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Acute diffuse peritonitis due to spontaneous rupture of a primary gastrointestinal stromal tumor of the jejunum: A case report

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ABSTRACT

INTRODUCTION: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract. Overt peritonitis caused by GIST rupture is very uncommon. Three types of GIST rupture have been described: closed perforation due to abscess (abscess type), hemoperitoneum leading to rupture of the hematoma capsule in the tumor (hemoperitoneum type), and perforation of the digestive tract via a fistula leading to central necrosis of the tumor (bowel perforation type). This report describes a patient with spontaneous tumor rupture and diffuse peritonitis, a variant of the bowel perforation type of GIST rupture.

PRESENTATION OF CASE: A 74-year-old man presented with symptoms of vomiting and abdominal pain. Computed tomography (CT) scan revealed an approximately 10 × 7-cm mass in the pelvis with free air and fluid collection. Emergency laparotomy revealed a tumor in the jejunum, which was ruptured with a hole measuring 5 mm in diameter. The tumor and part of the jejunum were resected. Immunohistochemically, the mass was diagnosed as a GIST originating from the gastrointestinal tract. Despite chemotherapy with imatinib mesylate, the patient died 22 months after surgery.

CONCLUSIONS: This report describes a patient with acute diffuse peritonitis due to spontaneous rupture of a primary GIST of the jejunum.

1. Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumor of the gastrointestinal tract [1]. The clinical symptoms of GIST complications include vague abdominal pain, hematemesis, and intestinal obstruction. However, overt peritonitis caused by GIST rupture is very uncommon [2]. Three types of GIST rupture have been described to date: closed perforation due to abscess (abscess type), hemoperitoneum leading to rupture of the hematoma capsule in the tumor (hemoperitoneum type), and perforation of the digestive tract via a fistula leading to central necrosis of the tumor (bowel perforation type). This report describes a patient with spontaneous tumor rupture and diffuse peritonitis, a variant of the bowel perforation type of GIST rupture. This case report has been prepared in line with the SCARE criteria [3].

2. Presentation of case

A 74-year-old man presented with symptoms of vomiting and abdominal pain for 10 h. His body temperature was 38.1 °C; blood pressure, 144/91 mmHg; radial pulse rate, 118 beats/minute. Abdominal examination revealed tenderness and muscular defense in the epigastric fossa. Blood tests showed a white blood cell count of 7470/mm^3, and a C-reactive protein concentration of 6.39 mg/dL. Computed tomography (CT) scan revealed a solid mass measuring approximately 14 cm × 7 cm within the pelvis, and free air around the gastric cardia and perihepatic fluid (Fig. 1a–c). These findings suggested peritonitis induced by organ rupture. Emergency laparotomy revealed an approximately 14-cm solid tumor in the jejunum, located 100 cm from Treitz's ligament (Fig. 2). The tumor was perforated, with a hole measuring approximately 5 mm. Segmental

Abbreviations: CA 19-9, cancer antigen 19-9; CEA, carcinoembryonic antigen; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; GIST, gastrointestinal stromal tumor; H&E, hematoxylin and eosin.

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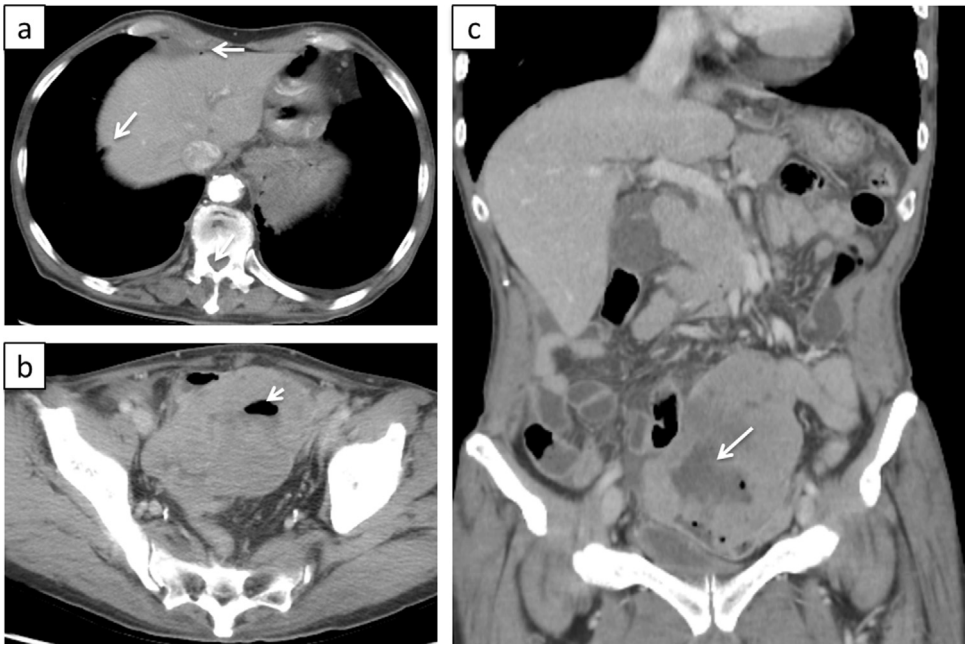

