

Case Report

Remnant pancreatectomy for recurrent or metachronous pancreatic carcinoma: a case report and literature review

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Abstract: Background: Due to the aggressive biological behavior, surgical resection is the only curative therapeutic option for pancreatic ductal adenocarcinoma (PDAC), yet only a third of patients with PDAC are eligible for surgery at initial diagnosis. However, the majority of patients with PDAC who undergo surgical resection develop local recurrences to the remnant pancreas or peritoneum or distant metastasis to the liver, leading to the inability to even perform a second resection. Case presentation: Here we report two patients on whom remnant pancreatectomy was both performed to treat recurrent or metachronous PDAC and then a literature review is included. To the best of our knowledge, there up to now has been only 11 related cases in the previous literature report. Conclusion: Remnant pancreatectomy should be considered as an effective treatment for recurrent or metachronous PDAC in selected patients, which could result in prolonged disease-free survival after the second operation.

Keywords: Remnant pancreatectomy, pancreatic ductal adenocarcinoma

Introduction

Of all pancreatic cancers, 80% are pancreatic ductal adenocarcinoma, presenting a worldwide annual incidence of 4.9 per 100,000 for men and 3.6 per 100,000 for women [1, 2]. With an aggressive biological behavior, PDAC might only be cured by surgery. However, due to the locally advanced infiltration or distant metastases, only a third of patients with PDAC are eligible for surgery at initial diagnosis [3]. Approximately 80% of all surgically-treated patients develop a recurrence, which is usually found in the remnant pancreas, liver or peritoneum [4], and that typically develops within 2 years after the initial resection [5]. Meanwhile, major advancements in gene detection for the postoperative treatments of PDAC have been seen in the last few years. Recently, we met with two patients in whom remnant pancreatectomy was both performed to treat recurrent or metachronous PDAC. Gene detection was used in one of the cases.

Case report

Case 1

In January 3rd 2016, a 51-year-old male patient was admitted into our hospital, manifesting with epigastric pain, nausea, and vomiting. Abdominal enhanced computed tomography (CT) detected a 2.0*2.0 cm low density mass in the head of his pancreas, with a visible dilatation of the main pancreatic duct (**Figure 1A**). Furthermore, the cancer antigen 19-9 (CA 19-9) in his blood was increased (78.17 U/ml; normal range: <22 U/ml). Classic pancreaticoduodenectomy was performed on January 7th 2016 for this patient. A moderately differentiated PDAC was pathologically diagnosed, with all negative surgical margins and without any regional lymph node metastasis. Postoperatively, this patient received adjuvant therapy with 3 cycles of gemcitabine monotherapy, followed by an additional 3 cycles of gemcitabine.

In January 2nd 2017, nearly 12 months after his first operation, a follow-up magnetic resonance

