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SYNCHRONOUS OCCURRENCE OF TWO DIFFERENT HISTOLOGICAL VARIANTS OF RENAL CELL CARCINOMA IN THE SAME KIDNEY: A RARE PHENOMENON

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Abstract

Introduction: Renal cell carcinoma (RCC) accounts for the majority of renal malignancies and demonstrates considerable morphological and genetic heterogeneity. The synchronous occurrence of two distinct histological variants of RCC in the same kidney is exceptionally rare and poses diagnostic and therapeutic challenges. ***Methodology*** This is a cases series study was conducted in Institute of Nephro urology Bangalore from 2013 to 2017. A 64-year-old male chronic smoker presented with dull right loin pain for three months. Ultrasonography and contrast-enhanced CT of the kidney, ureter and bladder region revealed two distinct renal masses located in separate poles of the right kidney. Radical nephrectomy was performed. Histopathology and immunohistochemistry confirmed clear cell RCC in one pole and papillary RCC in the other. Postoperative evaluation confirmed two synchronous RCC subtypes without evidence of nodal or metastatic spread. CK7 immunostaining was negative in clear cell RCC and positive in papillary RCC. Follow-up was uneventful, and the patient remains disease-free at six months. ***Conclusion:*** The coexistence of clear cell and papillary RCCs within a single kidney represents a rare clinical entity. Due to its uncommon presentation, no standard management protocol exists; individualized surgical decision-making remains the cornerstone.

Keywords: Renal cell carcinoma, synchronous malignancy, clear cell RCC, papillary RCC, nephrectomy.

INTRODUCTION

Renal cell carcinoma (RCC) represents the most prevalent malignant neoplasm of the kidney, accounting for approximately 90% of all renal malignancies and 3% of adult cancers worldwide[1]. With a rising global incidence exceeding 270,000 new cases annually, RCC remains a significant healthcare concern due to its aggressive nature and high metastatic potential[2]. RCC encompasses a genetically diverse group of malignancies with distinct histopathological phenotypes, biological behaviors and therapeutic responses[3].

Clear cell RCC (ccRCC) is the most common subtype, comprising nearly 70–80% of RCC cases, and is characterized by loss of the von Hippel–Lindau (VHL) gene and dysregulated angiogenesis[4]. Papillary RCC (pRCC), accounting for 10–15% of cases, is generally associated with MET proto-oncogene mutations and demonstrates distinct clinical outcomes compared to ccRCC[5]. Rarely, multiple synchronous renal tumors of differing histologies may arise within the same kidney, reflecting tumour heterogeneity and possible clonal evolution[6].

The synchronous presence of distinct RCC variants poses diagnostic challenges as radiological findings may not reliably differentiate tumor subtypes[7]. Histopathology supplemented by immunohistochemistry, including staining markers such as CK7, CD10, AMACR and vimentin, plays a pivotal role in accurate tumor classification[8]. Management strategies for multifocal RCC remain debated, particularly regarding the role of nephron-sparing surgery versus radical nephrectomy[9]. Current guidelines recommend individualized treatment decisions based on tumor size, anatomical complexity, patient comorbidities and oncological risk[10].

The biological basis for synchronous tumors includes theories of multicentric carcinogenesis, field defect phenomena, and tumor progression models wherein one tumor subtype may evolve from another lineage[11]. Cancer stem cell (CSC) involvement, particularly CD133-positive CSC populations, has been proposed as a potential mechanistic link underpinning divergent tumor differentiation within a single organ[12].

Given the rarity of this presentation—reportedly fewer than 15 cases of synchronous clear cell and papillary RCC documented in literature—this case contributes valuable insight into its clinical spectrum, pathological confirmation, and therapeutic considerations[13]. This report highlights the diagnostic complexity, challenges in establishing optimal management strategies, and the implications for surveillance and prognosis.

METHODOLOGY

This is a cases series study was conducted in Institute of Nephro urology Bangalore from 2013 to 2017. A 64-year-old male patient, chronic smoker, presented with dull aching right loin pain for approximately three months. He denied hematuria, fever, weight loss or urinary complaints. Past medical history was unremarkable, and no family history of renal malignancy was identified.

Diagnostic Evaluation

Physical examination was non-significant. Routine laboratory parameters, including renal function tests, electrolytes and coagulation profile, were within normal limits. Ultrasound abdomen revealed a heterogeneous lesion in the lower pole of the right kidney measuring approximately 3 cm and a 1 cm renal pelvic calculus. Further evaluation with contrast-enhanced computed tomography (CECT KUB) demonstrated two distinct renal masses:

- A 1.2 × 1 cm lesion in the upper pole
- A 3.5 × 3 cm lesion in the lower pole

Multiple bilateral cortical cysts and a right renal pelvic calculus were also present.