Fig. 1. Computed tomographic scans, showing (a) free air at the liver surface and the gastric cardia with fluid collection (white arrows) and (b, c) a solid mass within the pelvis, measuring approximately 14 cm × 7 cm, with some air (short arrows) and internal liquid (long arrows).

resection of the jejunum with the tumor showed that the resected mass was a well-circumscribed tumor, measuring 14 cm × 7 cm and penetrating the jejunum. The solid parenchyma contained an area central necrosis with a fistula to the lumen of the jejunum. (Fig. 3) Hematoxylin and eosin staining showed proliferation of spindle-shaped cells, and immunohistochemical staining showed that the tumor was positive for c-kit and CD34, with approximately 10% of the tumor cells positive for nuclear expression of the proliferation-associated antigen Ki-67. (Fig. 4) The patient was diagnosed with a high-risk GIST of the jejunum. Because of cardiac insufficiency and pneumonia, the patient could not be treated with adjuvant imatinib. A follow-up CT 1 year after surgery showed the appearance of liver metastases. Chemotherapy was initiated with a lower dose of imatinib mesylate, but the treatment was discontinued 3 months later due to cough and general malaise. The patient died 22 months after surgery.

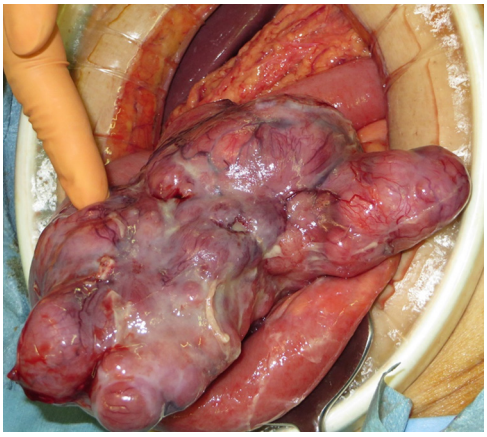

Fig. 2. Intraoperative photograph, showing an approximately 14 cm perforated tumor with a hole measuring approximately 5 mm (white arrow) in the jejunum. The tumor was located 100 cm from Treitz's ligament.

3. Discussion

GISTs are visceral tumors arising from any site within the gastrointestinal tract. Approximately 60–70% of these tumors occur in the stomach, 25–35% in the small intestine, and 10% in the jejunum, whereas the esophagus, colon, rectum, and appendix are rarely affected [4]. GISTs are usually associated with abdominal pain, palpable mass, and/or GI bleeding, accompanied by fever, anorexia, weight loss, and/or anemia [5]. Approximately 10% of GISTs are located in the jejunum [6]. The most commonly reported clinical symptoms are bleeding and obstruction [7]. However, GISTs originating from the small bowel rarely cause perforation or cause acute diffuse peritonitis. Common symptoms of small intestinal GISTs include abdominal pain and a palpable mass, with early satiety and abdominal fullness also occurring frequently [8]. Fever, anorexia and weight loss are rarely observed [9]. A MEDLINE search, using the key-words "GIST" AND "small intestine" AND "perforation" or "rupture," revealed only 15 cases of small intestinal GIST with perforation; including the present case (Table 1). Three types of GIST rupture have been identified: abscess; hemoperitoneum; and bowel perforation types.

