

## Life-threatening Bleeding from Gastrointestinal Stromal Tumor of the Stomach

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### Abstract

Here, we report on two patients with hemorrhagic shock due to hematemesis from a gastrointestinal stromal tumor (GIST) of the stomach. Patient 1 was a 64-year-old woman who was admitted to our hospital because of syncope due to hemorrhagic shock resulting from massive hematemesis. Emergent upper gastrointestinal (GI) endoscopy revealed a 5-cm-diameter submucosal tumor on the lesser curvature of the lower gastric body. In addition to the central ulceration of the tumor, a Dieulafoy-like lesion was present. Neither lesions showed active bleeding at the time of observation. Because the patient collapsed twice with fluminant hematemesis after admission, she underwent distal gastrectomy with Billroth-I reconstruction. Histological examination revealed a gastric GIST with no nodal metastasis and the mitotic count was less than 5 per 50 HPFs. Dilated vessels were prominent in the peritumoral submucosa, and a thrombus was seen in these vessels, which seemed to be a bleeding point. The patient had an uneventful postoperative course and has been alive without recurrence for 5 and a half years. Patient 2 was a 60-year-old man who presented with syncope due to hemorrhagic shock resulting from massive hematemesis. Because the source of the bleeding was not elucidated with an initial upper GI endoscopy, he was treated for a gastric ulcer. One week after admission, he suffered from hemorrhagic shock again, and a submucosal tumor 6 cm in size was revealed on the greater curvature of the upper stomach with upper GI endoscopy. The patient subsequently underwent wedge resection of the tumor. Histopathological findings were consistent with a GIST and the mitotic count was less than 5 per 50 high-power fields. The tumor showed no necrosis or intratumoral hemorrhage. A peritumoral submucosal artery, which was responsible for the massive hematemesis, was located at some distance away from the central ulceration. Postoperative recovery was without complications. After 4 years, the patient remains healthy and disease-free. Although hematemesis associated with gastric GIST has been said to originated from the central ulceration of the GIST, life-threatening, massive hematemesis is rare. The exact bleeding points of the gastric GISTs in these cases were submucosal vessels adjacent to the GIST, not the central ulceration. There have been no reports of peritumoral, submucosal vessels causing massive hematemesis from gastric GISTs. Because the origins and manner of bleeding varies

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in gastric GISTs, we must decide the methods of hemostasis immediately including the tumor excision.

(J Nippon Med Sch 2008; 75: 306–311)

**Key words:** gastrointestinal stromal tumor, stomach, hematemesis

## Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumor of the gastrointestinal (GI) tract. Although GISTs may arise throughout the gut, they are most often found in the stomach (60% to 70%), followed by the small intestine (20% to 30%), colon and rectum (5%), and esophagus (<5%)<sup>1-3</sup>. GISTs represent only 0.1% to 1.0% of gastric tumors<sup>4,5</sup>. The most common symptoms associated with gastric GISTs are abdominal pain and GI bleeding<sup>6,7</sup>. Although the degree of GI bleeding varies from asymptomatic occult bleeding to massive bleeding, life-threatening hematemesis that requires emergent surgery is rare<sup>8,9</sup>. Endoscopic injection of ethanol, laser, argon beam plasma coagulation, and hemostatic clipping are used to achieve emergent hemostasis of GISTs<sup>10</sup>. Next, the standard treatment of localized, resectable GIST is surgery, which can achieve complete hemostasis<sup>11</sup>. Here, we report on two patients with hemorrhagic shock due to hematemesis from a GIST of the stomach. The bleeding points of these GISTs were unusual, as revealed with detailed pathological examinations.

## Case Report

Patient 1 was a 64-year-old woman who was admitted to our hospital because of syncope due to hemorrhagic shock resulting from massive hematemesis. Laboratory analysis showed a hemoglobin level of 8.2 g/dL. Emergent upper GI endoscopy revealed a 5-cm-diameter submucosal tumor on the lesser curvature of the lower gastric body. In addition to the central ulceration of the tumor, a Dieulafoy-like lesion was present. Neither lesions showed active bleeding at the time of the observation (**Fig. 1a**). Hemostasis was achieved

through the application of 3 hemoclips to the Dieulafoy-like lesion.

Twenty-four hours after admission, the patient collapsed again because of hematemesis. Endoscopy was performed again and revealed recurrent bleeding from the Dieulafoy-like lesion of the tumor. This time, hemostasis was achieved with ethanol injection and the application of 2 hemoclips. However, 12 hours later, the patient began to vomit large amounts of blood, and showed a hemoglobin level of 3.4 g/dL. Because a third endoscopic examination revealed oozing from the Dieulafoy-like lesion of the tumor, we concluded that complete hemostasis could not be achieved with endoscopic procedures. The patient underwent laparotomy later that day.

