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Successful En Bloc Resection of Locally Advanced Pancreatic Tail Cancer with Colonic Perforation Following Neoadjuvant Chemotherapy: A Case Report

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Data Collection B
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Data Interpretation D
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Patient: Male, 66-year-old
Final Diagnosis: Pancreatic cancer
Symptoms: Abdominal pain
Medication: —
Clinical Procedure: Adjuvant chemotherapy • neoadjuvant chemotherapy • radical resection
Specialty: Surgery

Objective: Unusual setting of medical care

Background: Distal pancreatic cancers may be unresectable at the time of diagnosis because these cancers are asymptomatic and readily infiltrate neighboring organs. Radical resection of a pancreatic tail cancer with colonic perforation is rare. We describe successful resection of a locally advanced pancreatic tail cancer with colonic perforation using a multidisciplinary approach.


Case Report: A 66-year-old man presented to our hospital with a chief concern of high fever. Abdominal computed tomography revealed a pancreatic tail tumor infiltrating the neighboring organs and causing colonic obstruction with perforation, which resulted in an intra-abdominal abscess. Colonoscopy revealed obstruction of the descending colon by extramural invasion. Laboratory tests showed high tumor marker concentrations (carcinoembryonic antigen, 11.6 ng/dL; pancreatic cancer-associated antigen-2, >1600 U/mL). We clinically diagnosed locally advanced pancreatic tail cancer with an intra-abdominal abscess caused by colonic perforation. First, we performed transverse colostomy and percutaneous drainage. We then started neoadjuvant chemotherapy with FOLFIRINOX for tumor shrinkage and prevention of distant metastases. The therapeutic effect was a partial response, and no distant metastases was found. We therefore performed radical surgery comprising distal pancreatectomy with partial resection of neighboring organs. Although pathological examination revealed a pancreatic tail tubular adenocarcinoma with direct invasion of the neighboring organs, R0 resection was achieved. The patient was discharged with no perioperative complications. Tegafur/gimeracil/oteracil potassium were administered as adjuvant chemotherapy. The patient remained recurrence-free for 19 months after surgery.

Conclusions: We achieved successful en bloc resection of a locally advanced distal pancreatic cancer with colonic perforation by using a multidisciplinary approach.

Keywords: Colon • Neoadjuvant Therapy • Pancreatic Cancer, Adult


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Background

Some distal pancreatic cancers are unresectable at the time of diagnosis because they are characteristically asymptomatic and readily infiltrate neighboring organs or blood vessels and metastasize to distant locations. Therefore, the prognosis of distal pancreatic cancer is poor [1]. Solcie et al have reported that infiltration of the colon by pancreatic tail cancers is not rare, occurring in up to about 17% of cases [2]. However, most pancreatic tail cancers with colonic obstruction caused by infiltration are not resectable because of the presence of distant metastases. Diagnosis of pancreatic tail cancer on the basis of evidence of colonic perforation is unusual [3]. Attaining R0 resection of pancreatic cancers is important for achieving long-term survival after radical surgery [4]. However, R0 resection of pancreatic tail cancer with colonic perforation is relatively rarely achieved. Herein, we describe successful en bloc resection with negative surgical margins of a locally advanced pancreatic

tail cancer with colonic perforation, which result in intra-abdominal abscess following neoadjuvant chemotherapy (NAC).

Case Report

A 66-year-old Japanese man presented to our hospital with a chief concern of high fever. Abdominal computed tomography (CT) revealed a pancreatic tail tumor. The pancreatic tail tumor was infiltrating the abdominal wall, spleen, left kidney, and splenic flexure of the transverse colon. Colonic obstruction occurred by pancreatic cancer invasion, resulting in an intra-abdominal abscess formation near the splenic flexure of the transverse colon (Figure 1). No distant metastases were detected in the lungs, peritoneum, or other organs. Lower gastrointestinal endoscopy revealed that the tumor had compressed and obstructed the descending colon from the serosal wall (Figure 2). No malignant cells were found in a mucous