Abdominal pain is a chief symptom in patients with GIST. Statistical analysis revealed that 58% of patients with gastric GISTs experienced bleeding in the digestive tract and 61% experienced abdominal pain; these rates are higher than those in patients with GISTs at other locations are [10]. In contrast, acute abdominal symptoms were more frequent in patients with jejunal (40%) and ileal (60%) GISTs than in those with gastric GISTs ($p < 0.05$ each) were [10]. Patients with the hemoperitoneum type of GIST rupture frequently experience hypovolemic shock, short loss of consciousness, and sudden abdominal pain, whereas patients with the bowel perforation type of GIST rupture experience diffuse, worsening abdominal pain. Symptom duration is longer in patients with the abscess type than in those with the other types of GIST rupture (Figs. 3 and 4).

To date, all tumors in patients with GIST rupture originated in the jejunum, ranging in size from 6.5 cm to 21 cm. No differences in tumor origin and size have been observed among patients with the three types of GIST rupture. GIST perforations are more

Table 1
Summary of 15 cases of GIST perforation at the small intestine.

Author	Year	Age	Sex	Symptoms	Duration of symptoms	Size (cm)	Shape	Location (distance from Treitz' ligament)	Mitotic count	Adjuvant therapy (duration)	Outcome
Bowel perforation type											
Efremidou EI	2006	66	M	diffuse abdominal pain	10 h	7	irregular	jejunum	2/50 HPF	Imatinib (20 months)	44 months ANED
Feng F	2010	45	M	paroxysmal abdominal pain	3 days	10	irregular	jejunum (40 cm)	Ki-67 < 5%	non	N/A
Ku MC	2010	33	F	abdominal pain	3 days	6.5	irregular	jejunum	N/A	non	N/A
Memmi M	2012	59	M	acute abdominal pain	20 h	12	irregular	jejunum (150 cm)	7/50 HPF Ki-67 8%	non	N/A
Misawa S	2014	70	M	abdominal pain	N/A	10	irregular	jejunum (near)	Ki-67 26%	Imatinib (12 months)	12 months ANED
Cabral FC	2015	49	F	worsening abdominal pain	4 days	14	irregular	jejunum	N/A	non	N/A
Present case	2017	74	M	acute abdominal pain	10 h	14	irregular	jejunum (100 cm)	Ki-67 10%	Imatinib (3 months)	22 months PA
Hemoperitoneum type											
Ajduk M	2004	60	F	localized abdominal pain	2 days	7	smooth	jejunum	3/10 HPF	non	N/A
Cegarra-Nanarro MF	2005	76	M	acute abdomen, shock	acute	9	irregular	proximal jejunum	<5/50 HPF Ki-67 < 10%	non	31 months ANED
Hirasaki S	2008	87	F	short loss of consciousness	N/A	13	smooth	jejunum (130 cm)	N/A	non	16 months ANED
Nannini M	2013	45	F	acute abdomen	acute	12	smooth	jejunum	2/50 HPF	Imatinib (13 months)	13 months reccurence
Attaallah W	2015	46	M	vague abdominal pain	N/A	8	smooth	jejunum (50 cm)	Ki-67 10%	Imatinib (N/A)	N/A
Abscess type											
Karagulle E	2008	70	M	right-sided abdominal pain	7 days	6.6	irregular	jejunum (5 cm)	no mitotic activity	non	13 months ANED
Andican A	2012	48	M	vague abdominal pain	30 days	21	irregular	proximal jejunum	N/A	Imatinib (3 months)	12 months ANED
Chen HW	2012	22	M	abdominal pain	3 days	9.1	irregular	jejunum (100 cm)	low mitotic count	non	2 months ANED

