

Case Report

Multiple gastrointestinal stromal tumors of the duodenum and proximal jejunum: an unexpected finding in an emergency laparotomy

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Abstract: Gastrointestinal stromal tumors (GISTs) of the duodenum are relatively rare and difficult to diagnose in early stage because it lacks pathognomonic symptoms. Here, we report a case of multiple GISTs involving the third and fourth portions of the duodenum and proximal jejunum, which were revealed in an emergent laparotomy. A 40-year-old, previously healthy man was referred to the Emergency Department with perineal trauma and diagnosed with a rectal perforation. The rectal perforation was repaired and solid nodules were detected on the proximal jejunum during the laparotomy that proved to be GISTs after histological examination. The patient was then readmitted and an enhanced CT of the abdomen revealed two smooth-outlined solid masses in the fourth part of the duodenum, but no mass was found on the proximal jejunum. During laparotomy, there were two solid masses located on the third portion of duodenum and about 30 solid nodules on the proximal jejunum that were not revealed by the preoperative CT scan. A local resection and primary closure was performed on the four isolated GISTs on the third and fourth portions of the duodenum. The proximal jejunum (~35 cm) with crowded solid tiny nodules was removed and a feeding catheter was placed in the jejunum distal to the anastomosis for postoperative feeding. Local or segmental resection is recommended when the lesions are located on the third and fourth portions of the duodenum according to literature review. A jejunal feeding catheter may be considered to prevent anastomotic leakage and to hasten recovery.

Keywords: Multiple gastrointestinal stromal tumors, duodenal neoplasms, emergent laparotomy, local resection, surgery

Introduction

Gastrointestinal stromal tumors (GISTs) are considered to be originated from the interstitial cells of Cajal or their precursors. GISTs are defined by their expression of c-KIT protein (CD117) that is positive in about 95% of cases [1-3]. It is a relatively rare disease although GISTs are the most common type of mesenchymal tumor of the gastrointestinal (GI) tract. The most common sites for GISTs are the stomach (60%-70%) and the small intestine (20-30%) [1, 2]. There can be multiple small intestinal GISTs and they are found to occur anywhere along the length of the bowel [1-3]. GISTs of the duodenum are uncommon, which account for 10%-20% of small intestinal GISTs, or only 3-5% of

all GIST cases [4, 5]. Duodenal GISTs are pathologically similar to that involving other organs, however they pose some challenges for diagnosis and management in early stage [4]. Because of the potential for malignant transformation, radical surgical resection is still considered the best treatment choice for GISTs. There are few reports in the literature addressing surgical procedures for duodenal GISTs including pancreatoduodenectomy, pancreas-sparing duodenectomy, segmental duodenectomy or local resection [5-7].

In the present study, we describe the case of four isolated GISTs (about 5 to 20 mm in diameter) involving the third and fourth portions of the duodenum and crowded tiny GISTs on the

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Figure 1. Plain abdominal radiograph of a perforated hollow organ in the cavity, showing air under the diaphragm.

proximal jejunum, which were revealed in an emergency laparotomy. The patient was treated successfully by multiple wedge resections of the duodenum and segmental jejunectomy combined with jejunostomy for feeding. This surgical strategy is ideal for multiple isolated GISTs of the duodenum and crowded tiny GISTs on the proximal jejunum when the duodenal GISTs did not involve the ampulla. A jejunal feeding catheter may be considered for preventing anastomotic leakage and to hasten the recovery because of multiple anastomoses.

Case presentation

A 40-year-old man presenting with perineal trauma and abdominal pain was referred to our emergency department. A steel bar penetrated the patient through anorectum with minimal rectal bleeding at a building construction site 20 hours prior to presentation. His medical and family histories were unremarkable. He also had no history of previous abdominal surgery. On admission, his blood pressure was 124/68 mmHg, heart rate was 88 beats/min, and temperature was 38.9°C. Physical examination revealed acutely-ill patient, lower abdominal muscle guarding, tenderness and rebound tenderness. The anus was mildly damaged and there was blood on the gloved finger upon digi-

tal rectal examination. The rest of the examination was normal. Peripheral blood cell count indicated infections with a white blood cell of $16.13 \times 10^9/L$. Liver and renal function tests were normal. The erect plain abdominal radiograph showed air under the diaphragm (**Figure 1**). Based on the recent history, physical examination, and plain abdominal radiograph findings, the patient was diagnosed with an acute peritonitis and possible perforation of the rectum and other hollow abdominal organs.

