



## Primary Extra Renal Papillary Renal Cell Carcinoma Masquerading as A Metastatic Carcinoma: A Unique Case with Dual Malignancies

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Cite this article: Selvaraj S, Patil A, GC, Amirtham U: Primary Extra Renal Papillary Renal Cell Carcinoma Masquerading as A Metastatic Carcinoma: A Unique Case with Dual Malignancies. Ann Urol Oncol 2023, 6: 16. <https://doi.org/10.32948/auo.2023.09.10>

### Abstract

A 50-year-old male presented with abdominal pain, pain during defaecation, constipation, bleeding per rectum for 2 months. Colonoscopy showed an ulcero-proliferative growth, that is 2.5 cm from anal verge. Further PET-CT confirmed the growth in the lower rectum with mesorectal fat stranding and an irregular, lobulated, encapsulated solid-cystic mass in right perinephric fat, separated from the kidney (suggestive of metastasis), with intact bilateral kidneys. Biopsy of the rectum revealed an adenocarcinoma and biopsy of right perinephric mass revealed a papillary neoplasm. Following which abdominoperineal resection with perinephric mass excision was performed, due to encapsulation of mass. Histopathological evaluation and further immunohistochemistry performed was positive for vimentin, AMACR, CD10 and negative for other markers to rule out metastasis of either. This led to the diagnosis of synchronous primaries i.e., Extra-renal papillary renal cell carcinoma and adenocarcinoma of rectum.

**Key words** renal cell carcinoma, extra-renal renal cell carcinoma, papillary, metastasis, heterotopic kidney, synchronous tumors, dual malignancies

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## Introduction

Renal cell carcinoma (RCC) is the most common malignancy of kidney in adults, accounting for more than 90% of renal neoplasms. The most prevalent histologic subtype is clear cell carcinoma followed by papillary RCC. They are thought to be derived from the epithelium of proximal tubules of nephron[1]. However, there are countable number of cases of extra-renal type that have been reported in the medical literature. Extra-renal RCC is defined as presence of cancerous tissue in regions other than the native kidney. Our case is the thirteenth case to be reported worldwide, with the first case being reported in 2003[2] and first case of extrarenal papillary RCC reported in 2019[3].

Synchronous primary malignancies are defined by Warren and Gates's criteria, i.e they must be histologically confirmed, must be geographically separated and distinct lesions and the probability of metastasis of either has to be excluded.

Hereby, we present the first case of an extrarenal papillary RCC arising in the peri-renal adipose tissue along with synchronous primary adenocarcinoma of rectum. Literature review studies show that conventional clear cell RCC is the most common type of extra-renal RCC. However, our case was a papillary RCC; the second reported case at an extra-renal site.

## Case report

### Presenting symptoms and clinical evaluation

A 50-year-old male presented with abdominal pain, pain during defaecation, constipation, bleeding per rectum for 2 months. Colonoscopy showed an ulcero-proliferative growth that is 2.5 cm from anal verge.

