Small, spontaneously ruptured gastrointestinal stromal tumor in the small intestine causing hemoperitoneum: A case report

Shuichi Fukuda a,*, Yoshinori Fujiwara a, Tomoko Wakasa b, Keisuke Inoue a, Kotaro Kitani a, Hajime Ishikawa a, Masanori Tsujie a, Masao Yukawa d, Yoshio Ohta b, Masatoshi Inoue a

a Department of Gastroenterological Surgery, Kindai University Nara Hospital, Nara, Japan
b Department of Pathology, Kindai University Nara Hospital, Nara, Japan

A R T I C L E   I N F O
Article history:
Received 7 April 2017
Received in revised form 4 May 2017
Accepted 31 May 2017
Available online 17 May 2017

Keywords:
Case report
Gastrointestinal stromal tumour
Haemoperitoneum
Imatinib
Small intestine
Tumour rupture

A B S T R A C T

INTRODUCTION: Gastrointestinal stromal tumours (GISTs) are clinically asymptomatic until they reach a significant size; therefore, GISTs that are 2 cm or less are typically asymptomatic. Patients with symptomatic GISTs typically present with abdominal pain, gastrointestinal bleeding, or a palpable mass but rarely present with hemoperitoneum.

PRESENTATION OF CASE: A 72-year-old Japanese man presented to us with acute onset abdominal pain. Physical examination showed peritoneal irritation in the lower abdomen. Findings of abdominal computed tomography were suggestive of hemoperitoneum; therefore, urgent surgery was performed. Approximately 1500 ml of blood in the abdominal cavity was removed. A small, ruptured mass was found in the middle of the small intestine, and partial resection of the small intestine, including the mass, was performed. The resected tumor was 2 cm in size and exhibited an exophytic growth pattern. Immunohistochemical staining revealed that the tumor was positive for KIT and CD34; therefore, a final diagnosis of GIST was made. Treatment with imatinib at 400 mg per day was started from postoperative month 1. The patient is doing well without recurrence 5 months after surgery.

DISCUSSION: Even small GISTs in the small intestine can spontaneously rupture and cause hemoperitoneum. Moreover, when a patient presents with sudden abdominal pain and hemoperitoneum without an evident mass on imaging, clinicians should be aware of the possibility of bleeding from a small GIST in the small intestine.

CONCLUSION: We present an extremely rare case of a patient with a small, spontaneously ruptured GIST in the small intestine, resulting in hemoperitoneum.

© 2017 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract [1]. GISTs occur throughout the gastrointestinal tract, arising most commonly from the stomach (50–60%) followed by the small intestine (30–35%) [2]. Approximately two-thirds of GISTs in the small intestine are 5 cm or more in diameter at the time of diagnosis and rarely 2 cm or less [3]. The majority of GISTs are clinically asymptomatic until they reach a significant size; therefore, GISTs that are 2 cm or less are typically asymptomatic.

Symptomatic GISTs are generally associated with abdominal pain, gastrointestinal bleeding, or a palpable mass but rarely associated with hemoperitoneum [2]. Hemoperitoneum is a potentially life-threatening complication of GISTs caused by burst of the intratumoral blood vessel and rupture of the tumor capsule. Spontaneously ruptured GISTs have been reported to be generally over 5 cm [4]. Here we report an extremely rare case of a patient with a spontaneously ruptured GIST in the small intestine, only 2 cm in size, causing hemoperitoneum. The work has been reported in line with the SCARE criteria [5].
2. Presentation of case

A 72-year-old Japanese man presented to our hospital with sudden abdominal pain. His blood pressure was 108/72 mmHg, his pulse was 83 beats per minute, and his temperature was 37.0 °C. Physical examination showed slight abdominal distention and peritoneal irritation in the lower abdomen. The patient was a non-smoker and social drinker, and he had a past medical history of polycythemia vera and asthma. Laboratory data showed an increased white blood cell count of 24,900/\mu L, with 89% neutrophils, and a slightly increased C-reactive protein concentration of 1.9 mg/dL. Elevated blood urea nitrogen level of 36.2 mg/dL and creatinine level of 2.5 mg/dL were observed in addition to microcytic hypochromic anemia (hemoglobin, 10.0 g/dL).

Abdominal computed tomography (CT) revealed bilateral subphrenic fluid without free air and high concentrations of fluid in the pelvis, which was suggestive of hemoperitoneum (Fig. 1a and b). Urgent surgery was performed, although a definitive diagnosis was not made preoperatively. Laparoscopic exploration revealed hemorrhagic ascites in the entire abdominal cavity (Fig. 2). Major hemorrhages were suspected; therefore, laparoscopic surgery was converted to open abdominal surgery. Approximately 1500 ml of blood in the abdominal cavity was subsequently removed. A small, ruptured mass with a massive hematoma was found in the middle of the small intestine (Fig. 3a). Partial resection of the small intesti-
tine, including the mass, was performed, and functional end-to-end anastomosis of the small intestine was performed.

