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Peritonitis secondary to spontaneous perforation of a primary gastrointestinal stromal tumour of the small intestine: A case report and a literature review

Mario Alessiani[a,e], Marco Gianola[a], Sabina Rossi[b], Vittorio Perfetti[c], Piero Serra[a], Daniela Zelaschi[a], Enzo Magnani[a], Lorenzo Cobianchi[d,e,*]

[a] Department of General Surgery, Varzi Hospital, Italy
[b] Radiology Service, Voghera Hospital, Italy
[c] Department of Oncology, IRCCS San Matteo Hospital Foundation, Pavia, Italy
[d] Unit of General Surgery 1, IRCCS San Matteo Hospital Foundation, Pavia, Italy
[e] Department of Clinical, Surgical, Diagnostic and Paediatric Sciences, University of Pavia, Italy

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ABSTRACT

INTRODUCTION: A few cases of acute abdomen caused by perforation of small-intestinal gastrointestinal stromal tumours (GISTs) have been reported in the literature.
PRESENTATION OF CASE: Together with a review of the published cases, here we report a case of an elderly patient with peritonitis due to spontaneous perforation of a GIST of the jejunum. An 82-year-old man was admitted to the emergency unit of our hospital with fever and severe abdominal pain. An abdominal enhanced computed tomography scan detected a 6 cm solid mass in the left upper quadrant adherent to a jejunal loop and surrounded by free fluid and free air. Due to the radiological features of the mass, the diagnosis of a perforation of a GIST arising from the jejunum wall was suspected. The patient underwent emergency laparotomy. Intraoperative findings confirmed diffuse peritonitis secondary to jejunal tumour perforation. A segmental resection of the jejunum containing the mass was performed followed by a mechanical end-to-side anastomosis. The histopathologic examination of the mass confirmed the diagnosis of a perforated GIST of the small intestine (high-risk category). The post-operative course was uneventful and the patient was treated with adjuvant imatinib therapy.
DISCUSSION: Twenty-one other cases of spontaneous perforation of small intestine GISTs are reported in the literature and are summarized in the present review.
CONCLUSION: The described case is the tip of the iceberg and spontaneous rupture or perforation of GISTs are a far more frequent first presentation of this rare tumour.

1. Introduction

Gastrointestinal stromal tumours (GISTs) are mesenchymal neoplasms of the gastrointestinal tract (GI) that can arise anywhere from the oesophagus to the rectum [1]. GISTs accounts for less than 1% of all GI tumours; however they are the most common mesenchymal neoplasms of the GI tract. Population-based studies from different European countries report annual incidence rates ranging from 6.5 to 20 cases per million [2–6]. These studies also report an increase in the incidence of GISTs over the last two decades due to the improvement in their diagnosis and registration [2,3].

Few GISTs manifest as abdominal emergencies, such as GI haemorrhage, intestinal obstruction, or tumour perforation [7,8]. Although acute abdomen due to GIST perforation into the peritoneal cavity is rare, a few cases of peritonitis caused by perforation of small-intestinal GISTs have been reported in the literature [8–29]. Together with a review of the published cases, here we report a case of an elderly patient with acute abdomen due to spontaneous perforation of a GIST located in the jejunum.

2. Case presentation

An 82-year-old man was admitted to the emergency unit of our hospital with fever, vomiting, diarrhoea and diffuse abdominal pain that had been experienced for the previous 24 h. The patient

Abbreviations: GIST(s), Gastrointestinal stromal tumours; GI, Gastrointestinal; CT, Computed tomography; H&E, Hematoxylin and Eosin.

* Corresponding author at: Unit of General Surgery 1, IRCCS San Matteo Hospital Foundation, Pavia, Italy. Tel.: +393394421128; fax: +390382502447.
E-mail addresses: v.perfetti@smatteo.pv.it (V. Perfetti), piero_serra@ospedali.pavia.it (P. Serra), daniela_zelaschi@ospedali.pavia.it (D. Zelaschi), enzo_magnani@ospedali.pavia.it (E. Magnani), l.cobianchi@smatteo.pv.it (L. Cobianchi).

