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# Rare renaissance: Quadruple synchronous renal cell tumors in one kidney – A case report

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ABSTRACT

Multifocality in renal tumors is a rare occurrence, but not unheard of. Commonly the different foci correspond to the same histological pathology, however co-existence with other renal lesions, including both malignant and benign tumors, have also been reported. Here we present a 57-year-old male, ex-smoker who exhibited four distinct histological tumors in an ipsilateral kidney; multilocular cystic clear cell renal cell carcinoma (RCC) of low malignant potential, clear cell papillary RCC, renal oncocytoma, and renomedullary interstitial cell tumor. To our knowledge this is the first time these four tumors were found in the same patient, let alone the same kidney.

## 1. Introduction

Renal cell carcinomas (RCCs) represent the prevailing type of solid kidney lesions, comprising around 2–3% of all adult malignancies and accounting for 75–80% of adult kidney cancers. Among these, clear cell renal cell carcinoma stands as the most prevalent subtype, constituting approximately 70% of cases.[1] Other types of RCCs include papillary, chromophobe, collecting duct, and medullary types. Renal tumors encompass a diverse group of neoplasms that can be distinguished histologically and cytogenetically. Although the presence of synchronous multifocal renal malignancies within the same kidney is rare, it is not entirely unheard of.[2] In this context, we present a noteworthy case of RCC in a 57-year-old male exhibiting four distinct histologic subtypes. The patient received successful treatment through laparoscopic radical nephrectomy.

## 2. Case presentation

During a routine checkup, a 57-year-old ex-smoker with a medical history of hypertension, dyslipidemia, and gastroesophageal reflux disease (GERD) was found to have microscopic hematuria and proteinuria on urinalysis. The patient's physical examination was unremarkable and laboratory results were all within normal ranges, including his creatinine level. Further inquiry was undertaken through an ultrasound of the abdomen and pelvis, showing multiple renal cysts in the left kidney. Subsequently, a contrast-enhanced computed tomography (CT) scan was executed, revealing multiple bilateral renal cortical cysts (Fig. 1). The right kidney bore 2 cysts in the upper and lower polar regions, respectively; each categorized as Bosniak Type 1 lesions. On the left side however, multiple cystic masses were identified through all three regions of the kidney. The largest of these was an upper pole cyst, measuring 35 × 34 mm, bearing multiple thick septa (of around 7 mm thickness) and no calcifications (Bosniak type 3). Additionally, a complex contrast-enhancing, cystic mass was in the left mid calyceal region measuring 26 × 28 mm, with tiny calcifications, indicative of a Bosniak type 4 lesion. A third lesion, not originally reported by the radiologist, was identified in the mid-calyceal region, just proximal to this latter. This lesion showed mild enhancement, with a poorly defined interface with the surrounding normal parenchyma.

Upon further interviewing, the patient's family history revealed a positive correlation with both thyroid and breast cancer. An F18-FDG PET/CT scan was conducted, revealing hyper-metabolic suspicious lesions in the left renal upper and lower poles, warranting further histopathological confirmation. High-resolution computed tomography (HRCT) yielded no significant findings.

Following the review of the case by the Urology team, a decision was

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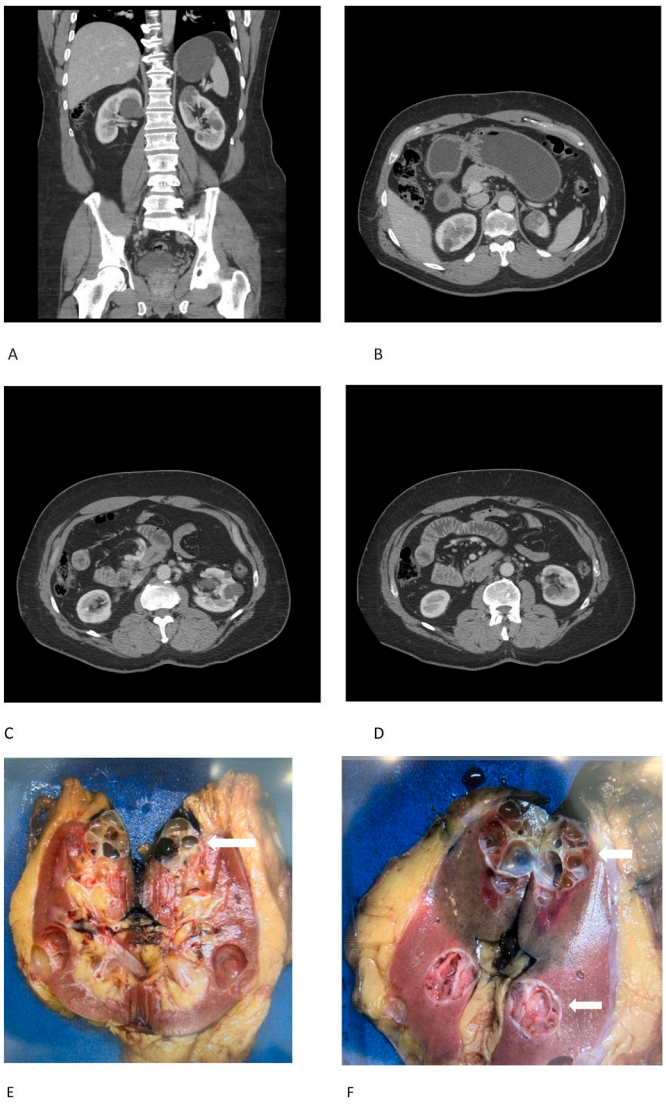


