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# Isolated Pancreatic Metastasis From Renal Cell Carcinoma 11 Years After Nephrectomy: A Case Report

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## Abstract

We report a case of isolated pancreatic metastasis from clear cell renal cell carcinoma (RCC) detected 11 years after nephrectomy in a 69-year-old man. A patient with a history of bilateral RCC was incidentally found to have a hypervascular mass in the pancreatic head during hospitalization for pneumonia. Contrast-enhanced CT and endoscopic ultrasonography demonstrated a well-defined hypervascular pancreatic lesion, while PET showed mild uptake without evidence of extra-pancreatic disease. Based on the patient's history and imaging findings, pancreatic metastasis from RCC or a pancreatic neuroendocrine tumor was suspected, with metastatic RCC considered more likely. Pylorus-preserving pancreaticoduodenectomy was performed with curative intent. Histopathological examination confirmed pancreatic metastasis of clear cell RCC, and R0 resection was achieved. The postoperative course was uneventful, and the patient was discharged on postoperative day 17. No adjuvant therapy was administered, and the patient remained recurrence-free at one year after surgery. This case highlights the potential for late pancreatic recurrence of RCC and the importance of considering metastatic RCC in the differential diagnosis of a hypervascular pancreatic lesion in patients with a history of RCC. Surgical resection may be a reasonable treatment option in carefully selected patients with isolated and resectable pancreatic metastasis.

**Categories:** General Surgery, Oncology
**Keywords:** late recurrence, metastasectomy, pancreatic metastasis, pancreaticoduodenectomy, renal cell carcinoma

## Introduction

Renal cell carcinoma (RCC) is the most common primary malignancy of the kidney in adults and is characterized by a heterogeneous clinical course. Although localized disease is usually treated with curative-intent surgery, some patients present with metastatic disease at diagnosis, whereas others develop metastatic recurrence after initial treatment for localized disease. Despite substantial advances in systemic therapies, including immune checkpoint inhibitors and tyrosine kinase inhibitors, metastatic RCC remains a major clinical challenge [1]. The lungs are the most common site of metastasis, followed by lymph nodes, bone, and liver [2]. In contrast, pancreatic metastases represent an uncommon manifestation of RCC [3]. Nevertheless, RCC is a recognized primary source of secondary pancreatic malignancies [4]. Pancreatic metastases from RCC exhibit distinctive clinical behavior, including prolonged disease-free intervals, a relatively indolent clinical course, and a tendency to remain confined to the pancreas in selected patients [3,4].

Several clinical features of pancreatic metastases from RCC are noteworthy. These lesions typically demonstrate marked hypervascularity and may closely resemble pancreatic neuroendocrine tumors (PNETs) on imaging, making preoperative differentiation challenging [4]. Distinguishing metastatic RCC from PNETs is clinically important because the underlying diagnosis may influence treatment selection, the extent of surgical resection, and consideration of alternative therapeutic approaches. Furthermore, RCC is characterized by the potential for late recurrence, with pancreatic metastases occasionally developing many years after nephrectomy. Pancreatic recurrence more than a decade after treatment of the primary tumor has been repeatedly reported, with occasional cases occurring several decades later [3,5-7].

Pancreatic resection is an important treatment option for carefully selected patients with resectable pancreatic metastases from RCC, particularly when disease is confined to the pancreas, and complete resection is feasible. Recent pooled analyses and meta-analyses have reported favorable long-term survival outcomes after pancreatic resection, with five-year overall survival rates of approximately 60-77% [8,9]. However, these findings are derived predominantly from retrospective observational studies and may reflect the indolent biology of pancreatic metastatic RCC and the selection of patients with favorable disease characteristics. Therefore, the optimal role of surgery relative to other treatment modalities remains uncertain. Herein, we report a case of isolated pancreatic metastasis from clear cell RCC detected incidentally 11 years after nephrectomy and treated with pylorus-preserving pancreaticoduodenectomy (PPPD). Although late pancreatic recurrence of RCC has been previously documented, this case highlights

the diagnostic challenge of distinguishing metastatic RCC from other hypervascular pancreatic neoplasms and the complexities of therapeutic decision-making in the absence of preoperative histological confirmation.