After an emergency preparation, he was taken to the operating theater. A midline incision was performed. Purulent material was found in the abdominal cavity as well as adhesion of the small intestines to the pelvis during surgical exploration. There was a rectal perforation (about 40% of circumference of laceration) located in peritoneal reflection after clean suctioning of purulent material and separation of the small intestines from the pelvis. The perforation was repaired and the patient underwent a loop sigmoid colostomy for protection. In order to avoid missing other perforated organs, exploration was extended to the entire digestive tract, liver, and other organs. It was during this time that some solid nodules on the proximal jejunum that were hard and smooth with distinct boundary were detected. The laparotomy was completed after one of the nodules was excised for pathological examination so as to come to an exact diagnosis. All the nodules were not excised at the same time in order to prevent possible infection.

The patient was discharged 10 days after an uneventful postoperative course and the histological examination revealed that the tumor was composed of spindle cells with a mitotic count of less than 5 mitoses per 50 high power fields. Immunohistochemical study revealed positive staining for CD117 (c-KIT) and CD34 (**Figure 2A-C**). Based on the above histopathological results, the tumor was finally diagnosed as a GIST with low-grade malignancy originating from the intestine.

The patient was readmitted two months after recovering from the rectal perforation confirmed by colonoscopy. Upper gastrointestinal endoscopy was performed, but there was no intraluminal mass detected. Enhanced computed tomography (CT) of the abdomen revealed two smooth-outlined hypervascular

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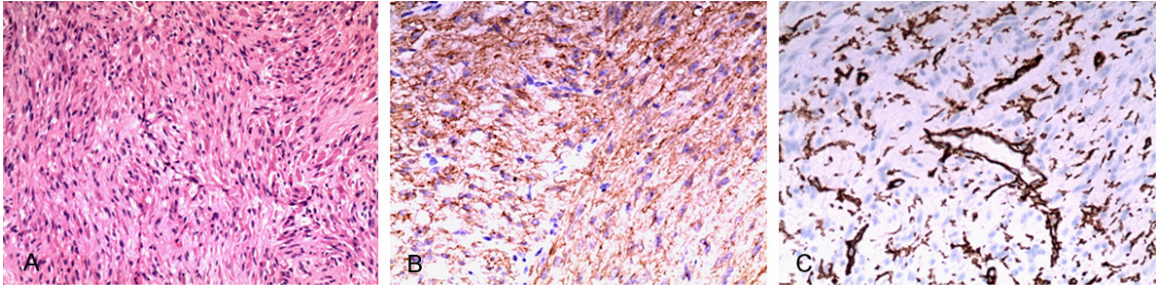


Figure 2. A. Microscopic examination revealed that the relatively uniform spindle cells are features of gastrointestinal stromal tumors (Hematoxylin and eosin, $\times 100$); B. Tumor tissue with moderately-strong staining of CD117 (original magnification, $\times 100$); C. Tumor tissue showing positive staining for CD34 (original magnification, $\times 100$).

