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

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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.

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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...
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 lymphatic 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 imatinib 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*        |
| Efremidou et al. [10]    | 2006 | M/66            | Ileum                | 7 x 5    | 2/50           | Peritonitis            | SBR + Imatinib | 44 Alive         |
| Karagüle et al. [11]     | 2008 | M/70            | Jejunum              | 5         | NR             | Abscess                | SBR        | 13 Alive          |
| Versaci et al. [12]      | 2009 | M/46            | Jejunum              | 12 x 7    | 5/50           | Peritonitis            | SBR + Imatinib | 12 Alive         |
| Tamaguchi et 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      | 5/50           | Peritonitis            | SBR        | 5 NR              |
| Ku et al. [15]           | 2010 | F/33            | Jejunum              | 6.5 x 4   | NR             | Peritonitis            | SBR        | NR                |
| Özben et al. [16]        | 2010 | M/65            | Jejunum              | 8          | <5/50          | Peritonitis            | SBR + Ileostomy | Dead POD 4       |
| Feng et al. [17]         | 2011 | M/45            | Jejunum              | 10 x 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 x 15   | 5/50           | Peritonitis            | SBR        | NR                |
| Asian 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 x 3.5 | <5/10          | Peritonitis            | SBR        | 48 Alive         |
| Sezer et al. [23]        | 2012 | F/61            | Jejunum              | 5 x 2     | 9/50           | Peritonitis            | SBR + Imatinib | 6 Alive         |
| Roy et al. [24]          | 2012 | M/46            | Jejunum              | 3 x 2     | NR             | Peritonitis            | SBR + Imatinib | 6 Alive         |
| Shojo et al. [25]        | 2013 | M/61            | Jejunum              | 9 x 7     | 0/50           | Peritonitis            | SBR + Imatinib | 36 Alive         |
| Beltrán et al. [26]      | 2013 | M/46            | Jejunum              | 7.5 x 7   | 15/50          | Abscess                | SBR + Imatinib | NR                |
| Misawa et al. [27]       | 2014 | M/70            | Jejunum              | 9          | NR             | Abscess                | SBR + Imatinib | 12 Alive         |
| Sharma et al. [28]       | 2014 | F/50            | Ileum                | 10 x 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 x 5     | 16/50          | Peritonitis            | SBR + Imatinib | 6 Alive         |

Legend: SBR = Small Bowel Resection; NR = Not Reported.

* 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  | 5.1 – 10.0     | 6–10                       | Gastric           |
| High risk     | Any            | Any                        | Any               |

* 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 chemotherapeutic 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.

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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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