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# Metastasectomy of Sequential Asynchronous Metastatic Renal Cell Carcinoma to the Pancreas, Thyroid, Skin, Contralateral Kidney, and Lung with Cumulative Survival Beyond 10 Years: A Case Report and Clinicopathologic Review

## Authors' Contribution:

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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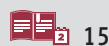
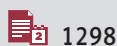
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**Patient:** Female, 46-year-old  
**Final Diagnosis:** Metastasis of renal clear cell carcinoma  
**Symptoms:** Renal carcinoma  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Urology

**Objective:** Unusual setting of medical care**Background:** One-third of renal cell carcinoma cases present with an initial metastasis to various organs, emphasizing the tumor's unpredictable behavior. Prognosis is poor once metastasis is discovered. Multiple-organ involvement with metastatic lesions has a particularly dismal survival rate. Surgical resection alone of metastatic masses can extend patient survival with reasonable quality of life.**Case Report:** Here, we present the case of a healthy 46-year-old woman who initially presented with an incidental localized clear cell renal cell carcinoma. During the follow-up period, she presented with sequential asynchronous metastasis to the pancreas, thyroid, skin, contralateral kidney, and lung. She has no family history of malignancy. Her physical examination and laboratory investigations were normal even upon presentation of most of her metastatic organs. The first metastasis was in her sixth year of follow-up. She underwent consecutive metastasectomy of all the organs described above, excluding the lung. She eventually was started on sunitinib after non-resectable lung nodules were discovered. Her survival is now over 10 years since her first metastasectomy, with good performance status.**Conclusions:** Metastasis to a single organ has a poor prognosis and dramatically affects survival. Nevertheless, our patient had multiple consecutive examples of metachronous metastasis, yet she has survived for over a decade since the occurrence of metastasis. Our case offers more information to fill the gaps in understanding the favorable role of surgical resection in advanced renal cell carcinoma metastasis.**Keywords:** Carcinoma, Renal Cell • Metastasectomy • Neoplasm Metastasis • Renal Cell Carcinoma 1Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/931696>

## Background

Metastatic clear cell renal cell carcinoma (ccRCC) is usually seen after primary tumor management. Nevertheless, one-third of newly diagnosed patients present with metastasis [1]. Dismal prognostic independent factors, including the number of metastatic organs, performance status, male sex, and disease-free interval <1 year, have been proposed. Additionally, tumor size, age, race, and family history are possible prognostic factors [2]. In the debate about metastatic ccRCC management options, surgical resection remains indispensable when metastatic lesions are resectable, with or without systemic therapy [3,4]. Surgical resection of synchronous and asynchronous metastases, including those in multiple unusual organs, are rarely reported in the literature. We present here a case of asynchronous consecutive metastatic ccRCC to different and unusual organs. This patient underwent complete surgical resection of metastases that had been presented 6 years after the primary tumor diagnosis and has survived for more than 10 years after diagnosis of the first metastasis.

## Case Report

A 46-year-old healthy woman with good performance status presented to our institution with an incidentally localized right renal mass, clinical stage 1, discovered during an investigation into gallstone. She had no active concerns upon presentation. A systemic review was unremarkable, with no history of renal masses or malignancies in her family. Results of the physical examination and laboratory investigations were normal. She underwent a right radical nephrectomy, and pathology revealed a ccRCC. Six years later, she presented to our emergency room with vague abdominal pain and vomiting. A pancreatic mass localized to the head was discovered by imaging, but her amylase and lipase levels were normal. She underwent a Whipple procedure and recovered well. The pathology showed metastatic ccRCC.

Two years later, she presented with difficult swallowing with no dyspnea, and a physical examination showed a thyroid mass obvious in both lobes. However, ultrasound confirmed 4 thyroid hypervascular nodules, the largest in the left lobe. Fine-needle aspiration of the thyroid nodules revealed inflammatory changes and was inconclusive. The pathological diagnosis was challenging and showed metastatic ccRCC after total thyroidectomy. One year later, a painless but suspicious well-circumscribed mass of soft tissue in the forearm was seen with a smooth surface and no skin discoloration, scales, or ulcers. Excisional biopsy with negative margins showed metastatic ccRCC. During follow-up, a suspicious incidental mass was detected and removed from the remaining pancreatic tissue almost 5 years after the Whipple procedure. Accordingly, she