## Case Presentation

A 69-year-old man had a history of bilateral RCC, for which he had undergone left partial nephrectomy followed by right radical nephrectomy at another institution 11 years before the current presentation. However, the original pathological reports were unavailable, and detailed histopathological information regarding the primary renal tumors, including histological subtype, pathological stage, tumor grade, and surgical margin status, could not be confirmed.

He was subsequently admitted to another hospital for treatment of pneumonia. After improvement of the pneumonia, he was transferred to the Department of Diabetology for glycemic control. During this admission, contrast-enhanced CT incidentally revealed a 20-mm hypervascular mass in the pancreatic head (Figure *1A*).

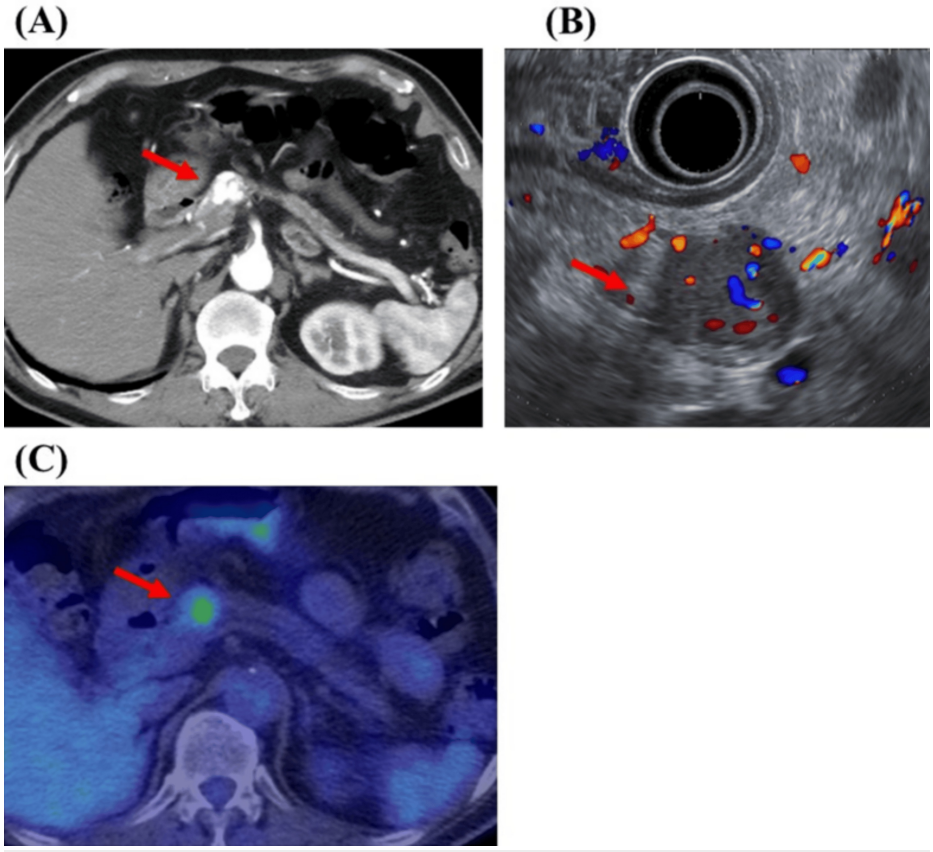



**FIGURE 1: Preoperative imaging findings.**

(A) Contrast-enhanced CT in the arterial phase showing a 20-mm hypervascular mass in the pancreatic head (arrow). (B) EUS with color Doppler imaging demonstrating a well-defined, hypervascular lesion measuring approximately 17 mm at the junction of the pancreatic head and body (arrow). (C) 18F-fluorodeoxyglucose PET/CT showing mild uptake in the pancreatic lesion (arrow; maximum standardized uptake value, 4.3), with no evidence of abnormal uptake in other organs.

EUS, endoscopic ultrasonography

The patient was referred to our hospital for further evaluation and treatment. At the time of surgical evaluation, his Eastern Cooperative Oncology Group performance status was 1. His medical history included diabetes mellitus treated with oral antidiabetic medications. Preoperative laboratory testing revealed a serum creatinine level of 1.58 mg/dL, and the patient was not receiving dialysis. Endoscopic ultrasonography (EUS) with color Doppler imaging demonstrated a well-defined mass measuring approximately 17 mm at the pancreatic head, with abundant intratumoral blood flow (Figure *1B*). EUS-guided tissue acquisition was not performed because of concerns regarding potential bleeding complications associated with the marked hypervascularity of the lesion. 18F-fluorodeoxyglucose (FDG) PET/CT demonstrated mild FDG uptake in the pancreatic lesion, with a maximum standardized uptake value of 4.3, and no abnormal uptake suggestive of

metastatic disease in other organs (Figure 1C).