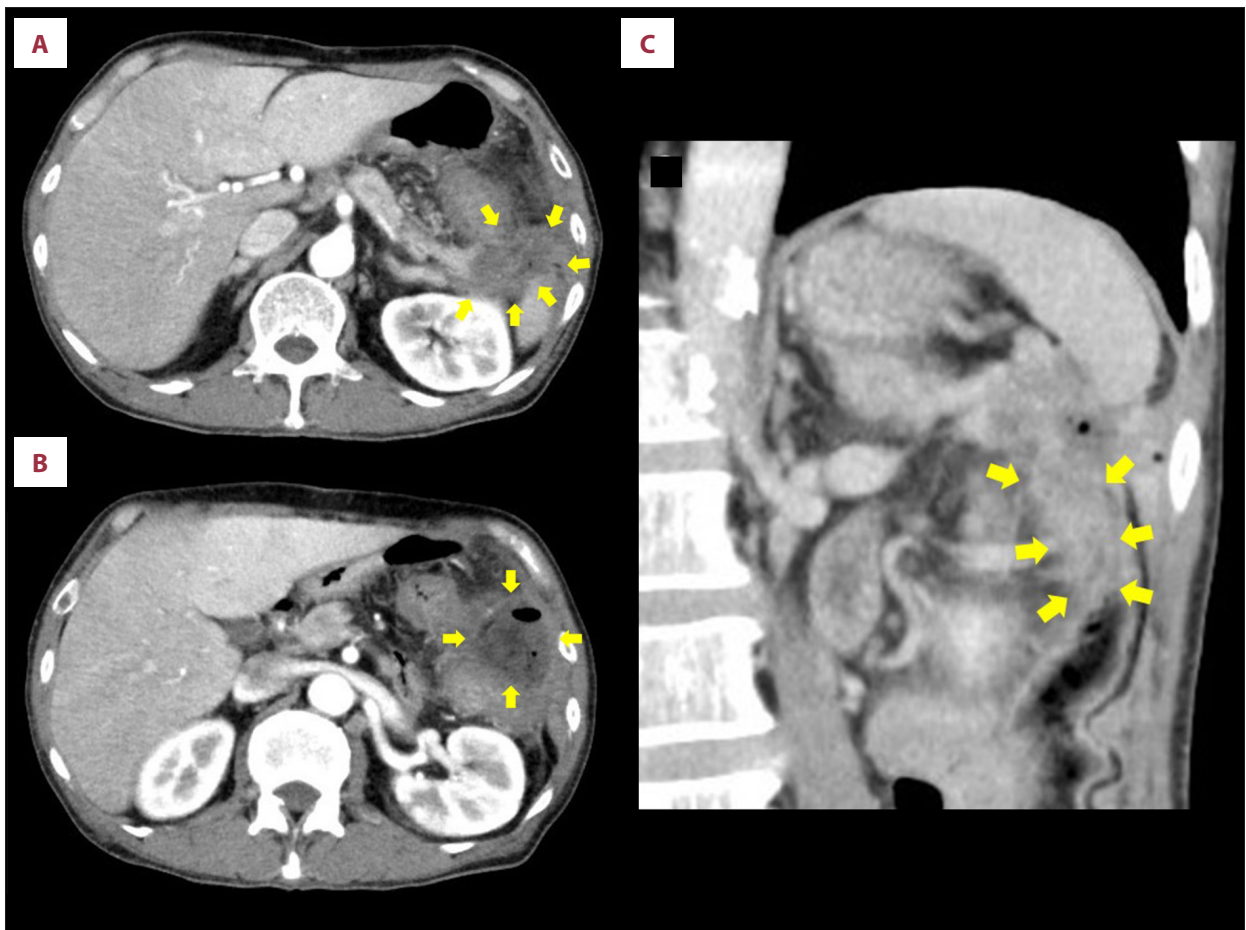


Figure 1. (A) Axial section view of the computed tomography images showing the pancreatic tail tumor seems to be infiltrating the other organs. Arrows indicate the pancreatic tail tumor. (B) Axial section view of the computed tomography images showing an intra-abdominal abscess near the pancreatic tail and splenic flexure of the transverse colon. Arrows indicate an intra-abdominal abscess. (C) Coronal section view of the computed tomography images showing the pancreatic tail tumor seems to be infiltrating the splenic flexure of the transverse colon. Arrows indicate compressed splenic flexure of transverse colon.

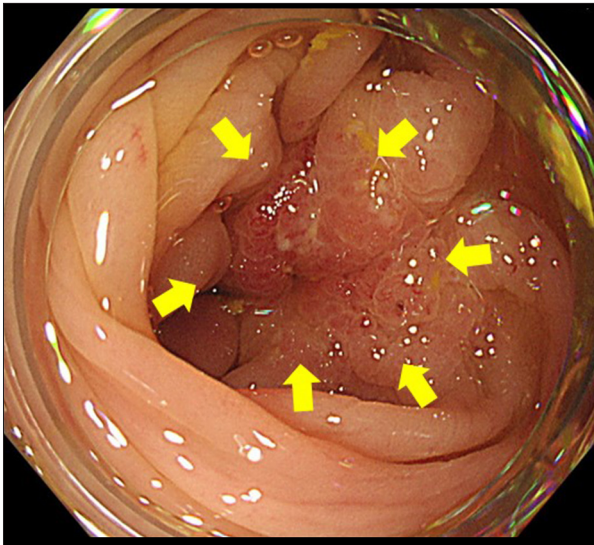


Figure 2. Colonoscopy image showing that the tumor appears to be compressing the descending colon from the serosal wall.