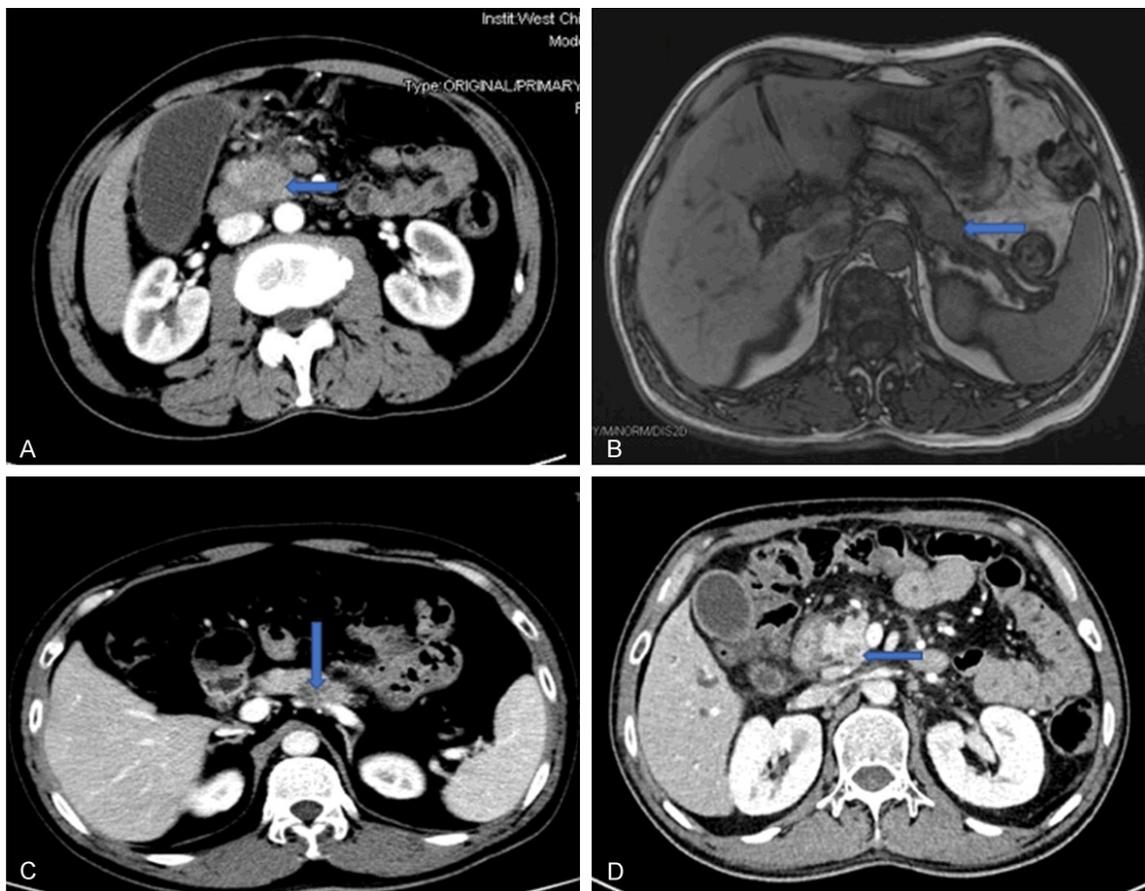


Figure 1. A: A 2.0*2.0 cm low-density mass in the head of the pancreas (Blue arrow). B: A solid lesions at the tail of the pancreas. C: A 1.9*1.7 cm mass in the body of the pancreas. D: A low-density lesion in uncinate process of pancreas.

imaging (MRI) examination detected a solid lesions at the tail of his pancreas (**Figure 1B**), with simultaneously notably increased CA 19-9 (173.70 U/ml), although he did not have any uncomfortable symptoms. After an intense multidisciplinary discussion, a radical resection of total remnant pancreatectomy with splenectomy was performed in January 4th 2017, which confirmed a moderately-to-poorly differentiated PDAC. To obtain as much information as possible, immunohistochemical staining was done for this patient, which revealed positive expression of CK7 and CK19, with a Ki-67 positive rate of approximately 10%~15%. Additionally, KRAS and TP53 gene mutations were identified. This patient is still alive in the last follow-up, about 23 months after the first operation and 11 months after the second.

Case 2

A 41-year-old male came into our hospital with slight hypogastralgia in November 3rd 2015. An

abdominal CT showed a 1.9*1.7 cm mass in the body of his pancreas without visible pancreatic duct dilatation (**Figure 1C**), and also with obviously elevated CA 19-9 (607.70 U/ml). In November 7th 2015, a radical distal pancreatectomy with splenectomy was performed, which postoperatively confirmed the pathological diagnosis of PDAC, without any regional lymph node or distant metastasis. A 6-month course of adjuvant chemotherapy was administered for this patient, without obvious recurrence evidence by CT or MRI in the followed periodic checkups, although the CA 19-9 level was slightly elevated at 1 year after operation (40.43 U/ml).

In April 20th 2017, about 17 months after his initial resection, this patient presented signs of obstructive jaundice, with notably elevated total bilirubin (232.0 umol/L; normal range: 5.0-28.0 umol/L), direct bilirubin (191.0 umol/L; normal range: <8.8 umol/L) and CA 19-9 in his blood (> 1000.00 U/mL). An abdominal en-

Remnant pancreatectomy for recurrent pancreatic carcinoma

Table 1. Features of patients with remnant PDAC who underwent a second pancreatic resection