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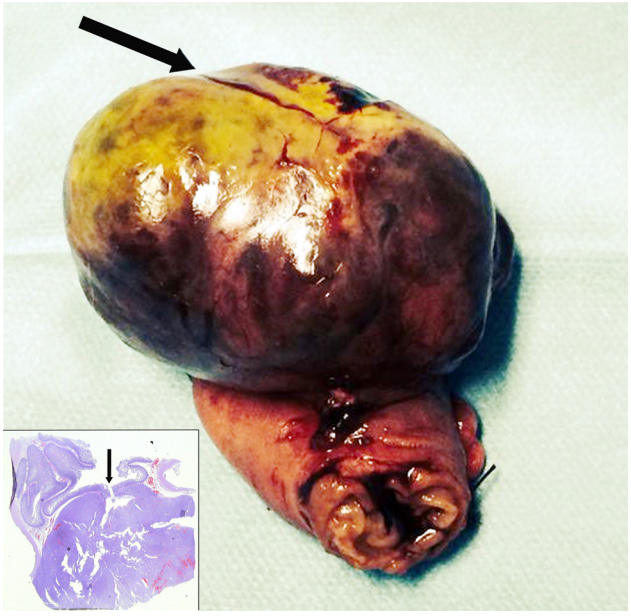

Fig. 1. Surgical specimen. The resected specimen includes the jejunal loop and the perforated GIST arising from the antimesenteric side of the loop. The arrow indicates the ruptured margin of the tumour. The insert shows the histology of the specimen: the perforation to the lumen of the jejunum is indicated by the arrow.

had a history of arterial hypertension. No other co-morbidities were reported. Vital signs were within normal limits and the rectal temperature was 38.6 °C. On examination, the abdomen was distended with generalized tenderness and muscular defence. Laboratory tests showed elevated white cell count (13.430/mm3, 92.7% neutrophils) and hyper-glycaemia (221 mg dl^{-1}).

Abdominal plain radiography showed gas-fluid levels in the small bowel without free intraperitoneal air. An abdominal enhanced computed tomography (CT) scan was urgently performed and revealed the presence of a 6 × 5.5 × 5.5 cm solid mass in the left upper quadrant towards the umbilicus, adherent to a jejunal loop, and surrounded by free fluid. A small layer of free extraluminal air was also seen close to the margin of the mass (Fig. 1). Due to the radiological features of the mass, the diagnosis of a perforation of a GIST located in the jejunum wall was suspected.

The patient underwent emergency laparotomy. Intraoperative findings showed free purulent exudate in the abdominal cavity and a diffuse inflammatory reaction of the peritoneum. The mass was located 10 cm away from the Treitz ligament, on the antimesenteric side of the first jejunal loop (Fig. 2). The perforation was identified on the external border of the mass. A segmental resection of the jejunum containing the mass was performed followed by a mechanical end-to-side anastomosis, peritoneal irrigation and toilet, and finally the placement of multiple drainages. A search for other gastrointestinal or peritoneal abnormalities was negative.

The post-operative course was uneventful and the patient was discharged 10 days after surgery. On histological examination, the specimen was described as a solid smooth grey and white mass (maximum diameter of 7 cm) arising from the wall of the resected segment of small bowel. H&E staining showed spindle-shaped cell proliferation (Fig. 3a). The mitotic index was 16/50 high-power field (HPF) and the Ki-67 value was 15%. The immunohistochemical staining was positive for C-KIT (Fig. 3b), focal positive for h-caldesmon, negative for smooth muscle actin, desmin, CD34, S-100, EMA and cytocheratine. All these findings led to the diagnosis of GIST of the jejunum, which was classified as high-risk using the prognostic classification by Fletcher et al. [30]. The surgical margins were disease-free. As soon as the diagnosis was confirmed by histology, the patient was started on imatinib mesylate therapy at the daily oral dose of 400 mg and he is currently under follow-up after six months of therapy.