membrane biopsy. Additionally, laboratory testing showed high tumor marker concentrations (carcinoembryonic antigen, 11.6 ng/dL; carbohydrate antigen 19-9, <2.0 U/mL; pancreatic cancer-associated antigen-2 >1600 U/mL) (Table 1). Therefore, we clinically diagnosed a locally advanced pancreatic tail cancer with the colonic obstruction with perforation and intra-abdominal abscess formation as a result of infiltration of the splenic flexure of the transverse colon. First, we urgently performed a transverse colostomy and percutaneous drainage for the intra-abdominal abscess for infection control. When we performed percutaneous drainage, we did not perform a cytology exam of the intra-abdominal abscess. After strict infection control, we started first-line treatment as neoadjuvant chemotherapy for locally advanced pancreatic cancer with FOLFIRINOX in

light of the patient's performance status. FOLFIRINOX consisted of oxaliplatin at a dose of 85 mg per square meter, given as a 2-hour intravenous infusion, immediately followed by leucovorin calcium at a dose of 200 mg per square meter, given as a 2-hour intravenous infusion, with the addition, after 30 minutes, of irinotecan hydrochloride hydrate at a dose of 180 mg per square meter, given as a 90-minute intravenous infusion through a bypass injection. This treatment was immediately followed by fluorouracil at a dose of 400 mg per square meter given by intravenous bolus, followed by a continuous intravenous infusion of 2400 mg per square meter over 46 hours given every 2 weeks.

After 6 courses of FOLFIRINOX without any adverse events, the size of the main tumor in the pancreatic tail was reduced from 36 mm at baseline to 23 mm in diameter at the end of neoadjuvant therapy. According to the RECIST guidelines [5], partial response was achieved. Although there was persistent invasion of the abdominal wall, spleen, descending colon, and left kidney, no distant metastases were detected by preoperative CT after NAC. We therefore considered that we could perform radical surgery comprising distal pancreatectomy (DP) and resection of other affected organs. We successfully performed DP with partial resection of the colon, stomach, jejunum, abdominal wall, left adrenal gland, and kidney and closure of the transverse colostomy. The resected specimen had a hard elastic mass in the pancreatic tail surrounded by the other organs, namely the stomach, jejunum, spleen, transverse colon, left kidney, and a part of abdominal wall (Figure 3A). Pathological examination of hematoxylin and eosin-stained sections of the resected specimen revealed that the main tumor, which was located in the pancreatic tail, was a tubular adenocarcinoma that had infiltrated the abdominal wall, spleen, transverse colon, and left renal capsule. Infiltration of the transverse colon into the muscularis propria was found (Figure 3B). Although

Table 1. Laboratory data on admission.

Complete blood count		Serum	
WBC	170×10 ² /μl	CRP	24.5 mg/dl
RBC	332×10 ⁴ /μl	Total protein	6.9 g/dl
Hb	10.9 g/dl	Albumin	2.9 g/dl
Plt	29.4×10 ⁴ /μl	Total-bilirubin	0.7 mg/dl
Tumor markers		AST	41 IU/l
CEA	11.2 ng/ml	ALT	36 IU/l
CA19-9	<2.0 U/ml	LDH	137 IU/l
DUPAN-2	>1600 U/ml	AMY	30 IU/l
		BUN	17 mg/dl
		Cr	0.88 mg/dl
		eGFR	88.9 ml/min/1.73 m ²

