

## A Case Report of Pancreatic Metastasis from Clear Cell Renal Carcinoma with Polycystic Liver and Kidney

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### Abstract

The treatment strategy for pancreatic metastasis from renal cell carcinoma (PM-ccRCC) is unclear due to its rarity. Pancreatic Metastasis from clear cell renal carcinoma are very rare, yet with a favorable prognosis compared to other pancreatic malignancies. We herein present a case of a women with metastatic disease in the pancreas following complete resection of RCC ten years ago. This case underlines the necessity of long-term follow-up of patients treated for kidney cancer.

### Keywords

Renal Cell Carcinoma; Pancreatic Metastasis; Polycystic Liver; Polycystic Kidney.

### 1. Introduction

Renal cell carcinoma (RCC) is a common cancer, but pancreatic metastasis of RCC is unusual, accounting for only 2% to 5% of all tumours affecting the pancreas [1]. The common metastases affecting the pancreas include renal cell carcinomas, lung cancer, mammary cancer, carcinoma of the large intestine, etc. In the present case, we report the case of a patient for metachronous pancreatic metastasis, ten years after nephrectomy.

### 2. Case Report

The patient, female, 58 years old, was admitted to the hospital on 26<sup>th</sup> June, 2021, due to “fatigue, poor absorbing for 1 month, and pancreatic lesion found for 1 day”. The patient was admitted to a local hospital a week ago for “weakness, poor appetite for 1 month with nausea and vomiting for 1 week”, and the symptomatic treatment such as acid suppression and gastric protection did not relieve the symptoms significantly. On 25<sup>th</sup> June, 2021, a CT scan of the upper abdomen was performed in this hospital, suggesting a pancreatic lesion, and now the patient has been transferred to our hospital for further treatment. Past medical history: the patient had undergone radical nephrectomy 10 years ago for right kidney tumour and clear cell renal carcinoma (ccRCC) was diagnosed by histologic examination. The patient was followed up regularly after the operation.

Hospitalization Examination: no obvious jaundice on the skin or sclera, belly flat and soft, no tenderness or rebound tenderness, the liver enlarged below the costal margin, negative for Murphy's sign, bowel sounds normal, old surgical incision scar seen on the right lumbar region with good healing. Laboratory examination did not show any significant abnormalities.

Imaging Examination: the liver lost its normal shape, multiple scattered cystic hypo-density shadows of varying size with clear borders were seen, with a maximum of about 8.0 X 6.5 cm and a CT value of about 6 HU, and enhancement CT showed no apparent enhanced lesions. The right kidney was absent after surgery and the left kidney was enlarged, with speckled hyper-

density and scattered capsular hypo-density shadows of varying size, some of high intensity. The cyst wall was calcified and its intracapsular density is homogeneous, with a maximum of approximately 6.6 X 6.1 X 6.2 cm, and no significant enhancement was found. The pancreas was significantly enlarged, several large round-like masses with internal separation can be seen in the head, body, and tail of the pancreas, the largest being approximately 9.8 X 7.5 cm. The enhancement scanning showed that the solid portion on the focus marginal is significantly intensified, with reduced intensification in the portal-venous-period and lag-period. In the low-density area of the focus, no intensification was showed, but the peripheral mesenteric-gastric compression has narrowed the gap. No significant dilatation of the pancreatic duct can be seen. Biopsy Results of Pancreatic Puncture: (Pancreatic lesion) Microscopically, the tumour cells were round and transparent, large in size, with a clear envelope and abundant cytoplasm. The nucleus was centrally located, round-like, and relatively uniform in size, the chromatin was fine, and the nucleolus was not prominent. The tumour cells were divided by abundant thin-wall sinusoidal vessels. Immunohistochemistry(IHC): PAX-8 (+), CK7 (-), EMA (foci+), TFE3 (-), CD10 (+), Syn (-), CgA (-), S-100 (-), Ki-67 approx. 5% (+). Considered consistent with metastatic clear cell renal carcinoma. This patient, with multiple pancreatic metastasis, requires total pancreatectomy if given surgical treatment. While the patient and her families refuse surgical operation due to poor quality of life after surgery. Based on the patient's condition and the relevant departmental consultation, the patient is given immunotherapy with sintilimab and targeted therapy with anlotinib and is still being followed up.

