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Case Report

Neoadjuvant FOLFIRINOX Followed by Pancreatoduodenectomy for Pancreatic Cancer in Patients with Previous Transhiatal Esophagectomy for Esophageal Cancer

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Keywords
Case report · Pancreatic cancer · Neoadjuvant chemotherapy · Pancreaticoduodenectomy · Transhiatal esophagectomy

Abstract
During pancreaticoduodenectomy after transhiatal esophagectomy, the preservation of the blood supply to the gastric conduit is technically difficult due to adhesion. Here, we present a case of successful pancreaticoduodenectomy after neoadjuvant chemotherapy in a patient with pancreatic head cancer who previously underwent subtotal esophagectomy with gastric reconstruction for esophageal cancer. A 69-year-old man who had undergone cholecystectomy 20 years prior and transhiatal esophagectomy 6 years prior for esophageal cancer presented to our hospital for indigestion. Computed tomography and magnetic resonance imaging revealed a 2.8-cm pancreatic head cancer, with focal abutment with the gastroduodenal artery, right gastroepiploic artery, and right colic vein. After discussion with the multidisciplinary team, the patient underwent neoadjuvant chemotherapy with six cycles of FOFIRINOX. The patient successfully underwent pancreatectomy, which preserved the pylorus. We preserved the gap between the gastric tube and the left lateral segment of the liver to

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avoid injuring the right gastric artery and vein. The tumor was found to be invading the gastroduodenal artery; thus, we performed R0 resection of the gastroduodenal artery and an end-to-end anastomosis between the gastroduodenal artery and the right gastroepiploic artery. After completing the surgical procedure, we added Braun anastomosis to reduce the incidence of delayed gastric emptying. Pancreaticoduodenectomy after transhiatal esophagectomy can be performed with preservation of the blood supply to the neogastric tube by reconstructing the major vessels, even in cases in which the tumor is invading or abutting the major vessels.

Introduction

To ensure the long-term survival of patients with pancreatic cancer, complete extirpation of pancreatic cancer using pancreatoduodenectomy (PD) and distal pancreatosplenectomy is essential. Various aspects must be considered when treating pancreatic cancer, such as resectability, the use of neoadjuvant chemotherapy, and whether malignant structural jaundice is present, and percutaneous transhepatic biliary drainage or endoscopic biliary drainage should be performed followed by surgery [1]. The retroperitoneal location of the pancreas, surrounding major vascular structures, and even small tributary vessels around the pancreas increase the complexity of this surgical procedure. Although pivotal clinical trials in pancreatic cancer have led to improvements in adjuvant chemotherapy, securing a negative resection margin remains the most important to oncologic outcome [2]. With advances in surgical techniques, combined major vascular resection is believed to be safe and appropriate for obtaining margin-negative resection in well-selected patients with pancreatic cancer [3] and should also be considered when planning elective radical pancreatectomy.

In addition, previous upper gastrointestinal surgery might be another factor that contributes to the difficulty of pancreatic surgery. We previously reported the surgical tactics used to achieve safe PD in patients who have undergone previous radical gastrectomy [4, 5]. When performing PD (resection and reconstruction) for pancreatic head cancer, previous operations that induced severe intra-abdominal adhesions around the major vessels and altered gastrointestinal alignment must be considered.

When performing radical surgery for esophageal cancer, preserving the right gastroepiploic artery (RGEA) and the right gastric artery (RGA) to maintain blood circulation of the neogastric tube is highly necessary to ensure future healthy reconstruction for cervical esophagogastrostomy. In recent years, along with the increased long-term survival of resected esophageal cancer, the number of patients with double primary cancers has increased. However, it remains unclear how to perform safe PD for pancreatic head cancer in patients with previous esophagectomy. To perform the usual PD, the division of the RGA, gastroduodenal artery (GDA), and RGEA must be resected to obtain a margin-negative resection or complete dissection of the lymph vessels and nodes. However, these vessels are critical for maintaining gastric tube perfusion for previous esophageal cancer surgery. Whether to preserve or resect these vessels can be critical in determining the cure of pancreatic cancer.

In this article, we present successful PD in patients with pancreatic head cancer who previously underwent transhiatal esophagectomy for esophageal cancer. The surgical considerations for safe PD will be discussed based on our experience.