### Radiological findings

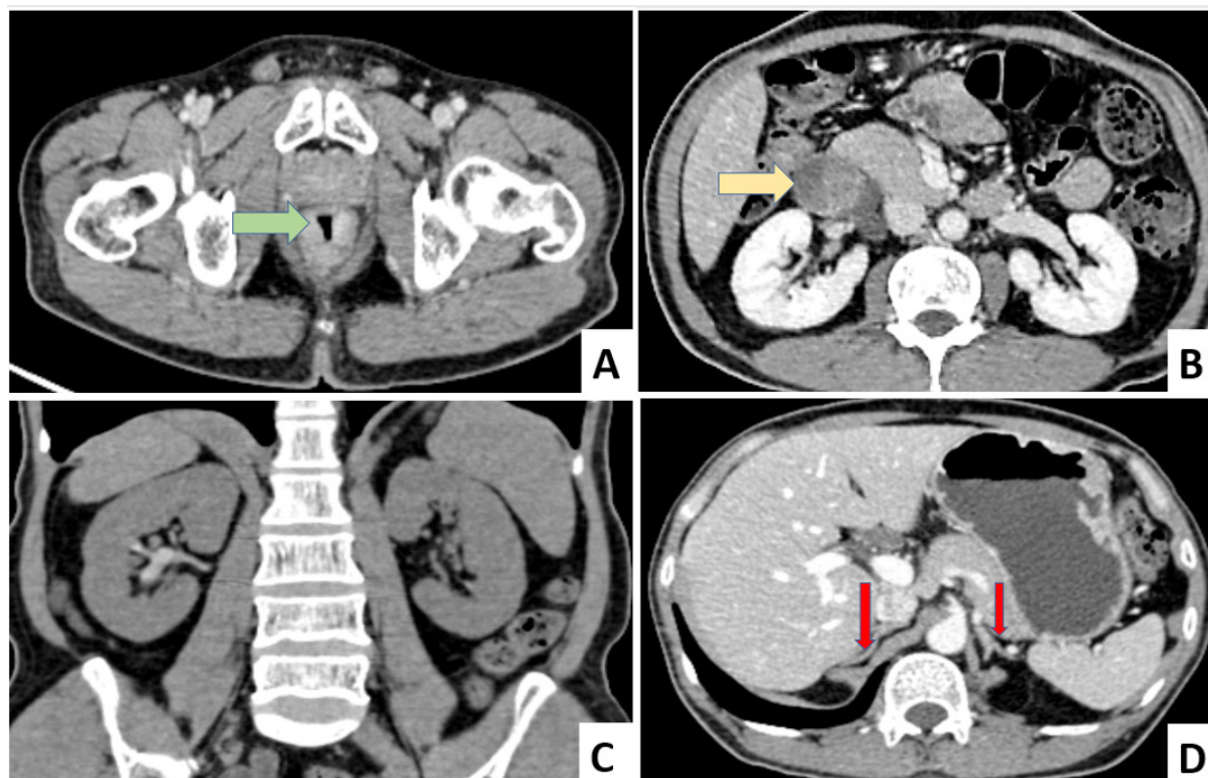
Further PET-CT was done for metastatic workup which confirmed the growth in lower rectum with mesorectal fat stranding. There was also an irregular, lobulated, encapsulated solid-cystic mass measuring 7 x 6 x 4 cm in right perinephric fat space separated from the renal capsule. Bilateral kidneys and adrenals were unremarkable. This perinephric mass was suggestive of metastasis radiologically with an SUV of 8.5 (**Figure 1**).

### Initial histopathological and IHC findings

Biopsy of the rectum revealed a moderately differentiated adenocarcinoma. Biopsy from the right perinephric mass revealed a papillary neoplasm morphologically. The histopathologic findings favoured a papillary renal cell carcinoma. Further IHC was performed, which showed positivity for vimentin, CK7, AMACR, focally positive for CD10 and SATB2 and negative for PAX-8, RCC, CA IX CK20, CDX2 (**Figure 2**). On correlating with clinical, radiological findings; which had strong suspicion of metastasis, the SATB2 positivity, made us err towards a metastatic adenocarcinoma of rectum in spite of inconclusive immunomorphology.