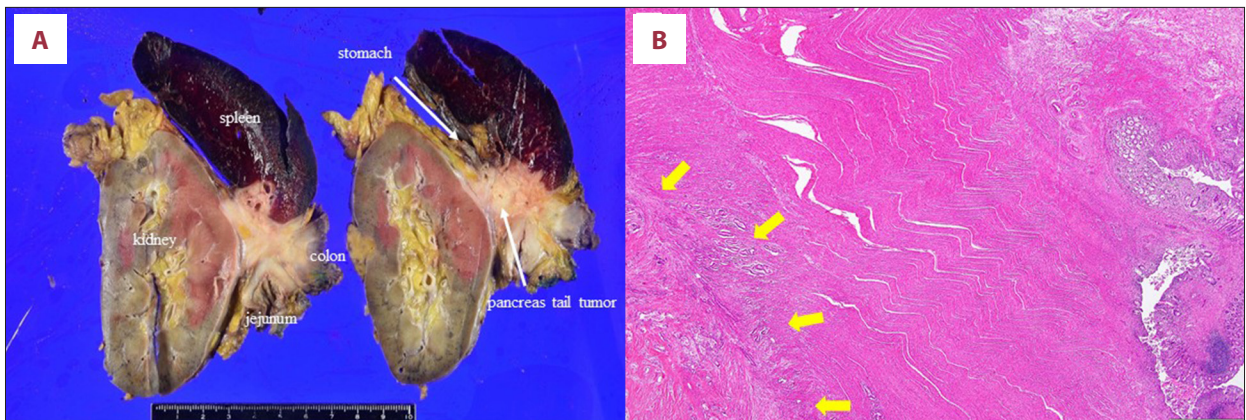


Figure 3. (A) Photograph of en bloc resected specimen comprising the pancreas, colon, spleen, stomach, jejunum, and kidney. (B) Photomicrograph showing tumor cells invading the colon up to the muscularis propria (hematoxylin eosin stain; magnification: $\times 20$).

the histological evaluation of resected specimen demonstrated colonic obstruction due to the stenosis of cancer infiltration, cancer infiltration was not histologically identified at the perforated site. The final pathological stage was T3N1M0, Stage IIb according to the eighth edition of the TNM classification of malignant tumors of UICC [6]. Although the tumor size was reduced by the NAC, the histological response to neoadjuvant chemotherapy was Evans grade I [7]. We succeeded in performing R0 resection with negative surgical margins by resecting all affected organs.

The postoperative course was uneventful. The patient was discharged on postoperative day 27 having had no perioperative complications. Adjuvant chemotherapy comprising tegafur/gimeracil/oteracil potassium was administered for 6 months. There has been no evidence of recurrence or complications in the 19 months since radical surgery.

Discussion

Thanks to developments in medical technology in recent years, we are now able to detect and treat many kinds of cancer at an early stage. However, because most pancreatic tail cancers are asymptomatic, some are classified as locally advanced cancers at the time of diagnosis [1]. Attaining R0 resection of pancreatic cancers is important for achieving long-term survival after radical surgery [4]. The International Study Group for Pancreatic Surgery has established a clear definition of extended DP associated with resection of any of the following involved organs: stomach, colon, small bowel, left adrenal gland, left kidney, diaphragm, and contiguous liver. Major arterial or venous resections are also included in the definition. Despite increased perioperative morbidity, extended pancreatectomy is warranted to achieve long-term survival of patients with pancreatic ductal adenocarcinoma if R0 resection

can be achieved [8]. Therefore, DP with resection of multiple viscera should be considered with the aim of achieving R0 resection in fit patients with locally advanced pancreatic cancer.

Several investigators have demonstrated that resection of multiple viscera in patients with pancreatic cancer may increase postoperative complications. This applies particularly to patients who undergo resection of a kidney or the colon, who require intraoperative transfusions, and whose operative procedures are lengthy. Nevertheless, these patients' long-term prognoses may be better than after standard DP [9,10]. However, extended DP did not increase the rates of postoperative pancreatic fistula, post-pancreatectomy hemorrhage, or major complications [11]. Although the safety and effectiveness of extended DP are still controversial, extended DP with the aim of achieving R0 resection and long-term survival is permissible. However, the indications for such radical surgery should be carefully considered, keeping in mind the possibility of complications such as anastomotic leakage, pancreatic fistula, and other major complications.

We have herein reported successful en bloc resection by extended DP following NAC of a pancreatic tail cancer with colonic obstruction, perforation, and formation of an intra-abdominal abscess secondary to infiltration of the splenic flexure of the transverse colon and other affected organs, without perioperative complications. Although this case was locally advanced case, we considered the case to be resectable by multivisceral organ resection without NAC. However, locally advanced cases often have early local and distant recurrences after surgery. Therefore, we consider and expect that neoadjuvant chemotherapy can contribute to not only the tumor reduction, but also the prevention of distant metastases. Although the response was partial, we considered that in this case NAC could contribute to a sufficient surgical margin to achieve R0 resection without distant metastases.

Table 2. The reported cases of pancreatic cancer with colonic perforation.