	Author	Sex	Age	First operation	Time interval of two surgery (months)	Symptom before the diagnosis of Remnant PDAC	Second operation	Outcome
1	Eriguchi N et al. [10]	Female	67	DP	88	No symptoms, the CA 19-9 level increased	Proximal remnant pancreatectomy	Alive 8 months
2	Wada K et al. [6]	Female	52	PPPD	12	NM	DP	NM
3	Takamatsu S et al. [7]	Male	63	PPPD	43	No symptoms, the CA 19-9 level increased	DP	Alive 10 months
4	Dalla Valle et al. [6]	Male	63	PD	12	No symptoms, the CA 19-9 level increased	DP	Alive 24 months
5	Miura et al. [8]	Female	72	PD	29	NM	DP plus liver resection	Dead 5 months
6	Miura et al. [8]	Female	52	PD	22	NM	DP	Dead 44 months
7	Koizumi et al. [11]	Male	65	PD	85	Hydrodipsia and polyuria, blood sugar level was elevated, the CA 19-9 level was within the reference limits	DP	Alive 10 months
8	Koizumi et al. [11]	Male	67	DP	25	No symptoms, the CA 19-9 level increased	Proximal remnant pancreatectomy	Alive 8 months
9	Ogino et al. [13]	Female	63	PD	66	Blood sugar level was elevated, the CA 19-9 level increased	DP	Alive 13 months
10	Ogino et al. [13]	Male	56	PD	37	No symptoms, the CA 19-9 level increased	DP	Alive 7 months
11	Hamner et al. [12]	Male	73	PD	48	No symptoms, the CA 19-9 level increased	DP	Alive 11 months
12	Present Case 1	Male	51	PD	12	No symptoms, the CA 19-9 level increased	DP	Alive 11 months
13	Present Case 2	Male	41	DP	17	Jaundice, the CA 19-9 level increased	PD	Dead 1 month

Note: PDAC=pancreatic ductal adenocarcinoma; DP=distal pancreatectomy; PPPD=pylorus-preserving pancreaticoduodenectomy; PD=pancreaticoduodenectomy; NM=not mentioned.

Remnant pancreatectomy for recurrent pancreatic carcinoma

hanced CT scan detected a low-density lesion in uncinate process of pancreas (**Figure 1D**). Pancreaticoduodenectomy was performed in April 26th 2017, which once again confirmed the pathological diagnosis of PDAC. Unfortunately, this patient died less than 1 month after the second resection, due to the postoperative complications of coagulopathy and superior mesenteric vein stenosis.

This study was approved by the Institutional Review Board of West China Hospital, Sichuan University. Informed consent was given by the patient.

Discussion

Repeated pancreatectomy for recurrent PDAC is extremely rare. Over the last 17 years, only 11 cases have been reported [6-13], which were detailed in **Table 1**. These cases include eight male and five female patients, with an average age at first resection of 60.4 years (Range: 41-73 years). The average interval time between the initial operation and the diagnosis of remnant PDAC was 38.2 months (Range: 12-88 months). The average survival time after the second operation was 12.7 months (Range: 1-44 months), with the longest one of 44 months.

For 10 out of 13 patients in the reviewed literature (**Table 1**), the CA 19-9 level in his/her blood increased obviously before the diagnosis of remnant PDAC, which was mostly prior to an abdominal enhanced CT or MRI examination, as the Case 2 occurred at 1 year after this operation. Therefore, we strongly believe that CA 19-9 is of great value for the diagnosis of remnant PDAC. CA19-9 is also a sensitive indicator to diagnosis of remnant PDAC, even if the abdominal CT or MRI was negative.

Recently, gene detection has been applied as an advanced technique for malignant tumors, such as carcinoma from stomach, lung, and ovary, etc, especially in indicating function of postoperative treatments. In Case 1 of our present report, KRAS and TP53 gene mutations were detected for this patient. As we have known, the Cancer Genome Atlas database (2017, cBioPortal) has shown that KRAS and TP53 mutations in pancreatic cancer are 86% to 95% and 13% to 69% [14] respectively, which might give us valuable information for the

patient's next treatments [14]. However, currently there are no KRAS or TP53 gene targeted bio-markers or drugs and targeted drugs that have been approved by Food and Drug Administration.

Conclusion

Altogether, remnant pancreatectomy should be considered as an effective treatment for recurrent or metachronous PDAC in selected patients, which could result in prolonged disease-free survival after the second operation. CA19-9 is a sensitive indicator to suspect or diagnose remnant PDAC in patients who underwent initial pancreatic resection because of PDAC. Gene detection can search the mutation gene for recurrent or metachronous PDAC, which is certainly promising to the postoperative treatments of selected patients with recurrent or metachronous PDAC.

Disclosure of conflict of interest

None.

Abbreviations

PDAC, pancreatic ductal adenocarcinoma; CT, computed tomography; CA19-9, cancer antigen 19-9; MRI, magnetic resonance imaging; DP, distal pancreatectomy; PPPD, pylorus preserving pancreaticoduodenectomy; PD, pancreaticoduodenectomy; NM, not mention.

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Remnant pancreatectomy for recurrent pancreatic carcinoma

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