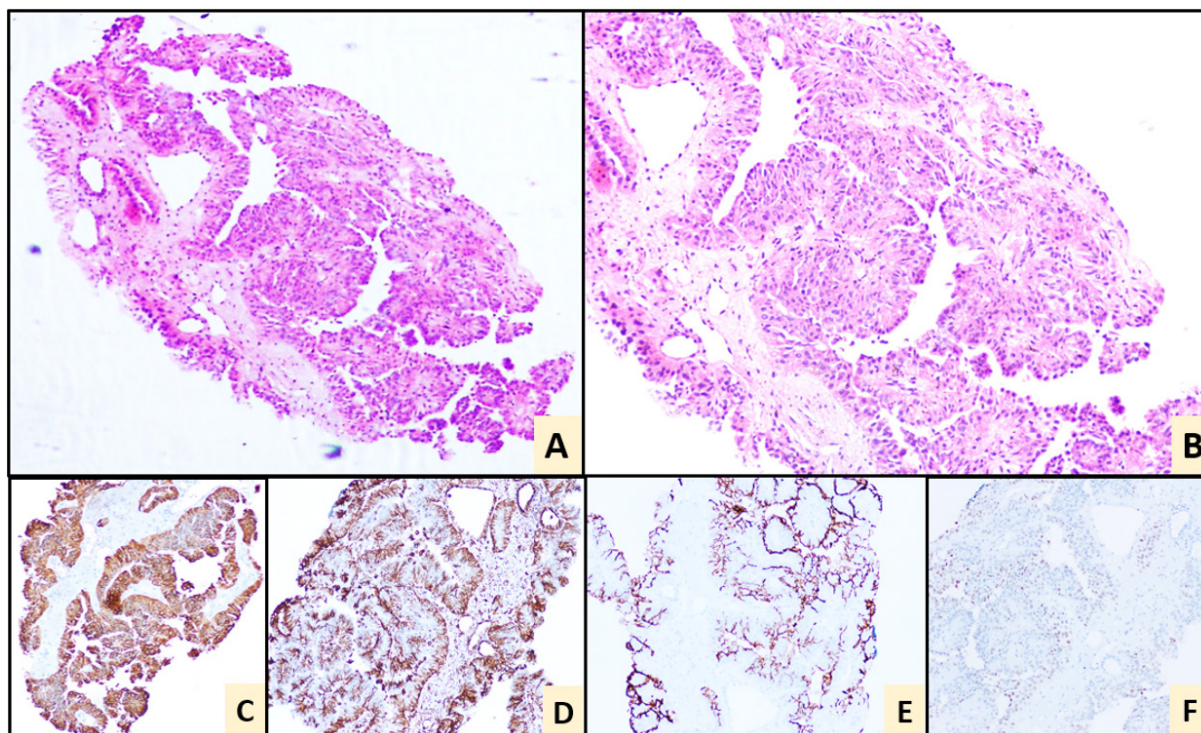
As the lesion was encapsulated, excision of the mass was performed along with abdominoperineal resection (APR). Grossly, the APR had a 6 x 4 x 1.5 cm tumour infiltrating into the muscularis propria. The perinephric mass was completely encapsulated grossly measuring 7 x 5 x 4 cm with a solid-cystic grey-brown cut surface.

### Final histopathologic evaluation



**Figure 1.** PET-CT. (A) Growth in the lower rectum with mesorectal fat stranding (marked by green arrow); (B) An irregular, lobulated, encapsulated solid-cystic mass identified in the right perinephric fat space which has no communication with the right kidney (marked by yellow arrow)- Suggestive of metastasis radiologically; (C) Bilateral normal Kidneys and (D) Bilateral normal Adrenals (marked by red arrow).





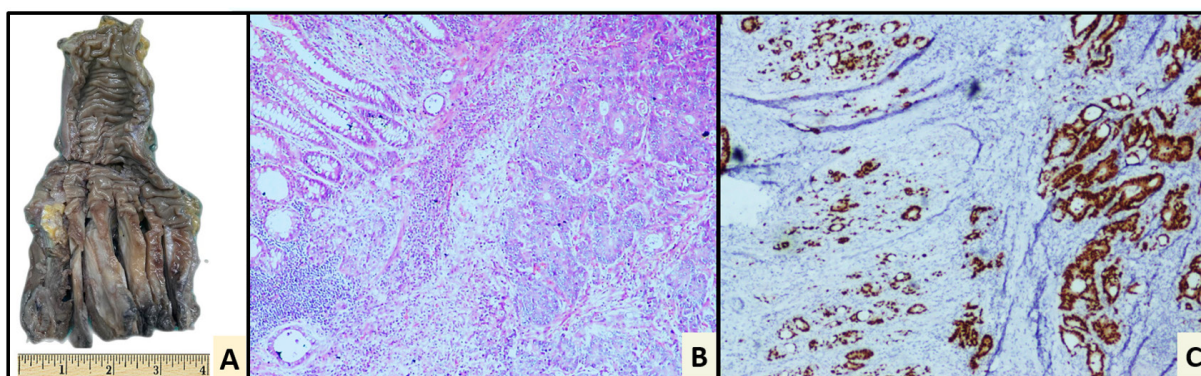
**Figure 2.** Perinephric mass biopsy. Haematoxylin and Eosin stain showing a papillary neoplasm (A, 10x) and (B, 20x). IHC: Positive for vimentin (C), AMACR (D) and focally positive for CD10 (E) & SATB2 (F). Negative IHC markers: PAX-8, RCC, CA IX, CK20, CDX2.

