SYNCHRONOUS IPSILATERAL CLEAR CELL RENAL CELL CARCINOMA AND RENAL ONCOCYTOMA: A CASE REPORT

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ABSTRACT

Introduction: *Synchronous clear cell renal cell carcinoma (ccRCC) and renal oncocytoma (RO) in the same kidney is rare.* ***Objective:*** *The report of dual tumour with ccRCC and RO is rarely seen in the medical literature. We report a case with this rare combination of synchronous tumours in ipsilateral kidney.* ***Case(s) presentation:*** *We report the case of a 66-year-old male with incidentally detected synchronous renal masses in the left kidney- a combination of clear cell renal cell carcinoma and oncocytoma.* ***Discussion:*** *The coexistence of two or more distinct renal tumours in the same kidney, though uncommon, have been reported in the literature, mainly renal oncocytoma in combination with Papillary RCC. The synchronous occurrence of oncocytoma and clear cell renal cell carcinoma is very rarely reported. A thorough review of the English medical literature did not reveal any prior case report documenting this type of synchronous renaltumour except for an online poster describing this combination. This poster was not seen as a peer-reviewed publication in the English medical literature. Hence, to the best of our knowledge, our case may be the first full peer-reviewed report of this type of synchronous renal tumour.* ***Conclusion:*** *A rare combination of renal tumours is being presented for awareness of clinicians and pathologists for correct diagnosis and appropriate management.*

Keywords: *Case report, clear cell renal cell carcinoma, ipsilateral, renal oncocytoma, synchronous renal tumour.*

ABSTRAK

Pendahuluan: *Karsinoma sel ginjal tipe clear cell (ccRCC) dan renal oncocytoma (RO) yang muncul secara bersamaan pada ginjal yang sama merupakan kondisi yang jarang terjadi.* ***Tujuan:*** *Laporan mengenai tumor ganda yang terdiri dari ccRCC dan RO jarang ditemukan dalam literatur medis. Kami melaporkan sebuah kasus dengan kombinasi langka tumor sinkron pada ginjal ipsilateral ini.* ***Presentasi Kasus:*** *Kami melaporkan kasus seorang pria berusia 66 tahun dengan massa ginjal sinkron yang terdeteksi secara insidental pada ginjal kiri suatu kombinasi antara karsinoma sel ginjal tipe clear cell dan onkositoma.* ***Diskusi:*** *Keberadaan dua atau lebih tumor ginjal yang berbeda secara bersamaan pada ginjal yang sama, meskipun jarang terjadi, telah dilaporkan dalam literatur medis; kombinasi yang paling sering dilaporkan adalah onkositoma ginjal bersama dengan karsinoma sel ginjal (RCC) tipe papiler. Kejadian sinkron antara onkositoma dan karsinoma sel ginjal tipe clear cell sangat jarang dilaporkan. Penelusuran menyeluruh terhadap literatur medis berbahasa Inggris tidak menemukan laporan kasus sebelumnya yang mendokumentasikan jenis tumor ginjal sinkron ini, kecuali sebuah poster daring yang mendeskripsikan kombinasi tersebut. Poster tersebut tidak dikategorikan sebagai publikasi yang telah melalui telaah sejawat (peer-reviewed) dalam literatur medis berbahasa Inggris. Oleh karena itu, sejauh pengetahuan kami, kasus ini mungkin merupakan laporan lengkap pertama yang telah melalui telaah sejawat mengenai jenis tumor ginjal sinkron ini.* ***Simpulan:*** *Kombinasi tumor ginjal yang jarang ditemui ini disajikan untuk meningkatkan kesadaran para klinisi dan ahli patologi demi tercapainya diagnosis yang tepat dan penatalaksanaan yang sesuai.*

Kata kunci: *Laporan kasus, karsinoma sel ginjal clear cell, ipsilateral, onkositomaginjal, tumorginjalsinkron.*

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INTRODUCTION

Renal cell carcinoma (RCC) is the most common malignant epithelial neoplasm of the kidney arising from proximal tubular epithelium. The prognosis depends on the stage, histological subtype and nuclear grade.Clear cell renal cell carcinoma (ccRCC) is the most common histological subtype. Renal oncocytoma (RO) a benign renal epithelial tumour arising from the intercalated cell of collecting duct, comoposed of oncocytic cells rich in mitochondria. RO is

histologically characterized by cells withabundant eosinophilic granular cytoplasm and benign nuclear features. RO should be distinguished from the malignant tumour, chromophobe RCC since both showoncocytic cells. A combination of different types of renal tumors has been reported.

A combination of oncocytic tumors with papillary RCC have been well documented in the English medical literature.1-4Hybrid oncocytic/chromophobe tumors (HOCT) especially in Birt-Hogg-Dubé syndrome has also been reported.5 The report of dual tumour with ccRCC and RO is rarely seen in the medical literature. We report a case with this rare combination of synchronous tumours in ipsilateral kidney. This tumour was detected during imaging for a single episode of hematuria when the patient was admitted in the neurology ward for the management of another unrelated condition.