Distal gastrectomy with Billroth-I gastroduodenostomy was performed because of the tumor's location and size. Neither peritoneal dissemination nor liver metastasis was observed. Gross examination revealed a 4.0 × 5.0-cm submucosal tumor covered by mucosa with central ulceration, which had not invaded adjacent organs. The cut surface of the tumor was white and firm and showed no hemorrhage or necrosis. Histological examination revealed a stromal cell neoplasm composed of spindle-shaped cells with oval nuclei (**Fig. 1b**). No lymph node metastasis was found and less than 5 mitoses per 50 high-power fields (HPFs) were found in the tumor. Dilated vessels were prominent in the submucosa adjacent to the tumor, and a thrombus was seen in these vessels, which indicated that the bleeding point (**Fig. 1c**). In the central ulceration, there was no evidence of massive hematemesis. Immunohistochemical studies revealed that tumor cells were positive for KIT and CD34 (**Fig. 1d, e**), but negative for S-100 and  $\alpha$ -smooth muscle actin, as markers of neurogenic and myogenic cells, respectively. On the basis of these findings, we finally diagnosed a gastric GIST. The

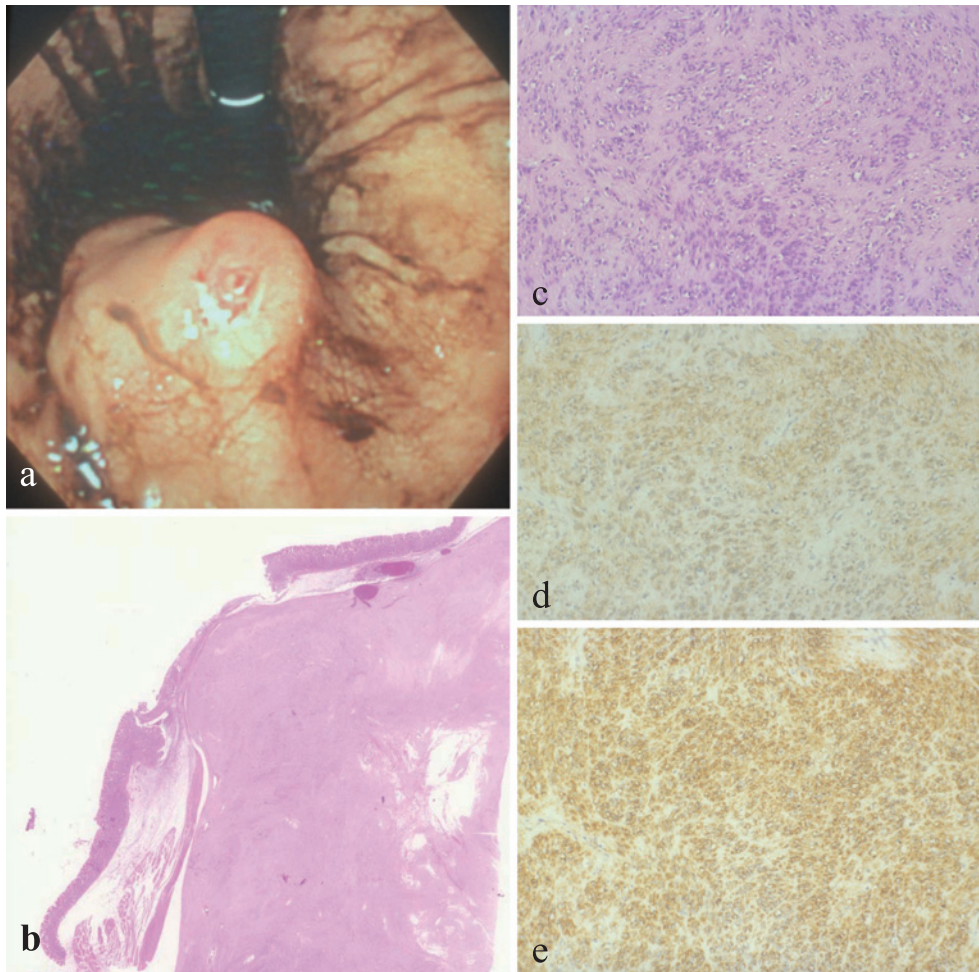


Fig. 1 **a:** Upper GI endoscopy revealed a submucosal tumor on the lesser curvature of the lower gastric body. **b:** Histological findings of tumor. The tumor was characterized by fascicular and interlacing proliferation of spindle - shaped cells (hematoxylin and eosin,  $\times 200$ ). **c:** Eroded vessels can be seen at the peritumoral submucosal layer with thrombus (hematoxylin and eosin,  $\times 10$ ). **d:** Photomicrograph of GIST with immunohistochemical staining for KIT ( $\times 200$ ). **e:** Photomicrograph of GIST with immunohistochemical staining for CD34 ( $\times 200$ ).

patient had an uneventful postoperative course and has been free from recurrence for 5 and a half years.

