CASE REPORT

Aggressive secondary surgery for local recurrence of pancreatic cancer

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SUMMARY

We report two cases of locally recurrent pancreatic cancer treated with repeated resection. In both cases, local recurrence was found in the cut end of the remnant pancreas after initial pancreatic resection, and total remnant pancreatectomy was performed. The postoperative course was uneventful and long-term survival was achieved. Aggressive repeated surgical resection could improve the prognosis of selected patients who are suffering from local recurrence of pancreatic cancer, and can be considered as a treatment option.

BACKGROUND

Pancreatic cancer still remains one of the most lethal diseases. While surgical resection is the only potential curative therapy, recurrence occurs in as high as 80% of the patients and the high incidence of recurrence is a cause of the poor prognosis.^{1 2} Although local recurrence without distant metastases is not a rare situation, there are no standardised treatments and the majority of these patients are treated with palliative chemotherapy or chemoradiotherapy alone.³ We report two cases of locally recurrent pancreatic cancer successfully treated with intensive multidisciplinary therapy including total remnant pancreatectomy.

CASE PRESENTATION**Case 1**

A 73-year-old woman showed dilation of the main pancreatic duct (MPD) on abdominal ultrasonography (US) at an annual medical check-up. CT scan and endoscopic retrograde cholangiopancreatography (ERCP) also demonstrated dilation of the MPD in the distal part of the pancreas. CA19-9 level was not elevated. Subtotal stomach preserving pancreaticoduodenectomy was performed, and histopathological examination proved well-differentiated tubular adenocarcinoma in the pancreatic head (figure 1A), without any lymph node metastasis (T1N0M0StageIA). Surgical margin was free from cancer cells, but pancreatic intraepithelial neoplasia was present in the cut end of the MPD. Adjuvant therapy was not carried out because of the patient's refusal.

Seventeen months after the initial operation, CT scan showed dilation of the MPD of remnant pancreas (figure 1B,C), and CA19-9 level was elevated to 702 U/mL. Thus, local recurrence was strongly suspected.

Case 2

A 67-year-old man was referred to our hospital for pancreatic tumour detected on screening abdominal US. Carcinoembryonic antigen (CEA) and Duke pancreatic monoclonal antigen type-2 (DUPAN-2) level was elevated to 13.9 ng/mL and 436 U/mL, respectively. CT scan showed low-density lesion in the body of the pancreas (figure 2A), and ERCP revealed dilation of the MPD in the distal part of the pancreas. On the basis of these findings, pancreatic body cancer was suspected and distal pancreatectomy was performed. Histopathological examination demonstrated mucinous carcinoma (figure 2B), and negative surgical margin (T2N0M0StageIB). After the operation, three cycles of gemcitabine therapy (1000 mg/m²) was carried out.

Nineteen months after the initial operation, CT scan showed a new low-density lesion in the remnant pancreas (figure 2C), and CEA level was elevated to 7.9 ng/mL, from which local recurrence was suspected. Although gemcitabine therapy was resumed, the tumour size was increased.

TREATMENT

In both cases, whole-body evaluation including positron emission tomography revealed no evidence of distant metastasis, and surgical resection was performed. Remnant distal pancreatectomy with splenectomy was performed in case 1, and remnant proximal pancreatectomy with duodenectomy was performed in case 2.

OUTCOME AND FOLLOW-UP

The operations were performed safely with good postoperative glycaemic control. Histopathological examination of the second tumour confirmed well-differentiated tubular adenocarcinoma in case 1 (figure 1D), and tubular adenocarcinoma with mucinous components in case 2 (figure 2D). Similar histopathological findings and brief time interval between the first and the second tumours in these two cases are compatible with the idea of tumour recurrence, although it is difficult to distinguish local recurrence from second primary cancer.

Both patients received chemotherapy following the second operation. In case 1, the patient showed multiple liver metastases, and died 34 months after the second operation (55 months after the first operation; figure 3). In case 2, the patient is still doing well without any recurrence 14 months after the second operation (41 months after the first operation; figure 4).

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Figure 1 Images and pathological findings in case 1. (A) A well-differentiated tubular adenocarcinoma was proved at the initial operation. (B) Abdominal CT 12 months after the initial operation showed no sign of recurrence including dilation of the main pancreatic duct (MPD). (C) Dilation of MPD in the remnant pancreas was detected by CT scan 17 months after the initial operation (arrows). (D) A well-differentiated tubular adenocarcinoma similar to the initial pancreatic cancer was demonstrated in the cut end of the remnant pancreas at the second operation.