Histopathological evaluation of APR revealed a moderately differentiated adenocarcinoma of rectum, and pathologic stage of pT3 N1. Histopathological evaluation of right perinephric mass revealed a tumor arranged in papillary pattern composed of tumour cells exhibiting moderate nuclear pleomorphism, vesicular nuclei, prominent nucleoli and moderate eosinophilic cytoplasm. There were numerous psammoma bodies also identified. The above features were morphologically suggestive of a papillary renal cell carcinoma. However, the intact kidneys radiologically gave us a set back and could not explain it. The periphery of the mass showed dilated tubules lined by bland cuboidal epithelium, which were suspected to be renal tubules. Further sampling of the mass revealed a glomerulus and renal tubules exhibiting

thyroidisation. This confirmed the mass to be a heterotopic kidney with papillary renal cell carcinoma arising from it. We ruled out the possibility of supernumerary kidney as radiologically, the mass did not have a separate collecting system.

#### *IHC findings*

Immunohistochemistry (IHC) performed on tumor from perinephric mass showed positivity in tumor cells for vimentin, AMACR and focally positive for CD10. PAX-8 was positive in the adjacent cystically dilated tubules. The tumor cells were negative for CK7, CK20, CAIX, NapsinA, CDX2 (**Figure 3**). The presence of psammoma bodies raised a suspicion of translocation associated RCC. However, TFE-3 was negative. IHC done on the rectal tumor



**Figure 3.** Abdominoperineal resection (apr). (A) Gross photograph of APR showing an ulcero-infiltrative tumour in the lower third of rectum; Haematoxylin and Eosin stain showing features of adenocarcinoma, Grade 2 (B, 20x). IHC: Positive for CDX2 (C). The tumor was MMR proficient on IHC. Negative IHC markers: PAX-8, CK7, AMACR CA-IX and CD10.



Table 1. Summary of IHC markers.

IHC Marker	Perinephric Mass	Abdominoperineal Resection
CK7	Negative	Negative
CK20	Negative	Positive
CDX2	Negative	Positive
Vimentin	Positive	Negative
AMACR	Positive	Negative
CD10	Positive(focally)	Negative
PAX-8	Positive (dilated tubules)	Negative
CA-IX	Negative	Negative
Napsin-A	Negative	N/A
TFE-3	Negative	N/A

revealed positivity for CDX2, CK20 and negative for PAX-8, CK7, AMACR and CD10 (**Figure 4**). This ruled out metastasis of either tumors. Summarised in **Table 1**.

The final diagnosis was given as dual malignancies

with synchronous primary extra-renal papillary RCC and adenocarcinoma of rectum.

