Limited pancreatectomy for metastatic pancreatic tumors from renal cell carcinoma

Running title: Limited pancreatectomy for metastasis from RCC

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Case Report

Key words: Multifocal pancreatic metastasis, Renal cell carcinoma, Limited pancreatectomy

Abbreviations:

RCC: renal cell carcinoma, QOL: quality of life, CT: computed tomography, US: ultrasonography, TAE/TAI: transcatheter arterial embolization/transcatheter arterial infusion chemotherapy, ENPD: endoscopic naso-pancreatic drainage, MPD: main pancreatic duct, SMV: superior mesenteric vein, SMA: superior mesenteric artery, OGTT: oral glucose tolerance test, PFD test: pancreatic functional diagnostant test

ABSTRACT

BACKGROUND/AIMS: Metastasis of renal cell carcinoma (RCC) to distant organs occurs commonly, even after radical nephrectomy, but metastatic lesions are rarely detected in the pancreas. Our objective was to improve the postoperative quality of life of a patient with pancreatic metastasis of RCC through limited resection of the pancreas. *METHODOLOGY*: Since therapeutic modalities including chemotherapy or radiation are ineffective for metastatic tumors, surgical intervention is a treatment of choice in selected patients. In patients with multiple pancreatic metastases, however, near-total or total pancreatectomy may result in a lower quality of life postoperatively due to endocrine and exocrine pancreatic insufficiency. *RESULTS*: We used limited resection of the pancreas combined with removal of the uncinate process and distal pancreatectomy for a 65-year-old woman with multifocal pancreatic metastases located in the uncinate process, body, and tail of the pancreas, which were detected 6 years after radical nephrectomy for RCC. This surgical procedure allowed preservation of about 40% of the pancreatic parenchyma, with complete excision of metastatic tumors in the pancreas. *CONCLUSIONS*: The patient has had an excellent quality of life with well-preserved pancreatic function and no evidence of tumor recurrence for 31 months after pancreatic surgery.

INTRODUCTION

A metastatic pancreatic tumor is uncommon, accounting for only 2% of resected pancreatic tumors in a recent large series[1]. The primary sites of pancreatic metastasis are predominantly colorectal, lung, breast, and kidney[1-4]. Metastasis to the pancreas from renal cell carcinoma (RCC) sometimes appears many years after radical nephrectomy and is often detected as multiple lesions of the pancreas[5-11]. Although surgical treatment often provides a good outcome in patients with metastatic tumor of the pancreas from RCC[3-11], a lower postoperative quality of life (QOL) with endocrine and exocrine pancreatic insufficiency may become a serious problem after near-total or total pancreatectomy for multiple pancreatic metastases. With the aim of preserving pancreatic function, we performed removal of the uncinate process of the pancreas combined with distal pancreatectomy for a 65-year-old woman with multifocal pancreatic metastases that appeared 6 years after radical nephrectomy for RCC.

CASE REPORT

A 65-year-old woman underwent right radical nephrectomy for RCC in September 1998. Pathological findings revealed renal cell carcinoma of the clear cell type: G2, T1b, n0, M0, stage I. The patient was followed by a urologist and did not receive cancer chemotherapy. Six years after RCC resection, multiple well-enhanced masses in the pancreas were detected in follow-up enhanced computed tomography (CT). Metastatic pancreatic tumors from RCC were suspected and the patient was referred to our hospital in July 2004. Laboratory findings on admission were within normal limits. Tumor markers, including carcinoembryonic antigen, carbohydrate antigen 19-9, SPan-1 and DUPAN-2, were normal. Abdominal ultrasonography (US) and an enhanced CT scan

showed four masses in the pancreas: one in the uncinate process and the others in the body and tail of the pancreas (Fig. 1). Angiography demonstrated hypervascular masses in the pancreas, corresponding to the CT findings, and small tumor stains in segments 4, 6 and 8 of the liver (Fig. 2). Chest CT and bone scintigraphy indicated no metastatic lesions. Based on these findings and the past history, we diagnosed delayed multiple metastases to the liver and pancreas from RCC.