The resected tumor was 2 cm in size. The tumor grew exophytically, and the mucosal side of the resected small intestine was clear (Fig. 3b). Hematoxylin–eosin staining revealed a bundle-like growth of the spindle-shaped tumor cells with acidicophilic cytoplasm and enlarged nuclei with increased chromatin (Fig. 4a). Hemorrhage within the tumor was noted (Fig. 4b), and the mitotic count was 3 per 50 high-power fields. The tumor cells grew externally from the proper muscle layer of the small intestine. Resection margins were free of the tumor cells, and immunohistochemical staining revealed that the tumor was positive for KIT and CD34 and negative for desmin and S-100 proteins (Fig. 4c and d). The MIB-1 labelling index of the tumor cells was 3%. Based on these findings, a final diagnosis of GIST in the small intestine was made. Because macroscopic tumor rupture was identified, this case was classified into the high-risk category according to the modified Fletcher’s classification [6]. Tumor genotyping with sequencing for mutations in KIT gene (exon 9 and 11) disclosed a heterozygous mutation of 1721del25insC (N567T, Y568Q575delC) at exon 11. The patient had an uneventful postoperative course and was discharged from the hospital on postoperative day 12. Treatment with imatinib at 400 mg per day was started from postoperative month 1. The patient is doing well without recurrence 5 months after surgery.

3. Discussion

The small intestine is the second most common primary site for GISTs [2]. Previous reports showed that the median tumor size of GISTs in the small intestine was 7 cm at the time of diagnosis, and a size of 2 cm or less is rare [3]. Small GISTs generally do not produce any symptoms and rarely progress or metastasize [1]. In this study, we report an extremely rare case of a patient with spontaneously ruptured GIST in the small intestine, only 2 cm in size, causing hemoperitoneum. Table 1 shows 13 cases of spontaneously ruptured GISTs in the small intestine causing hemoperitoneum previously reported in the English literature, including this report [7–18]. Nine of the 13 patients (69.2%) were male, with a median age of 54 years (range, 28–87 years). Except for the undescribed cases, all tumors exhibited an exophytic growth pattern. Twelve of the 13 patients (92.3%) were without concurrent peritoneal dissemination. Nine of the 13 tumor sizes (69.2%) were 10 cm or more, and our case is the smallest. Our case demonstrates that GISTs in the small intestine can spontaneously rupture and cause hemoperitoneum even if they are small.

In the present study, resected tumor histologically showed an intratumoral hemorrhage. Hemoperitoneum is thought to be caused by hematoma formation due to intratumoral hemorrhage, followed by increased intratumoral pressure and subsequent rupture of the tumor capsule [12,18]. The histological findings of our case are compatible with this theory, although the mechanisms behind intratumoral hemorrhage are uncertain. Because of their high vascularity, ruptured GISTs can be associated with massive hemoperitoneum. In fact, as shown in Table 1, the amount of hemoperitoneum is generally 1000 ml or more in ruptured GISTs; furthermore, hemorrhagic shock can occur. Hemoperitoneum can lead to sudden abdominal pain and unstable circulatory dynamics; therefore, prompt diagnosis and intervention are imperative. Owing to its convenience and diagnostic ability regardless of the skill of the operator, CT may be a useful modality for the diagnosis of hemoperitoneum. When large, ruptured GISTs cause hemoperitoneum, contrast-enhanced CT can show a heterogeneously enhanced mass with hemoperitoneum [19]; however, when the tumor size is small, only hemoperitoneum is likely to be found, as in our case. When a patient presenting with sudden

