GEM + nab-PTX Therapy for Pancreatic Body Cancer cStage IVb for Conversion Surgery: A Case Report

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A 67-year-old woman presented with a chief complaint of umbilical region mass and epigastric pain. Carbohydrate antigen 19−9 (CA19−9) level was 177.5 U/mL; computed tomography (CT) showed a hypovascular mass lesion of 20 mm × 20 mm in the pancreas, infiltration into the superior mesenteric artery and dilation of the main pancreatic duct. Peritoneal dissemination to the omentum and abdominal wall was observed. The patient was diagnosed with T4N0M1, cStage IV unresectable pancreatic body cancer and was started on GEM + nab-PTX therapy. She underwent chemotherapy for 10 months for a total of 10 cycles. The CA19−9 level returned to normal, CT showed reduction in tumor size to 11 mm × 8 mm, and peritoneal dissemination also disappeared. Disappearance of peritoneal dissemination was also observed on Positron emission tomography (PET). Laparoscopic surgery was planned, and rapid pathological examination results of ascites washing cytology and peritoneal mass were negative. Laparoscopic distal pancreatectomy was then performed, which transitioned to hand-assisted laparoscopic surgery; R0 resection was achieved. The patient underwent outpatient postoperative adjuvant chemotherapy with orally administered S-1 and has been recurrence-free for 1 year postoperatively. This case demonstrates that patients with pancreatic body cancer with distant metastasis can undergo R0 resection following GEM + nab-PTX combination therapy.

Key words: pancreatic cancer, peritoneal dissemination, conversion surgery, GEM + nab-PTX therapy

INTRODUCTION

Many cases of pancreatic cancer are discovered with multiple metastases, and many of them relapse early even if the patients are able to undergo surgery [1]. Their prognosis is poor, and long-term survival is difficult to achieve. Only 10%−15% of cases become indications for surgery; the 5-year survival rate after surgery is said to range between 20.7% and 23.9% [2], showing poor prognosis. In patients with cStage IV pancreatic cancer with liver metastasis or peritoneal dissemination, extension of median survival time cannot be expected from combination of surgery with chemotherapy compared with chemotherapy alone. Thus, there is no indication for surgery and prognosis is poor [3]. Here along with relevant literature review, we report a case of pancreatic cancer with peritoneal dissemination in which R0 resection was achieved by conversion surgery following gemcitabine (GEM) + nab-paclitaxel (nab-PTX) therapy.

CASE REPORT

Case: A 67-year-old woman

Chief complaint: An umbilical mass and epigastric pain

History of present disease: The patient presented to our hospital with an umbilical mass and epigastric pain in May 2017.

Medical history: type 2 diabetes and lumbar spinal stenosis

Family history:None

Hematological test findings at the initial visit: Carbohydrate antigen 19−9 (CA19−9) and s-pancreas-1 antigen (SPAN-1) levels were high: CEA, 2.5 ng/mL; CA19−9, 177.5 U/mL; DUPAN, 44 U/mL; and SPAN-1, 85 U/mL.

Contrast-enhanced computed tomography (CT) of the abdomen at the initial visit: A hypovascular neoplasm of 20 mm × 20 mm was observed in the pancreatic body in the arterial phase, and the main pancreatic duct was dilated. Infiltration into the superior mesenteric artery (SMA) and splenic artery (SPA) was also found. A mass that appeared to be peritoneal dissemination was found in the greater omentum/umbilical region. Ascitic fluid was found in the Pouch of Douglas (Fig. 1).

Fluorodeoxyglucose-positron emission tomography (FDG-PET) at the initial visit: Accumulation of FDG was found within the masses in the abdominal wall, abdominal cavity, and rectovesical pouch. The maximum standardized uptake value (SUV-max) was 6.1 for the umbilical mass. A mass of SUV-max 4.1 was also found in the pancreatic body (Fig. 2).