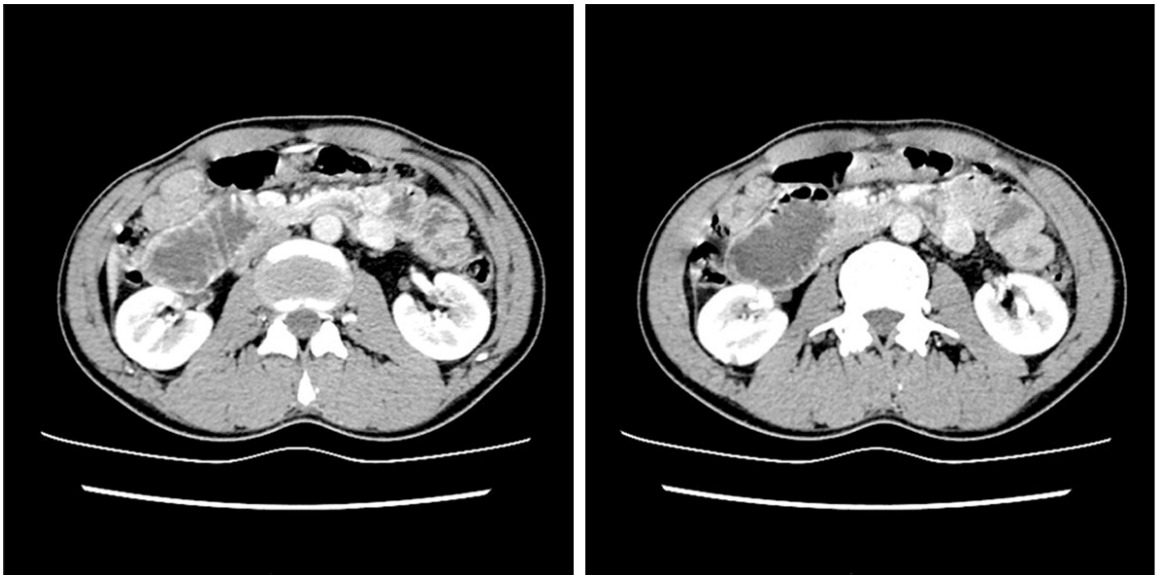


Figure 3. The preoperative enhanced abdominal CT scan demonstrated two well-demarcated enhancing tumors with 20×17 mm and 12×10 mm in diameter at the fourth part of the duodenum.

solid masses ($20 \text{ mm} \times 17 \text{ mm}$ and $12 \text{ mm} \times 12 \text{ mm}$) in the fourth part of the duodenum (no mass was revealed in the third part of duodenum and proximal jejunum in the preoperative enhanced CT scan) (**Figure 3A** and **3B**). Neither lymphadenopathy nor metastasis was observed. Various blood tests including blood routine, liver and renal function tests, were normal. The levels of serum tumor markers, including carcinoembryonic antigen and carbohydrate antigen 19-9 were within normal limits.

After full preparation, the patient was taken to the operating theater for a second operation. A midline incision over the previous scar was performed. In order to expose the duodenum, the incision was extended to 8 cm above the umbilicus after the loop sigmoid colostomy was

closed. At laparotomy, four isolated solid masses (5 to 20 mm in diameter) in the submucosa were identified arising from the third and fourth portions of the duodenum that did not involve the pancreas. There were two isolated solid masses (5 mm in diameter) located on the third portion of duodenum and more than 30 crowded solid nodules on the proximal jejunum (about 3 to 5 mm in diameter) that were not revealed in the preoperative CT scan. The junctional part about 40 cm between the duodenum and the lesions on the proximal jejunum was normal. No evidence of local invasion of the pancreas or distant metastases was found and the duodenal wall was carefully dissected from the inferior border of the pancreas. Since the pancreas and major papilla were not involved, a local resection and primary closure was per-

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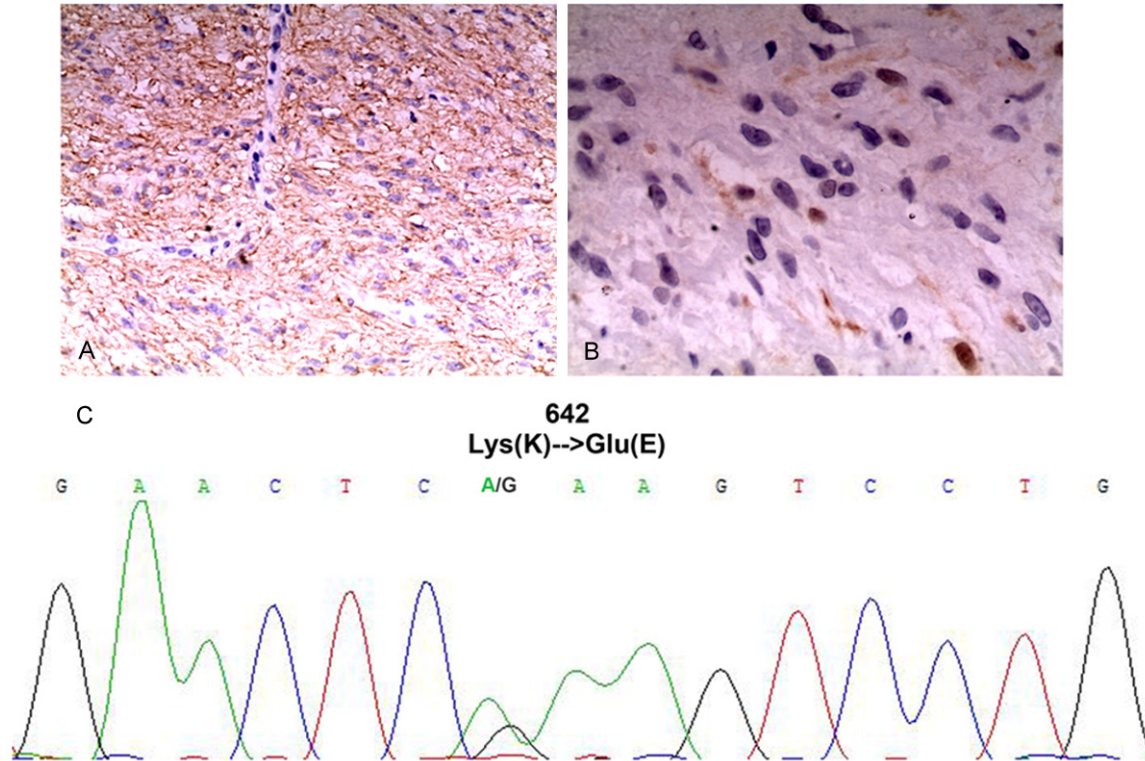