| Case | Author | Gender | Age | Diagnosis | Modality | Size | Motive | Count | HPFs | Growth | Amount of hemorrhage | Outcome | Treatment | Recurrence |
|------|--------|--------|-----|----------|----------|-----|--------|-------|------|--------|---------------------|--------|-----------|------------|
| 1    | Dellah | M      | 48  | GIST     | CT       | 15 cm | Yes    | 1200 ml | Exophytic | No     | No       | Yes                 | No     | PR        | No         |
| 2    | Djakic | F      | 62  | GIST     | CT, US  | 75 cm | Exophytic | 600 ml | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 3    | Gepart | F      | 76  | GIST     | CT, US  | 13 cm | Exophytic | 1000 ml | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 4    | Hazalsi| M      | 87  | GIST     | CT, US  | 10 cm | Exophytic | 2500 ml | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 5    | Wang   | M      | 71  | GIST     | CT, US  | 8 cm  | Yes    | 300 ml  | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 6    | Yudico | M      | 76  | GIST     | CT, US  | 8 cm  | Yes    | 1000 ml | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 7    | Mabidha| M      | 87  | GIST     | CT, US  | 10 cm | Exophytic | 2000 ml | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 8    | Varas  | F      | 71  | GIST     | CT, US  | 13 cm | Yes    | 500 ml  | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 9    | Azinali | M      | 46  | GIST     | CT, US  | 15 cm | No     | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 10   | Lai     | M      | 54  | GIST     | CT, US  | 2 cm  | No     | Exophytic | No     | No       | No                 | No     | PR        | No         |
| 11   | Our case|        | 72  | GIST     | CT, US  | 2 cm  | No     | Exophytic | No     | No       | No                 | No     | PR        | No         |

GIST, gastrointestinal stromal tumor; PD, peritoneal dissemination; CT, computed tomography; US, ultrasonography; HPF, high-power field; PR, partial resection of the small intestine; IM, imatinib.
abdominal pain has concurrent hemoperitoneum without an evident mass on imaging, clinicians should be alerted to the possibility of bleeding from a small GIST in the small intestine.

Tumor rupture is a significant risk factor of recurrence [6]; therefore, our case is considered a high-risk GIST patient, although the tumor was small and the mitotic count was low. Adjuvant imatinib for high-risk GIST patients who have undergone surgery is helpful for improving both recurrence-free survival and overall survival [20]. As shown in Table 1, surgery followed by imatinib administration can improve survival for spontaneously ruptured GISTs in the small intestine causing hemoperitoneum. GISTs with KIT exon 11 mutations are highly sensitive to imatinib [20]. Moreover, KIT exon 11 mutations that involve codons 557–558 indicate a poor prognosis [21]. In the present study, a KIT exon 11 mutation that did not involve codons 557–558 was observed. Therefore, the patient is likely to have a favorable prognosis.

Small, spontaneously ruptured GISTs in the small intestine causing hemoperitoneum are relatively rare; therefore, the number of patients treated in a single institution limits the amount of insight that can be gleaned about the description of this rare tumor. The accumulation of prospective evidence from multiple case reports and institutions is needed to clarify the clinicopathological features and adequate treatment strategies.

4. Conclusion

We reported an extremely rare case of a patient with a small, spontaneously ruptured GIST in the small intestine causing hemoperitoneum. Learning points of this case report are 1) it is important to consider the possibility of spontaneous rupture with resultant hemoperitoneum of even small GISTs in the small intestine and 2) when a patient presents with sudden abdominal pain and hemoperitoneum without an evident mass on imaging, one should consider a potential bleeding from a small GIST in the small intestine.

Conflicts of interest

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

This study was approved by the Ethics Committee of our institution (approval number: 17-5).

Consent

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 Editor-in-Chief of this journal on request.

Author contribution

SF designed the study and drafted the manuscript. SF and YF performed the operation. TW and YO performed the histopathological examination. KI, KK, HI, MT, MY, and MI participated in the manuscript revision process. All authors read and approved the final manuscript.

Registration of research studies

Not applicable.
Guarantor

The guarantor of this manuscript is Shuichi Fukuda, corresponding author.

Acknowledgement

The authors would like to thank Enago (www.enago.jp) for the English language review.