The preoperative diagnosis was T4N0M1, cStage IV,

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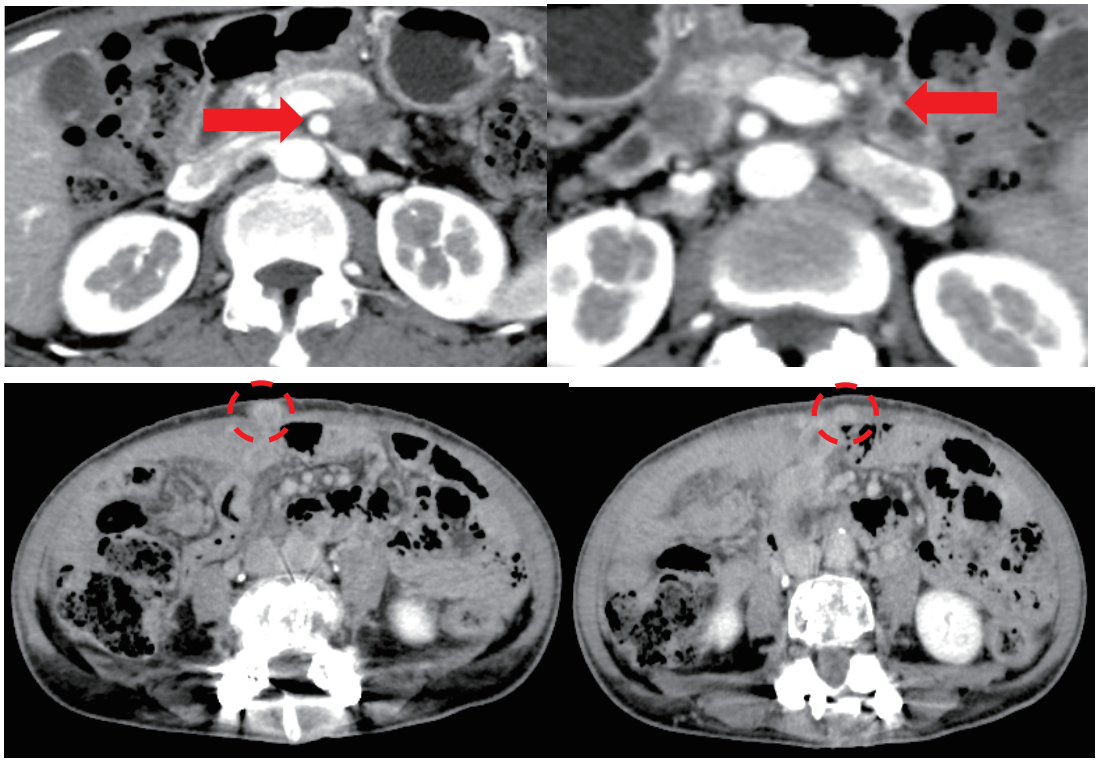

Fig. 1 CT of the abdomen at the initial visit.
A hypovascular mass of 20 mm × 20 mm with infiltration into SMA/PSA (➡). An umbilical mass appearing to be peritoneal dissemination (○).

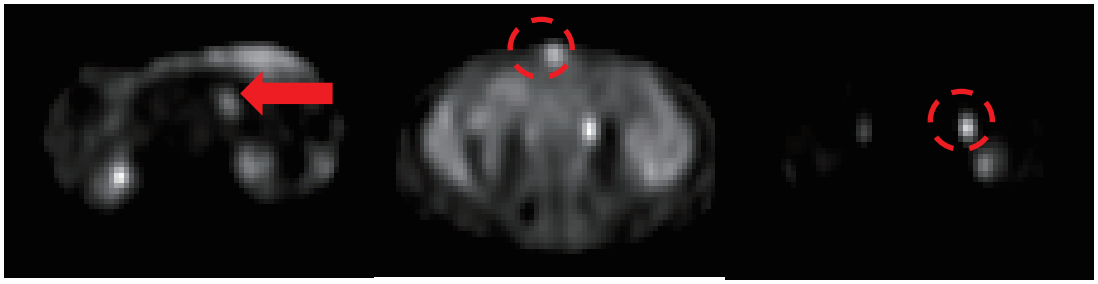

Fig. 2 FDG-PET at the initial visit.
FDG is accumulated in the pancreatic body (➡). Masses with FDG accumulation are seen in the umbilical region and abdominal cavity (○).

and GEM + nab-PTX was selected as the therapy. The patient underwent chemotherapy for 10 months for a total of 10 cycles. No major side effects were observed during chemotherapeutic drug administration.