Discussion

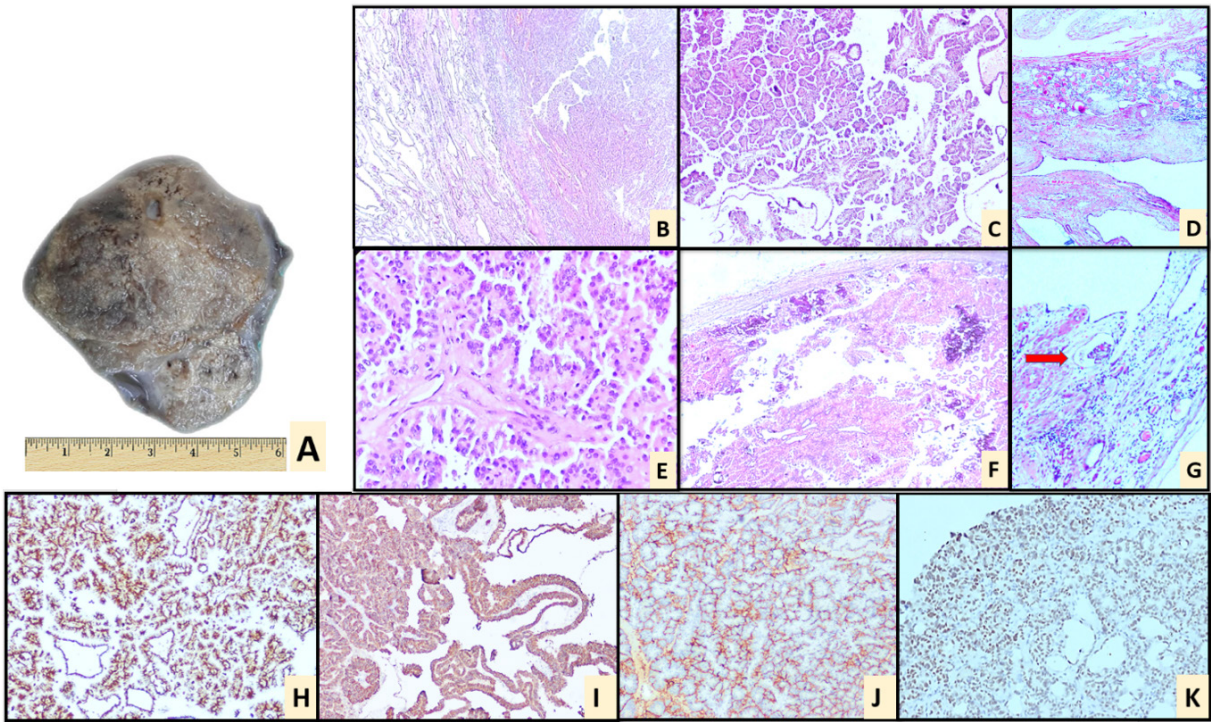


Figure 4. Perinephric mass excision. (A) Gross photograph of right perinephric space mass showing an encapsulated mass with a solid, grey-brown cut surface; Haematoxylin and Eosin stain showing an encapsulated neoplasm exhibiting a papillary architecture with adjacent tissue showing cystically dilated tubules (B, 10x), (C, 20x), (E, 40x); There are numerous psammoma bodies seen (F); On further sampling, renal tubules were identified with evidence of thyroidisation (D) along with an occasional glomerulus (marked with red arrow) (G); IHC: Excised specimen of Perinephric mass showing diffuse positivity for vimentin (H) and AMACR (I); CD10 (J) shows focal positivity, PAX-8 (K) is positive in the adjacent cystically dilated tubules. Negative IHC markers: CK7, CK20, CAIX, NapsinA, CDX2, TFE3.

**Table 2. Literature review of relative case.**

Author	Year	Location of Tumour	Pathologic Subtype	TFE3/TFEB Positivity	Second Primary
Singh et al.[2]	2003	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Pal and Chowdhury[6]	2007	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Permi et al.[7]	2011	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Terada et al.[8]	2011	Peri-renal adipose tissue	Renal-type Clear Cell Carcinoma	N/A	No
Hasan et al.[9]	2015	Adrenal gland	Renal-type Clear Cell Carcinoma	N/A	No
Patne et al.[10]	2015	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Wang and Xue[11]	2015	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Sato et al.[12]	2016	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Liao et al.[13]	2018	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Li et al.[3]	2019	Adjacent to inferior Vena Cava	Type II Papillary RCC	TFE3 and TFEB positive	No
Han and Lim[14]	2020	Prostate	Renal-type Clear Cell Carcinoma	N/A	No
Petrinec et al.[15]	2021	Retroperitoneum	Renal-type Clear Cell Carcinoma	TFE3 positive	No
Current case	2022	Right Peri-renal adipose tissue	Type II Papillary RCC	TFE3 negative	Yes-Adenocarcinoma, Rectum