3. Discussion

Nearly a third of patients with GISTs are asymptomatic and the diagnosis is made incidentally during surgical, endoscopic, radiologic procedures or at autopsy [1,31]. Most of the symptomatic patients present with vague, nonspecific abdominal pain or discomfort, sometimes associated with nausea and vomiting. Patients may also complain of early satiety or a sensation of abdominal fullness. More frequently, GISTs larger than 4 cm may produce symptoms secondary to obstruction or GI bleeding. The bleeding can be either chronic, often leading to anaemia, or acute with episodes of haematemesis or melena. Very few cases manifest as other abdominal emergencies, such as haemoperitoneum secondary to intra-abdominal tumour rupture, or peritonitis secondary to tumour perforation.

This latter emergency has been reported for all gastrointestinal tracts [32–34]. However GIST perforation seems to occur more frequently in the small bowel compared to other anatomic sites [35]. Our literature search revealed 21 cases of acute abdomen with diffuse or localized peritonitis caused by spontaneous perforation of small intestine GISTs (Table 1) [9–29]. Two more cases are reported in the case-series of Mansour and Coll [8]. They are not included in Table 1 because the details of the cases are not available. In another two cases not listed in Table 1, spontaneous ruptures of the small intestinal GISTs were associated with an intraperitoneal abscess without perforation to the intestinal lumen [35,36].

Of the 22 cases reported in Table 1, including this case, 16 patients were male and five were female. GIST perforation can occur irrespective of the age, since the patients' ages ranged from 22 up

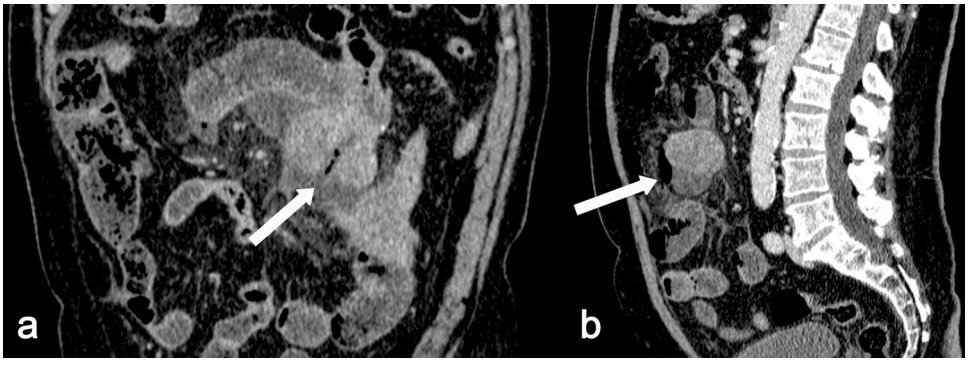

Fig. 2. Preoperative computed tomography (CT). (a) CT image showing air in the perforation track of the tumour (arrow); (b) CT image showing free air and intraperitoneal free fluid (arrow) around the jejunal tumour.

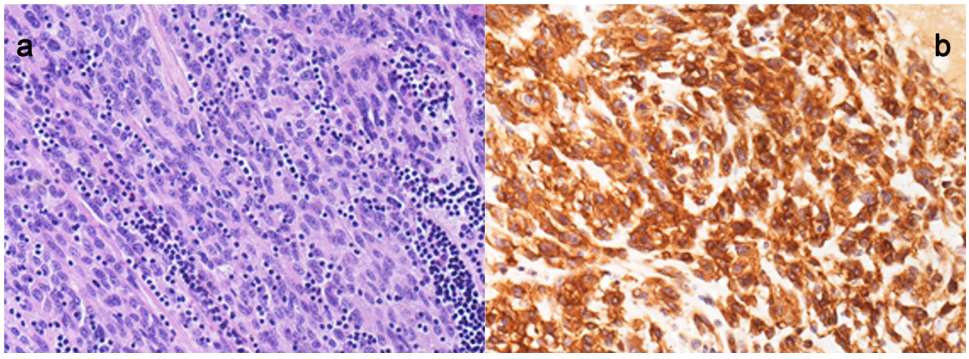

Fig. 3. Histological findings. (a) H&E staining shows spindle-shaped cell proliferation; (b) immunoistochemical staining shows positivity for c-kit.

to 82 years. The jejunum was the more common location of perforation compared to the ileum (15 vs 4). In three other cases it was not specified at what level of the small intestine the perforated GIST was located. These were all undiagnosed primary GISTs tumours. In one patient the small intestinal GIST was associated with hepatic metastases [9], in the other two cases small bowel GISTs were multifocal [26,29]. In all the other 19 patients there was a primary localized single GIST.