Figure 4. A. Immunohistochemical staining showing Dog-1 positive cells (original magnification, $\times 100$); B. Negative staining for S-100 (original magnification, $\times 200$); C. A K642E mutation in exon 13 of c-KIT was observed by molecular genetic analysis for c-KIT and PDGFR α gene mutation.

Table 1. Risk of aggressive behavior in gastrointestinal stromal tumors

Risk	Size (cm)	Mitotic count (mitoses per 50 high powered fields)	Location of primary tumors
Very low risk	< 2.0	≤ 5.0	Any site
Low risk	2.1-5.0	≤ 5.0	Any site
Intermediate risk	2.1-5.0	> 5.0	Stomach
	≤ 5.0	6-10	Nongastric sites
	5.1-10.0	≤ 5.0	Stomach
High risk	Any size	Any mitotic rate	Tumor rupture
	> 10	Any mitotic rate	Any site
	Any size	> 10	Any site
	> 5.0	> 5	Any site
	2.1-5.0	> 5	Nongastric sites
	5.0-10.0	≤ 5	Nongastric sites

Adapted from Joensuu [8].

formed with the dissection kept outside the capsule of the four tumors, taking care not to rupture the tumor. The proximal jejunum about 35 cm with matted solid nodules was removed with end-to-end anastomosis. The normal junctional part about 40 cm between the duode-

num and the lesions on the proximal jejunum was preserved. A feeding catheter was placed in the jejunum distal to the anastomosis through a tunnel to the outside of the abdominal wall for postoperative feeding. Operative time was 240 min and estimated blood loss was 100 ml. Essential diets were fed through the jejunal-feeding catheter as soon as the peristaltic activity of the intestines recovered two days later. The patient started to eat food by mouth two weeks later. He tolerated the procedure well and had an uneventful recovery.

The jejunal feeding catheter was removed without complication after forty days.

The operative specimen revealed multiple GISTs (3 to 20 mm in diameter) with less than 5 mitosis per 50 high-power fields. The patient

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Table 2. Reported cases of gastrointestinal stromal tumors of the fourth portion of duodenum in the last five years

Age (yr)	Gender	Symptoms	Size (cm)	Surgery	Risk degree	Reference	Year
51	Male	Abdominal Pain	3.0	LR	Low	[12]	2009
57	Male	Melena	2.5	LR	Low	[12]	2009
49	Female	Melena	4.5	SR	Low	[13]	2010
40	Male	Abdominal Pain	5.5	SR	Intermediate	[14]	2010
49	Female	Upper GI Bleeding, Melena	4.5	SR	Low	[6]	2011
60	Male	Health Examination	6.2	SR	Low	[15]	2012
50	Male	Health Examination	5.0	SR	Intermediate	[15]	2012
55	Female	Abdominal Pain	7.0	SR	High	[15]	2012
81	Male	Health Examination	8.0	SR	Low	[15]	2012
55	Female	Melena	8.0	SR	High	[16]	2013
52	Male	Abdominal Pain	20.0	SR	High	[16]	2013

Abbreviations: LR, Local Resection; SR, Segmental Resection.

was classified in the low-risk group according to Joensuu's criteria for risk stratification of GISTs. Immunohistochemical study revealed positive staining for CD117 (c-KIT), CD34 and Dog-1, but is negative for SMA and S100 protein. A molecular genetic analysis for c-KIT and PDGFR α (platelet derived growth factor receptor alpha) gene mutation showed c-KIT exon 13 mutation (**Figure 4A-C**). Based on the above findings, the tumors were finally diagnosed as multiple GISTs with low-grade malignancy originating from the duodenum and proximal jejunum. There was no lymph node metastasis. The patient was discharged 18 days after an uneventful postoperative course.