Extrarenal RCC is defined as the presence of RCC in regions other than normal native kidneys[4]. Based on urinary tract embryogenesis; the metanephric blastema arises from the metanephros and ancestral intermediate mesoderm, which further develop into the bilateral native kidneys[5]. There is a school of thought which suggests that postnatal life has some remnants of mesonephric structures, identified in the perirenal adipose tissue, adrenal gland and adjacent to inferior vena cava that may be predispose to cancer transformation and are termed as extra-renal RCC[2]. These extrarenal RCCs arise from ectopic tissue or even supernumerary kidney, which were both part of our differentials initially after the perinephric mass biopsy. However, radiologically our case did not have a separate collecting system and blood supply related to the urinary system. This ruled out the possibility of a supernumerary kidney and the perinephric space mass was confirmed to be an ectopic kidney tissue being part of mesonephric remnants; which gave rise to the RCC.

There are twelve reported cases of extra-renal RCC[9] of them arising from prostate, 1 from adrenal gland, peri-nephric adipose tissue, retroperitoneum, adjacent to inferior vena cava each respectively. Summary of the reported cases in medical literature are represented in the **Table 2**. Eleven of twelve cases were clear cell RCC and 1 case was a type II papillary RCC. Our case is a type II papillary RCC. There were areas of psammomatous calcifications identified which was further worked up for Microphthalmia translocation associated RCC and turned out to be negative. The second synchronous primary in our case was adenocarcinoma of the rectum.

The differential diagnoses while working up these cases of

extra-renal RCC is very intricate and unique for each case. In our case, the first possibility considered was a metastasis as we had an established diagnosis of adenocarcinoma arising from rectum. The morphology and immunohistochemistry did not complement this possibility. The positivity of SATB2 and negativity of PAX-8 added on to the clinico-radiological suspicion, complicating the scenario. SATB2 shows variable positivity in RCCs and is shown to be a poor prognostic factor in clear cell RCC. PAX-8 is negative in 10% of renal cell carcinomas[7]. After the resection of the perinephric mass with APR, we worked up both the tumors extensively and arrived at the final diagnosis. This is first reported case of extra-renal RCC presenting as a dual malignancy and the second reported case of papillary extra-renal RCC in English literature.

The second synchronous primary in our case was adenocarcinoma of the rectum with tumour budding and deposits in serosa. The patient was in Stage III - pT3N2a. This case fulfilled the Warren and Gate's criteria for multiple primary malignancies and was given this final diagnosis of Synchronous primaries being extrarenal Papillary RCC and carcinoma rectum. The patient is now planned for adjuvant chemotherapy for carcinoma rectum as priority following the resection.

## Conclusion

Although accounting for its rarity, we would like to emphasise on the awareness of Extra-renal type of RCC being a unique and intriguing entity, which are hypothesised to arise from the mesonephric remnants. Establishing a precise diagnosis is essential for planning appropriate treatment and assessing the prognosis in

such cases.

## Acknowledgements

None.

## Ethical policy

There were no human participants involved. The data was collected from archival resources.

## Availability of data and materials

All data generated or analysed during this study are included in this publication.

## Author contributions

SS: archival retrieval and collection of data, writing the report, review of literature; AP: manuscript correction and review of literature; CG: manuscript correction and review of literature; UA: manuscript correction and review of literature.

## Competing interests

No conflicts of interest.

## Funding

No funding required .

## Consent

Institutional consent was obtained. However, no patient details are disclosed in the case report. IRB approval was not obtained as it was only a case report.

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