References

[1] T. Nishida, O. Goto, C.P. Raut, N. Yahagi, Diagnostic and treatment strategy for small gastrointestinal stromal tumors, Cancer 122 (2016) 3110–3118.
[2] H. Joensuu, P. Hohenberger, C.L. Corless, Gastrointestinal stromal tumour, Lancet 382 (2013) 973–983.
[3] M. Miettinen, H. Makhlouf, L.H. Sobin, J. Lasota, Gastrointestinal stromal tumors of the jejunum and ileum: a clinicopathologic, immunohistochemical, and molecular genetic study of 906 cases before imatinib with long-term follow-up, Am. J. Surg. Pathol. 30 (2006) 477–489.
[4] Y. Hwangbo, J.Y. Jang, H.J. Kim, Y.W. Kim, S.D. Park, J. Shim, et al., Spontaneous rupture of a sigmoid colon gastrointestinal stromal tumor manifesting as pneumoretroperitoneum with localized peritonitis: report of a case, Surg. Today 41 (2011) 1085–1090.
[5] R.A. Agha, A.J. Fowler, A. Saetta, I. Barai, S. Rajmohan, D.P. Orgill, for the SCARE Group, The SCARE Statement: consensus-based surgical case report guidelines, Int. J. Surg. 34 (2016) 180–186.
[6] H. Joensuu, Risk stratification of patients diagnosed with gastrointestinal stromal tumour, Hum. Pathol. 39 (2008) 1411–1419.
[7] S.R. Dubenec, E.K. Davies-Higgs, R.J. Higgs, P.G. Trussett, Haemoperitoneum caused by spontaneous rupture of a gastrointestinal stromal tumour, ANZ J. Surg. 71 (2001) 612–614.
[8] M. Ajudiuk, D. Mikulic, B. Sebeci, S. Gasparov, L. Patrlj, L. Erdelez, et al., Spontaneously ruptured gastrointestinal stromal tumor (GIST) of the jejunum mimicking acute appendicitis, Coll. Antropol. 28 (2004) 937–941.
[9] M.F. Cegarra-Navarro, M.A. de la Calle, E. Girela-Baena, J.M. Garcia-Santos, F. Lloret-Estalt, E.P. de André, Ruptured gastrointestinal stromal tumors: radiologic findings in six cases, Abdom. Imaging 30 (2005) 535–542.
[10] S. Hirasaki, K. Fujita, M. Matsubara, H. Kanzaki, H. Yamane, M. Okuda, et al., A ruptured large extraluminal ileal gastrointestinal stromal tumor causing hemoperitoneum, World J. Gastroenterol. 14 (2008) 2928–2931.
[11] C.Y. Wang, F. Du, S.M. Huang, Y.C. Tsai, Nontraumatic hemoperitoneum due to spontaneous gastrointestinal stromal tumor rupture: a case report, Chin. J. Radiol. 34 (2009) 293–297.
[12] T.A. Worley, S.S. Abadin, E. Revesz, G.I. Salti, Gastrointestinal stromal tumor with hemoperitoneum masquerading as appendicitis, Int. Surg. 95 (2010) 8–11.
[13] D. Isuco, M. Jannaci, A. Grassi, S. Bonomi, I. Ismail, G. Navarra, et al., Giant ileal gastrointestinal stromal tumour presenting as an intestinal subocclusion and subsequent haemoperitoneum: a case report and a review of the literature, Updates Surg. 62 (2010) 189–193.
[14] E.A. Mahmoud, F. Fadhel, M. Amin, R. Wael, D. Amin, B. Haykel, et al., A ruptured ileal GI stromal tumor causing hemoperitoneum, Gastrointest. Endosc. 71 (2010) 185–186.
[15] M. Varras, N. Vlachakos, C. Akrivis, T. Vasilakaki, E. Skafida, Malignant gastrointestinal stromal tumor presenting with hemoperitoneum in puerperium: report of a case with review of the literature, World J. Surg. Oncol. 8 (2010) 95.
[16] M. Nannini, M.A. Pantaleo, F. Catena, S. Romano, S. Tondo, M.G. Pirini, et al., Surgical second-look in high risk gastrointestinal stromal tumor of small intestine: a case report, Int. J. Surg. Case Rep. 4 (2013) 7–10.
[17] W. Attaallah, Ş. Çöpkun, G. Özden, H. Mollanemisoglu, C. Yeşen, Spontaneous rupture of extraluminal jejunal gastrointestinal stromal tumor causing acute abdomen and hemoperitoneum, Ulus. Cerrahi Derg. 31 (2015) 99–101.
[18] E.C. Lai, K.M. Chung, S.H. Lau, W.Y. Lau, A ruptured recurrent small bowel gastrointestinal stromal tumour causing hemoperitoneum, Front. Med. 9 (2015) 108–111.
[19] K. Sandrasageran, A. Rajesh, D.A. Rushing, J. Rydberg, F.M. Akisik, J.D. Henley, Gastrointestinal stromal tumors: CT and MRI findings, Eur. Radiol. 15 (2005) 1407–1414.
[20] H. Joensuu, M. Eriksson, K. Sundby Hall, A. Reichardt, J.T. Hartmann, D. Pink, et al., Adjuvant imatinib for high-risk GI stromal tumor: analysis of a randomized trial, J. Clin. Oncol. 34 (2016) 244–250.
[21] J. Martín, A. Poveda, A. Llombart-Bosch, R. Ramos, J.A. López-Guerrero, J. García del Muro, et al., Deletions affecting codons 557–558 of the c-KIT gene indicate a poor prognosis in patients with completely resected gastrointestinal stromal tumors: a study by the Spanish Group for Sarcoma Research (GEIS), J. Clin. Oncol. 23 (2005) 6190–6198.