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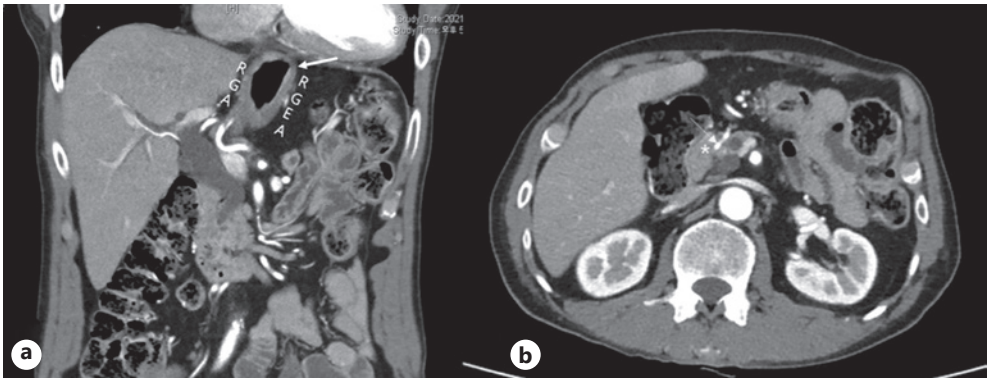

Fig. 1. Preoperative CT scan. **a** Status of transhiatal esophagectomy. **b** Tumor abutting the gastroduodenal artery (yellow star: tumor; yellow arrow: GDA). CT, computed tomography; RGA, right gastric artery; RGEA, right gastroepiploic artery; GDA, gastroduodenal artery.

Case Presentation

A 69-year-old man visited our hospital for indigestion. He had undergone cholecystectomy 20 years prior and subtotal esophagectomy with gastric reconstruction 6 years previously for esophageal cancer (Fig. 1a). Preoperative computed tomography (CT) scan revealed abrupt tapering of the dilated main pancreatic duct in the head and a 2.8-cm mass of the pancreatic head.

Laboratory testing did not indicate any hepatorenal abnormalities. In the tumor marker test, carcinoembryonic antigen (CEA) was 6.17 ng/mL (reference range: 0–2.5 ng/mL), and carbohydrate antigen 19-9 (CA 19-9) was 48.8 U/mL (reference range: 0–37 U/mL).

In addition to the CT scan, magnetic resonance imaging showed a 2.8-cm focal lesion at the head of the pancreas and a focal abutment with GDA, RGEA, and the right colic vein (shown in Fig. 1b). Positron-emission tomography with fluoro-2-deoxyglucose (FDG) confirmed a mass of increased FDG uptake involving the pancreas head, suggesting malignancy. No distant metastases were observed. We performed a pathological examination by endoscopic ultrasound with fine-needle aspiration biopsy, and adenocarcinoma was diagnosed. Through multidisciplinary discussion, we decided to administer neoadjuvant chemotherapy first followed by surgery to reduce the tumor burden, which was abutment with GDA and RGEA. The patient was administered oxaliplatin, leucovorin, irinotecan, and 5-FU (FOFIRINOX) for a total of six cycles of chemotherapy at 2-week intervals. After neoadjuvant chemotherapy, no significant changes were detected in the follow-up CT scan, and the tumor marker decreased slightly from 5.78 to 4.64 ng/mL for CEA and from 48.8 to 21.8 for CA 19-9. The operation for pancreatic cancer was performed 1 month later, after the last chemotherapy.

Operation

Laparotomy was performed using an inverted L-incision, and intra-abdominal exploration was conducted. No distant metastases were observed. We dissected the gastrocolic ligament and exposed the pancreas. We attempted to expose the superior part of the first portion of the duodenum, but severe adhesions were found around the left lateral segment of the liver and the neogastric tube due to previous surgery. The RGA and right gastric vein (RGV) passed through this part to the gastric tube. We preserved this area between the gastric tube and the left lateral segment of the liver so as not to injure the RGA and RGV. We dissected the superior border of the pancreas and performed eight lymph node dissection of the station. The common bile duct was skeletonized and divided. The resection margin of the bile duct was sampled for frozen section and was found to be negative for malignancy. Although we dissected

