

## A Spontaneously Ruptured Gastric Stromal Tumor with Cystic Degeneration Presenting as Hemoperitoneum : A Case Report

We report a case of a 38-yr-old man with a spontaneously ruptured gastric stromal tumor presenting as hemoperitoneum in outpatient clinic. He visited our hospital with generalized abdominal pain after abdominal CT scan for the evaluation of the asymptomatic palpable abdominal mass. Repeated abdominal CT scan showed a size decrement of cystic mass compared with the previous abdominal CT scan, and newly developed fluid collection in the left paracolic gutter. An emergency laparotomy revealed a ruptured gastric stromal tumor with bloody fluid in the peritoneal cavity. Immunohistochemical examination revealed positive reactivity to C-kit protein and CD34. The patient presented with hemoperitoneum due to spontaneous rupture of the tumor, which is an extremely rare complication.

**Key Words :** *Stomach Neoplasms; Gastric Stromal Tumor; Rupture; Hemoperitoneum; Proto-Onco-gene; Protein c-kit*

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## INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are specific mesenchymal tumors of the gastrointestinal (GI) tract that may occur in the entire length of the GI tract. The results of recent molecular pathologic studies showing that most GISTs are immunoreactive for CD34, a marker for dendritic fibroblastic interstitial cells, and CD117, a c-kit proto-oncogene protein seem to support the concept of GISTs as biologically distinct entity (1, 2).

GISTs may be detected during a gastroscopy as submucosal tumors or occasionally as incidental radiologic findings. The symptomatic GISTs of the esophagus typically present with dysphagia. Gastric and small intestinal GISTs often present with vague symptoms leading to their gastroscopic or radiologic detection, but sometimes they cause upper gastrointestinal bleeding (3). Colorectal GISTs may manifest with lower GI bleeding, colonic perforation, pain, obstruction, or combination thereof (4). There were few reports of spontaneous rupture of the GISTs in the stomach. This report describes the case presented with hemoperitoneum due to spontaneous rupture of the tumor, which is an extremely rare complication.

## CASE REPORT

A 38-yr-old man visited our hospital with generalized abdominal pain. He visited our hospital 1 week ago because he felt the painless abdominal mass. A plain abdominal radiography showed a huge opaque area in the left upper quadrant and displaced neighboring bowel loop. Initial abdominal CT scan showed a 15 × 10 cm sized oval-shaped, low density mass in peritoneal cavity with central thickened septa like enhancing solid component, which showed broad abutment with the stomach in part (Fig. 1). The next day he visited the emergency department of our hospital due to severe abdominal pain. At that time, on physical examination, the palpable mass in epigastric area was decreased in size compared before. The body temperature was 36.6°C, pulse rate was 85 beats/min, and respiration rate was 20 times/min. The blood pressure was 130/90 mmHg. The laboratory findings revealed no abnormalities except for a low hemoglobin level of 11.9 g/dL. Therefore we performed the follow up abdominal CT scan. On physical examination, abdomen was distended and accompanied with generalized rebound tenderness, but there was no muscle guarding. The abdominal pain was spontaneously subsided one day after admission.