We considered resection of the pancreatic lesions if the liver metastases were controllable. Therefore, transcatheter arterial embolization/transcatheter arterial infusion chemotherapy (TAE/TAI) was first performed for the multiple liver metastases, and the patient was discharged from the hospital. Two months later, the patient was readmitted for reevaluation. CT examination confirmed no progression of the metastatic lesions in the liver and pancreas, and there was no evidence of metastasis to other organs, such as lung and brain, or to bones; therefore, the patient was considered to be a candidate for surgery. Endoscopic retrograde pancreatography and magnetic resonance cholangiopancreatography demonstrated that the metastatic lesion in the uncinate process of the pancreas did not affect the main pancreatic duct. In consideration of preserving pancreatic endocrine and exocrine functions, we resected the uncinate process of the pancreas in combination with distal pancreatectomy in October 2004.

Under general anesthesia, a 5F-size endoscopic naso-pancreatic drainage (ENPD) tube was inserted deep into the main pancreatic duct (MPD) to identify the MPD intraoperatively and to avoid injury to the duct. After laparotomy, the gastrocolic membrane was incised and the pancreas was exposed widely from head to tail. One tumor in the uncinate process and three tumors in the body and tail of the pancreas were identified. The ENPD tube placed in the MPD was clearly and easily detected by

intraoperative US, and thus the distance between the MPD and the tumor in the uncinate process was confirmed to be 10 mm. The gastric branch of the gastrocolic trunk was ligated and divided. The superior mesenteric vein (SMV) was isolated and taped at the lower border of the pancreas. Then, the anterior inferior pancreaticoduodenal vein draining into the SMV from the uncinate process was ligated and divided. The uncinate process was detached from the third part of the duodenum. During detachment of the uncinate process, the anterior inferior pancreaticoduodenal artery branched from the superior mesenteric artery (SMA) was identified and this artery was ligated and divided. Mobilization of the uncinate process was performed along with preservation of the mesoduodenum situated on the posterior off the pancreas. The posterior inferior pancreaticoduodenal artery identified on the mesoduodenum was preserved.

After mobilization of the uncinate process, we reconfirmed that the excision line of the uncinate process had a safe margin from the tumor and was also distal to the MPD, using intraoperative US. The pancreatic parenchyma was then dissected carefully with forceps and resection of the uncinate process was completed. This procedure was followed by distal pancreatectomy (Fig. 3). After the pancreatic resection, pancreatography through the ENPD tube was performed using a mixture of indigo carmine and contrast material. The leak points at the cut surface of the pancreas were then closed by interrupted sutures. After the procedure, about 40% of the pancreatic parenchyma was preserved without residual tumor in the pancreas.

Macroscopically, the pancreatic tumors were yellowish, well capsulated, and clearly bordered from surrounding normal pancreatic tissue. Histological examination showed that these tumors were composed of clear cells with alveolar proliferation, similar to the pathological features of the RCC removed 6 years earlier (Fig. 4).

Postoperative endocrine and exocrine functions of the pancreas were well preserved. A 75g oral glucose tolerance test (OGTT) showed a normal pattern in both the pre- and postoperative course. The value of hemoglobin A1c (HbA1c) was 5.1% before surgery and 4.9% after multiple pancreatectomies. Pre- and postoperative pancreatic functional diagnostant (PFD) tests gave results of 63.7% and 63.6%, respectively.

Metastatic liver tumors were well controlled with the second and third TAE performed at 17 months and 25 months after the pancreatic resection, respectively. The patient has maintained normal pancreatic function without medication and has an excellent QOL without tumor recurrence in the remnant pancreas at the time of writing.

DISCUSSION

A series of autopsies suggested that metastatic pancreatic tumors account for almost 10% of all pancreatic malignancies[12], and Roland and van Heerden[1] found that 2% of patients who underwent surgical exploration for pancreatic malignancies had a tumor metastasis. However, the pancreas is rare as a site of RCC metastasis; RCC tends to metastasize by venous and lymphatic routes and the most common sites of metastasis are the lung, bone, liver and brain[13]. In addition, latent distant metastasis is a characteristic feature of RCC. McNichols et al.[14] found that 11% of RCC patients developed metastasis more than 10 years after nephrectomy. In the present case, multiple metastases to the pancreas and liver occurred 6 years after radical nephrectomy for RCC.

