

## Resection of Pancreatic Metastasis from Renal Cell Carcinoma and an Early Gastric Cancer

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### Abstract

An 81-year-old woman, who had undergone left radical nephrectomy for renal cell carcinoma 17 years previously, was found to have a mass approximately 5 cm in diameter in the body of the pancreas and an early gastric cancer. The patient was suspected of having pancreatic metastasis from renal cell carcinoma and an early gastric cancer and underwent distal pancreatectomy, splenectomy, and distal gastrectomy. Histologic examination showed that the pancreatic tumor was a clear cell renal cell carcinoma that had metastasized to the body of the pancreas and that the gastric cancer was a well-differentiated adenocarcinoma that had invaded the mucosa. Twenty months after the operation, the patient was well, without any evidence of recurrence. Renal cell carcinoma metastatic to the pancreas with gastric cancer rarely occurs, and surgical resection might have improved the quality of life in this patient. Careful long-term follow-up is necessary for patients who have undergone surgery for renal cell carcinoma.

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**Key words:** pancreatic metastasis, renal cell carcinoma, gastric cancer

### Introduction

Renal cell carcinoma (RCC) accounts for approximately 3% of the adult malignancies and has a rate of metastasis of more than 25%<sup>1</sup>. The most common sites of metastasis of RCC are the lungs, bone, lymph nodes, adrenal glands, brain, liver, and contralateral kidney<sup>1–3</sup>. The pancreas is not a common site of metastasis of RCC. A solitary pancreatic metastasis is especially rare after surgical

resection of a primary RCC, and such a metastatic tumor is difficult to differentiate from a primary pancreatic tumor. Furthermore, metastasis many years after nephrectomy is common in RCC<sup>4</sup>. However, there have been few reports of cases in which a solitary pancreatic metastasis from RCC with allopatriotic cancer were surgically resected together. We herein report the case of a patient with double cancer: metastatic RCC in the pancreas and early gastric cancer.

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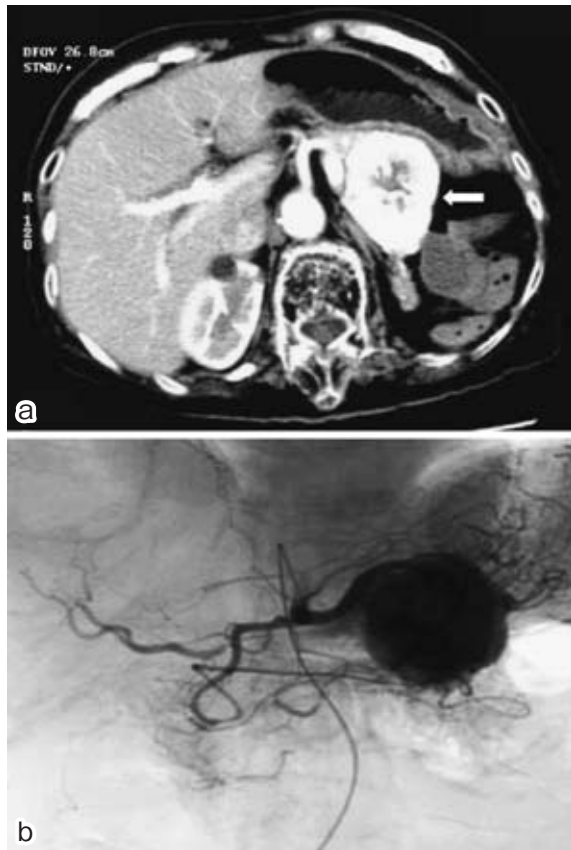


Fig. 1 (a) Abdominal CT scan showing a strongly enhanced mass in the body of the pancreas (**arrow**). (b) Celiac arteriogram showing a hypervascular mass in the body and tail of the pancreas, fed by an enlarged splenic artery in the arterial phase.

### Case Report

An 81-year-old Japanese woman was admitted to our hospital complaining of dull back pain. She had undergone left radical nephrectomy for RCC at another hospital in 1987, 17 years earlier. She was not given adjuvant chemotherapy or immunotherapy at the time and was followed up annually by a urologist. She had no evidence of recurrent disease until 2 years before the present admission. Gastric cancer was diagnosed during a gastroscopy performed to evaluate the patient's chief complaint.

