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Author(s)	Gunji, Shutaro; Okabe, Hiroshi; Obama, Kazutaka; Sakai, Yoshiharu
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27	Shutaro Gunji, Hiroshi Okabe, Kazutaka Obama, Yoshiharu Sakai
28	Department of Surgery, Graduate School of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin,
29	Sakyo-ku, Kyoto, Japan
30	hokabe@kuhp.kyoto-u.ac.jp
31	Tel: +81-75-751-4108
32	Fax: +81-75-751-4646
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1 Abstract

- 2 Fistulas between the aorta and the digestive tract are rare complications. There are some reports of
- 3 aortoesophageal fistulas that are rare but fatal complications after esophagectomies or esophageal stent
- 4 implantations. An aortoenteric fistula (AEF) occasionally occurs after an aortic intervention or
- 5 vascular procedures; however it is quite rare after gastrointestinal surgeries. This paper demonstrates a
- 6 case of an AEF after laparoscopic total gastrectomy for an advanced gastric cancer. This is the first
- 7 case report describing an AEF after the so-called overlap method of esophagojejunal anastomosis.
- 8 This report describes a case of 77-year-old Japanese woman who underwent laparoscopic total
- 9 gastrectomy and esophagojejunal anastomosis with Roux-en-Y reconstruction for advanced gastric
- 10 cancer. The patient exhibited bacterial peritonitis five days after the operation, due to a partial necrosis
- 11 and perforation of the small intestine. The patient was treated successfully with laparoscopic partial
- 12 resection of the small intestine. However, the patient died of massive hematemesis caused by the AEF
- 13 30 days after the primary surgery.
- 14
- 15 Key word; Aortoenteric fistula, laparoscopic total gastrectomy, overlap anastomosis
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1 Introduction

 $\mathbf{2}$ Fistulas between the aorta and a digestive tract are quite rare complications after 3 gastrointestinal surgeries. There are some reports of aortoesophageal fistulas after esophagectomy as 4 fatal complications. Previous studies reported anastomotic leakage or peptic ulceration of the gastric tube as a cause of fistula formation [1-4]. However, an aortoenteric fistula (AEF) after total 5 6 gastrectomy is a quite rare complication. Recent technical advancements in endoscopic surgery have 7 increased the number of laparoscopic gastrostomies for gastric cancer. Several types of anastomotic 8 techniques have been developed; experienced surgeons have even made advancements that allow 9 completely laparoscopic total gastrectomies [5-7]. This paper describes a case of an AEF at the site of 10 esophagojejunal anastomosis after laparoscopic total gastrectomy. This is the first case report 11 describing an AEF after applying the so-called overlap method of esophagojejunal anastomosis [6, 7].

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14 **Case presentation**

The patient was a 77-year-old Japanese female referred with a diagnosis of advanced gastric cancer. The patient had been receiving medication for type II diabetes and hypertension. Preoperative examinations included computed tomography, endoscopy, and an upper gastrointestinal series. Endoscopy showed that the tumor had invaded the esophagus about 15mm above the esophagogastric junction. Computed tomography demonstrated lymph node metastasis around the cardia and the

20 esophageal hiatus. The patient was diagnosed withT3N2M0 Stage IIIB, according to the TNM

21 classification of Union for International Cancer Control (UICC) edition 6.

22The patient received neoadjuvant chemotherapy using a combination of S-1 and cisplatin. S-1 (80 23mg/day) was orally administered for three weeks, and cisplatin (60 mg/m²) was given intravenously on day 248. This regimen was repeated every five weeks for a total of two cycles. Two courses of chemotherapy did 25not significantly change the size of the primary lesion or the metastatic lymph nodes. There were no new 26lesions or progression, thus the disease was judged to be stable disease (SD) according to the response 27evaluation criteria in solid tumors (RECIST, version 1.1). Because her tumor was still diagnosed as 28resectable, total gastrectomy was planned. The patient participated in a clinical trial of a phase II study of 29laparoscopic gastrectomy for clinical stage II or higher gastric cancer (UMIN000002085), and successfully 30 underwent a laparoscopic total gastrectomy with D2 lymph node dissection and a radical lymph node 31resection in the lower mediastinum; this included lymph nodes No. 20, 110 as per the UICC edition 6 32classification. During the operation, SonoSurg[™] (Olympus Medical, Tokyo, Japan) was used. 33 Following the removal of the specimen, laparoscopic Roux-en Y reconstruction was done. The 34lower esophagus was resected to obtain a safety margin, and esophagojejunostomy was created in the lower 35mediastinum using linear staplers, using the overlap method. A side-to-side anastomosis was created

