



Two Sessions of Radiotherapy Were Successful in Treating Gastric Cancer with Bleeding

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Introduction

The radical treatment for gastric cancer, which accounts for the highest malignancy-related morbidity in Japan, is surgery, and chemotherapy is often provided in addition to surgical treatment [1–5]. On the other hand, in Europe and America, chemoradiotherapy is often provided after and/or before perioperative therapy.

Radiotherapy is a well-known treatment option to achieve hemostasis in patients with bleeding organs [1, 2, 6–11], the most common of which are the esophagus, stomach, colon (rectum), bronchus, and uterus. However, the optimal protocol of radiotherapy is not established. The protocol followed in Murakami Memorial Hospital to treat gastric cancer cases with organ bleeding is as follows: to initially irradiate the entire organ at 20 Gy/5 fractions. In cases that rebleed, 3–5 clips are placed endoscopically near the tumor and salvage radiation of the bleeding site at 15 Gy/5 fractions is performed [12]. Herein, we report a case of successful salvage radiotherapy for bleeding gastric cancer, which resulted to 15 months of local control and enabled the patient to resume his activities of daily living in 12 months and subsequently received chemotherapy as an outpatient.

Case

A 60-year-old man consulted his family doctor because of anorexia and was referred to the Department of Gastroenterology in our hospital for further workup of the cause of anemia. As for the patient, hematochezia and the stomach ache were absent. He had history of diabetes from 7 years ago. He did not have a significant family history.

Endoscopy revealed advanced gastric cancer with obstruction of the pyloric ring and invasion of the duodenum (Fig. 1), which rendered the tumor inoperable. One week after endoscopy, the patient underwent bypass surgery of the jejunum instead. Intraoperative findings revealed vascular invasion of the lower, middle, and upper portions of the duodenum, which corresponded to cStage 4 (Type 3, cT4b, cN2, cH1, pP1, CY1, cM0). The pathologic diagnosis was poorly differentiated adenocarcinoma with greater omentum metastasis. Preoperative tumor marker levels were as follows: CEA, 149.2; CA19-9, 17.3; AFP, 3.3; and CA-125, 76.5.

One month after the bypass operation, he was discharged from the hospital because there was no progression of anemia. Subsequently, he was started on chemotherapy (as an outpatient) using the usual dosages of SOX regimen: tegafur/gimeracil/oteracil (100 mg/m²), and oxaliplatin L-OHP (130 mg/m²). However, because he developed side effects including anorexia, diarrhea, and nausea from the first cycle, in the second cycle, the dose of the drugs was reduced to 80% of the initial dose.

Three months after the initiation of chemotherapy, he suddenly developed hematemesis, which was found to be due to peritumoral hemorrhage on endoscopy; the hemorrhage did not resolve with argon plasma laser coagulation (APC) (Fig. 2). During this time, he was transfused with a total of 10 units of red cell concentrate (RCC). However, the progression of anemia was observed in 2 weeks after APC. In order to stop the bleeding, we started him on radiotherapy of the entire stomach at 20 Gy/5 fractions within 5 days (Fig. 3a).

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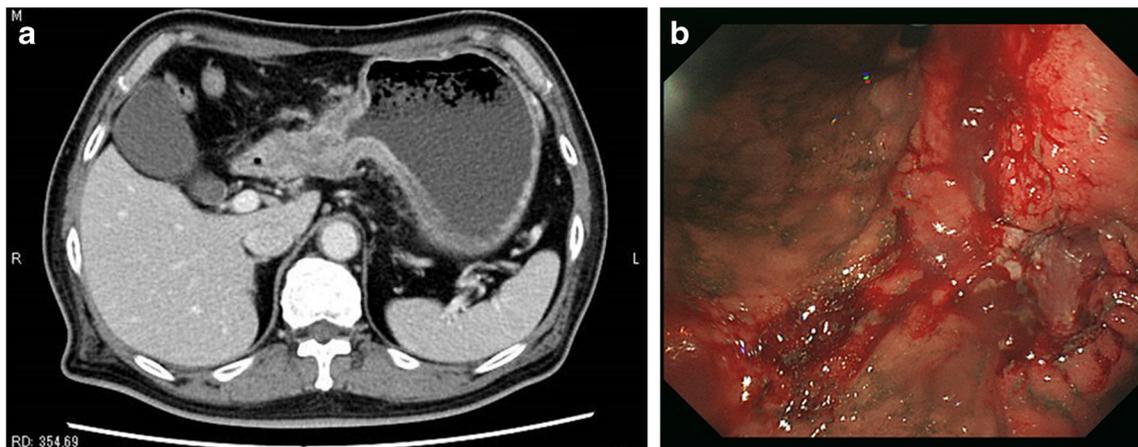