Based on the patient's history of RCC and the hypervascular characteristics of the pancreatic lesion, pancreatic metastasis from RCC was considered the most likely diagnosis, although a PNET remained an important differential diagnosis. Although the lesion was relatively small, it was located in close proximity to the main pancreatic duct. Tumor enucleation was therefore considered to carry a high risk of postoperative pancreatic fistula due to potential injury to the main pancreatic duct. Given these anatomical considerations and the need to achieve complete resection, PPPD was selected despite the absence of a preoperative histological diagnosis. Macroscopic examination of the resected specimen demonstrated a well-circumscribed tumor in the pancreatic head (Figure 2).

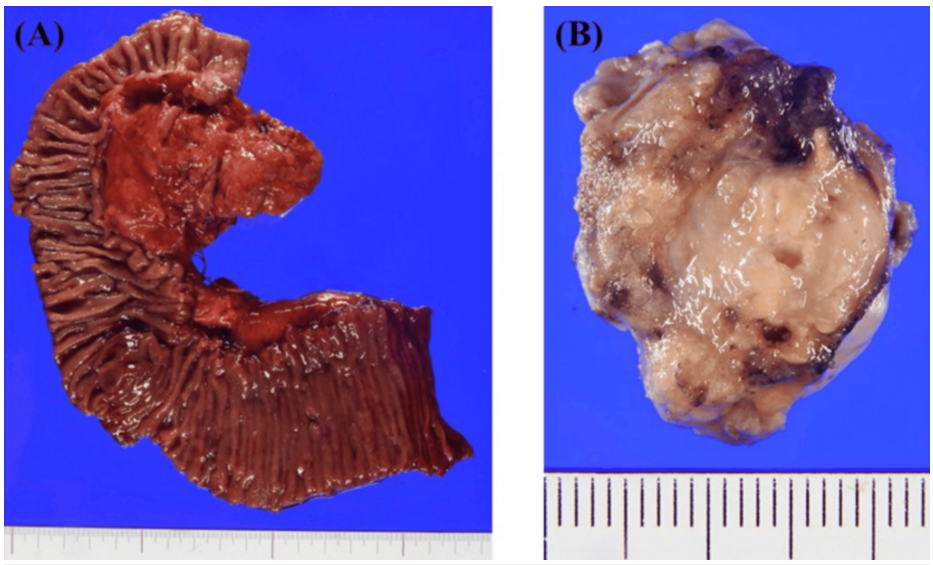



**FIGURE 2: Macroscopic findings of the resected specimen.**

(A) Gross appearance of the specimen obtained by PPPD. (B) Cut surface of the resected specimen showing a well-circumscribed tumor in the pancreatic head.

PPPD, pylorus-preserving pancreaticoduodenectomy

Histopathological examination revealed tumor cells with clear cytoplasm. Immunohistochemically, the tumor cells were positive for cytokeratin AE1/AE3, carbonic anhydrase IX, and CD10, supporting the diagnosis of pancreatic metastasis from clear cell RCC (Figure 3). R0 resection was achieved.