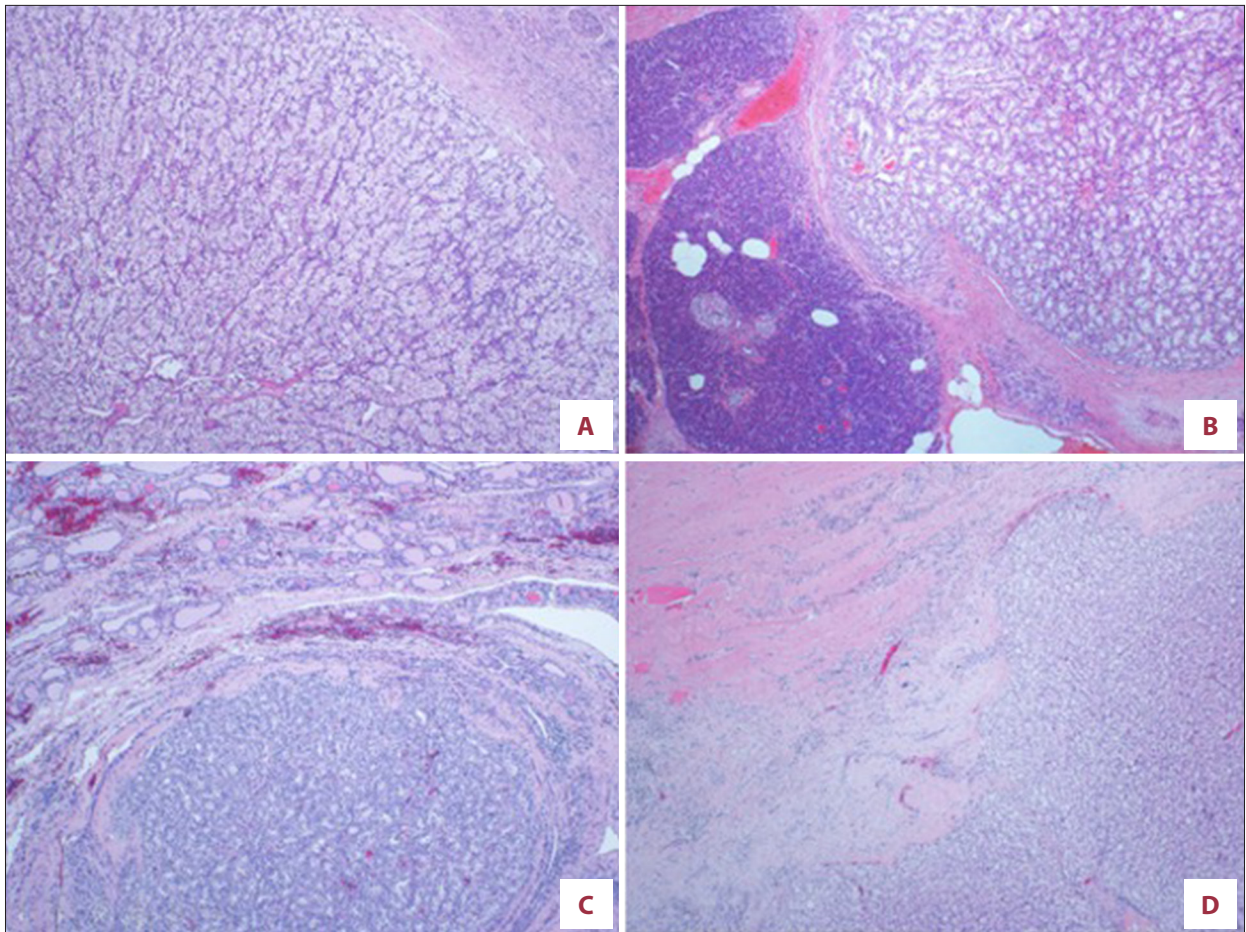
**Figure 1.** The arrow points to a metachronous endophytic renal mass.

had a total pancreatectomy and splenectomy, and the pathologist report classified it as ccRCC metastasis.

Twelve years after her right radical nephrectomy and 6 years since her first metastasis, a left renal mass was seen on follow-up imaging. This mass was a candidate for a partial nephrectomy, which was performed; pathology revealed metastatic ccRCC (Figure 1). Pathology sections of primary kidney cancer, as well as pancreas, thyroid, and soft tissue masses, are illustrated in Figure 2. However, her partial nephrectomy was complicated by perirenal hematoma and hydronephrosis, which were managed conservatively via the insertion of a DJ stent (classified as Clavien IIIb). Her later follow-up showed the resolution of her peri-renal hematoma and improvement of her hydronephrosis. Her renal function was maintained with a stable creatinine level. One year after partial nephrectomy, she developed several stable non-resectable pulmonary nodules. She was started on a tyrosine kinase inhibitor (sunitinib). Follow-up images showed multiple stable pulmonary nodules with no clinical problems. Bone and positron emission/computed tomography (PET/CT) scans revealed no evidence of bone metastasis. Her Eastern Cooperative Oncology Group (ECOG) score was insignificant, and results of laboratory investigations were unremarkable. No genetic testing was done due to limited facilities at our institution. The patient's consent was obtained to report her case while respecting her confidentiality.