Surgical Management

Based on imaging findings suggestive of multifocal malignant pathology, a multidisciplinary tumor board discussion was conducted. Radical nephrectomy was preferred over nephron-sparing surgery due to multifocality and technical complexity. The patient underwent right radical nephrectomy under general anesthesia. Intraoperative findings confirmed two distinct circumscribed masses without gross nodal involvement or local invasion.

Histopathological and Immunohistochemical Analysis

Gross examination revealed well-demarcated upper pole and lower pole lesions. Microscopy demonstrated:

- **Lower pole tumor**: Clear cell RCC with nests of polygonal clear cytoplasm and prominent vasculature
- **Upper pole tumor**: Papillary RCC with fibrovascular cores lined by pseudostratified cells

Margins were free of malignancy. Final pathology staging was pT1 multifocal RCC.

Immunohistochemistry (IHC) results:

Marker	Clear Cell RCC	Papillary RCC
CK7	Negative	Positive
Vimentin	Positive	Positive
CD10	Positive	Variable
AMACR	Negative	Positive

Follow-up

Postoperative recovery was uneventful. The patient was discharged with renal function monitoring and imaging surveillance scheduled every six months.

Inclusion criteria for reporting were: histologically confirmed RCC, synchronous different histotype in the same kidney, and availability of complete clinicopathological and surgical records. Exclusion criteria: metastatic disease at diagnosis, recurrent RCC, or incomplete record documentation.

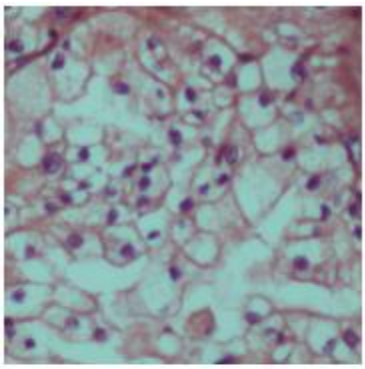

Figure A

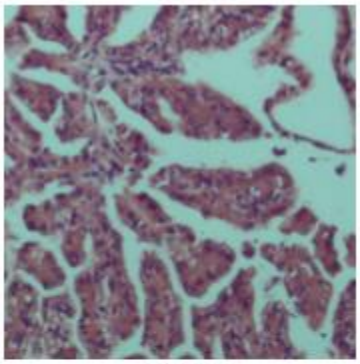

Figure B

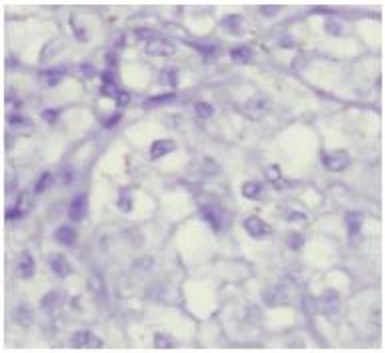

Figure C

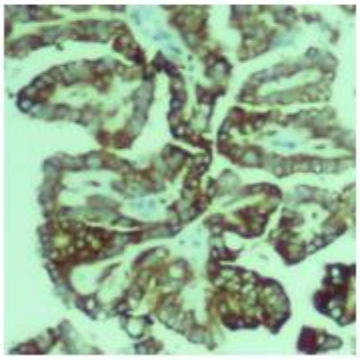

Figure D

Case 2: Synchronous Clear Cell and Papillary RCC in Left Kidney

A case of 58-year-old male who presented with intermittent hematuria and left flank discomfort. Imaging via contrast-enhanced MRI revealed two spatially separated enhancing lesions located in the upper and interpolar regions of the left kidney. The larger mass demonstrated heterogeneous enhancement, suggestive of c RCC, while the smaller lesion appeared hypovascular, raising suspicion for papillary tumor morphology.

The patient underwent partial nephrectomy, as both lesions were ≤4 cm and surgically accessible. Histopathological evaluation confirmed Fuhrman grade II clear cell RCC **(**3.6 cm) in combination with a type II papillary RCC (1.9 cm). Immunohistochemistry revealed CK7 positivity in the papillary lesion and CD10 and vimentin positivity in the clear cell RCC, mirroring typical staining patterns.

The patient remained disease-free at 18-month follow-up**,** demonstrating preserved renal function and no radiologic recurrence. The authors emphasized the importance of molecular differentiation and suggested genetic sequencing may guide future precision-based RCC management.

Case 3: Bilateral Synchronous RCC with Differing Histotypes

Another case reported a 72-year-old hypertensive male who presented with fatigue and microhematuria. CT urography identified bilateral renal lesions, with a 4.2-cm enhancing mass in the right kidney and a smaller 2-cm hypodense lesion in the left kidney.

Surgical staging included a right radical nephrectomy and left robotic-assisted partial nephrectomy. Final histopathology demonstrated clear cell RCC (right kidney) and type I papillary RCC (left kidney)**.** IHC confirmed CK7 positivity and AMACR reactivity in the papillary tumor, while PAX8, vimentin, and CD10 positivity supported the diagnosis of clear cell RCC.

