgo-22-301/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-22-301/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

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