On admission, physical examination and blood tests revealed no abnormal findings, except for an operative scar on the left flank. Levels of carcinoembryonic antigen (CEA), carbohydrate

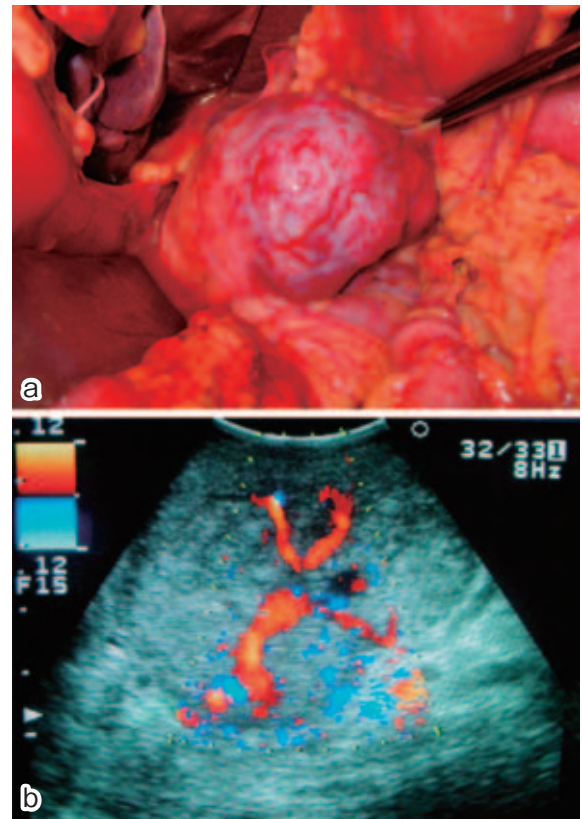


Fig. 2 (a) Intraoperative view showing a hypervascular tumor in the body of the pancreas. (b) Intraoperative Doppler ultrasonogram showing a hypervascular mass in the body and tail of the pancreas.

antigen 19-9 (CA 19-9), DUPAN2, tissue polypeptide antigen (TPA), basic fetoprotein (BFP) and immunosuppressive acidic protein (IAP) were within normal limits. Levels of insulin, glucagon, gastrin, and somatostatin levels were also within their normal ranges. Abdominal computed tomography (CT) revealed a well-enhanced irregularly shaped mass approximately 5 cm in diameter in the body of the pancreas (**Fig. 1a**). No enlarged lymph nodes or liver metastases were detected. Celiac angiography revealed a hypervascular tumor in the body of the pancreas (**Fig. 1b**). Gastroduodenoscopy revealed a IIc early gastric cancer in the lower body of the stomach. Other preoperative examinations, including chest X-ray and abdominal ultrasonography, did not reveal any evidence of extrapancreatic lesions.

The pancreatic tumor was well demarcated from the normal pancreatic tissue. A noninvasive oval mass with dense tumor vessels on its surface was found in the pancreatic body (**Fig. 2a**).

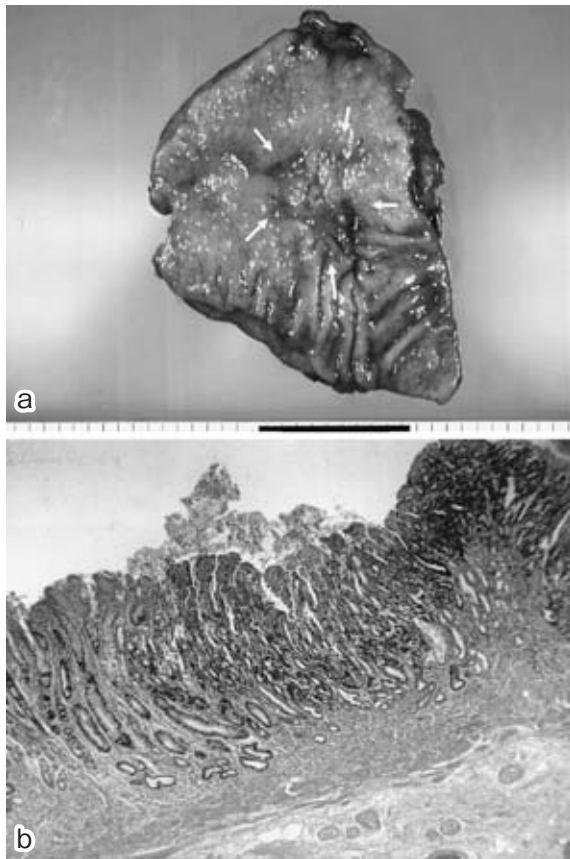


Fig. 3 (a) The gross appearance of the resected specimen with an early gastric cancer (**arrows**). (b) Photomicrograph showing a well-differentiated adenocarcinoma with invasion limited to the mucosa (hematoxylin-eosin stain,  $\times 40$ ).

