Case Report

Endoscopic Ultrasound-Guided Drainage of Intra-Abdominal Abscess after Gastric Perforation in a Patient Receiving Ramucirumab and Paclitaxel for Advanced Gastric Cancer

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Keywords

Advanced gastric cancer · Endoscopic ultrasound-guided drainage · Gastric perforation · Intra-abdominal abscess · Ramucirumab

Abstract

Gastrointestinal perforation is a serious adverse event that occurs in approximately 1% of patients receiving ramucirumab and paclitaxel. A 67-year-old man with unresectable advanced gastric cancer was admitted to our hospital and treated with ramucirumab and paclitaxel. Gastric perforation occurred during the second cycle of chemotherapy. Although the patient's condition improved without surgery, an abscess developed in the intra-abdominal fluid collection resulting from the perforation. We performed endoscopic ultrasound-guided abscess drainage. The patient improved and was discharged in satisfactory condition. Endoscopic ultrasound-guided drainage is a treatment option for patients with intra-abdominal abscess following gastric perforation due to ramucirumab.

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Introduction

The RAINBOW trial, reported in 2014, was a randomized, placebo-controlled, double-blind, phase 3 trial comparing paclitaxel plus ramucirumab with paclitaxel plus placebo in patients with previously treated advanced gastric or gastroesophageal junction adenocarcinoma [1]. This study indicated the combination of ramucirumab and paclitaxel could serve as a standard second-line treatment for patients with unresectable advanced gastric cancer with an acceptable frequency and severity of adverse events. However, the reported incidence of gastrointestinal perforation in the ramucirumab plus paclitaxel group was higher than in the placebo plus paclitaxel group. Here we report a case of intra-abdominal abscess following gastric perforation during the second cycle of chemotherapy with ramucirumab plus paclitaxel for advanced gastric cancer treated with endoscopic ultrasound (EUS)-guided drainage.

Case

A 67-year-old man was referred to our hospital for treatment of a gastric tumor detected by esophagogastroduodenoscopy (EGD). He reported abdominal discomfort, occasional vomiting, and weight loss of 10 kg during the 4 months preceding his presentation. Following admission to our hospital, we performed an EGD that showed copious gastric food debris and a tumor involving the entire stomach (Fig. 1). Because definite stenosis caused by the tumor was absent, the accumulation of gastric debris appeared to result from reduced peristalsis due to tumor extension throughout the stomach. The histological diagnosis was human epidermal growth factor receptor 2 (HER2)-negative well-differentiated gastric adenocarcinoma. Abdominal computed tomography (CT) showed cancer invasion of the pancreas and metastatic lymph nodes near the aorta. We diagnosed the lesion as an unresectable advanced gastric cancer. The patient's performance status was sufficiently good, and chemotherapy was indicated. In Japan, for patients with HER2-negative gastric cancer, S-1 plus cisplatin combination chemotherapy is the standard of care [2]. However, our patient sometimes vomited due to delayed gastric emptying (DGE), and oral treatment was difficult. We started intravenous nutrition and chemotherapy with ramucirumab plus paclitaxel. After the chemotherapy was started, the patient's oral intake gradually increased, and he ceased vomiting. He was discharged in satisfactory condition after finishing the first cycle of chemotherapy.

The patient continued chemotherapy as an outpatient but developed sudden severe upper abdominal pain on the seventh day of the second cycle of the chemotherapy. A CT examination showed perforation at the lesser curvature of the gastric body (Fig. 2a), and he was readmitted to our hospital. Because he had been taking a proton pump inhibitor, we did not think that the perforation was caused by acid-induced ulceration, and we attributed the perforation to ramucirumab. We began treatment with analgesic medication and decompression using a nasogastric tube. The patient's condition improved with conservative treatment. On the 15th hospital day, his CT scan showed improvement of the gastric perforation, and we removed the nasogastric tube. He started to take a liquid diet but developed a fever (39.0°C) on the 24th hospital day. His laboratory data showed an increased white blood cell count and elevated C-reactive protein level. A CT examination on the 27th hospital day showed enlargement of the fluid collection outside the stomach (Fig. 2b). We considered an intra-abdominal abscess following the gastric perforation and performed EUS-guided fine-