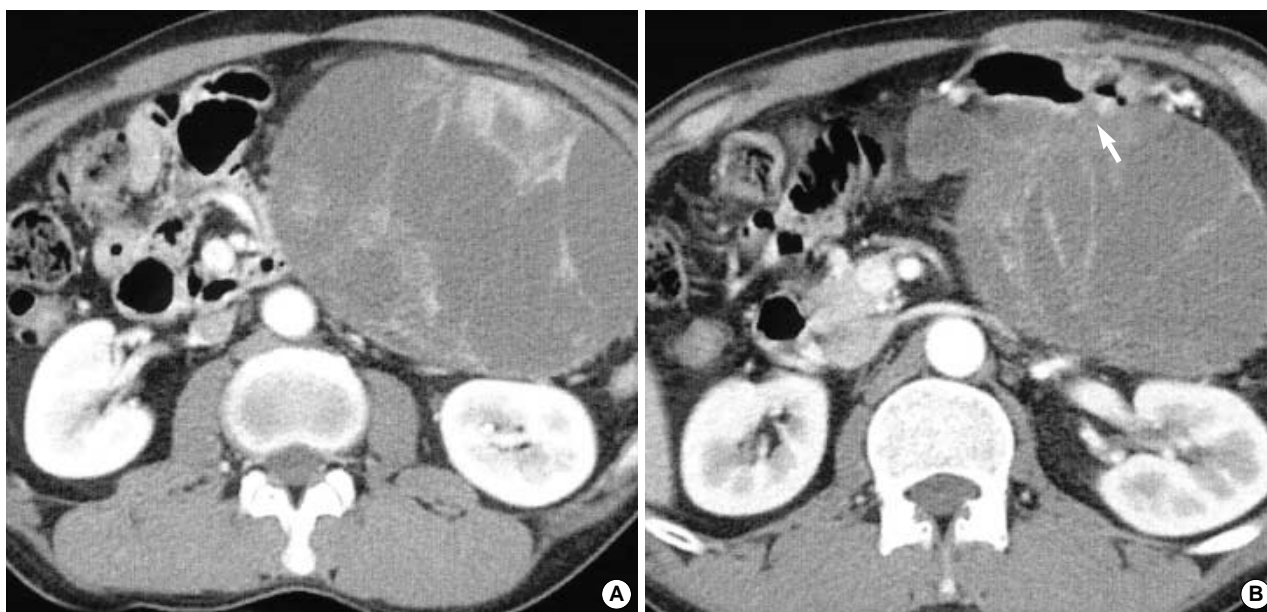


Fig. 1. Initial abdominal CT scan shows a 15 × 10 cm sized oval shaped low dense mass in peritoneal cavity with central thickened septa like enhancing solid component (A), which shows broad abutment with stomach in part (B, arrow).

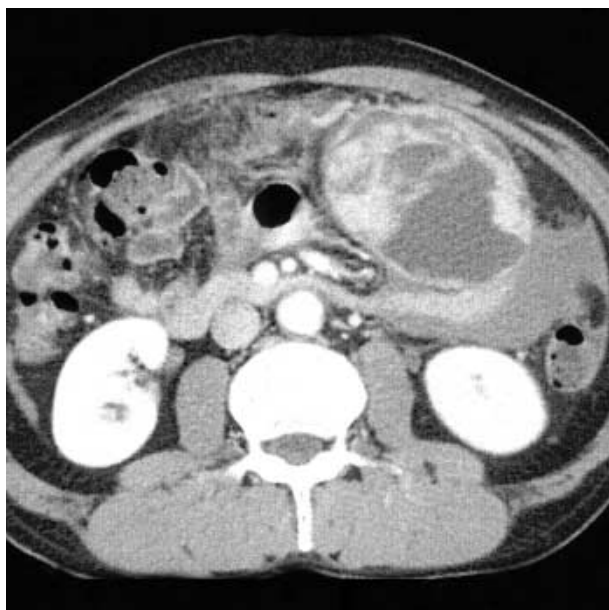


Fig. 2. Follow up abdominal CT scan shows a decreased size mass compared with the finding of the initial abdominal CT scan, and demonstrates a newly developed fluid collection in left paracolic gutter.

Follow-up abdominal CT scan showed a decreased mass size compared with the finding of the initial abdominal CT scan, and it demonstrated a newly developed fluid collection in left paracolic gutter (Fig. 2).

Under the diagnosis of hemoperitoneum due to the ruptured intraabdominal cystic mass, an emergency laparotomy was performed. When the peritoneum was opened, bloody ascites was

encountered, and the exploration revealed a ruptured large tumor arising from posterior wall of the middle part of stomach.

The resected tumor was a well-circumscribed mass, measuring 10 × 9 × 6 cm in size (Fig. 3A). Tumor was focally attached to the gastric wall. On section it consisted of irregular solid trabeculae with large areas of cystic degeneration and hemorrhage (Fig. 3B). The solid portion was pink gray, soft, and fish-flesh in appearance. Microscopically, tumor cells were epithelioid or spindle-shaped in ill-defined fascicular arrangement (Fig. 4A). The tumor cells were growing exophytically from the gastric muscular propria. There were a few foci of nuclear pleomorphism. The mitotic count was about 4 mitoses/50 HPF (high power field) with atypical forms (Fig. 4B). Immunohistochemical staining of the tumor tissue demonstrated positive reactivity to c-kit (Fig. 5A) and CD34 (Fig. 5B), but demonstrated negative reactivity to S-100 protein and to smooth muscle markers. The Ki-67 proliferation index was less than 2%. Therefore it could be diagnosed as gastric stromal tumor of borderline malignancy.