Hematological test findings after chemotherapy: Tumor marker values were normal: CEA, 5.1 ng/mL and CA19−9, 14.4 U/mL.

CT scan of the abdomen after chemotherapy: The pancreatic tumor reduced to 11 mm × 8 mm, and infiltration into the SMA was not found. The umbilical mass also reduced in size (Fig. 3).

FDG-PET examination after chemotherapy: No evidence of FDG accumulation in the pancreas or peritoneal dissemination was found (Fig. 4).

Tumor markers became negative and CT and PET showed the absence of SMA infiltration and disappearance of peritoneal dissemination; therefore, resection was considered possible. Laparoscopic examination was performed.

Surgical findings: A 12-mm camera port was inserted from the umbilical region. At this time, a tissue sample from the umbilical part was sent for rapid pathological examination. The intraperitoneal area was examined, but no obvious peritoneal nodes or liver metastasis was found. Peritoneal washing cytology was performed. No cancer cells were found in the umbilical region tissue or by peritoneal washing cytology; laparoscopic distal pancreatectomy was therefore performed. Laparoscopy was performed up to completing tunneling of the pancreas directly above the superior mesenteric vein (SMV) and its resection. The pancreatic tumor was adhered to the junction of the superior pancreatic vein (SPV) and SMV, and resection was determined to be difficult under laparoscopy. A 6-cm incision was made at the midline of the upper abdomen, and management of SPA and displacement of the spleen were performed under hand-assisted laparoscopic surgery. Plexuses surrounding SPV and SMA were treated under direct vision, and R0 resection was achieved.

Histopathological findings: Invasive ductal carcinoma of the pancreas, post chemotherapy state, Pb,

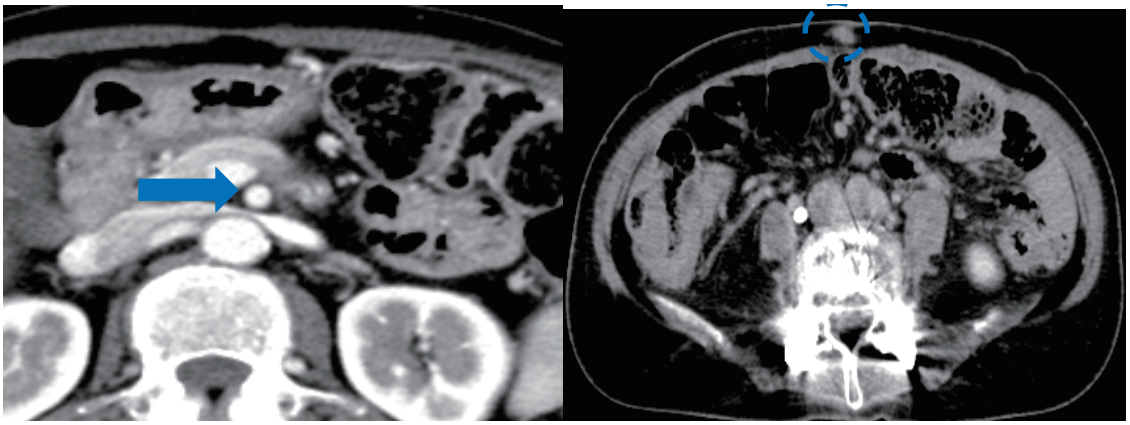

Fig. 3 Contrast-enhanced abdominal CT after chemotherapy.
The pancreatic body neoplasm reduced to 11 mm × 8 mm. No infiltration into SMA is found (➡). The mass in the umbilical region reduced in size (○).