Diffuse peritonitis was described in 19 patients, while in the remaining three the intraoperative presentation was a localized abscess adjacent to the anatomical site of the perforated GIST. Despite perforation and concomitant peritonitis, all authors but one reported good post-operative outcome. The only death occurred on postoperative day four due to septic shock in a complicated case of perforated GIST of the ileum with concomitant small bowel necrosis secondary to internal herniation [16]. A possible explanation of the very low morbidity and mortality in the reported cases is the relatively low peritoneal contamination due to the predominant proximal anatomic site of perforation, and the expeditious resuscitation followed by emergency surgical intervention in all patients with diffuse peritonitis. Primary small bowel anastomosis was safely performed in all cases but one. The only exception was a terminal ileostomy performed in the very compromised patient reported by Özben et al. [16].

Complete surgical resection is considered the only potential curative treatment for localized GISTs. However, the potential risk of recurrence after surgery is consistent. Complete resection can be achieved in approximately 85% of patients and the estimated incidence of recurrence or metastasis after radical surgery is 50% [31]. Using the widely accepted prognostic classification proposed by Fletcher et al. [30], based on the size of the tumour and the mitotic count, GISTs are classified as very low-, low-, intermediate- and high-risk for potential malignancy. Joensuu and Coll have proposed a classification that includes tumour rupture and tumour site (Table 2) [37–39]. Based on this risk classification, all the patients with tumour rupture should be considered at high risk for recurrence [39,37].

Imatinib mesylate, a tyrosine kinase inhibitor, has been found to be beneficial after radical resective surgery of high-risk GISTs [39,40]. More recently, adjuvant therapy with imitinab has been used with wider indications, such as intermediate-risk tumours with size > 3 cm and primary tumours with rupture or perforation. [41,42]. Of the 21 surviving patients reported in Table 1, 13 were treated with imatinib, including our case. In the other eight cases, there is no mention of imatinib therapy. Follow-up data are reported for 12 patients, of which 10 were on imatinib adjuvant therapy. All but one were alive without recurrence, with a follow-up ranging from six to 48 months. The only exception was the case

Table 1
Summary of spontaneous perforated gastrointestinal stromal tumors (GISTs) of small intestine in the available medical literature.

First author (reference)	Year	Sex/age (years)	Small-bowel location	Size (cm)	Mitotic counts	Intraoperative findings	Treatment	Follow-up (months)
Yamamoto et al. [9]	2003	M/32	NR	15	28/50	Peritonitis	SBR + Imatinib	24 Alive[a]
Efremidou et al. [10]	2006	M/66	Ileum	7 × 5 × 4	2/50	Peritonitis	SBR + Imatinib	44 Alive
Karagülle et al. [11]	2008	M/70	Jejunum	5	NR	Abscess	SBR	13 Alive
Versaci et al. [12]	2009	M/46	Jejunum	12 × 7	5/50	Peritonitis	SBR + Imatinib	12 Alive
Taniguchi ey al. [13]	2009	M/59	NR	7,5	<5/50	Peritonitis	SBR + Imatinib	14 Alive
Licursi et al. [14]	2009	M/47	Jejunum	12,5 × 5	<5/50	Peritonitis	SBR	NR
Ku et al. [15]	2010	F/33	Jejunum	6.5 × 5 × 4	NR	Peritonitis	SBR	NR
Özben et al. [16]	2010	M/65	Ileum	8 × 5	NR	Peritonitis	SBR + Ileostomy	Dead POD 4
Feng et al. [17]	2011	M/45	Jejunum	10 × 8	<5/50	Peritonitis	SBR	NR
Paramythiotis et al. [18]	2011	M/56	Jejunum	3	<5/50	Peritonitis	SBR + Imatinib	48 Alive
Bhandarwar et al. [19]	2011	F/55	Jejunum	36 × 15 × 10	5/50	Peritonitis	SBR	NR
Aslan et al. [20]	2012	F/50	Jejunum	13	NR	Peritonitis	SBR	NR
Memmi et al. [21]	2012	M/59	Jejunum	12	7/50	Peritonitis	SBR	NR
Choudhary et al. [22]	2012	M/35	Jejunum	4,5 × 3,5 × 2,5	>5/10	Peritonitis	SBR	48 Alive
Sezer et al. [23]	2012	F/61	Jejunum	5 × 2	9/50	Peritonitis	SBR + Imatinib	6 Alive
Roy et al. [24]	2012	M/46	Jejunum	3 × 2	NR	Peritonitis	SBR + Imatinib	6 Alive
Shoji et al. [25]	2013	M/61	Jejunum	9 × 7	0/50	Peritonitis	SBR + Imatinib	36 Alive
Beltrán et al. [26]	2013	M/46	Ileum	7.5 × 7	15/50	Abscess	SBR + Imatinib	NR
Misawa et al. [27]	2014	M/70	Jejunum	9 × 9	NR	Abscess	SBR + Imatinib	12 Alive
Sharma et al. [28]	2014	F/50	Ileum	10 × 8	NR	Peritonitis	SBR + Imatinib	NR
Mansoor [29]	2014	M/41	Multiple	NR	NR	Peritonitis	SBR + Imatinib	NR
Present case	2014	M/82	Jejunum	7 × 5	16/50	Peritonitis	SBR + Imatinib	6 Alive