He was discharged from hospital on the 18th postoperative day and has been treated with chemotherapy with imatinib (Gleevec, Novartis, Switzerland) in the outpatient clinic without any medical problems.

## DISCUSSION

In the GI tract, CD117-positive cells are the interstitial cells of Cajal, autonomous nerve-related GI pacemaker cells that regulate intestinal motility (5). Because of the immunohistochemical and ultrastructural similarities between Cajal cells



Fig. 3. (A) The resected tumor is 10×9×6 cm in size. A stump of gastric wall is noted (arrow). (B) On section it consists of irregular pink gray fish-flesh solid trabeculae with large areas of cystic degeneration and hemorrhage.

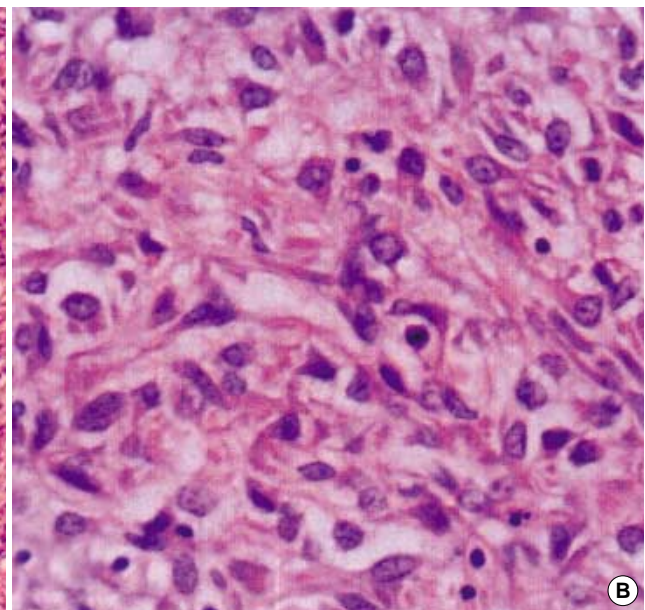
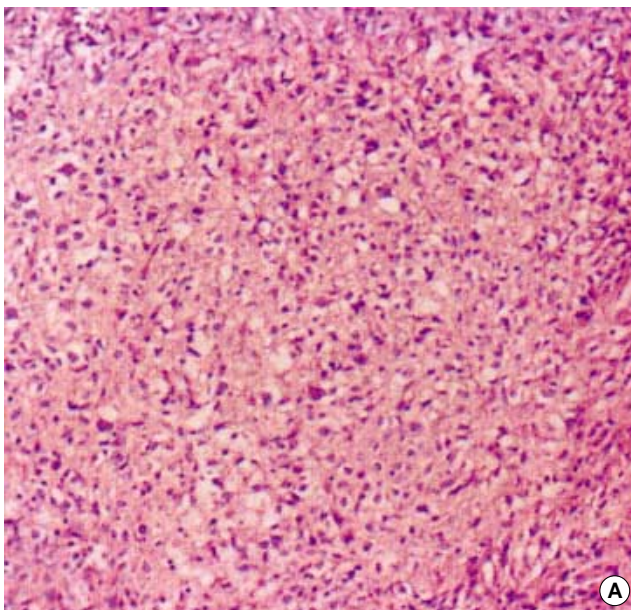


Fig. 4. (A) A microscopically, epithelioid or spindle-shaped tumor cells are arranged in ill-defined fascicles (H&E, ×100). (B) There are mild nuclear pleomorphism and occasional mitotic figures (H&E, ×400).

and GISTs, the histogenetic origin of GISTs from Cajal cells has been proposed (6). Another possibility is that GISTs originate from primitive stem cells that can differentiate into Cajal cells and smooth-muscle cells (2). GISTs are defined here as cellular spindle cells, epithelioid, or occasionally pleomorphic mesenchymal tumors of the gastrointestinal tract that express the c-kit (CD117, stem cell factor receptor). Immunohistochemical analysis of the tumor from our patient showed positive staining for CD34 and c-kit.