Surgical intervention for pancreatic metastasis of RCC may improve the prognosis when the pancreas is the only site of metastasis[5-11, 15-17]. In addition, pancreatic resection may offer prognostic benefits to RCC patients with both pancreatic and extra-pancreatic

metastases if the extra-pancreatic metastasis is controlled[16,17]. Although our patient had multiple liver metastases, these tumors were well controlled by TAE/TAI and thus the patient was considered to be eligible for pancreatectomy.

Pancreaticoduodenectomy or distal pancreatectomy has been used for treatment of patients with solitary pancreatic metastasis of RCC. In contrast, total pancreatectomy is usually considered for multifocal metastatic tumors of the pancreas[5-11]. However, a decrease in QOL becomes a serious problem after total pancreatectomy because of the abolition of pancreatic function. The present case showed multifocal pancreatic metastases located in the uncinate process, body and tail of the pancreas, which is usually an indication for total pancreatectomy. Application of limited resection of the pancreas is controversial in the treatment of multifocal pancreatic metastases from RCC[7,11,18], and there are some reports describing the risk of recurrence after atypical resection[18,19,20]. However, we employed removal of the uncinate process of the pancreas combined with distal pancreatectomy for our patient. For safe and certain resection of the uncinate process, we utilized an ENPD tube during surgery, which enabled precise evaluation of the distance between the MPD and tumor in the uncinate process. Subsequently, the tumor was excised with a negative surgical margin without injury to the MPD. Moreover, pancreatography through the ENPD tube with a mixture of indigo carmine and contrast material[21] was also helpful in demonstrating pancreatic leakage as a visible blue point at the cut surface of the pancreas, and thus we were able to manage the leak easily with sutures. Otherwise, the risk of duodenal necrosis also remains on the resection of the uncinate process. For preventing this risk, certain preservation of the posterior inferior pancreaticoduodenal artery, which supplies vital blood to the duodenum, is important. Our surgical procedures allowed preservation of about 40% of

pancreatic volume with complete excision of pancreatic tumors. As a result, pancreatic functions were well maintained postoperatively and the patient has an excellent QOL without tumor recurrence in the remnant pancreas.

In conclusion, a combination of limited resections of the pancreas for multifocal pancreatic metastases from RCC may offer advantages over near-total or total pancreatectomy in preserving pancreatic endocrine and exocrine function and giving an excellent postoperative QOL.

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FIGURE LEGENDS

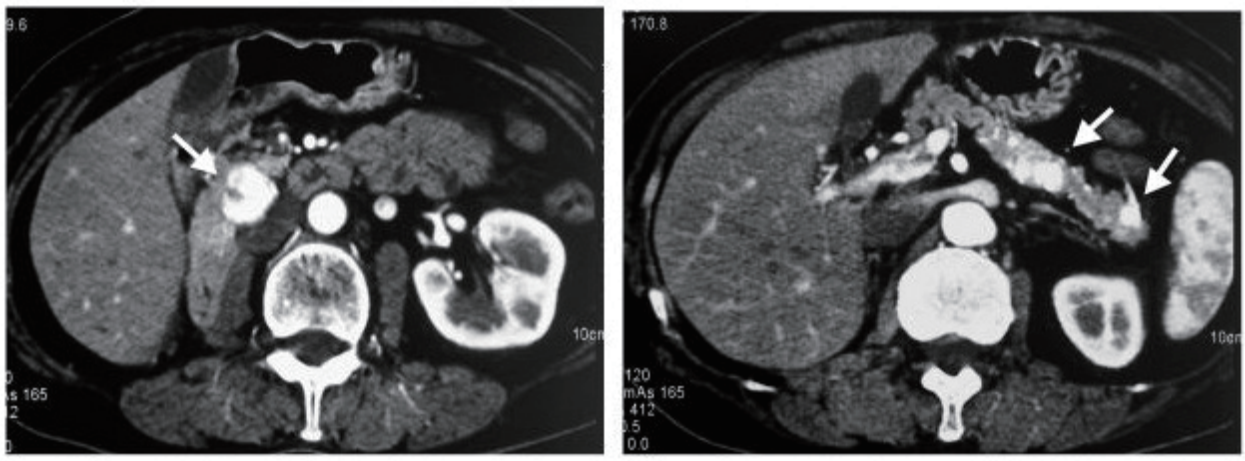

Fig. 1. Abdominal computed tomography showing multiple well-enhanced masses in the uncinate process (**A**), and body and tail (**B**) of the pancreas (arrows).