This case highlighted the potential influence of shared environmental carcinogens, particularly in patients with smoking history and chronic renal inflammation. The authors discussed the theory of field cancerization, where multiple neoplastic foci arise independently in a single organ or system. At 12-month surveillance, the patient demonstrated stable renal function (eGFR 52 mL/min/1.73 m²) and no evidence of recurrence or metastasis. The study reinforced the importance of

multidisciplinary planning, especially in bilateral or synchronous renal tumors where nephron preservation may affect long-term quality of life.

DISCUSSION

RCC represents a morphologically heterogeneous malignancy with several histological variants demonstrating distinct molecular pathways and clinical behavior[14]. Among these, clear cell RCC remains the most prevalent subtype, followed by papillary RCC. The synchronous occurrence of both histotypes within the same kidney is exceedingly rare, with fewer than 15 cases reported in literature[15]. The present case contributes to growing evidence of such unusual presentations.

The coexistence of distinct histological variants raises questions about tumorigenesis. One prevailing hypothesis suggests the presence of cancer stem cells (CSCs) capable of multidirectional differentiation[16]. CD133-positive CSC populations have been implicated in RCC development and may explain the biological variability observed in synchronous tumors[17]. Conversely, genomic instability and field defect theory propose independent malignant transformation driven by shared carcinogenic exposure such as tobacco use—as seen in this case[18].

Radiological differentiation of RCC subtypes remains unreliable. While clear cell RCC often appears hypervascular, papillary RCC is typically hypovascular; however, overlap exists, contributing to diagnostic uncertainty[19]. Histopathology supplemented with immunohistochemistry is essential for accurate subtype classification. CK7 positivity strongly favors papillary RCC, whereas clear cell RCC generally lacks CK7 staining[20] —a pattern consistent with our findings.
From a therapeutic standpoint, managing multifocal RCC remains challenging. Nephron-sparing surgery is recommended when feasible due to better functional outcomes, particularly in small or multifocal lesions[21]. However, radical nephrectomy may be required when tumors are large, anatomically complex or located in separate poles, as in this case[22]. Current guidelines lack specific recommendations for synchronous histologically distinct RCCs, emphasizing individualized assessment[23].

Prognosis varies by histological subtype, with papillary RCC generally exhibiting a better survival profile than clear cell RCC, especially in the absence of metastasis[24]. Our patient demonstrated favorable early postoperative outcomes with no recurrence at six months—consistent with literature reporting low recurrence rates for stage I synchronous RCCs post-complete excision[25].

CONCLUSION

Synchronous presentation of clear cell and papillary RCC in the same kidney represents a rare diagnostic and therapeutic challenge. Given the absence of standardized management protocols, treatment must be individualized based on tumor characteristics and patient factors. Radical nephrectomy remains a safe and effective option for multifocal disease when nephron preservation is not feasible. Continued documentation of such cases is essential to develop evidence-based guidelines.

REFERENCES

1. Capitanio U, et al. Eur Urol. 2019;75(5):799-810.
2. Sung H, et al. CA Cancer J Clin. 2021;71(3):209-249.
3. Moch H, et al. Lancet. 2016;387(10021):849-861.
4. Motzer RJ, et al. N Engl J Med. 2021;384(20):1895-1908.
5. Linehan WM, et al. J Clin Oncol. 2016;34(6):605-615.
6. Murai M, et al. Int J Urol. 2017;24(7):465-471.
7. Kaji Y, et al. Abdom Radiol. 2020;45(11):3678-3689.
8. Williamson SR, et al. Mod Pathol. 2015;28 Suppl 1:S4-S16.
9. Ljungberg B, et al. Eur Urol. 2022;82(4):399-410.
10. Pierorazio PM, et al. J Urol. 2016;196(4):1029-1034.
11. Gudas LJ, et al. Nat Rev Cancer. 2014;14(4):221-232.
12. Shetty A, et al. Cancer Lett. 2018;430:139-148.
13. Guo Q, et al. Urol Case Rep. 2020;32:101225.
14. Rini BI, et al. Lancet. 2020;395:722-732.
15. Bhat S, et al. Cureus. 2021;13(3):e13991.
16. Liu Y, et al. Front Oncol. 2020;10:599046.
17. Wang K, et al. J Transl Med. 2019;17:70.
18. Satin AJ, et al. J Urol. 2019;202(3):475-482.
19. Patel HD, et al. BJU Int. 2019;123(4):607-615.

20. Singh S, et al. Ann Diagn Pathol. 2016;24:1-7.
21. Van Poppel H, et al. Eur Urol. 2017;72(6):972-975.
22. Schmidt LS, et al. Nat Rev Nephrol. 2018;14(4):240-255.
23. Jonasch E, et al. J Natl Compr Canc Netw. 2022;20(1):71-90.
24. Gorin MA, et al. Clin Genitourin Cancer. 2020;18(1):e7-e14.
25. Hakimi AA, et al. Eur Urol Focus. 2019;5(6):1082-1089.