In our review of the literature on ruptured GISTs, we were able to find only two other similar case reports (7, 8); one case

was an 83-yr-old patient presenting with intraperitoneal hemorrhage and hypovolemic shock who was successfully treated by a total gastrectomy. However, c-kit expression was not investigated in this case. The other one was a 75-yr-old patient who was also presenting with generalized peritonitis and severe abdominal pain; c-kit expression was investigated in this case. Hasegawa et al. (9) reported that the clinical features of 171 cases of GIST with a long follow-up period were investigated for accurate diagnosis. 107 cases (62.6%) were identified incidentally through endoscopic screening. The most common symptoms were pain, followed by GI bleeding, signs of obst-



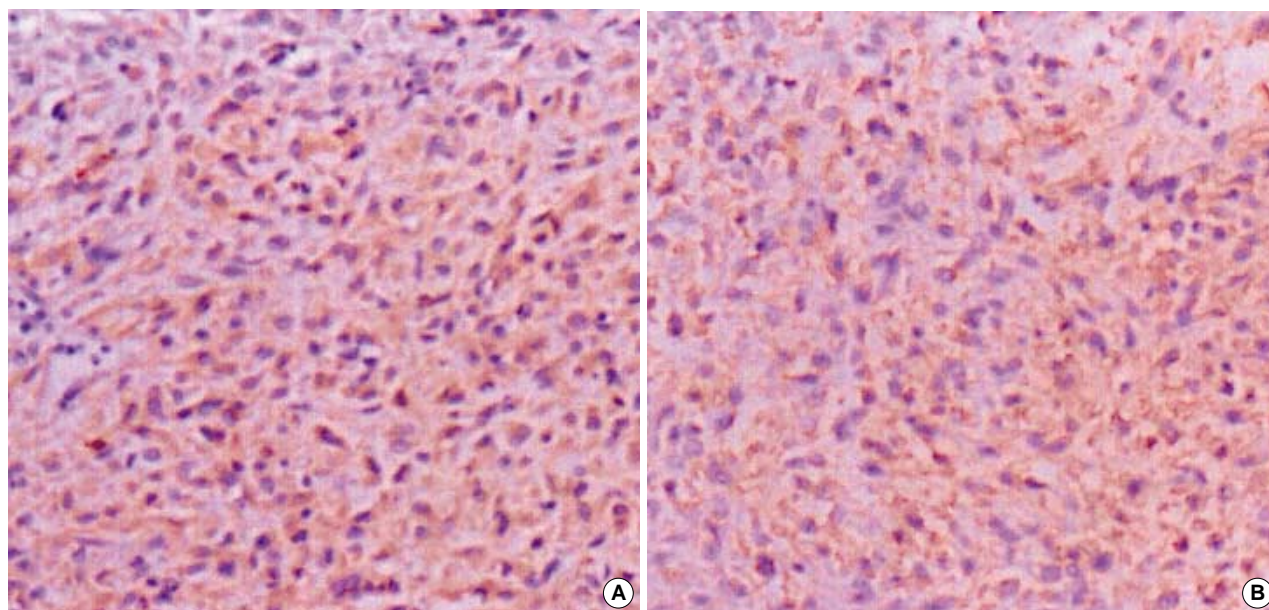


Fig. 5. Immunohistochemical staining of the tumor tissue demonstrates positive reactivity to c-kit (A) and CD34 (B) by avidin-biotin complex method ( $\times 200$ ).

ruption, and masses. These tumors appeared primarily as endophytic polypoid submucosal growth, often with surface ulceration and bleeding, although some appeared as exophytic subserosal lesions extending into the mesentery or retroperitoneum of the small intestine. We do not know the precise reason of spontaneous rupture of the GIST. However, we think that the rupture may be at the weakened wall of mass, which may be due to cystic degeneration within the mass. The patient's ordinary activity or physical impact by the movement of intestine may trigger the rupture of the weakened mass wall.

The clinicopathologic adverse prognostic factors tested in large series of GISTs and found significant in at least one investigation to include aneuploidy on DNA flow cytometry (10, 11), tumor size more than 5–6 cm (9, 10), presence of coagulative tumor necrosis (12), and high Ki67-labelling index (more than 5%) (11, 13). Ng and colleagues (14) reported the factors that were associated with a significantly better outcome in gastrointestinal leiomyosarcoma: complete resection without tumor rupture, localized lesions, low grade of tumor (low mitotic figure), and tumor smaller than 5 cm. There is no evident report of the prognosis yet due to the rare case of the rupture in the GISTs. We believe, however, that the prognosis will not be so good either because the complete tumor removal is not possible in case of the ruptured GISTs as reported above.