Patient 2 was a 60-year-old man who presented with syncope due to hemorrhagic shock resulting from massive hematemesis. The hemoglobin level, at admission, was 10.2 g/dL. The exact source of bleeding could not be identified with emergent endoscopy because of the large amount of blood in the stomach. The patient had had a gastric ulcer since 25 years, and we started treatment with proton-pump inhibitors to control the bleeding.

One week after admission, hemorrhagic shock developed again because of hematemesis. The hemoglobin level had decreased to 6.4 g/dL.

Emergent upper GI endoscopy was performed, and gastric lavage with cold saline was performed repeatedly. A 6-cm-diameter submucosal tumor was found on the greater curvature of the upper stomach, from which oozing continued (**Fig. 2a**). In the week after the first episode of hemorrhagic shock, endoscopy was not performed because the patient's symptoms had resolved. Regrettably, the chance to establish the diagnosis and to start appropriate treatment was lost. Computed tomography of the abdomen showed a 6- cm-diameter in diameter extragastric tumor in the greater curvature of the stomach (**Fig. 2b**).

After a submucosal tumor of the stomach without

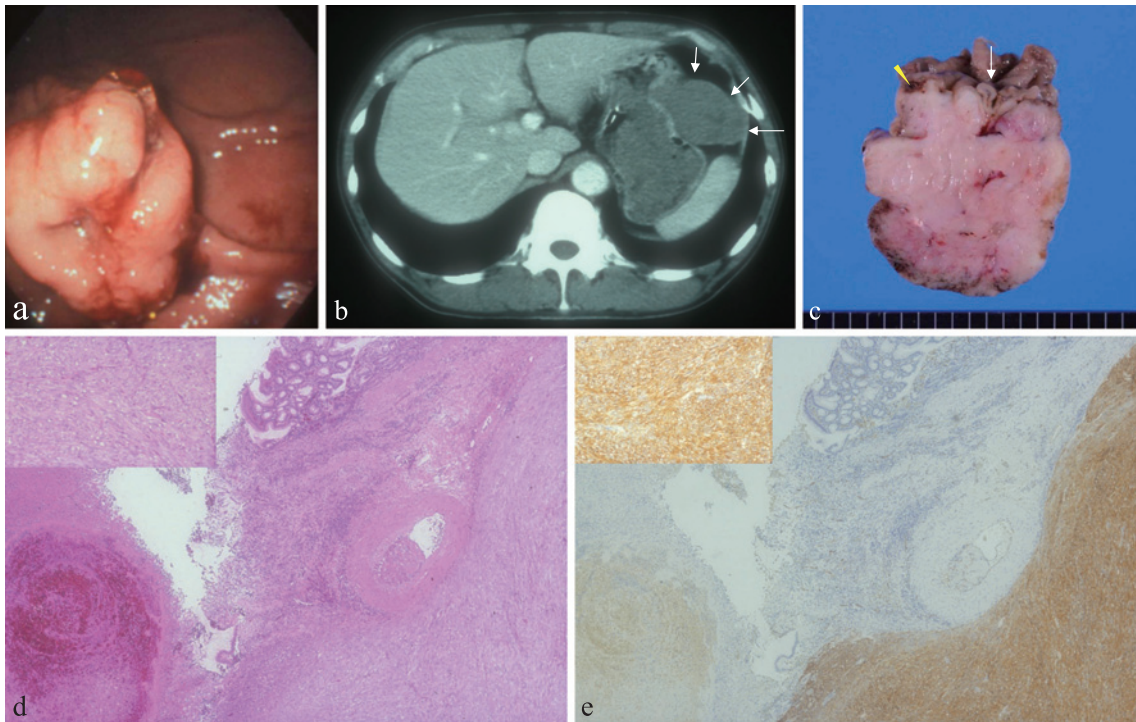


Fig. 2 **a:** Upper GI endoscopy revealed a submucosal tumor on the greater curvature of the upper stomach. **b:** Computed tomography scan of the abdomen showing an extragastric tumor on the greater curvature of the stomach (**arrows**). **c:** The cut surface of the tumor. An eroded artery (**arrow-head**) was present beside the central ulceration (**arrow**). **d:** Histological findings of the tumor. Owing to the defect of the normal mucosa, an artery with a thrombus was shown to have massive bleeding. Below the artery, a submucosal tumor grew expansively (hematoxylin and eosin,  $\times 40$ ). **e:** Photomicrograph of GIST with Elastica van Gieson staining ( $\times 40$ ).