CASE(S) PRESENTATION

A 66-year-old malepatient, a known case of cerebrovascular accident (CVA) due to left middle cerebral artery thrombosis developed right hemiplegia one year earlier.Type 2 diabetes mellitus and hypertension were detected one year back when the patient was hospitalized for the CVA and is on oral medication. Now, the patient is having residual hemiparesis of right side with deviation of angle of mouth. The patient was admitted in the neurology ward for regular check-upand management of hemiparesis. On 2nd day of admission, the patient had an episode of dysuria for which the patient was investigated.

His blood investigations showed normal blood counts with a Hb% of 12.4g/l. The preoperative serum creatinine was 2.1 mg/dl., blood urea-36 mg/dl,Serum sodium, potassium and calcium were within normal limits.Liver function tests, lipid profile and coagulation studies were all within normal limits. Urine examination showed microscopic hematuria with occult blood in Dipstick and 8-10 RBCs/HPF on microscopy.

Computed Tomography (CT) scan of abdomen was done. Left kidney showed two lesions- a larger lesion well defined enhancing with central non enhancing area in the parenchyma of the upper pole and mid portion (Figure 1a) and a smaller exophytic lesion in the upper pole towards the peripheral cortex (Figure 1b). The clinical and radiological diagnosis was multifocal RCC.

Patient underwent left radical nephrectomy with a clinical and radiological diagnosis of multifocal of Renal cell carcinoma. Post operative period was uneventful. Post operative creatinine was 1.8mg/dl.

We received the specimen in the pathology department. The renal capsule has been stripped when received but was present in the specimen. On cutting open, a larger partially encapsulatedtumour was seen in the parenchyma of the upper pole extending to the mid portion which was tan brown in colour and measured 5x4.9x3 cms. No central scar was noted within this neoplasm. This tumour wasclose to, but not extending to the renal sinus.Another unencapsulated exophytic growth was seen projecting from the upper pole with attachment to the peripheral cortical area just beneath the renal capsule far away from the renal sinus and hilar structures. This tumour was soft, yellowish white in colour and measured 2.5x1.5x0.5cms (Figure: 1c, 1d).There was a clear narrow rim of demarcation between the two lesions. Grossing and sampling was done according to standard protocol followed by our department.

Sections were stained with hematoxylin and eosin andmicroscopic examintionrevealed a thin rim of normal renal tissue separating the two tumours (Figure 2a). The yellow exophytic smaller tumourwas ccRCC with cells having clear cytoplasm arranged in sheets and lobules separated by a fine branching capillary network. The cells showed clear cytoplasm, round nuclei and inconspicuous, basophilic nucleoli at x400 magnification, indicating WHO/ISUP grade1 with scanty mitosis (Figure 2b). No lymphovascular invasion, tumor necrosis, sarcomatoid/rhabdoid change noted.ccRCC was limited to the kidney with renal sinus, renal artery, renal vein, renal capsule, perinephric fat, resected end of ureter, all free of neoplasm. No lymph nodes were received or found in the specimen. The ccRCC was reported as per College American Pathologists (CAP) Protocol (June 2025) with pathological stage assigned as pT1a. The larger tan tumour showed oncocytic cells arranged in nests and lobules. The cells showed abundant eosinophilic, granular cytoplasm, round regular nuclei, with inconspicuous nucleoli. Edematous stroma noted. No mitosis or resinoid nucleus noted. This tumour was histologically diagnosed as RO (Figure 2c).For confirmation immunohistochemistry with Anti-Vimentin (Clone V9, PathnSituBiotecnologies), CD10 (clone 56c6

DAKO), CK7 (Clone EP16, PathnSituBiotecnologies), CD117, E cadherin (Clone EP6, PathnSituBiotecnologies), and Ki67 (Clone MIB1, PathnSituBiotecnologies) were done using standard protocol in VENTANA BenchmarkGX of Roche Diagnostics, with 3,3'-diaminobenzidine (DAB) as chromogen giving a brown colour result if positive. On-slide external control was kept for each marker. Vimentin was strongly and diffusely positive in the cytoplasm of cells ofccRCC (Figure: 3a) and negative in RO (Figure: 3b).CD10 showed patchy membranous positivity in ccRCC (Figure: 3c) and negative in RO (Figure: 3d).