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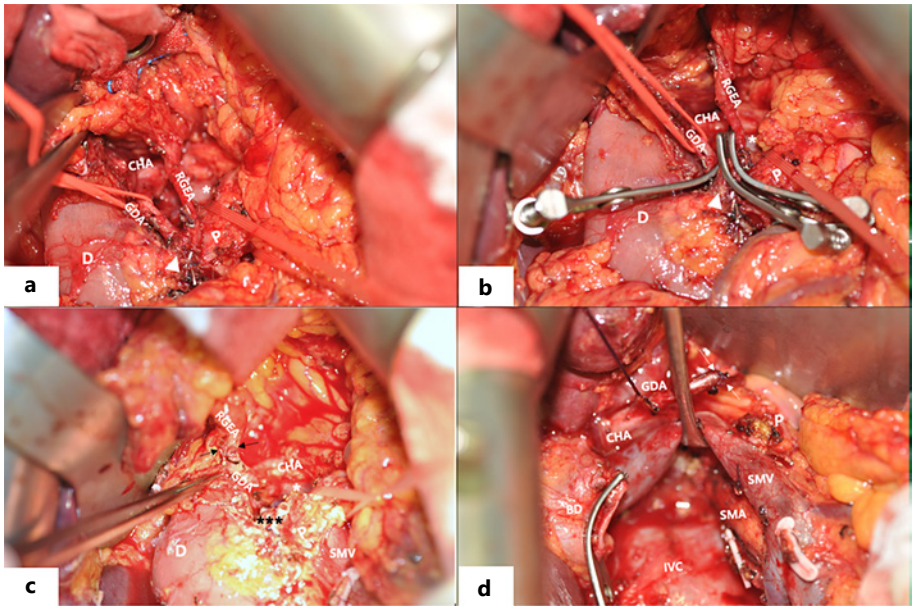

Fig. 2. Intraoperative view. **a** Pancreatic head cancer invading the GDA proximal to the RGEA (white arrowhead: abutment or invasion of cancer and GDA). **b** Clamping of the GDA and RGEA (white arrow: abutment of cancer and the GDA). **c** Vascular restoration by segmental resection and end-to-end anastomosis of the GDA. Note the well preserved GDA (black arrows: anastomosis site of the GDA and RGEA; black three stars: resected GDA). **d** Intraoperative view after extraction of the specimen (white arrows: anastomosis site of the GDA and RGEA). GDA, gastroduodenal artery; RGEA, right gastroepiploic artery; RGA, right gastric artery; D, duodenum; CHA, common hepatic artery; P, pancreas; SMV, superior mesenteric vein; SMA, superior mesenteric artery; IVC, inferior vena cava; BD, bile duct; black star (*), portal vein.

the common hepatic artery and attempted to isolate the GDA from the pancreas to preserve the RGEA, the tumor had invaded the GDA (as shown in Fig. 2a). We clamped the GDA with a bulldog, and the flow of the RGEA was determined by intraoperative ultrasound and Doppler. However, blood flow pulsation was weak (shown in Fig. 2b). For R0 resection, we resected the tumor-involved GDA segment and performed an end-to-end anastomosis for GDA and RGEA in an interrupted suture using Prolene 8-0 and 9-0 (shown in Fig. 2c, d). Using Doppler ultrasound, we confirmed that blood flow and pulse were preserved in the anastomosis. We cut the duodenal bulb 2 cm distal to the pyloric ring using a stapler. The inferior border of the pancreas was dissected, and the tributaries of the gastric colic trunk were ligated. We created a small window between the anterior border of the SMV and the posterior neck of the pancreas. The neck of the pancreas was divided, and full kocherization was performed to mobilize the duodenum and head of the pancreas. We sampled the para-aortic lymph node for frozen section biopsy, and the result showed that it was tumor-free. The jejunum was cut approximately 15 cm distal to the Treitz ligament, and the mesentery was resected. We carried out dissection of the uncinate process and divided the uncinate process along the lateral wall of the SMA. The specimen was excised, and bleeding control was performed.

We performed an interrupted suture, two-layer, duct-to-mucosa pancreatiocojejunostomy with a short internal stent. We placed continuous posterior and interrupted anterior sutures for hepaticojejunostomy without stent. A 50-cm Roux-en-Y limb jejunum was anastomosed from the hepaticojejunostomy site with the duodenum side by side. We also performed additional Braun anastomosis at the infracolic site. A closed drain was placed near the hepaticojejunostomy and pancreaticojejunostomy. The incision was closed layer by layer. The operation time was 512 min, and the estimated blood loss was 550 mL.