Fig. 1 Initial examination of the patient. **a** Contrast-enhanced CT shows thickness of the lower gastric wall. **b** Gastrointestinal endoscopy shows Borrmann type 3 with bleeding and obstruction of the pyloric ring of the stomach

Two weeks later, the anemia was improved and he was subsequently discharged. On surveillance imaging, there was no thickness of the gastric and duodenal wall (Fig. 3b). He was started on second-line chemoradiotherapy with XELOX regimen, which comprised oxaliplatin L-OHP (130 mg/m^2) and capecitabine (1000 mg/m^2 , administered orally twice daily on days 1–14). The patient remained stable and in a good condition for 7 months after the initial radiotherapy and 10 months after the bypass operation.

However, he developed malaise. Further workup revealed positive fecal occult blood and the cause of his malaise was examined by upper gastrointestinal tract endoscopy, and the pyloric region of the stomach was seen to have gradual bleeding (Fig. 4a). He was transfused with a total of 6 units of RCC and was subsequently recommended to radiation for hemostasis of the rebleeding organ. Radiotherapy was given to a portion of the residual tumor at 15 Gy/5 fractions within 5 days; the area for irradiation was planned based on the 3–5 clips

placed endoscopically near the tumor. The radiation treatment field was guided by the clips placed during the initial surgery (Fig. 4b). He was discharged at 2 weeks after radiotherapy as no progression of the anemia was observed.

At 14 months after the initial treatment including surgery, chemotherapy, and two sessions of radiotherapy (4 months after the second radiotherapy), he was brought to the emergency room and immediately admitted to the hospital because of difficulty in breathing and disturbance in consciousness. There was no hematemesis or hematochezia. Systemic examination revealed a large quantity of left-sided pleural effusion (on whole-body CT) and a punctate abnormal signal in the brain MRI (on diffusion-weighted imaging) (Fig. 5). Based on these findings, we diagnosed the patient as having lymphangitic carcinomatosis with brain metastasis. Twenty days after hospitalization, his clinical manifestations remained refractory to treatment and he eventually passed away.

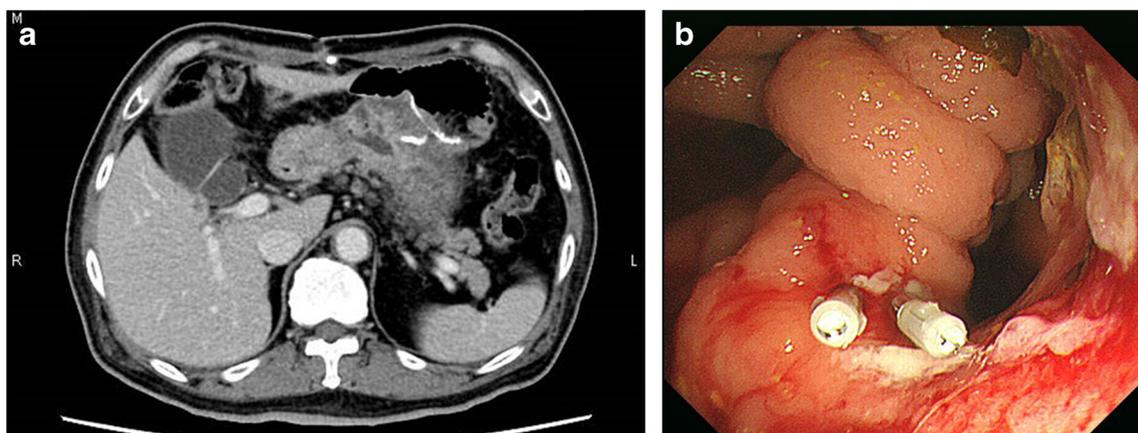


Fig. 2 Status of the patient after Braun bypass operation. **a** There is shrinkage of the gastric tumor, but there is persistence of duodenal thickening. **b** Argon plasma laser coagulation of the residual bleeding after operation