## Discussion

Studies addressing metastatic ccRCC consist of retrospective studies and case reports, with no higher levels of evidence. Management options for metastatic ccRCC are a subject of ongoing debate; novel immunotherapies have made the options more diverse. Metastasectomy is preferred, either alone or as part of multimodal therapy, in patients with good performance



**Figure 2.** (A) Histological examination of the kidney tumor shows infiltration by malignant clear epithelial cells arranged in nests typical of clear cell renal cell carcinoma (ccRCC); Hematoxylin and eosin (H&E) 100×, (B-D) Sections of the pancreas, thyroid, and soft tissue masses, respectively, showing metastatic ccRCC with similar primary tumor features (H&E, 40×, 100×, 100×).

status and resectable metastasis, regardless of the organs involved. Still, a positive surgical margin might defer patients from further surgical resection of metachronous metastasis, and immunotherapy alone would be preferred [3,4].

Inconstant sites of metastatic ccRCC have been published in the literature. The lung is a common site of metastases, but the pathophysiology of such involvement is unknown. The literature describes lung involvement as a favorable site. Nevertheless, solitary lesions, small lesion sizes, and absence of lymph node involvement collectively give a favorable survival rate, with 5-year patient survival rate of about 45% [5]. Thomas et al stated that bone metastasis is the second most common metastatic organ for renal cell carcinoma and is seen in about 20% of patients [4,6]. Renal cell carcinoma metastasizes to the pancreas in 1% to 2% of patients. No understanding of metastasis from renal mass to the pancreas exists [3]. However, Nagakawa et al proposed a role for lymphatics as a possible explanation. Saitoh et al explained the role of the pro-venous system in pancreatic metastasis [7,8]. Patient history

and normal pancreatic enzymes along with a hypervascular lesion on imaging increase the suspicion of metastasis to the pancreas. The Whipple procedure or complete pancreatectomy with or without adjunct immunotherapy can increase survival, as proposed in the literature [9]. Thyroid metastases is an uncommon presentation of the thyroid mass, and metastatic renal cell carcinoma to the thyroid is found in about 1% of cases [10]. However, renal cell carcinoma is a culprit when thyroid metastasis is discovered.

Heffess et al studied 36 patients with thyroid metastases secondary to renal mass and found that diagnosis can be challenging, especially if the renal cell metastasis initially presented with a solitary thyroid mass. Thyroid metastases have an average presentation from initial renal cell carcinoma of about 5 to 10 years [4,10]. An abnormal thyroid gland can be a trigger for metastases, as postulated by Behrs et al. On the contrary, many reports in the literature found no differences in the incidence of thyroid metastases among normal and abnormal thyroids [11,12]. Skin metastasis of renal cell carcinoma is rare



and is seen in less than 1% of renal carcinoma patients. The scalp and face are typical areas for metastases. Other areas can also be involved. The mode of skin metastases is poorly understood and hard to differentiate from more common skin lesions like hemangioma, pyogenic granuloma, or even primary skin cancer [13]. Bilateral synchronous and metachronous nonfamilial renal masses are often ccRCC and account for more than 85% of such cases. Metachronous renal cell carcinoma can be detected a decade after primary tumors [14]. Syed et al studied more than 80 000 patients with renal cell carcinoma, about 1% develop metachronous renal mass, and more than 70% of them were diagnosed 10 years from primary renal cell carcinoma [15].

In our case, consecutive surgical resections of metastasis increased our patient's survival by more than 10 years from the first metastasis. The clinical presentation and laboratory investigations of the metastasis mentioned above were nonspecific; proper imaging has an essential role, and careful pathology reporting is critical for not missing such rare metastatic presentations. Flanigan et al described a low median survival rate of 6 months for patients with no metastasis treatment. On the contrary, the beneficial role of surgery in prolonging patient survival is well described in review articles, retrospective cohort studies, and case series [1,3,4].

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## Conclusions

Our patient survived for 10 years in the face of multiple sequential organs metastasis that were surgically resected, apart from lung lesions. Complete surgical resection of metastases has worthwhile benefits for survival in selected patients. Moreover, supporting enrollment of such patients in clinical trials for metastasectomy in advanced renal carcinoma will help demonstrate its clinical utility.

## Institution Where Work Was Done

King Fahad Specialist Hospital in Dammam, Dammam, Saudi Arabia.

## Conflict of Interest

None.