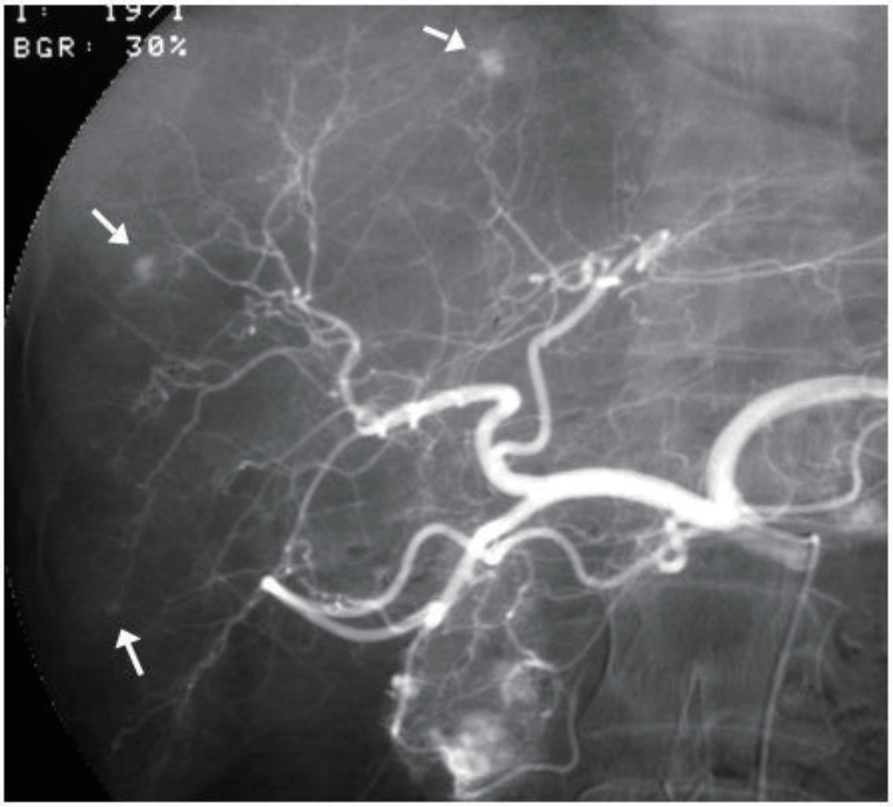

Fig. 2. Selective celiac angiography showing small tumor stains in segments 4, 6 and 8 of the liver (arrows).