**Fig. 1.** CT scan of the abdomen and pelvis, with contrast and gross pictures of the kidney
(A) Coronal Section, showing both kidneys. Simple cyst in left upper pole. Left kidney showing three suspicious regions, in upper pole and mid calyceal regions.
(B) Axial Section, showing a left upper pole lesion.
(C) Axial Section, showing multiple left middle pole lesions.
(D) Axial Section, showing suspicious region in lower part of mid pole of left kidney.
(E) Cross section of upper pole, highlighting the malignant area (with arrow).
(F) Cross section of middle calyceal area. Suspicious regions marked with arrows.

made to proceed with a laparoscopic left radical nephrectomy. During the procedure, the left kidney was carefully removed while ensuring the three renal cysts enclosed within Gerota's fascia remained intact, avoiding any rupture. The post-operative period was uneventful, except for an elevation in creatinine levels, peaking at 197 μmol/L, and an estimated glomerular filtration rate (eGFR) of 35 ml/m on post-operative day four. Thereafter, the patient was discharged. A week following the surgery, the patient's condition remained satisfactory except for a creatinine level of 210 μmol/L and an eGFR of 29 ml/m potentially indicative of his new baseline.

## 3. Histopathology

During macroscopic examination, the left kidney (Fig. 1e and f ) exhibited four distinct lesions, manifesting different types of RCC. The largest lesion (Fig. 2) , situated in the upper pole and measuring 3.5 × 3.0 × 3.0 cm, displayed a multilocular cystic appearance with thin fibrous septa and contained serous to gelatinous light brown fluid, ultimately diagnosed as **multilocular cystic clear cell RCC of low malignant potential.**

Moving to the junction between the mid and lower zone of the kidney, two well-demarcated cysts came into view. The first cyst (Fig. 3) , measuring 2.5 × 2.2 × 2.0 cm, resided in the renal medulla, presenting a solid, fleshy, and hemorrhagic appearance with cystic characteristics. Considering the morphology, we gave a diagnosis of **clear cell papillary RCC.**

Furthermore, an additional solid and hemorrhagic nodule (Fig. 4) , measuring 1.5 × 1.2 × 1.1 cm, was observed in the renal cortex. Unencapsulated with well-demarcated borders pushing into perirenal fat giving it a solid, brown to tan color was identified as a **renal oncocytoma.**

A **renomedullary interstitial cell tumor** was the fourth pathology identified microscopically; (Fig. 5) shows a well-demarcated, medullary based tumor composed of small stellate cells in a background of loose fibrotic/basophilic stroma with entrapped tubules.

Importantly, all these lesions remained confined to the left kidney and showed no signs of invasion or involvement of the renal sinus, fatty tissue, blood vessels, or lymph nodes. Pathologic examination also confirmed the presence of a normal adrenal gland.