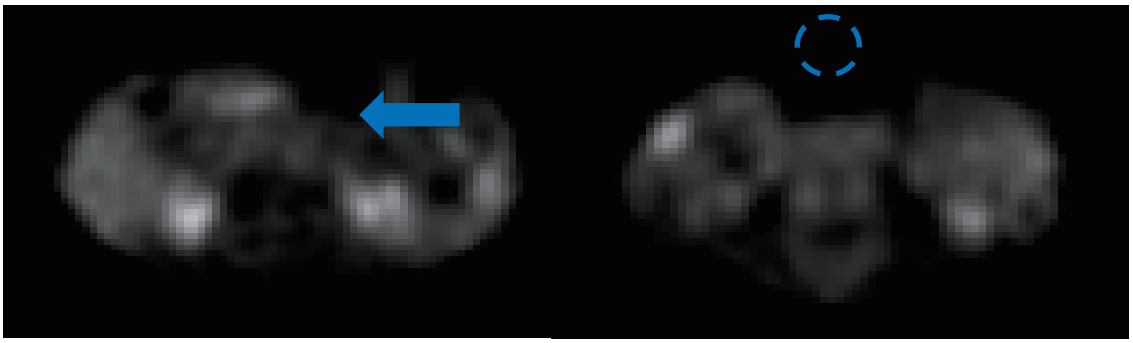

Fig. 4 FDG-PET examination after chemotherapy.
There is no accumulation of FDG in the pancreatic body (➡). There is no accumulation of FDG in the mass of the umbilical region or abdominal cavity (○).

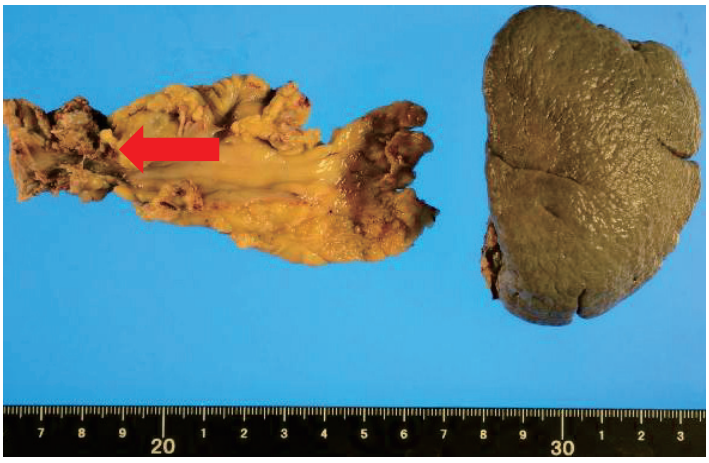

Fig. 5 Macroscopic findings.
Tumor in the pancreatic body (➡).

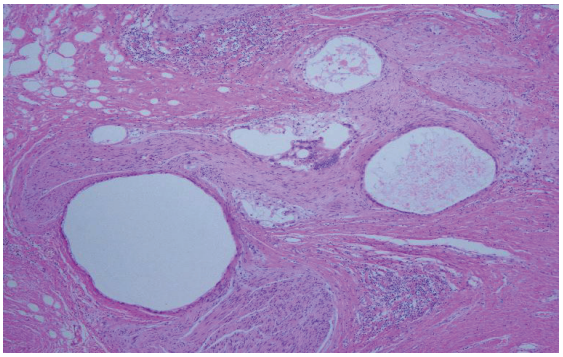

Fig. 6 Histopathological findings.
The pancreatic tissue had a high degree of fibrosis and fatty change. A very limited amount of cancer glands remained. Histological therapeutic efficacy was grade III by the Evans Classification.

TS2 (13 × 7 × 30 mm), infiltrative type, tub1, pT3, sci, INFc, ly0, v0, ne3, mpd1, pSX, pRP1, pPV0, pA0, pPL1, pPCM0, pDM0, pN0, pR0, and histological therapeutic efficacy: The tumor was grade 3 fStage IB. The tumor margin was macroscopically unclear (Fig. 5). Histologically, the pancreatic tissue had a high degree of fibrosis and fatty change (Fig. 6). The cancer gland remained slightly, accompanying neuroinvasion (PL1). Cancer cells were extended to the main pancreatic duct; however, invasion of cancer cells was not confirmed around the SPA/SPV, where only high degree of fibrosis was seen. Histological therapeutic efficacy was grade III by the Evans Classification.

The umbilical part was a fibrous connective tissue.

Postoperative course: On postoperative day 3, chylous ascites was detected from the drain, but the patient followed a course of spontaneous remission. On day 10, the drain was removed and the patient was discharged from hospital on foot. After being discharged from the hospital, the patient underwent outpatient postoperative adjuvant chemotherapy using 100 mg/body S-1 (6 weeks as one cycle consisting of

4 weeks oral administration and 2 weeks off). The patient is relapse-free for 1 year postoperatively.