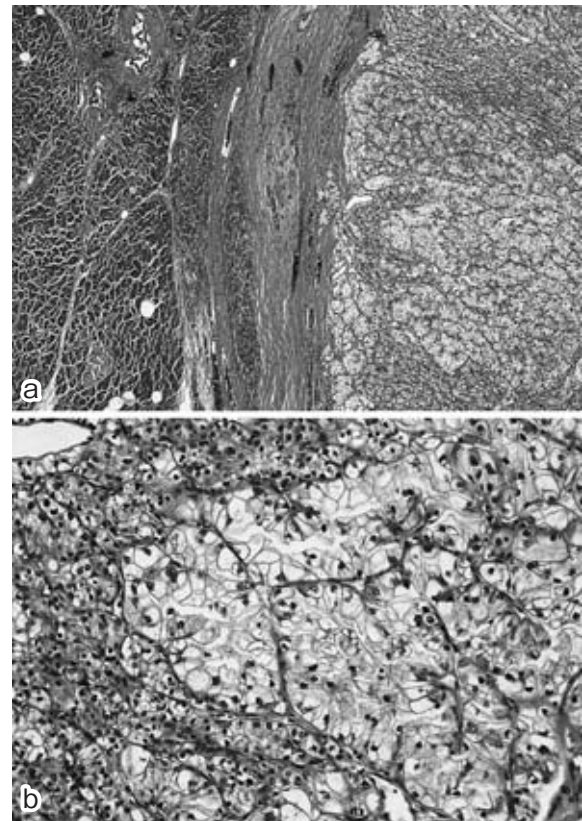


Fig. 4 Histologic specimen of pancreatic metastasis from RCC. (a) Hematoxylin-eosin staining  $\times 100$ . Invasive borders of a metastasis from RCC (right) to the pancreas (left, up). (b) Hematoxylin-eosin staining  $\times 400$ . Microscopic appearance of a RCC with the classic clear-cell pattern.

Intraoperative Doppler ultrasonography revealed an axial and hypervascular tumor that was characteristic of RCC (**Fig. 2b**). No other masses were felt in the remainder of the pancreas, and abdominal exploration revealed no further evidence of metastatic disease. Distal gastrectomy with lymph node dissection and distal pancreatectomy with splenectomy were performed. The left gastric artery, which is a feeding artery to the gastric remnant after distal pancreatectomy with splenectomy, was not ligated because the gastric remnant would have had insufficient blood flow from only the inferior phrenic artery or the proper esophageal artery. A pancreatic tumor,  $5.0 \times 5.2 \times 5.3$  cm in size, was found to occupy the body of the pancreas. The cut surface showed a well-defined, yellowish-white tumor with necrotic foci and central hemorrhage. A slightly ulcerative tumor was found

in the lower body of the stomach (**Fig. 3a**). Final pathological examination of the resected specimens revealed that the pancreatic tumor comprised typical RCC clear cells (**Fig. 4**), and that the gastric tumor was a well-differentiated adenocarcinoma with invasion limited to the mucosa (**Fig. 3b**). We performed immunohistochemical studies to confirm the origin of the pancreatic tumor. Immunohistochemical studies performed with paraffin blocks of the pancreatic tumor demonstrated that none of tumor cells were positive for Wilms' Tumor 1 (DAKO, Glostrup, Denmark), cytokeratin-7 or cytokeratin-20 (DAKO). No metastasis was found in the regional lymph nodes. All surgical margins were free of carcinoma. The tumor was negative for pancreatic endocrine markers, such as glucagon, insulin, gastrin, and somatostatin. On the basis of these results, we

concluded that the pancreatic tumor was not a Wilms tumor, a metastatic tumor from gastric adenocarcinoma, or an endocrine tumor of the pancreas. Therefore, we concluded that the pancreatic tumor was a metastasis from RCC. The gastric cancer was classified as stage IA (T1, N0, M0) according to the TNM classification system. The postoperative course was uneventful, and at the time of writing the patient has survived for 20 months after surgery without further treatment or any evidence of recurrence or metastasis.