needle aspiration of the fluid collection using a 19-gauge needle (SonoTip Pro Control; Medi-Globe GmbH, Achenmühle, Germany). Because malodorous yellowish-white pus was aspirated, we diagnosed the lesion as an intra-abdominal abscess and conducted EUS-guided drainage (Fig. 3a). The procedure was performed using a convex-type echoendoscope (GF-UCT260; Olympus Medical Systems, Tokyo, Japan). A 0.025-inch guidewire (VisiGlide, Olympus Medical Systems) was introduced through the needle and coiled into the abscess under fluoroscopic guidance. The fistula was dilated using a dilation catheter (ES dilator; Zeon Medical, Tokyo, Japan), and a 6-Fr pigtail nasal biliary catheter (nasal biliary drainage set; Cook Medical, Bloomington, IN, USA) was subsequently placed (Fig. 3b). Gram staining and culturing of an aspirate sample confirmed anaerobic bacteria (*Prevotella melaninogenica* and *Peptostreptococcus micros*). Meropenem (3 g/day) was administered because the antibiotic sensitivity test showed that all the causative bacteria were sensitive to meropenem and it had the lowest minimum inhibitory concentration. The external drainage catheter placed via the nose was irrigated once daily with 10–20 mL of sterile saline.

The clinical course after drainage was uneventful and the external drainage catheter was removed on the 34th hospital day. The patient had not vomited since he started oral intake on the 36th hospital day, and we observed that his DGE was improved by the first cycle of the chemotherapy with ramucirumab plus paclitaxel. Therefore, we started chemotherapy with S-1 plus cisplatin on the 41st hospital day, and the patient was discharged after the first cycle of this chemotherapy was finished. The patient gave informed consent for each treatment he received.

Discussion

Japanese gastric cancer treatment guidelines suggest that S-1 plus cisplatin combination chemotherapy is a standard first-line treatment for patients with HER2-negative unresectable gastric cancer. The combination of ramucirumab and paclitaxel is regarded as a standard second-line treatment [2]. Because our patient had DGE and tolerated oral medications poorly, we started intravenous chemotherapy with ramucirumab plus paclitaxel. The patient's symptom of DGE-induced vomiting improved during the first cycle of chemotherapy, and the treatment was effective. However, gastric perforation occurred during the second cycle of chemotherapy and, as the patient was taking a proton pump inhibitor, we believe this perforation was caused by ramucirumab.

Gastrointestinal perforation is a serious adverse event reported in approximately 1% of patients treated with ramucirumab plus paclitaxel [1]. Although the mechanism by which ramucirumab causes gastrointestinal perforation is not completely understood, this adverse event is associated with most antiangiogenic treatments. In our case, the CT scan revealed that the perforation occurred in the portion of the stomach affected by the tumor rather than in normal tissue. Due to our concern that a perforation through cancerous tissue would not close naturally, we considered surgical treatment. However, antiangiogenic medications may cause a failure to heal, and gastrectomy was impossible because the tumor had invaded the pancreas. These considerations led us to avoid surgery. Fortunately, the perforation closed with conservative treatment and the patient's condition improved although the fluid collection outside the stomach developed an abscess. EUS-guided drainage has been reported to be a safe and effective method not only for patients with a peripancreatic fluid collection but also for those with an abdominal abscess [3, 4]. We performed EUS-guided transgastric

drainage for this patient with advanced malignancy because EUS-guided drainage is less invasive than surgical drainage.

In conclusion, we present a case of intra-abdominal abscess following gastric perforation during the second cycle of chemotherapy with ramucirumab plus paclitaxel. EUS-guided drainage improved the patient's condition allowing S-1 plus cisplatin combination chemotherapy to be started. EUS-guided drainage is a treatment option for patients with intra-abdominal abscess following gastric perforation due to ramucirumab.

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Statement of Ethics

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from the patient to be included in this report. This article does not contain any studies with human or animal subjects performed by any of the authors.

Disclosure Statement

There are no conflicts of interest to declare.

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Fig. 1. Esophagogastroduodenoscopy image from the first hospitalization. Esophagogastroduodenoscopy shows a tumor and food debris in the stomach.

Fig. 2. Computed tomography images. Computed tomography performed on the 7th day of the second cycle of the chemotherapy shows perforation (red arrow) at the lesser curvature of the gastric body (a). Computed tomography performed on the 27th hospital day of the second hospitalization shows the fluid collection (yellow arrow) outside the stomach (b).

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Fig. 3. Endoscopic ultrasound-guided drainage performed on the 27th hospital day of the second hospitalization. Endoscopic ultrasonography reveals an anechoic lesion outside the stomach. A 19-gauge needle is present aspirating the lesion (a). A fluoroscopic image shows the 6-Fr pigtail nasal biliary catheter placed in the lesion (b).