Although the patient was in the low risk group according to Joensuu's criteria for risk stratification of GISTs (**Table 1**) [8], he was placed on imatinib for one year because of the multiple lesions and potential risk of recurrence. He has been doing well with no recurrence during the two years of follow-up.

Discussion

GISTs account for approximately 30% of all primary duodenal tumors. It is a low-grade malignant mesenchymal tumor of the GI tract considered to arise from any tissue with Cajal cells including the stomach, small intestine, colon, rectum, omentum, oral cavity, biliary tree, and liver [9]. These cells are intestinal pacemaker cells or mesenchymal stem cells [1-10]. Most data on duodenal GISTs are from case reports or a few small series and they commonly involve the second part of the duodenum followed by

the third, fourth, and first parts [10, 11]. GISTs located at the fourth part of the duodenum are relatively rare. There are about thirty reported cases of GISTs of the fourth part of the duodenum obtained from the literature according to a Medline search using the key words "duodenum" and "gastrointestinal stromal tumor" in the last five years, but only eleven cases were described with detailed information [6, 12-16] (**Table 2**). The patients in the published reports were seven men and four women between 40 and 81 years of age. Our case was the youngest among these. Eight cases exhibited certain symptoms such as abdominal pain, upper GI bleeding and melena. Three cases were found in apparently healthy individuals.

Duodenal and small intestinal GISTs are usually asymptomatic and difficult to diagnose early, especially when it is small in size. GISTs can reach a large size before causing any symptoms. The GISTs in our case would not have been diagnosed if the patient did not undergo the laparotomy for rectal perforation because he had no symptoms of digestive system abnormalities in his medical history. The clinical presentation of duodenal GISTs varies depending on their size, location and the presence of mucosal ulceration. Most duodenal GISTs present with GI bleeding manifested as melena and occasionally with massive acute bleeding, as well as some other symptoms such as abdominal pain or discomfort, early satiety, bloating or obstructive jaundice due to the involvement of the papilla of Vater. The median size of the lesion is reported to be 4 cm in contrast to the median size of gastric and small intestinal

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GISTs of 6 to 7 cm, respectively [10-17]. The tumor sizes in **Table 2** ranges from 2.5 to 20 cm. The largest tumor size is 2.0 cm in our case, which is smaller than that in the literature probably because it was an unexpected finding at an emergency laparotomy.

Although gastrointestinal endoscopy may be diagnostic when the tumors are located in the stomach or in the upper duodenum, some problems may arise when the tumor is relatively small in diameter with very nonsignificant outward expansion. In such conditions, endoscopic ultrasound is helpful in determining whether the lesion is submucosal and it can also be performed to clarify the layer of origin of the intramural lesion. On the other hand, GISTs of the distal duodenum or small intestines may remain undetected at gastrointestinal endoscopy unless an enteroscope is used. Alternative diagnostic means include contrast-enhanced CT, magnetic resonance imaging (MRI), and barium swallow examination. However, CT and MRI are the best imaging modalities for estimating the primary lesion and detection of metastasis. On contrast-enhanced CT scan, GISTs may present as small homogenous to large necrotic masses. Small tumors are typically shown as sharply marginated, smooth, homogenous masses with moderate contrast enhancement while large tumors show heterogeneous contrast enhancement and tend to have mucosal ulceration, cavitation and central necrosis [18].

Surgery remains the mainstay of treatment for non-metastatic, resectable GISTs. Unlike carcinomas, there is little submucosal spread in GISTs and locoregional lymphatic involvement is infrequent. Therefore, wide margins with routine lymph node dissection may be unnecessary [12-17]. Complete enbloc surgical resection of the tumor with negative surgical margins and avoidance of tumor rupture, which can lead to peritoneal spread, should be the goal of surgery. Selection of the type of surgical resection depends on the primary tumor site, location and proximity to the duodenal papilla. Although complete excision with wide margins in the stomach or small intestine provides definitive cure, wide resection of tumors involving the duodenum will always entail a pancreatoduodenectomy due to the unique and complex anatomy of the pancreatoduodenal region. Major resection through a pancreatoduodenectomy