Figure 2 Images and pathological findings in case 2. (A) A tumour approximately 3 cm in diameter was detected in the pancreatic body on abdominal CT before the initial operation (arrows). (B) Mucinous carcinoma was proved at the initial operation. (C) A new tumour was detected in the cut end of the remnant pancreas 19 months after the initial operation (arrows). (D) Tubular adenocarcinoma with mucinous components was demonstrated at the second operation.

Figure 3 Postoperative clinical course of the patient in case 1. Gemcitabine therapy was introduced, but CA19-9 level was gradually increased and multiple liver metastases were revealed 29 months after the second operation.

DISCUSSION

Pancreatic cancer is a lethal disease with 5-year survival rate of up to 20% even after curative resection.⁴⁻⁷ The poor prognosis is mainly owing to the high recurrence rate of the cancer. Despite improvements in surgical techniques and advances in adjuvant treatment, recurrence occurs in as high as 80% of the patients.^{1 7 8} The location of recurrence can vary, but is most commonly observed in the liver, peritoneal cavity or locally in the remnant pancreas. Although in most patients the prognosis is deteriorated by distant metastasis or combined locoregional and distant failure, local recurrence without any evidence of distant metastasis can be found in 8–35% of patients.^{3 7-11}

There are no established therapeutic strategies for recurrent pancreatic cancer, and palliative chemotherapy or chemoradiotherapy

has been chosen historically. Indeed in most cases with recurrence, there is no indication for surgical resection because the tumour is far advanced or distant metastases are present, but isolated local recurrence seems to be a potentially curable situation, although it has so far not been clear whether resection of remnant pancreatic recurrence could provide improved survival.²

There are few reports regarding repeated resection for local recurrence of pancreatic cancer.^{1-4 12 13} These literature suggest that repeated pancreatectomy might provide some benefits for selected patients. Lavu *et al*¹ reported that repeated resection was safe and viable option with postoperative morbidity of 18% and 1-year survival rate of 71%. Kleeff *et al*⁴ reported that there was a tendency of increased median survival in patients who received remnant pancreatectomy (17.0 months) compared

Figure 4 Perioperative clinical course of the patient in case 2. In spite of the gemcitabine therapy, the recurrent tumour was increased in size and second operation was performed. The patient goes on with chemotherapy and is still doing well without any recurrence 14 months after the second operation.

with those who underwent only exploration or palliative bypass (9.4 months). To the best of our knowledge, there are no large studies which compared the overall survival after repeated resection to the survival with palliative treatment, but our cases seem to have achieved longer survival (55 months and 41 months after the first operation) than ever.

To achieve radical resection for recurrent pancreatic cancer, total remnant pancreatectomy is required in most cases. A major concern following total pancreatectomy is an impact of the resultant apancreatic state on the patient's quality of life. Diabetes mellitus and malabsorption as a sequel to total pancreatectomy are well recognised and significant clinical problems.^{14 15} Although the permanent pancreatic endocrine insufficiency associated with total pancreatectomy was previously regarded as a cause of brittle diabetes leading to morbidity, recently long-acting insulin glargine along with supplemental sliding scale insulin at meals has made it possible to control diabetes adequately.^{1 16} Pancreatic exocrine insufficiency can be managed by pancreatic enzyme replacement with few complications.^{1 15}

In our cases, the operations were performed safely with good postoperative glycaemic control, and long-term survival with satisfactory quality of life was achieved. The result demonstrated that repeated resection for local recurrence of pancreatic cancer could provide improved prognosis. Aggressive resection may be considered as a treatment option for isolated local recurrence of pancreatic cancer.

Learning points

- ▶ Local recurrence of pancreatic cancer without evidence of distant metastases is sometimes recognised after initial pancreatectomy.
- ▶ Total remnant pancreatectomy is a potentially curative treatment for the local recurrence, and may provide long-term survival.
- ▶ Endocrine and exocrine pancreatic insufficiency following total pancreatectomy can be managed more easily than previously thought, owing to long-acting insulin and pancreatic enzyme replacement.

Contributors AT, TF and HM operated and managed patients perioperatively. NS prepared a manuscript and TF reviewed it.

Competing interests None.

Patient consent Obtained.

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