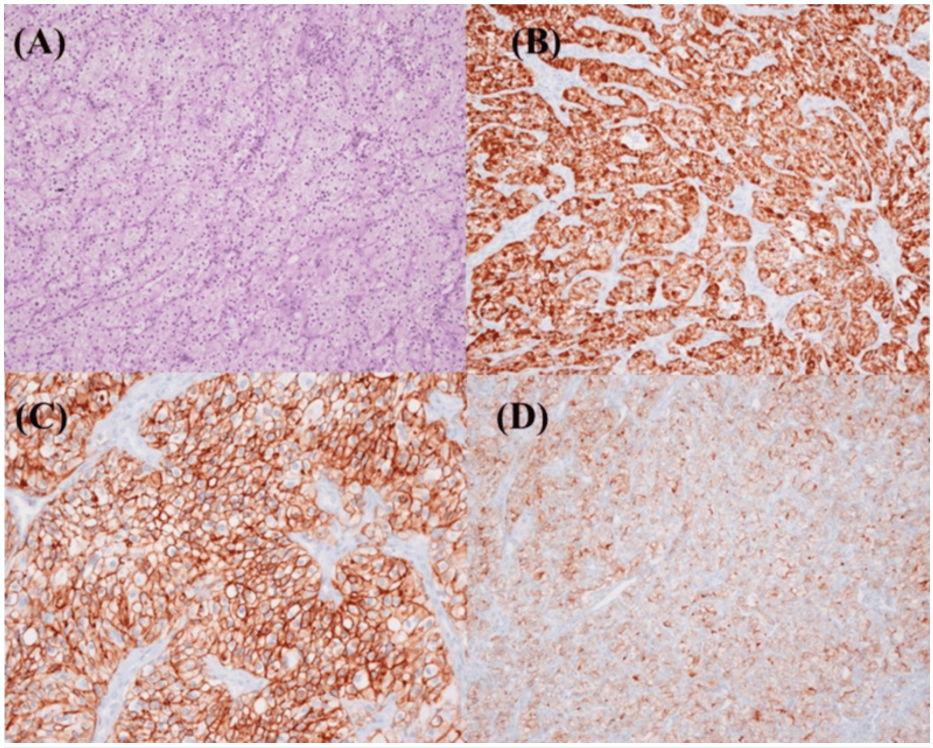



**FIGURE 3: Histopathological findings of the pancreatic tumor.**

(A) Hematoxylin and eosin staining showing tumor cells with clear cytoplasm arranged in an alveolar and nested growth pattern (original magnification, ×200). (B) Immunohistochemical staining showing positivity for cytokeratin AE1/AE3 (original magnification, ×200). (C) Tumor cells showing strong membranous positivity for carbonic anhydrase IX (original magnification, ×400). (D) Tumor cells showing membranous positivity for CD10 (original magnification, ×200). These histopathological and immunohistochemical findings were consistent with pancreatic metastasis of clear cell RCC.

RCC, renal cell carcinoma

The postoperative course was uneventful, with no postoperative pancreatic fistula, delayed gastric emptying, post-pancreatectomy hemorrhage, or other postoperative complications. The patient was discharged on postoperative day 17. No adjuvant therapy was administered. Follow-up CT examinations performed at six months and one year after surgery demonstrated no evidence of recurrence.

## Discussion

Pancreatic metastases from RCC are rare and exhibit distinctive clinical and pathological characteristics, including prolonged disease-free intervals, relatively indolent tumor behavior, and a tendency to remain confined to the pancreas in selected patients [3,4]. These features are clinically important when considering local treatment strategies for isolated pancreatic metastases.

Late recurrence is a well-recognized characteristic of RCC. Among patients who remained disease-free for five years after nephrectomy for localized RCC, Kim et al. reported subsequent renal recurrence and distant metastasis in 4.3% and 11.8%, respectively [10]. In a study of 1,398 patients, Noguchi et al. reported that clear cell RCC could recur more than 10 years after surgery. They also observed that the proportion of recurrences involving typical metastatic sites, including the lung, bone, liver, and lymph nodes, decreased from 83.9% within five years to 40.0% beyond 10 years, whereas recurrence in retroperitoneal organs, including the pancreas, became proportionally more frequent over time [11]. Pancreatic metastases occurring more than a decade after nephrectomy have been repeatedly documented, including cases presenting several decades later [3,5-7]. The 11-year interval in the present case is consistent with this pattern and underscores the importance of considering late metastatic recurrence in patients with a history of RCC.

Pancreatic metastases from RCC typically demonstrate marked hypervascularity on contrast-enhanced imaging. On contrast-enhanced CT, these lesions typically demonstrate avid enhancement during the early contrast-enhanced phases, with attenuation differences of approximately 50-100 Hounsfield units relative to the surrounding pancreatic parenchyma, followed by reduced conspicuity during the delayed phase [12,13]. Smaller lesions generally exhibit homogeneous enhancement, whereas larger lesions may

demonstrate heterogeneous or peripheral enhancement with central necrosis [4]. On MRI, these metastases are typically hypointense on T1-weighted images and hyperintense on T2-weighted images, with prominent enhancement after contrast administration [14,15]. Their hypervascular appearance may closely resemble that of PNETs. Although differences in multiplicity, tumor size, location, and enhancement patterns may assist in differentiation, substantial imaging overlap remains [16]. In contrast, pancreatic ductal adenocarcinoma is typically hypovascular [4,12,17]. Therefore, a hypervascular pancreatic lesion in a patient with a remote history of RCC should raise suspicion for metastatic disease, although imaging findings alone may not establish a definitive diagnosis.