invading adjacent organs was diagnosed, the patient underwent wedge resection of the tumor. There was no nodal metastasis, liver metastasis and peritoneal dissemination. Gross examination of the resected specimen revealed a well-demarcated, lobular tumor  $6.0 \times 6.0$  cm in size with a central ulceration. The cut surface of the tumor showed a white and homogeneous mass arising from the submucosal layer of the gastric wall with an eroded vessel located far away from the central ulceration (**Fig. 2c**). Histopathological examination results were consistent with the diagnosis of a GIST, with less than 5 mitoses per 50 HPFs. A peritumoral submucosal artery with thrombus, which was responsible for the massive hematemesis, was observed (**Fig. 2d, e**). Immunohistochemical staining was positive for KIT and CD34, but negative for S-100,  $\alpha$ -smooth muscle actin, and desmin. On the basis of these results, the tumor was diagnosed as a GIST. Postoperative recovery was without complications.

After 4 years the patient remains healthy and disease-free.

### Discussion

GISTs are the most common mesenchymal tumors of the GI tract, originating from Cajal cells, which express KIT (CD117) or CD34<sup>12</sup> or both. Although GISTs may arise anywhere in the GI tract, the most frequent location is the stomach<sup>1-3</sup>. Clinical presentation of gastric GIST depends on tumor size and location. The most common symptoms are abdominal pain and GI bleeding<sup>6,7</sup>. Although the severity of GI bleeding ranges from asymptomatic occult bleeding to massive bleeding, life-threatening hematemesis that requires emergent surgery is rare<sup>8,9</sup>. In this report, we have described massive hematemesis from gastric GISTs was in 2 patients. Both patients had episodes of hemorrhagic shock due to the bleeding from gastric GISTs.

As a GIST grows, a central ulcer forms and penetrates deeply into the tumor mass, which has been considered to result in hematemesis<sup>7</sup>. In some reports, intraluminal bleeding in gastric GISTs is due to central ulceration<sup>9,10</sup>. Recently, endoscopic hemostasis has been achieved by applying hemoclips to an actively bleeding vessel arising from an ulcer crater in gastric GISTs<sup>10</sup>. In 2006, Vats et al. reported a case of massive GI bleeding from a Dieulafoy-like lesion overlying a gastric GIST. It was the first report of a gastric GIST presenting with massive hematemesis from a Dieulafoy-like lesion. With simple irrigation, a typical Dieulafoy-like lesion overlying a large gastric GIST was observed. It bled easily and caused massive hemorrhage<sup>13</sup>. Regrettably, a detailed pathological description of the lesion was not provided in the report. Regarding the growth pattern, most gastric GISTs are classified as having intraluminal, extramural, transmural, and mixed growth patterns<sup>14</sup>. However, the relationship between the growth pattern and the incidence of hematemesis is poorly understood. In our patients, peritumoral submucosal vessels were responsible for the massive hematemesis from the gastric GISTs. No bleeding point was observed in the central ulceration. There have been no reports of peritumoral submucosal vessels causing massive hematemesis from gastric GISTs.

The preoperative diagnosis in both our cases was gastric submucosal tumor with massive bleeding. Once the diagnosis of GIST has been established, the standard treatment for localized, resectable GIST is surgery. The goal of surgery is complete resection of macroscopic and microscopic disease<sup>11</sup>. Fletcher et al. have classified gastric GISTs into the following 4 groups: very low risk (<2 cm in diameter and <5 mitoses per 50 HPFs), low risk (2–5 cm in diameter and <5 mitoses per 50 HPFs), intermediate risk (<5 cm in diameter and <6–10 mitoses per 50 HPFs or 5–10 cm in diameter and with <mitoses per 5/50 HPFs), and high risk (>5 cm in diameter and >5 mitoses per 50 HPFs or >10 cm in diameter and any number of mitoses or any diameter with >10 mitoses per 50 HPFs)<sup>2</sup>. According to this classification, our patients 1 and 2 had low-risk and intermediate-risk GISTs, respectively. Tumor size

and mitotic index have been accepted as independent prognostic factors. Carrillo et al. have reported that a high MIB-1 index is the most powerful predictor of poor survival. The highest MIB-1 index value for these patients was less than 3%, suggesting a benign tumor<sup>15</sup>. Yokoi et al. have classified GISTs on a clinical basis with new histological malignant criteria. In addition to tumor size and Ki-67- labeling index, the presence of tumor hemorrhage or necrosis or both were emphasized<sup>16</sup>. Because our patients showed no accompanying hemorrhage or necrosis in the tumor, a better prognosis can be expected. However, careful follow-up is needed for both patients. Massive hematemesis from gastric GISTs is a life-threatening symptom that requires immediate treatment. Because the origin and manner of bleeding varies in gastric GISTs, we must decide the methods of hemostasis including the excision of the tumor.

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(Received, March 11, 2008)

(Accepted, July 1, 2008)