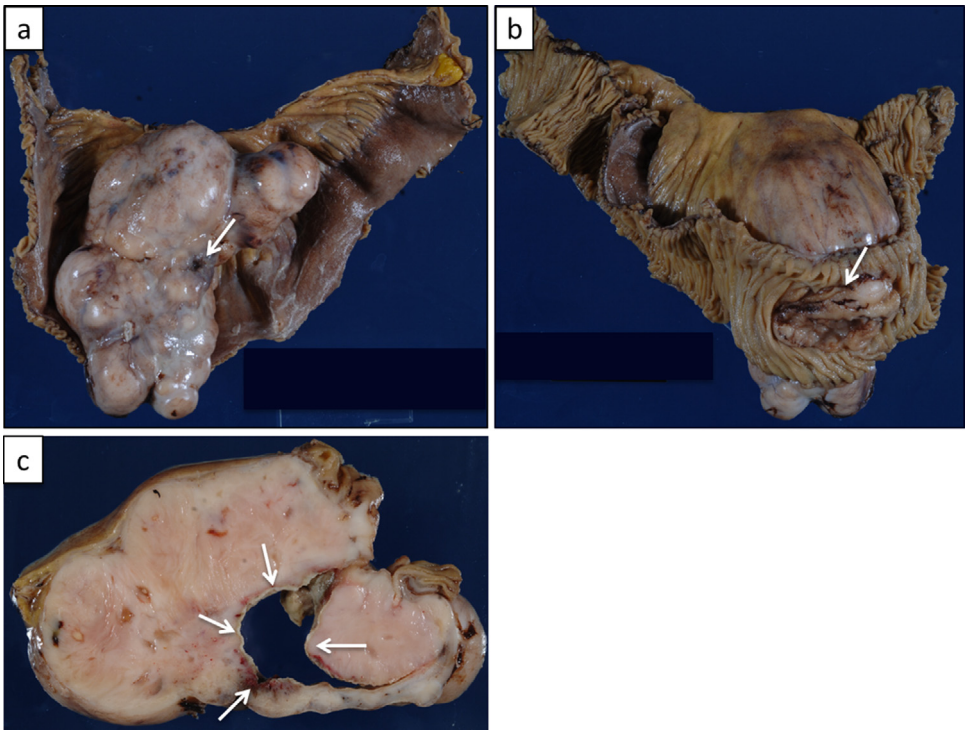

Fig. 3. a, b. Isolated specimens arising from the jejunal wall, with a small perforation of the intestinal tract (white arrow). c. The cut surface of the solid parenchyma, revealing a central necrotic cavity with a fistula to the lumen of the jejunum.

frequent in the perforation than in the ileum [11]. Surgical specimens have revealed the pathognomonic features of the ruptured tumors. For example, the shapes of the abscess and bowel perforation types are irregular, whereas the shapes of the hemoperitoneum type are smooth. An asymmetric, irregular, extremely thickened wall should suggest a diagnosis other than simple infection [12]. Tumor shape has been associated with the mechanism of formation. Mechanisms underlying the abscess type include increased intraluminal pressure due to tumor obstruction, replacement of the bowel wall by tumor cells followed by necrosis, and bowel ischemia