## 4. Discussion

Though single, unilateral tumors make up most renal neoplasms, the coexistence of concomitant primary tumors in a single kidney are rare, yet not completely unheard of. The more frequent combination often constitutes different histological variants of RCC, namely papillary and clear cell. The occurrence of ipsilateral multifocal renal tumors is observed in a small subgroup, comprising 0.5–5.4% of all renal tumor patients.[3] In a study performed by Simhan et al., a total of 2569 patients with renal tumors were examined, among whom 97 individuals were found to have unilateral synchronous multifocal renal masses, with 8 patients presenting with mixed RCCs comprising both papillary and clear cell RCC types.[4] Similarly, in their retrospective analysis of 1071 patients who underwent radical nephrectomy, Richstone et al. identified 57 cases of multifocality, with 6 of them being bilateral synchronous renal tumors.[5] In these multifocal cases, 74% had the same histological subtypes, with papillary subtype RCC being significantly associated with multifocality. The study also reported 9 patients with pathologic discordance between primary and satellite tumors, including cases with clear cell RCC and papillary type RCC.

Synchronous presentation of benign and malignant lesions has also been reported in literature; most frequently with angiomyolipoma (AML).[6] In our case along with the clear cell and multilocular clear variants of RCC, the specimen also revealed the presence of renal oncocytoma and renomedullary interstitial cell tumor. Renal Oncocytoma, often dubbed as the "Great Mimicker", is the most common benign solid renal tumor, characterized by cells with eosinophilic cytoplasm, and accounts for 4–7% of all kidney tumors resected in adults.[2,7,8] Authors have reported the propensity of renal oncocytomas towards multifocality within the same kidney. Often this is either with different foci of oncocytoma, or with coexisting AML, or chromophobe variants of RCC.[8,9] However, no clear genetic link between these lesions has yet been established.

Renomedullary interstitial cell tumors; formerly known as "Medullary Fibromas", are benign lesions, usually discovered incidentally in autopsies. These are more frequently found in the fifth decade of life and carry an excellent prognosis.[10]

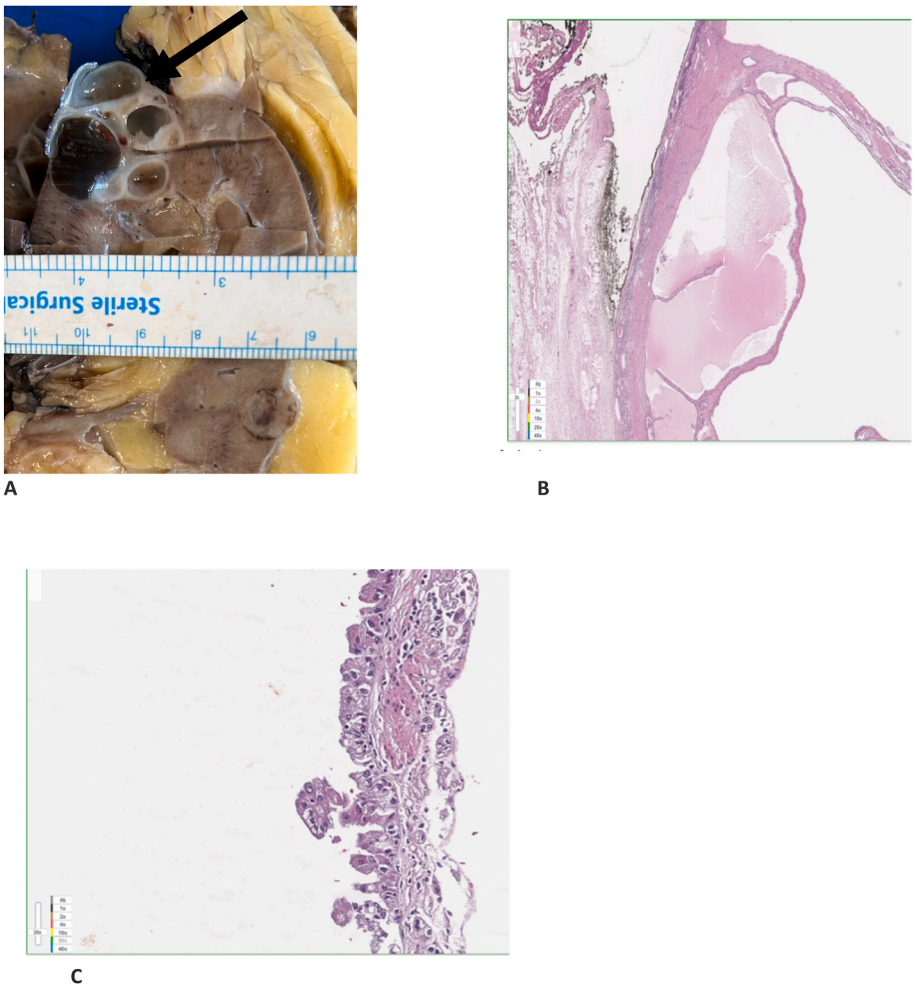


**Fig. 2.** Multilocular Cystic Clear Cell Neoplasm of Low Malignant Potential
(A) Gross specimen.
(B) Low magnification.
(C) High magnification.