Legend: SBR = Small Bowel Resection; NR = Not Reported.
[a] Patient with metastatic disease at presentation.

Table 2
Definition of the risk categories in the Joensuu classification (39).

Risk category	Tumor size (cm)	Mitotic index (per 50HPF*)	Primary tumor site
Very low risk	≤ 2.0	≤ 5	Any
Low risk	2.1 – 5.0	≤ 5	Any
Intermediate risk	≤ 5.0	6–10	Gastric
	5.1 – 10.0	≤ 5	Gastric
High risk	Any	Any	Tumor rupture
	> 10.0	Any	Any
	Any	> 10	Any
	> 5.0	> 5	Any
	≤ 5.0	> 5	Non-gastric
	5.1 – 10.0	≤ 5	Non-gastric

* HPF, high-power field

reported by Yamamoto and Coll. This patient had multiple hepatic metastases at the time of surgery and later developed peritoneal dissemination. At that time (2001) imatinib was still an investigational chemiotherapic agent and the patient was treated with this experimental therapy with dramatic clinical improvement [9].

4. Conclusions

Emergency presentation with a GIST is not uncommon and one of its manifestations is acute abdomen secondary to intraperitoneal rupture or perforation of a primary GIST of the small intestine. Emergency surgery is mandatory and should achieve radical resection. Primary anastomosis has been reported to be safe. Since there is an increased risk of recurrence after spontaneous intraperitoneal rupture/perforation of GISTs, patients should be evaluated by a multidisciplinary team in order to assess the indications for imatinib adjuvant therapy and for close monitoring and follow-up.

Competing interests

The authors declare that they have no competing interests.

Authors' information

MA is associate professor of the Department of Clinical, Surgical, Diagnostic and Paediatric Sciences, University of Pavia, and director of the Department of General Surgery, Varzi Hospital; MG, PS, EM and DZ are staff assistants of the Department of General Surgery, Varzi Hospital; SR is staff assistant of the Radiology Service, Voghera Hospital; VP is staff assistant of the Department of Oncology, IRCCS San Matteo Hospital Foundation, Pavia; LC is staff assistant of the Unit of General Surgery 1, IRCCS San Matteo Hospital Foundation, Pavia and assistant professor of the Department of Clinical, Surgical, Diagnostic and Paediatric Sciences, University of Pavia.

Authors' contribution

MA and LC developed the concept and designed the paper. MA, MG, PS, EM, DZ collected and analyzed the data and were involved in the care of the patient. SR and VP were involved in the interpretation of the diagnostic and oncologic data, in the diagnosis and in the follow-up of the patient. All the authors contributed equally to drafting the article or revising it critically for important intellectual content and for the final approval of the version to be published.

Consent

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

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