36 between the left dorsal side of the esophagus and the jejunal limb, and the entry hole was closed using an

37 interrupted hand-sewn technique [5, 7].

38 The tumor was histopathologically diagnosed as a poorly differentiated adenocarcinoma of

the stomach. Lymph node metastases were found in 10 among 28 removed nodes, and the pathological

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stage was pT3N2M0, Stage IIIB (Fig 1 A&B). The proximal and distal margins were negative, thus
 R0 resection was achieved.

On postoperative day 4, the patient exhibited severe abdominal pain. A computed 3 4 tomography (CT) scan was taken after administration of gastrographin, and it did not reveal any sign of anastomotic leakage. (Fig. 2A&B) However, a significant amount of gram positive and negative 5 6 cocci were detected from the drainage fluid, indicating a bacterial peritonitis. During the emergency 7 operation, a segmental necrotic change of the ileum with small perforation was found, which was 8 located at 45cm on the oral side from the ileocecum, and we thought that this caused peritonitis. The 9 affected ileum was resected, and the abdominal cavity was washed with large amounts of saline. 10 Neither the abscess nor any evidence of leakage was observed in the upper abdomen, and ischemic 11 ulcer associated with thromboembolic occlusion of a mesenteric artery was determined pathologically. 12Following the operation, the patient was treated with endotoxin absorption therapy, continuous 13hemodiafiltration, appropriate intravenous antibiotics, and total parenteral nutrition in the intensive 14 care unit. The patient gradually recovered and restarted a soft diet 17 days after the emergency 15operation. We measured the concentration of amylase in the drainage fluid multiple times, although 16the level had been less than 107 IU/L during the clinical course. 17 However, the patient had a sudden hematemesis on postoperative day 30. An aortoenteric

18 fistula (AEF) was suspected in addition to the massive amount of hematemesis. The patient was 19 immediately transferred to an angiography room for a radiological intervention. However, the patient 20 died from hemorrhagic shock before the procedure was initiated. The autopsy revealed AEF at the site 21 of esophagojejunostomy (**Fig 3**). Neither a hemorrhage nor abscess was observed in the abdominal 22 cavity. Rapid exsanguination from the fistula was determined to have been the cause of death.

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25 **Discussion**

26Fistulas between the aorta and a digestive tract are quite rare complications after 27gastrointestinal surgeries. AEFs occur after aortic interventions or vascular procedures, most 28commonly after an open abdominal aortic aneurysm repair because of mechanical erosion or infection 29of the suture line and the prosthetic graft into the overlying duodenum [8]. The other causes of AEFs 30 are gallstones, periaortic malignancies or metastases, peptic ulcers, complicated diverticulitis, appendicitis, and radiation therapy [9-13]. There are some recent reports of large-scale randomized 3132control studies of gastric surgery [10, 14-16]. Major complications after total gastrectomy include 33 anastomotic leakage, pancreatic fistulas, abdominal abscesses, intestinal obstructions, and pneumonia 34[17-19]. However, there are no reports of AEF following either open or laparoscopic total gastrectomies [5-7]. 3536 This rare but devastating complication requires prompt surgical or interventional

This fale but devastating complication requires prompt surgical of interventional

37 management. There are a few cases of successful treatment of aortoesophageal fistulas [20, 21].

- 38 Treatment generally requires closing of the aortic stump and repair of the fistula or endovascular
- intervention [20, 22, 23]. As a result, the difficulty in predicting this complication remains a critical

1 problem [8, 24].