Chemotherapy with imatinib (Gleevec, Novartis, Switzerland) was performed in our patient due to the large tumor size ( $>5$  cm), presence of coagulative tumor necrosis, borderline mitotic activity (4/50 HPF), and ruptured state. Although GISTs seldom responds to conventional chemotherapeutic agents, several experiences with tyrosine kinase inhibitor (Gleevec), have been extremely encouraging (15, 16).

## REFERENCES

1. Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, Kawano K, Hanada M, Kurata A, Takeda M, Muhammad Tunio G, Matsuzawa Y, Kanakura Y, Shinomura Y, Kitamura Y. *Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science* 1998; 279: 577-80.
2. Miettinen M, Lasota J. *Gastrointestinal stromal tumors; definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. Virchows Arch* 2001; 438: 1-12.
3. Ueyama T, Guo K-J, Hashimoto H, Daimaru Y, Enjoji M. *A clinicopathologic and immunohistochemical study of gastrointestinal stromal tumors. Cancer* 1992; 69: 947-55.
4. Miettinen M, Sarlomo-Rikala M, Sobin LH, Lasota J. *Gastrointestinal stromal tumors and leiomyosarcomas in the colon: a clinicopathologic, immunohistochemical, and molecular genetic study of 44 cases. Am J Surg Pathol* 2000; 24: 1339-52.
5. Maeda H, Yamagata A, Nishikawa S, Yoshinaga K, Kobayashi S, Nishi K, Nishikawa S. *Requirement of c-kit for development of intestinal pacemaker system. Development* 1992; 116: 369-75.
6. Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. *Gastrointestinal pacemaker cell tumor (GIPACT). Gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. Am J Pathol* 1998; 152: 1259-69.
7. Pera M, Saenz A, Fernandez-Cruz L. *Hemoperitoneum due to a ruptured gastric stromal tumor. Dig Surg* 1999; 16: 248-9.
8. Kitabayashi K, Seki T, Kishimoto K, Saitoh H, Ueno K, Kita I, Takashima S, Kurose N, Nojima T. *A spontaneously ruptured gastric stromal tumor presenting as generalized peritonitis: report of a case. Surg Today* 2001; 31: 350-4.
9. Hasegawa T, Matsuno Y, Shimoda T, Hirohashi S. *Gastrointestinal*

- stromal tumor: consistent CD117 immunostaining for diagnosis, and prognostic classification based on tumor size and MIB-1 grade. Hum pathol* 2002; 33: 669-79.
10. Cunningham RE, Federspiel BH, McCarthy WF, Sobin LH, O'Leary TJ. *Predicting prognosis of gastrointestinal smooth muscle tumors. Role of clinical and histologic evaluation, flow cytometry, and image cytometry. Am J Surg Pathol* 1993; 17: 588-94.
  11. Rudolph P, Gloeckner K, Parwaresch R, Harms D, Schmidt D. *Immunophenotype, proliferation, DNA-ploidy, and biological behavior of gastrointestinal stromal tumors: a multivariate clinicopathologic study. Hum Pathol* 1998; 29: 791-800.
  12. Lerma E, Oliva E, Tugues D, Prat J. *Stromal tumors of the gastrointestinal tract: a clinicopathological and ploidy analysis of 33 cases. Virchows Arch* 1994; 424: 19-24.
  13. Ando N, Goto H, Niwa Y, Hirooka Y, Ohmiya N, Nagasaka T, Hayakawa T. *The diagnosis of GI stromal tumors with EUS-guided fine needle aspiration with immunohistochemical analysis. Gastrointest Endosc* 2002; 1: 37-43.
  14. Ng EH, Pollock RE, Munsell MF, Atkinson EN, Romsdahl MM. *Prognostic factors influencing survival in gastrointestinal leiomyosarcomas. Ann Surg* 1991; 215: 68-77.
  15. Joensuu H, Roberts PJ, Sarlomo-Rikala M, Andersson LC, Tervahartiala P, Tuveson D, Silberman S, Capdeville R, Dimitrijevic S, Druker B, Demetri GD. *Effect of the tyrosine kinase inhibitor STI571 in a patient with a metastatic gastrointestinal stromal tumor. N Engl J Med* 2001; 344: 1052-6.
  16. van Oosterom AT, Judson I, Verweij J, Stroobants S, Donato di Paola E, Dimitrijevic S, Martens M, Webb A, Sciot R, Van Glabbeke M, Silberman S, Nielsen OS, European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. *Safety and efficacy of imatinib (STI571) in metastatic gastrointestinal stromal tumours: a phase I study. Lancet* 2001; 358: 1421-3.