Surgical resection is an important treatment option for carefully selected patients with isolated pancreatic metastases from RCC. In a pooled analysis of 436 patients, the median overall survival after pancreatic resection was 116 months, with five- and 10-year overall survival rates of 76.6% and 46.5%, respectively. Postoperative morbidity and 90-day mortality rates were 38.1% and 3.4%, respectively [8]. A separate meta-analysis of 553 patients reported a pooled five-year overall survival rate of 60.7% [9], while an institutional series reported a five-year overall survival rate of 92.8% following R0 resection [18]. Nevertheless, these favorable outcomes should be interpreted cautiously because the available evidence is predominantly retrospective and subject to selection bias. Furthermore, recurrence remains common after metastasectomy, with a reported 10-year cumulative incidence of recurrence of 62.7% [19]. In a multicenter retrospective study, Santoni et al. found no statistically significant difference in median overall survival between patients undergoing pancreatic resection and those receiving tyrosine kinase inhibitors (103 vs. 86 months; $p = 0.201$) [20]. However, differences in patient characteristics, disease burden, and treatment selection may have confounded this comparison, and the absence of statistical significance does not establish therapeutic equivalence. Thus, although pancreatic resection remains a reasonable option for selected patients with resectable disease, its survival benefit relative to other treatment strategies has not been definitively established.

Stereotactic body radiotherapy (SBRT), also referred to as stereotactic ablative radiotherapy, has emerged as a potential alternative local treatment for pancreatic metastases from RCC. van Vulpen et al. reported a two-year freedom from local progression rate of 95% following magnetic resonance-guided SBRT in 11 patients with 31 pancreatic metastases [21]. Similarly, Teriaca et al. reported a two-year local control rate of 89% in a multicenter retrospective study involving 33 patients with 46 pancreatic metastases [22]. Although these findings are encouraging, the available evidence remains limited by small sample sizes and nonrandomized study designs. The comparative efficacy and long-term safety of SBRT versus surgical resection remain uncertain, emphasizing the importance of individualized treatment selection.

The present case highlights the diagnostic and therapeutic challenges of isolated pancreatic metastasis from RCC. Although the original renal tumor pathology was unavailable and preoperative tissue acquisition was avoided because of bleeding concerns, postoperative histopathological and immunohistochemical findings supported the diagnosis of metastatic clear cell RCC. Despite the small tumor size, PPPD was selected because the lesion was located in close proximity to the main pancreatic duct, and tumor enucleation was considered to carry a high risk of postoperative pancreatic fistula due to potential main pancreatic duct injury. R0 resection was achieved without complications, and no recurrence was observed during one year of follow-up. Nevertheless, prolonged surveillance remains essential. This case emphasizes the importance of individualized surgical decision-making based on anatomical considerations and diagnostic uncertainty.

## Conclusions

Pancreatic metastasis from RCC is uncommon and may occur many years after nephrectomy. In patients with a history of RCC, even remote, metastatic RCC should be considered in the differential diagnosis of a hypervascular pancreatic lesion. Surgical resection may represent a reasonable treatment option for carefully selected patients with isolated and resectable pancreatic metastases. However, treatment decisions should be individualized through multidisciplinary evaluation. Although R0 resection was achieved in the present case, the absence of recurrence at one year does not establish long-term oncological benefit. Prolonged postoperative surveillance and further studies with long-term follow-up are therefore warranted.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Ryosuke Nakano, Shihoko Katayama, Yasuhiro Matsugu, Hideki Nakahara

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**Critical review of the manuscript for important intellectual content:** Ryosuke Nakano, Masakazu Hashimoto, Masashi Miguchi, Nobuaki Fujikuni, Satoshi Ikeda, Yasuhiro Matsugu, Hideki Nakahara

## Disclosures

**Human subjects:** Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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