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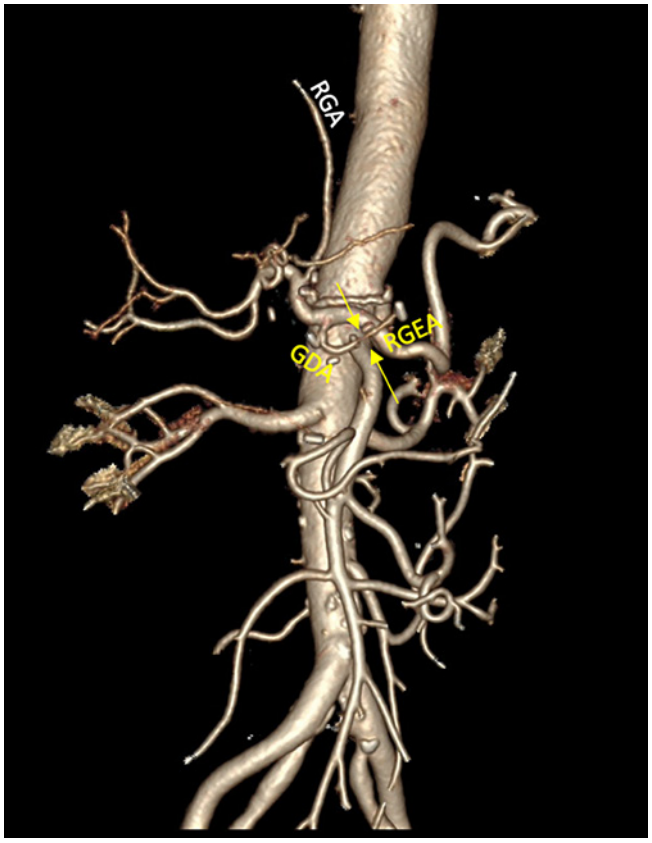

Fig. 3. Postoperative CT scan with three-dimensional reconstruction. Yellow arrow: anastomosis site. RGA, right gastric artery; RGEA, right gastroepiploic artery; GDA, gastroduodenal artery.

Postoperative Course

On the fifth postoperative day, the patient started oral intake and all drains were removed. There were no postoperative complications or abnormal findings on the follow-up CT scan conducted on the sixth postoperative day. Stomach perfusion was found to be well preserved, and the vascular anastomotic site appeared to be intact (shown in Fig. 3). The patient was discharged on day 15 after the operation.

Pathologic Examination

As a result of the pathological report of the sample, we diagnosed moderate differentiated ductal adenocarcinoma, and the entire resection margin was found to be free of carcinoma. No direct invasion of the GDA was observed, but abutment was found. The tumor size was 3.5 × 1.7 cm (ypT2), and the modified Ryan scheme for tumor regression score was 3 points, indicating a poor response to chemotherapy. There was no evidence of lymph node metastasis among the four lymph nodes recovered during surgery, corresponding to stage 1B (ypT2N0M0) according to the 8th American Joint Committee on Cancer.

Discussion

Based on our experience, we will consider the following points when performing PD in patients who have received previous esophagectomy followed by a gastric pull-up procedure. First, it is desirable, or perhaps even mandatory, to preserve both the RGA and RGEA for the safety of these patients. In several reports, the authors preserved one of these. In our case, we

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confirmed that gastric perfusion was diminished when clamping the GDA by intraoperative Doppler. However, it is not necessary to completely dissect the lesser sac side of the neogastric tube to identify and preserve the RGA and RGV. In our patient, we noted severe adhesion around the lower side of the neogastric tube due to the previous intra-abdominal process for gastric pull-up. Therefore, incidental injury to the RGA and RGV can occur when attempting to identify and preserve them. By this principle, the RGV could also be well preserved without injury (no dissection, no injury).

Second, from that point of view, pylorus-preserving PD is more appropriate than conventional PD. We recommend dissecting the duodenum, which will be divided for PD, from the vascular pedicles (RGA, RGEA).

Third, not only RGA but also RGEA should be preserved for the safety of PD in these patients. But is GDA-preserving PD oncologically safe? Nagai et al. [6] investigated this clinical issue. They reported 10 cases of PPPD preserved by GDA for periampullary cancer in cases without direct invasion, lymphatic spread, or lymph node metastasis around the GDA. However, they did not include patients with pancreatic head cancer in their case series. According to our present experience, it seemed easy to preserve the GDA because it had been retracted due to a previous gastric pull-up procedure, leading to a more superficial location as compared with the usual cases. However, in patients with pancreatic cancer, pancreatitis and possible cancer invasion around the GDA, as shown in the present case, may affect procedural and oncologic safety. Segmental resection followed by reconstruction of the RGEA to GDA [7] or the midcolic artery [6] has been reported. The present case also suggests that segmental GDA resection and end-to-end anastomosis of the RGA and GDA were feasible and safe for curative-intent radical surgery.