or pancreatic sparing duodenectomy is advisable when the tumor is found in the second portion of the duodenum and involves the papilla, pancreas or the duodenal bulb or if the common bile duct tend to be smaller in diameter causing problems while reconstructing and an increased chance of stenosis of the anastomosis after pancreatoduodenectomy [19, 20]. Nowadays, pancreatoduodenectomy has been reported to be associated with a low mortality rate, but it remains a complex surgical procedure associated with significant short and long-term morbidity. Therefore, extensive surgery with significant morbidity and possible mortality such as pancreatoduodenectomy should be avoided when possible and surgical resection with clear margins is the desirable primary treatment of GISTs, and local excision may be appropriate for duodenal GISTs when technically feasible [11, 12].

According to the above theory, various techniques of limited resection for duodenal GISTs have been advocated for some years. Wedge resection with primary closure can be performed for small lesions if the resulting lumen is adequate and the ampulla can be preserved. Segmental duodenectomy with side-to-end or end-to-end duodenojejunostomy can be performed for larger tumors located at the third and fourth portions of the duodenum [5, 6, 12-16, 20]. Partial duodenectomy with Roux-en-Y duodenojejunostomy can be performed for larger tumors involving the antimesenteric border of the second and third portions of the duodenum [20]. On the whole, local wedge resection of the duodenum is suitable for small lesions less than 2 cm except those lesions located within 2 cm from the ampulla of Vater. Segmental resection is indicated for large tumors on the third and fourth portions of the duodenum, while Whipple's resection is indicated for periampullary GISTs and for large tumors of the first and second portions of the duodenum. In this report, local wedge resection or segmental resection was performed when the tumor is located in the fourth portion of the duodenum. We describe a case of multiple isolated GISTs involving the third and fourth portions of the duodenum and matted solid tiny nodules on the proximal jejunum that were discovered during an emergency laparotomy. Because reconstruction after segmental resection of the third and fourth portions of the duodenum and the proximal jejunum was very chal-

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lenging and some complications may occur, we performed the operation via multiple wedge resections of the duodenum and segmental jejunectomy with end-to-end anastomosis. In order to protect several anastomoses and hasten recovery, jejunostomy was performed for feeding after the operation. This technique should be considered as a possible treatment option for multiple isolated GISTs located at the third and fourth portions of the duodenum together with jejunostomy to prevent anastomotic leakage and hasten recovery.

All GISTs have a certain potential for malignancy and the most important prognostic factors are their size, mitotic count and sites. Joensuu [8] established a risk stratification based upon tumor diameter, mitotic activity and sites (**Table 1**). The tumor in our case belonged to the low risk group as the mitotic index was less than 5 per 50 high power fields and the tumor size was 2 cm. Imatinib mesylate is a tyrosine kinase inhibitor. The efficacy of imatinib mesylate for a patient with GIST was first reported in 2001. A number of studies have reported the efficacy of imatinib mesylate for GISTs. In our case, although the patient was in the low risk group according to Joensuu's criteria for risk stratification of GISTs, he had to take imatinib for one year because of multiple lesions and potential risk of recurrence. There was no recurrence during the 2 years of follow-up. However, his prognosis will be clearer after a prolonged follow-up.

As far as we know, this is the first reported case of multiple isolated GISTs involving the third and fourth portions of the duodenum and matted solid tiny nodules of the proximal jejunum that were found during an emergency laparotomy. As a result, the prognosis of the patient is good because of the timely intervention. Jejunostomy distal to the anastomosis for feeding is a proper technique to protect the anastomosis in the duodenum and hasten recovery. It is obvious that the prognosis would have been different if the tumors were not diagnosed during the emergency laparotomy.

Conclusion

We report a case of multiple GISTs involving the third and fourth portion of the duodenum and proximal jejunum that were revealed in an emergency laparotomy.

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Disclosure of conflict of interest

None.

Authors' contributions

ZGZ and LJ evaluated the clinical significance of this case and drafted the manuscript. SCN, XZY, ZQL and HYS devised the study concept and corrected and revised the manuscript. All authors read and approved the final manuscript.

Abbreviations

GISTs, Gastrointestinal stromal tumors; GI, gastrointestinal; CT, computed tomography; PDGFR α , platelet derived growth factor receptor alpha; MRI, magnetic resonance imaging.

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