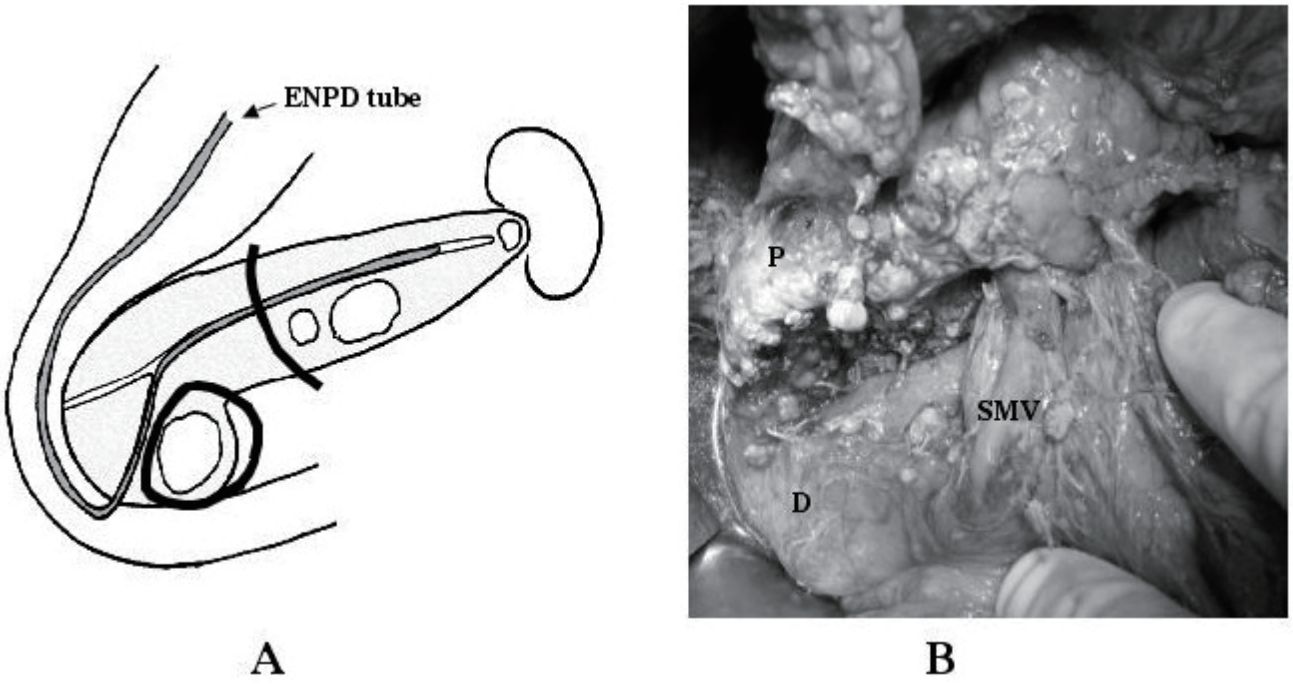

Fig. 3. A. Schematic demonstration of resection of the pancreatic metastatic tumors. **B.** Operative view after resection of the uncinate process of the pancreas. (P: pancreas, D: duodenum, SMV: superior mesenteric vein.)

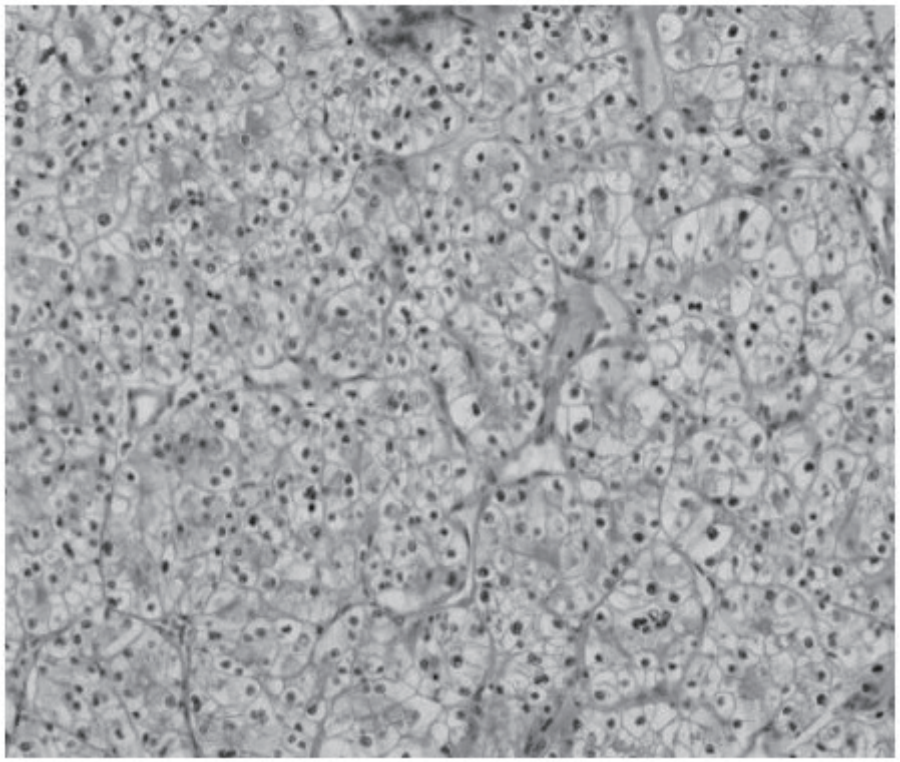

Fig. 4. Histological specimen of resected tumor. The tumors were composed of clear cells with alveolar proliferation, similar to the pathological features of the RCC removed 6 years earlier.