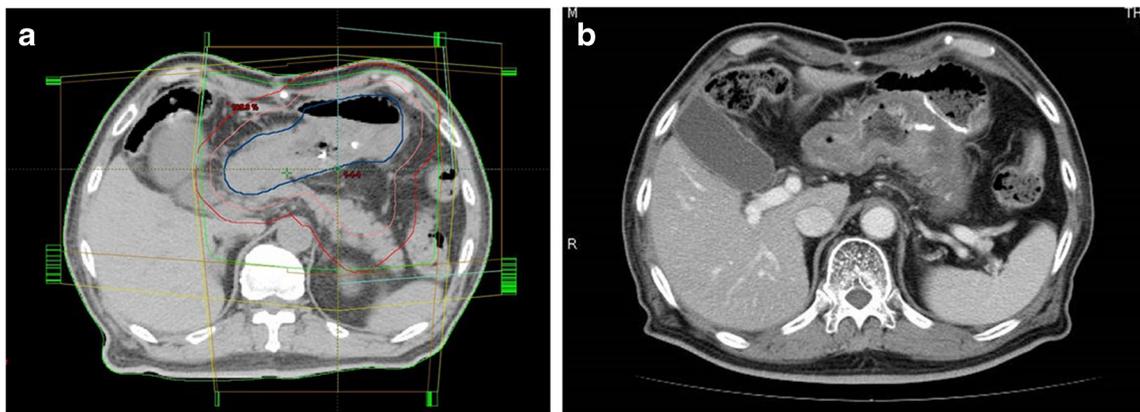


Fig. 3 First radiotherapy of the entire stomach for hemostasis. **a** External beam planning to target the entire stomach. Blue line: gross target volume (GTV), pink line: clinical target volume (CTV) (whole stomach), red line:

planning target volume (PTV) (2 cm margin for CTV), green line: 95% coverage of planning dose (20 Gy/5 fx). **b** There is resolution of the gastric and duodenal wall thickness

Discussion

In Japan, gastric cancer has been reported to have a high morbidity [4, 6, 10, 11] and the development of hematemesis in cases of progressive cancer. Although surgery is the standard treatment for gastric cancer, inoperable cases are usually managed with systemic chemotherapy [2]. Radiation for hemostasis was reported to be effective not only for the gastrointestinal tract but also for the bladder and uterus [2, 4, 5]. Radiotherapy for hemostasis has been reported to be effective in 50 to 80% of gastric cancer cases with tumor bleeding [5, 7, 8]. However, the optimal dosage, number of fractions, and the radiation method are not established. One study reported that irradiation with more than 36 Gy was more effective than that with dosages of 36 Gy or less [8]. On the other hand, Tey et al. reported that the response rates of bleeding were not different between a high-BED regimen of > 39 Gy and a low-BED

regimen of < 39 Gy [5]. Hence, there is no established method to treat bleeding gastric cancer [4, 7, 10].

In this case, the depth of gastric cancer invasion was difficult to measure by endoscopy and CT. Similar to the protocol followed in a previously reported case [12], this patient was given two sessions of irradiation for bleeding gastric cancer. After the second radiotherapy, the patient was discharged from the hospital. Notably, although the patient died 10 days after discharge, he had no manifestations of hematemesis and hematochezia; moreover, he was able to eat his usual meal 1 day before his death. These indicated that bleeding from gastric cancer was the unlikely cause of death; instead, the cause of death was thought to be a coagulation disorder. The patient needed a second radiotherapy when the tumor bleeding recurred 36 days after the first radiotherapy. Although he was eventually deemed fit to be discharged from the hospital, he died 26 days after the second radiotherapy [12]. On the other