### Discussion

RCC is known for the clinical symptoms it produces and its tendency to metastasize via both venous and lymphatic routes. Ritchie and deKernion<sup>5</sup> have reported that patients with RCC present with metastatic disease in 23% of cases and that metastasis occurs within 5 years of nephrectomy in 25% of cases. Metastatic pancreatic tumors are usually found at a preterminal stage when other sites of metastasis are involved and when the prognosis is poor. Ritchie and Chisholm<sup>1</sup> have reported 3- and 5-year survival rates of 4.4% and 2.7%, respectively, in 443 patients with untreated metastatic RCC. The most common primary origins of pancreatic metastases are carcinomas of the colon, lung, breast, and kidney and melanoma of the skin<sup>4</sup>. Metastatic tumors account for less than 5% of all pancreatic malignancies<sup>6</sup>. It has been reported that pancreatic metastasis from RCC is present at autopsy in 1.3% to 1.9% of patients with RCC<sup>7,8</sup>. Solitary metastasis occurs in only 1% to 2% of patients with RCC<sup>8,9</sup>.

Pancreatic metastasis from RCC is asymptomatic in approximately 50% of cases, and is difficult to diagnose<sup>10</sup>. In their study of 109 patients with pancreatic metastases of RCC, Thompson and Heffess have found that 24% of cases were discovered incidentally during routine follow-up and that the interval between initial nephrectomy and presentation of the metastasis was 14.6 years on average (range, 1 month to 32.7 years)<sup>10</sup>. Late recurrence of RCC metastases after surgery is relatively common, especially when the primary

tumor is well-differentiated<sup>11</sup>. McNichols et al.<sup>4</sup> have found that 11% of patients with RCC had pancreatic metastasis more than 10 years after radical nephrectomy and that late metastasis can occur even after complete resection of the primary cancer at an early stage. Furthermore, the chance of discovering asynchronous cancer might increase due to a late recurrence of RCC after nephrectomy. There have only been 2 reported cases of pancreatic metastasis from RCC accompanied by both gastric cancer and gallbladder carcinoma, which occurred 17 years and 20 years after nephrectomy<sup>2,13</sup>. Therefore, this is a very rare case of double cancer: metastatic RCC in the pancreas and early gastric cancer.

Pancreatic metastasis of RCC in our patient was identified with contrast-enhanced CT and angiography as a hypervascular tumor. It is difficult to differentiate a primary islet cell tumor of the pancreas from metastatic tumors. Therefore, it is very important that special attention is paid to the patient's medical history. The patient's medical history in the present case increased the likelihood of a pancreatic metastasis from RCC. Imaging techniques, such as ultrasonography, CT, and magnetic resonance imaging are useful noninvasive modalities for follow-up.

According to recent studies, metastatic pancreatic tumors from RCC can be resected successfully. Hirota et al.<sup>14</sup> have reported that pancreatic metastasis of RCC was successfully surgically resected in 49 (74%) of 66 patients. Tuech et al.<sup>15</sup> have reported a 5-year survival rate of 68% after surgical resection of pancreatic metastasis from RCC. Patients with solitary pancreatic metastasis of RCC have a better prognosis, with a mean survival of 6.2 years<sup>10</sup>. Several factors may be associated with this good prognosis after resection of such metastasis, including: 1) a long interval between primary tumor resection and metastasis, 2) evidence of a solitary or isolated lesion in the pancreas, and 3) slow evolution or growth of the tumor and a lack of clinical symptoms. Many reports suggest that surgical resection is the treatment of choice for pancreatic metastasis, because it is more effective than other treatments, including radiation therapy,

chemotherapy, immunotherapy, and hormonal therapy<sup>9,10,15,16</sup>. Interferon therapy has produced promising results for the treatment of pancreatic metastasis in some studies, but its efficacy remains controversial<sup>16,17</sup>. Furthermore, the role of adjuvant therapy after pancreatic resection is still unclear.

In conclusion, long-term follow-up with appropriate imaging techniques is necessary to find pancreatic metastases of RCC. Curative resection of a solitary pancreatic metastasis of RCC achieved good results in the present case.

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