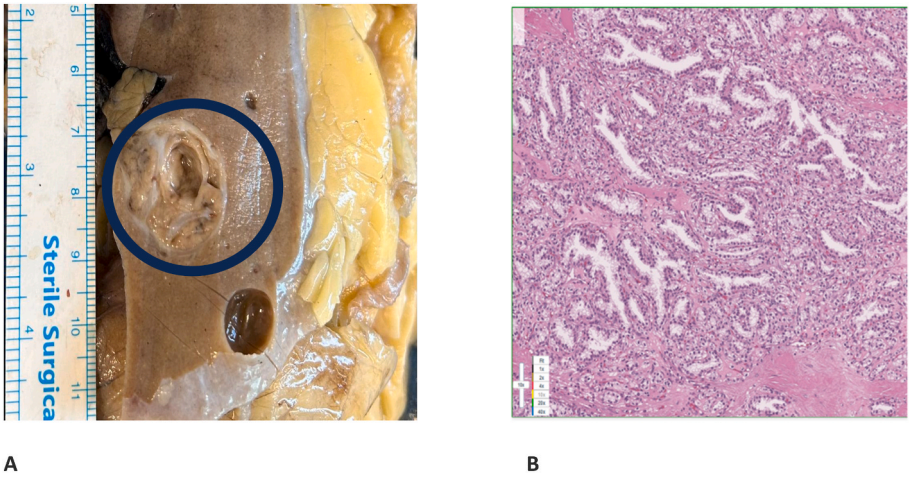


**Fig. 3.** Clear Cell Papillary Renal Cell Carcinoma
(A) Gross section.
(B) High magnification microscopic slide.

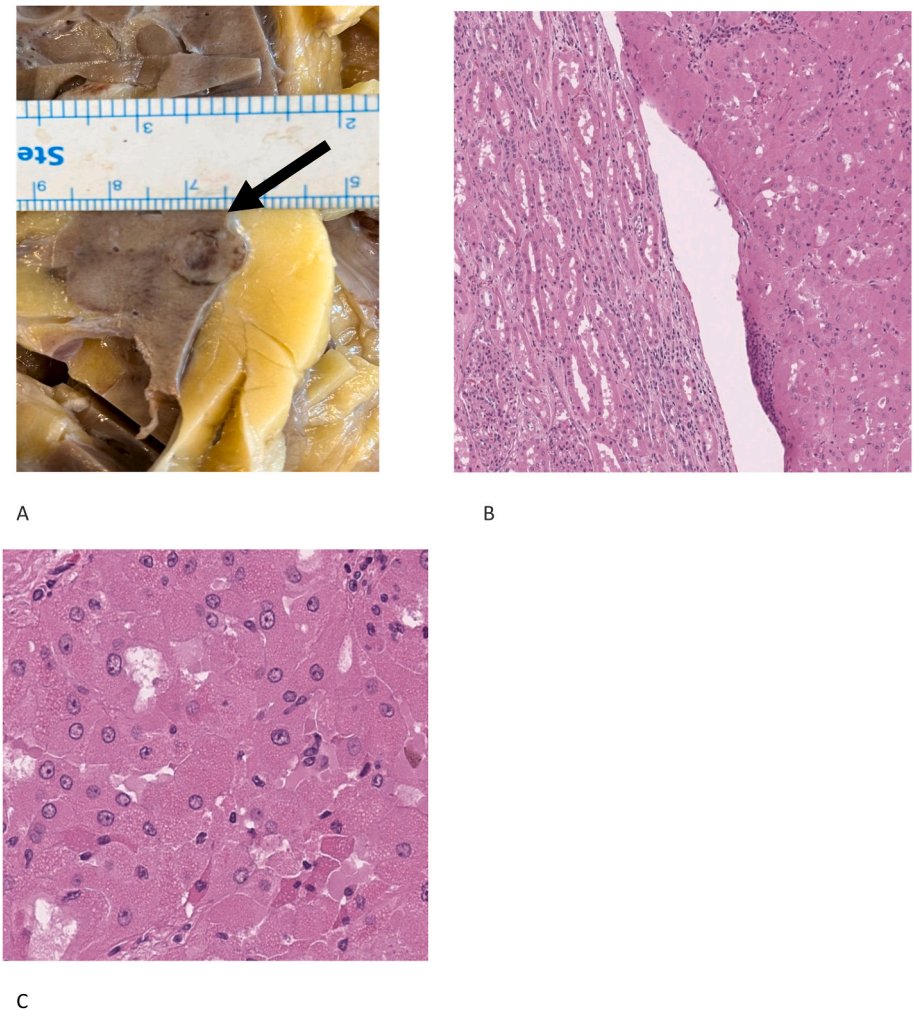


**Fig. 4.** Oncocytic Lesion
(A) Gross lesion.
(B) Microscopy, low magnification.
(C) High magnification.

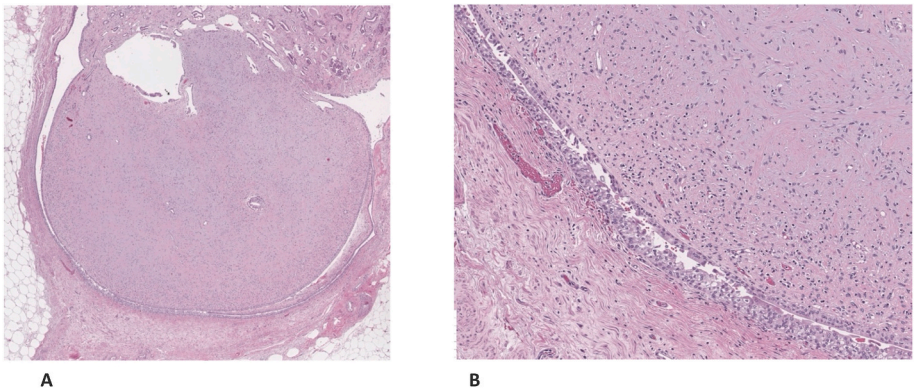


**Fig. 5.** Renomedullary Interstitial Cell Tumor
(A) low magnification microscopic slide.
(B) high magnification microscopic slide.

When taking into consideration the prognosis of cases with multiple neoplastic lesions, the more aggressive of the lesions usually bears the most influence. In our case, as mentioned above two of the four identified histopathology correlates with benign lesions and are often associated with excellent prognosis (in the absence of metastasis, in case of oncocytomas). The most malignant of these, however, correlates with a pathological T1a, clear cell papillary lesion. Provided there was no local invasion, venous invasion, nor evidence of metastasis, this

corresponds to an overall favorable prognosis, with no indication for further therapy.

Furthermore, it cannot be emphasized enough that renal tumors, malignant or otherwise encompass a wide cacophony of diseases; each manifesting their own histological and pathological features, as well as genetic characteristics. Certain genetic disorders have even been identified to be linked to different lesions, case in point being the infamous von Hippel Lindau syndrome (attributed with the VHL gene); which has shown to be associated with Angiomyolipoma, Oncocytoma and Clear Cell RCC.[11] However, there is no clear evidence of any association between either of the four histological entities found in our case.

After meticulous literature review, we found one similar report of 63-year-old lady, with four synchronous renal pathologies across both her kidneys, who had required bilateral partial nephrectomy. Her left kidney revealed a chromophobe lesion, and her right kidney bore both clear cell RCC, and medullary fibroma, as well as angiomyolipoma.[6] To our knowledge, however, this is the first reported case of four synchronous lesions in the same kidney.

## 5. Conclusion

In conclusion, this case report highlights an exceedingly atypical occurrence of a 57-year-old male diagnosed four distinct types of renal neoplasms within the same kidney - a phenomenon not yet documented in existing literature. Further research and reporting of such cases can contribute to a deeper understanding of the complexities of renal cell carcinoma and potentially guide future management decisions for similar presentations. More work into the intricacies behind the genetic associations between varying renal pathologies may also be beneficial in terms of offering genetic counselling, detailed investigations, and alternative treatment options, where applicable.

## Consent

The patient provided written informed consent for the publication of this case report and any associated images.

## Author statement

All the authors were involved in the conception and design, drafting/revision and final approval of the manuscript being submitted.

## Declarations of competing interest

The authors declare that there are no conflicts of interest or financial relationships to disclose in relation to this case report.

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