Author	Year	Age	Gender	Chief concern	Location	Neoadjuvant therapy
Slam KD	2007	78	M	Abdominal pain Nausea Distention	Tail	–
Takiuchi	2019	69	F	Abdominal pain	Tail	–
Kurata	2019	82	M	Abdominal pain	Tail	–
Our case		66	M	Fever	Tail	FOLFIRINOX

Author	Perforated site	Therapeutic strategy	Resected involved organs	Adjuvant chemotherapy	Prognosis (month)	Notification
Slam KD	Cecum	(1) Right hemicolectomy (2) Extended DP (after 5 days)	Left colon	–	3	
Takiuchi	Unknown	Colostomy Transabdominal drainage Chemotherapy	–	–	24	Classified unresectable because of peritoneal dissemination
Kurata	Splenic flexure of transverse colon	Extended DP	Colon	S-1	9	Infected pancreatic cyst was treated by antibacterial drugs
Our case	Splenic flexure of transverse colon	(1) Transverse colostomy percutaneous drainage (2) Extended DP (after 5 months)	Partial colon, stomach, jejunum, left kidney, abdominal wall	S-1	19	

Successful extended DP with a partial resection of the thoracic wall after downstaging by NAC using FOLFIRINOX was first reported in 2020 by Giuliani et al [12]. These authors stressed the importance of administering neoadjuvant strategies such as chemotherapy and radiotherapy with the aim of downstaging or reducing the tumor size in patients with locally advanced or borderline resectable pancreatic cancer [12]. Additionally, it has been shown that neoadjuvant therapy such as chemotherapy or chemoradiotherapy facilitates attainment of negative margins after resection of originally borderline or locally advanced pancreatic cancer [13].

In the present patient, we selected and administered FOLFIRINOX based on a meta-analysis showing that neoadjuvant chemotherapy with FOLFIRINOX for locally advanced pancreatic cancer achieves better overall and R0 resection rates than does therapy with gemcitabine [14]. The objective response rate of the FOLFIRINOX group was better than that of the gemcitabine group (31.4% versus 9.4%) [15]. A

meta-analysis reported that the complete response rate after treatment with FOLFIRINOX was 2.9%, the partial response rate was 35.9%, and the stable disease rate was 41.2% [16]. Another report showed that partial response was more common with FOLFIRINOX than with gemcitabine and nab-Paclitaxel (19% versus 6%) [17].

FOLFIRINOX as NAC is required to achieving radical resection and long-term survival because the operative outcomes and survival of the patients treated with neoadjuvant FOLFIRINOX are better than those of patients with borderline resectable/locally advanced cancer who undergo upfront resection [18].

Therefore, in this case, we were able to perform extended DP and achieve en bloc R0 resection with no complications using NAC with FOLFIRINOX with the aim of downstaging, tumor shrinkage, and prevention of distant metastases and early postoperative recurrence.

Abscess formation caused by colonic perforation is a very rare complication associated with pancreatic cancer. Searches for the terms “pancreatic cancer with colonic perforation” in PubMed from inception to 2020 yielded only 4 cases, including our case (Table 2) [19-21]. The pancreatic tumor was located in the pancreatic tail of all 4 patients. Two patients, including ours, had developed perforation at the splenic flexure of the transverse colon by direct infiltration [21]. The perforation in 1 patient had occurred at the cecum by increasing intra-colonic pressure [19]. Two patients, including ours, underwent urgent colostomy and percutaneous or transabdominal drainage [20]. The other 2 patients underwent right hemicolectomy or treatment with anti-bacterial drugs [19,21]. Because 1 patient had peritoneal dissemination, radical resection was not performed [20]. NAC was administered only in our case. Additionally, adjuvant chemotherapy was performed in 2 cases, including ours [21].

As mentioned above, because NAC is a requisite for locally advanced pancreatic cancer to achieve R0 resection and long-term survival, infection control is very important before NAC. In our case, by performing urgent percutaneous drainage of the intra-abdominal abscess and temporary colostomy for a strict infection control, NAC could be introduced promptly and safely. Of course, administration of adjuvant chemotherapy is also important for prevention of postoperative recurrence. Through

multidisciplinary treatment, our present patient achieved recurrence-free survival for 19 months after surgery despite the locally advanced nature of the cancer.

Conclusions

In conclusion, although colonic perforation and the intra-abdominal abscess formation were very rare and difficult complications, we achieved successful en bloc R0 resection of a locally advanced distal pancreatic cancer with colonic perforation by using a multidisciplinary treatment that included infection control by colostomy, drainage, and NAC with FOLFIRINOX.

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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