 $\mathbf{2}$ The role of NAC in the treatment of gastric cancer has been under discussion. [25] NAC can 3 increase the rate of achievement of R0 resection or pathological complete response (pCR). However, 4 Yeong et al. reported that NAC increased the incidence of surgical complications, although there were no deaths directly related to surgical site failures. [26] Schuhmacher et al. also reported that the total 5 6 number of postoperative complications was higher in the neoadjuvant cohort than the surgery-alone 7 cohort. [27] However, there were no fatal complications documented during surgery. On the other 8 hand, Ge et al. reported the rate of complications in the neoadjuvant cohort was not obviously higher 9 than in the surgery-alone cohort. [28] According to these reports, it seems to be difficult to deny the possibility that NAC may have affected the incidence of AEF in our case. However, there are no 10 11 reports that describe the incidence of AEF not only after NAC but also after surgeries in gastric cancer 12patients. 13The current case was similar to esophageal fistulas between the aorta and the gastric tube. Le

Roux reported 8 cases of fistulas between the gastric tube and aorta from 418 patients after 14 15esophagectomy [29]; the fistula was located at the anastomosis in 7 cases and it was at the closure line 16of the gastric tube in one case. He suggested that the two most common etiological factors of AEFs 17were anastomotic leakage, and the exposure of aortic sheath by extensive lymph node dissection. In 18 the current case, a radical lymph node resection in the lower mediastinum was performed because of 19evident lymph node metastasis. This resulted in the exposure of the descending aorta. A review of CT 20after the first operation revealed that the staple line of the anastomosis was in direct contact with the 21descending aorta (Fig 2A&B).

22There may be some reasons for the fistula in our case, for example, anastomotic leakage, 23pancreatic fistula, infection, sustained contact between the staples and the aorta, chemotherapy, 24energized devices such as ultrasonically activated scalpels and so on. Among them, we thought the 25persistent contact of the staple line could have caused erosion of the aortic wall and lead to the 26formation of the aortoenteric fistula, because there was no sign of anastomotic leakage, pancreatic 27fistula or concomitant abscess formation during the clinical course or autopsy (Fig 3 &4). Therefore, 28we would like to emphasize the importance of being mindful of the direction of the closure line of the 29anastomosis or adverse covering the staple line by adding sero-muscular sutures to avoid direct contact 30 with other organs. This anastomotic technique is new, and we don't have enough experience to discuss 31the pros and cons of this technique. More data is necessary for further clinical practice.

In conclusion, though we couldn't obtain the clear reason for the cause of the fistula from the autopsy, we hypothesized that it could have been the result of persistent contact of and subsequent abrasion by the staple line upon the aortic sheath. We would like to declare the importance of immediate intervention or surgery if AEF is suspected.

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1	Figure legends
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3	Figure 1
4	(A) The resected stomach. The tumor occupied the lesser curvature of the gastric corpus. However, no
5	tumor cell was detected at the proximal end (*) and the distal end (**).
6	(B) The tumor was histopathologically diagnosed to be a poorly differentiated adenocarcinoma (por1)
7	of the stomach. Lymph node metastasis was detected among ten of the twenty-eight resected lymph
8	nodes. The pathological stage was pT3 (SE) N2 M0 Stage IIIB.
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10	Figure 2
11	Contrast enhanced CT taken 4 days after the first operation demonstrated a small amount of fluid
12	collection at the subphrenic lesion and atelectasis. Arrows indicate the site of the anastomosis and
13	staples, which are close to the descending aorta. (A) Axial plane. (B) Coronal plane.
14	
15	Figure 3
16	An autopsy revealed the fistula at the site of the anastomosis (A) and communicated to the descending
17	aorta (B). Arrows indicate the site of fistula. The broken line indicates the anastomosis between the
18	esophagus (*) and the jejunum (**).
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20	Figure 4
21	The fistula located at the top of a triangular anastomosis, where the staple line might have been
22	exposed to the descending aorta.
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26	Conflict of interest statement: Yoshiharu Sakai and other co-authors have no conflict
27	of interest.
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