DISCUSSION

Pancreatic cancer is an extremely stroma — rich, hard, and scirrhous tumor [4]; the desmoplastic stroma prevents access of chemotherapeutic agents into the tumor [5], causing refractoriness to chemotherapy. Thus, the stroma is one of the important factors contributing to poor prognosis in patients with pancreatic cancer [6]. There are some patients with pancreatic cancer who show a discrepancy in the antitumor effect of the chemotherapy between the primary lesion and metastatic lesions; this could be attributable to the rich stroma in the primary lesion as compared with metastatic lesions.

Due to advancements in chemotherapy, extension of survival in pancreatic cancer patients has been achieved in recent years [7, 8]. Currently, GEM + nab-PTX combination therapy is one of the standard treatments for unresectable pancreatic cancer. [9].

A clinical trial conducted in Japan showed that the response rate of GEM + nab-PTX combination therapy was 58.8% in patients with metastatic pancreatic cancer, indicating its powerful tumor-reducing effects [10]. This is anticipated to become a new choice of preoperative therapy for patients with locally advanced pancreatic cancer. There are some cases of patients with locally advanced pancreatic cancer who underwent GEM + nab-PTX combination therapy and who were able to undergo conversion surgery [11]. In terms of therapies on pancreatic cancer patients with distant metastasis, Furuse *et al.* reported a case of a patient with pancreatic head carcinoma with liver metastasis who underwent FOLFIRINOX therapy and was then able to undergo primary tumor resection [12]. Schneitler *et al.* reported two cases of patients with metastatic pancreatic cancer who were able to undergo R0 resection following FOLFIRINOX therapy [13]. It was rare to report in which conversion surgery was performed following GEM + nab-PTX combination therapy, and our case appears to be valuable. Radical surgery may become possible in patients with pancreatic cancer with distant metastasis in the future.

There is no definitive consensus on postoperative adjuvant chemotherapy, and it is difficult to decide whether to continue with chemotherapy that was effective preoperatively. In Japan, efficacy of S-1 adjuvant chemotherapy in patients with pancreatic cancer has been shown in a multicenter, randomized, phase 3 trial [2]. From this evidence, we decided that S-1 oral administration was the best treatment choice for postoperative adjuvant chemotherapy; S-1 was therefore administered to the patient in this case.

The response rate to GEM + nab-PTX therapy is high, and we expect that there will be more future reports on similar cases. Upon compiling more case reports, building a definitive consensus will be a future task so that patients who responded to chemotherapy can undergo resection at their best timing. Satoi *et al.* performed a retrospective analysis on patients with unresectable pancreatic cancer whose disease progression was under control for ≥ 6 months with chemotherapy or chemoradiotherapy, and the effects of conversion surgery on extension of prognosis was reported. The results of their study demonstrated that patients who underwent treatment for 240 days or more had significantly better prognosis [14]. In our case, the patient underwent chemotherapy for 10 months followed by conversion surgery and is in a state of relapse-free survival for 1 year postoperatively.

Patients with pancreatic cancer often undergo chemotherapy with high response rates, such as FOLFIRINOX therapy or GEM + nab-PTX therapy. Thus, cases of patients with cStage IV pancreatic cancer who may be suitable for undergoing conversion surgery may continue to increase. We will need to accumulate reports on more cases of patients who had complete response to chemotherapy, and must obtain a consensus for the best timing to perform surgical resection. This will improve treatment outcomes for patients with pancreatic cancer.

Japanese guidelines do not allow conversion surgery for unresectable pancreatic cancer. Whether it is involved in extending OS or BFS is still unknown at this time. It is necessary to accumulate such cases and establish a consensus for conversion surgery for unresectable pancreatic cancer.

CONCLUSIONS

Here, we report our experience of a case of complete response to GEM + nab-PTX therapy in a patient with cStage IV pancreatic cancer with peritoneal dissemination who could undergo conversion surgery, in which R0 resection was achieved.

DECLARATIONS

List of abbreviations

CT, computed tomography; GEM: gemcitabine; PET, positron emission tomography; SMA, superior mesenteric artery; SMV, superior mesenteric vein; SPV, superior pancreatic vein; SPA, splenic artery; SPAN-1: s-pancreas-1 antigen; SUV-max, maximum standardized uptake value

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