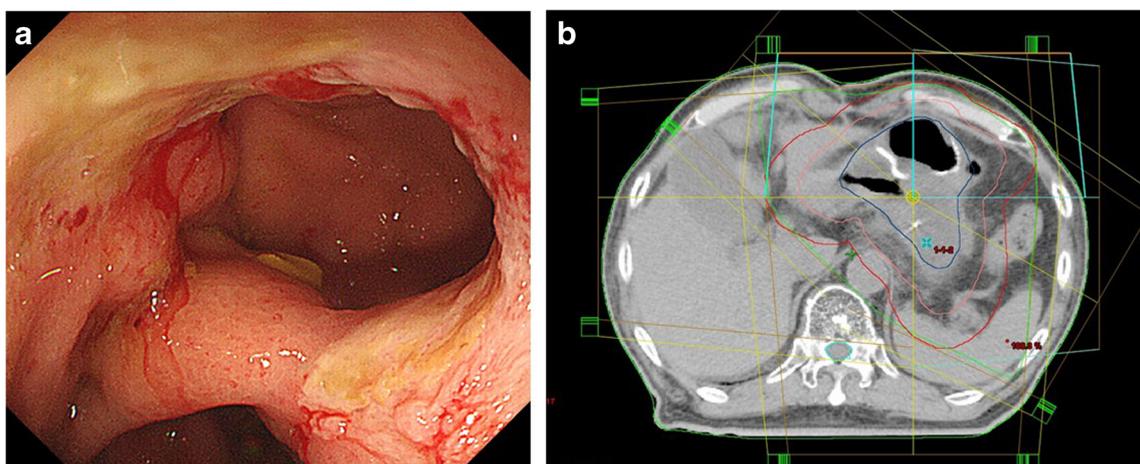
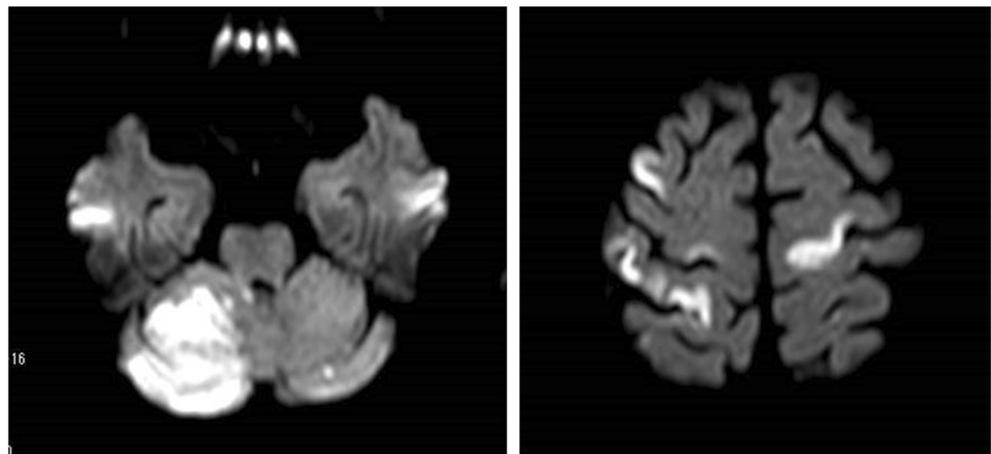


Fig. 4 Second or salvage radiotherapy for hemostasis on a localized area of the stomach. **a** The pyloric region of the stomach is seen to have gradual bleeding, which was not stopped with argon plasma

coagulation (APC). **b** The settings of the GTV, CTV, and PTV were the same as those for the initial radiotherapy, but the cancer site to irradiate was narrowed down based on the surrounding four clips

Fig. 5 Magnetic resonance imaging of the brain. There are punctate areas of hyperintensity in all areas of the brain on diffusion-weighted image



hand, the patient of this case was able to sustain the effects of the first radiotherapy for 7 months and could receive chemotherapy as an outpatient. The second salvage radiotherapy effects persisted for 5 months until he died.

Previously, we reported a case of gastric metastasis from liver cancer that was successfully treated by radiotherapy using a similar regimen [13]. The patient described in that case was able to tolerate dietary intake after radiotherapy. However, his condition worsened 35 days after radiotherapy and he subsequently died. There was emesis immediately before death, but there were no admixed blood, no melena, or any evidence of bleeding from the gastrointestinal tract. Although we were unable to identify the direct cause of death of this patient, radiotherapy was able to control the worsening anemia, improve gastrointestinal motility and obstruction, and improve his quality of life.

Currently, we are conducting prospective clinical trials on radiotherapy in two sessions to achieve hemostasis in cases of bleeding gastric cancer. To the best of our knowledge, no other report describing this treatment method has been published. Although the depth of gastric cancer invasion is difficult to measure by endoscopy and CT, one-time irradiation of a large area of the stomach may lead to perforation. Therefore, we plan to evaluate the efficacy and safety of administering radiotherapy in two sessions to achieve hemostasis in cases of bleeding gastric cancer as, if found to be effective, it would help shorten the hospital stay for correction of anemia, improve the quality of life, and prevent perforation.

Conclusion

In this case, radiotherapy in two sessions was successful in achieving hemostasis in bleeding gastric cancer. Although there are several methods, such as surgery, APC, and

medications to achieve hemostasis, radiotherapy in one or two sessions is a noninvasive option that can be considered.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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