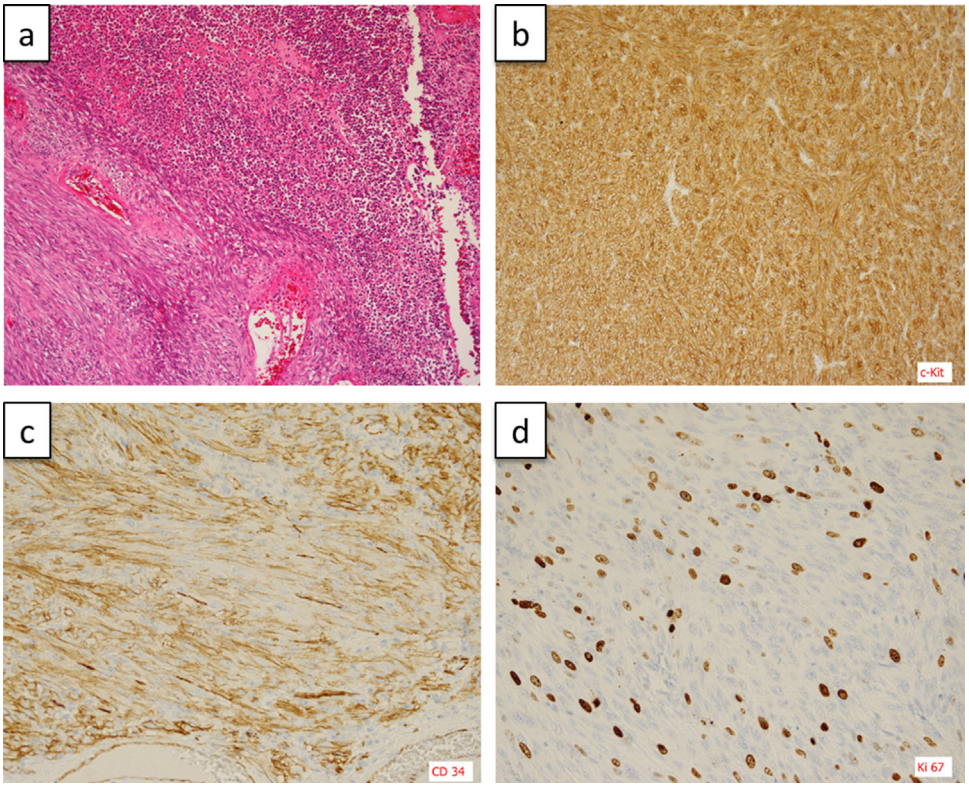

Fig. 4. a. Microscopic examination (hematoxylin-eosin staining, original magnification: ×100) showing proliferation of spindle-shaped cells. b, c. Immunohistochemical staining, showing that tumor cells were positive for (b) c-kit and (c) CD34. d. The cell proliferation index (Ki67) was approximately 10%.

due to tumor embolization [13]. The hemoperitoneum type may result from bleeding within the tumor, leading to hematoma and rupture of the capsule, or transudation of blood components from the tumor [14]. The bowel perforation type may be caused by a longstanding obstruction with increasing intraluminal pressure or an erosive tumor leading to mural necrosis and perforation [15]. Cytopathological examination of our patient revealed a fistulation to the lumen through the distorted parenchyma containing areas of central necrosis.

Surgical resection is considered the only potential curative option for patients with localized GISTs. However, only about 85% of tumors can be completely resected, and the estimated incidence of recurrence or metastasis after radical surgery is 50% [16]. A prognostic classification system [7] has revealed factors prognostic of the possible malignant potential of GISTs, including mitotic activity (>5 mitotic figures per 50 × high power field) and tumor size (>5 cm). Moreover, a Ki-67 index >22% in the most active area was found to be the most powerful predictor of poor survival [17]. Patient prognosis is dismal when tumors are accompanied by symptoms or signs such as perforation or rupture, multifocal location, or metastatic lesions. Because all perforated tumors identified to date (Table 1) were larger than 5 cm, all were classified as high-risk malignant GIST. Imatinib mesylate, a tyrosine kinase inhibitor targeting KIT, was found to be beneficial after radical resective surgery of high-risk GISTs [18]. Of the 15 patients described to date, only five were treated with imatinib. At a follow-up from 2 to 44 months, all but two, including the present patient, remain alive without recurrence. The second patient who experienced recurrence showed peritoneal dissemination during imatinib treatment 13 months after surgery because of cardiac insufficiency and pneumonia. Our patient could not be treated with adjuvant imatinib immediately after surgery. After the appearance of liver metastases, however, chemotherapy was initiated with a lower dose of imatinib mesylate 22 months after surgery.

4. Conclusions

This report describes a patient with acute diffuse peritonitis caused by the spontaneous rupture of a primary GIST of the jejunum.

Conflicts of interest

None of the authors has anything to disclose.

Funding

None of the authors has anything to disclose.

Ethical approval

All procedures used in this research were approved by the Ethical Committee of Chugoku Rosai Hospital.

Consent

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

Authors contribution

Sato and Tazawa wrote the manuscript. Sato performed the surgery. Fujisaki, Imaoka, Hirata, Takahashi, and Sakimoto participated in the surgery. Fukuda and Kuga participated in the clinical treatments. Nishida performed the pathological analysis. All authors conceived of the study and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Guarantor

Hirofumi Tazawa has accepted full responsibility for this work and the decision to publish it.

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