Lastly, delayed gastric emptying (DGE) was believed to have an adverse effect on cardiopulmonary function after PPPD in this patient. Furthermore, as a result of the severe adhesion induced by the previous operation, the duodenum was fixed near the common hepatic artery area. Therefore, in an effort to reduce the incidence of DGE, we added Braun anastomosis after completing the surgical procedure. It remains controversial whether adjunctive Braun anastomosis can reduce the incidence of DGE in PD. However, our previous prospective randomized control study [8] supports the potential benefit of Braun anastomosis in PD. These specific concerns should also be validated based on a large-scale study.

When reviewing the literature, 11 cases, including ours [7, 9–17], were reported (shown in Table 1). Because only 11 cases have been reported to date, accumulation of additional evidence is needed on the method of vascular reconstruction to preserve the gastric conduit. In addition, further studies are needed that report the details of the operative method such as operation time, blood loss, complications, and postoperative digestive function based on each method. Most cases have been reported in the past 10 years, and an analysis is expected of multicenter, long-term results and surgical details of the method of vascular reconstruction in the next 5 years.

Unfortunately, due to the short follow-up period, we were unable to analyze the long-term follow-up data, such as a detailed survey regarding the improvement in the patient's nutritional status and long-term oncologic outcome. This kind of case seems very rare. However, pancreatic surgeons must prepare for PD in patients with pancreatic head cancer who have undergone previous esophagectomy. As the long-term survival of early esophageal cancer patients improved, patients with esophageal cancer are increasingly diagnosed with pancreatic cancer after long-term follow-up. In addition, potent neoadjuvant chemotherapy is currently available, leading to conversion surgery and increasing the difficulty of the clinical circumstances. Pancreatic surgeons should consider the oncologic impact of potent systemic chemotherapy, and appropriate intraoperative surgical decision-making based on operative risk should be considered. Because margin-negative pancreatectomy is believed

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Table 1. Review of the literature reporting PD for pancreatic cancer after esophagectomy

Author	Age	Gender	Years after esophagectomy	Operative procedure, detail	Prognosis
Present 2021	69	M	6	GDA, RGEA resection; anastomosis between GDA and RGEA	2 months f/u, no recurrence, no complication
Minagawa et al. [16]	76	M	8	RGEA resection; anastomosis between RGEA and MCA	15 months f/u, no recurrence
Appelbaum et al. [14]	65	M	2	Preserved GDA, RGEA	8 months f/u, no recurrence
Takashi et al. [11]	79	M	11	Preserved RGA, RGV, RGEA, RGEV	5 years 3 months f/u, no recurrence, no complications
Sugimoto et al. [17]	40	F	6	Not described	POPF B
Izumi et al. [15]	78	M	7	Preserved GDA, RGEA	5 months f/u, no recurrence
Okochi et al. [8]	70	M	5	Anastomosis between RGEA and MCA	No complication
Nandy et al. [10]	70	M	3	Not described	3 months f/u, liver metastasis, dead d/t biliary sepsis
Inoue et al. [7]	72	M	10	RGEA resection; anastomosis to the terminus of the GDA; RGEV resection; lateral anastomosis to the left renal vein	6 months f/u, no recurrence, no complication
Fraguilidis et al. [12]	50	M	13	Preserved GDA, RGEA	14 months liver metastasis
Addeo et al. [13]	73	M	6	Preserved GDA, RGEA	POPF B

GDA, gastroduodenal artery; RGEA, right gastroepiploic artery; RGEV, right gastroepiploic vein; RGA, right gastric artery; RGV, right gastric vein; MCA, middle colic artery; POPF, postoperative pancreatic fistula; f/u, follow-up; d/t, due to.

to be essential to guarantee the long-term survival of patients with pancreatic cancer, more experience must be accumulated to address the safe and effective use of PD in this specific group of patients.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval is not required for this study, in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Juwan Kim and Chang Moo Kang researched the literature and drafted the manuscript. Seung-Soo Hong and Jae Guen Lee participated in the surgery. Choong-Kun Lee performed neoadjuvant chemotherapy. Sung Hyun Kim, Ho Kyoung Hwang, Woo Jung Lee, and Chang Moo Kang critically revised the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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