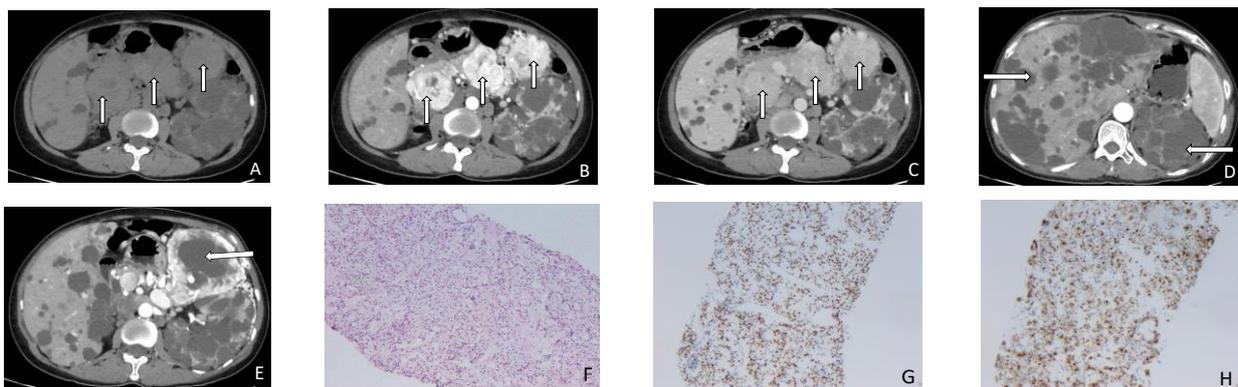


Figure 1. CT scan findings reveals three masses in pancreas(A,B,C);The enhancement scanning of the pancreatic mass, showed marked enhancement in the arterial phase(B), and greatly diminished enhancement in the lag phase(C) (D)Polycystic liver and kidney; Computed tomography images of a tissular corporeal pancreatic mass, enhanced in periphery with a central necrosis (E). On microscopic low power, the tumour cells were round and transparent, large in size, with a clear envelope and abundant cytoplasm. The nucleus was centrally located, round-like, and relatively uniform in size, the chromatin was fine, and the nucleolus was not prominent. The tumour cells were divided by abundant thin-wall sinusoidal vessels(F).IHC stains were positive for PAX-8 (G) and for CD10(H).

### 3. Discussion

Metastatic tumour of the pancreas is rare, accounting for 2-5% of all pancreatic tumours [1]. Pancreatic clear cell carcinoma is usually metastasised from other malignant tumours, commonly from lung cancer, mammary cancer, carcinoma of the large intestine, renal carcinoma, etc., among which only 1-2% of ccRCC metastases to the pancreas [1-4]. Currently, the shortest duration of pancreatic metastasis after nephrectomy was reported in the literature

[5] as 1 month and the longest as 32.7 years. In this case, the pancreatic metastases from clear cell renal carcinoma (PM-ccRCC) is 10 years after the resection of the right kidney. Therefore, long-term follow-up is needed after renal carcinoma (RC) surgery to detect tumour recurrence and distant metastases. Since the PM-ccRCC tend to occur late, and the pancreas is often the only organ affected by metastases of heterochronous ccRCC, relevant literature has proposed the “seed and soil” theory of the pancreatic metastases from clear cell renal carcinoma [6,7]. That is, specific tumour cells (seeds) tend to metastasise to specific organs (soil), and will only grow when the soil is suitable for the seeds and then successful metastasis occurs. How does postoperative pancreatic metastasis of RC happen is still unclear. One theory suggests the lymph gland is the origin, i.e., retroperitoneal lymph node is invaded by the tumour, thereby causing the inverse lymphatic metastasis. The other theory is that the tumour thrombus in the renal vein metastasised to the pancreas through a collateral vein formed by the vascularization of the tumour, or through an existing portal vein [8].

About 55% renal cell carcinoma (RCC) could metastasise to the pancreas without obvious symptoms, usually occur in a long time. Pancreatic tumour is usually detected during follow-up examinations after surgery on the primary lesion [9]. In fact, pancreatic tumour originating from renal carcinoma can be the first clinical manifestation in patients with renal cell carcinoma after surgery. The symptoms are usually non-specific, including abdominal pain, weight loss, vomiting, jaundice, gastrointestinal bleeding, etc. In this case, the patient presented with fatigue, poor absorbing, vomiting, symptoms of mass compression of the gastrointestinal canal, polycystic liver, and polycystic kidney. Yet the MR of the patient’s head did not show significant abnormalities, and there is no specialty in her family history, therefore Lindau’s syndrome can temporarily be excluded.

CT or MRI of pancreatic metastases from ccRCC shows marked enhancement in the arterial phase, diminished enhancement in the venous phase, and greatly diminished one in the lag phase, presenting a fast-in-fast-out pattern. This can be differentiated from the primary pancreatic carcinoma which is lack of blood supply, but has similar imaging features to pancreatic neuroendocrine tumours (PNET), thus the differential diagnosis needs to be made based on the patient’s clinical presentation and past medical history. Ultrasound-guided aspiration biopsy can be used if necessary, and post-operative pathology and immunological findings can clarify the diagnosis.

Compared to metastases from other sites, a large body of literature suggests that pancreatic metastases from ccRCC have a relatively better prognosis, which can be related to the biological inertness, enhanced angiogenesis, and absence of interstitial inflammation of ccRCC [10]. In recent years, the surgical management of metastatic renal cell carcinoma has changed, with the development of targeted therapy and immunotherapy. Resection of heterochronic metastases is more common than concurrent metastases. For heterochronous metastases, surgery is currently considered the most ideal treatment [11]. In the study by Grassi et al., among the 274 patients with PM (both heterochronous and synchronous), the researchers found that patients who received surgery doubled their mOS compared to those who received targeted therapy [12]. In a meta-analysis of 311 patients with PM, the overall survival rate at 5 years after surgery was 72.6% [13], and in the largest series of surgically resected RCC pancreatic metastases, Schwarz et al. [14] reported 3-, 5-, and 10-year overall survival rates of 72%, 63%, and 32%, respectively highlighting the beneficial long-term impact of surgery in these patients and therefore the preference for surgical treatment. Moreover, there is still no effective target identified for targeted therapy and no reliable research data to prove that targeted therapy can be used alone for the treatment of PM.

## 4. Conclusion

Though rare, most PM-ccRCC occur after a long period post-nephrectomy, thus, long-term follow-up examinations should be maintained. Based on the biologically inert nature of ccRCC and its good prognosis, more clinical studies are still needed to demonstrate the benefits of targeted therapy or immunotherapy over surgical treatment. Besides, further exploration of its molecular markers and elucidation of the mechanisms of PM should be done to develop an individualised treatment for patients.

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