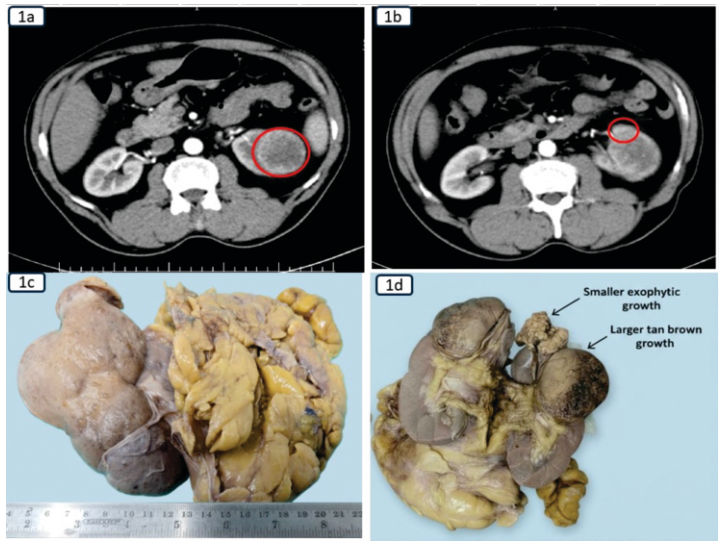

Figure 1. (a) CT picture of Renal Oncocytoma (Marked with red circle). (b) CT picture of ccRCC (Marked with red circle). (c) Gross appearance of left kidney shows irregular outer surface with stripped capsule along with perinephric fat. (d) Cut section of the kidney showing the 2 tumours- larger tantumuor-oncocytoma and smaller exophytic growth- ccRCC.

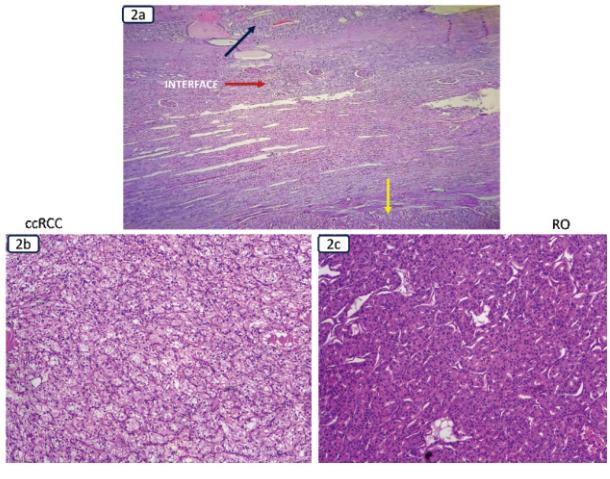

Figure 2. a- Interface of two tumours - ccRCC (blue arrow) and Oncocytoma (yellow arrow) separated by a rim of normal parenchyma (RED ARROW). (b) ccRCC. (c) Renaloncocytoma

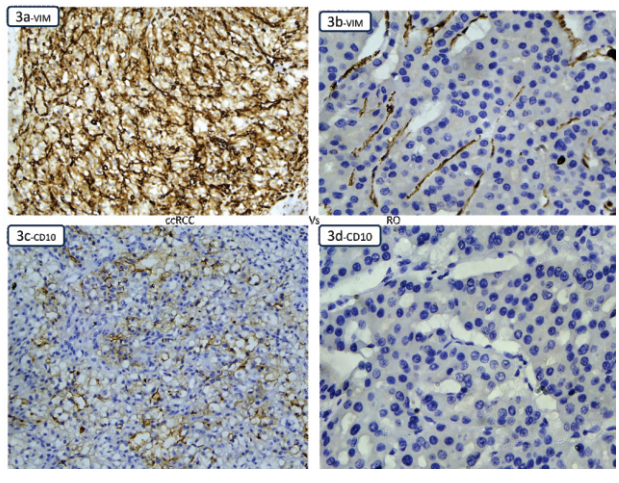

Figure3. (a) Anti- vimentin positive in ccRCC. (b) Anti-vimentin negative in RO. (c) Anti CD10 positive in ccRCC. (d) Anti CD10 negative in RO.

The CK7 was negative in both tumours.(Figure:4a, b). E cadherin was negative in ccRCC and showed strong, diffuse membranous positivity in oncocytoma (Figure: 4c, d).CD117 was negative in ccRCC and positive in RO seen as strong diffuse membranous and cytoplasmic positivity (Figure: 5a, b).Ki 67 was low (2%) in oncocytoma and 10% in ccRCC indicating a low proliferating tumour (Figure: 5c, d). The Gross appearance, histology and immunoprofile confirmed the diagnosis of dual synchronous tumour with ccRCC and RO in the left kidney.

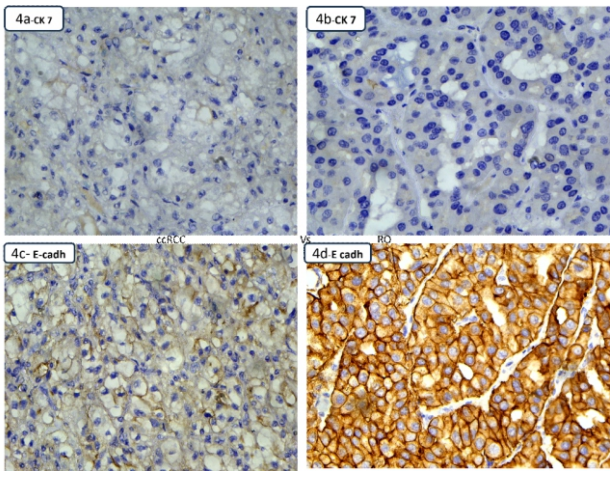

Figure 4. (a) Anti CK7 negative in ccRCC. (b) Anti CK7 negative in RO. (c) Anti E- cadherin negative in ccRCC. (d) Anti E cadherin positive in RO.

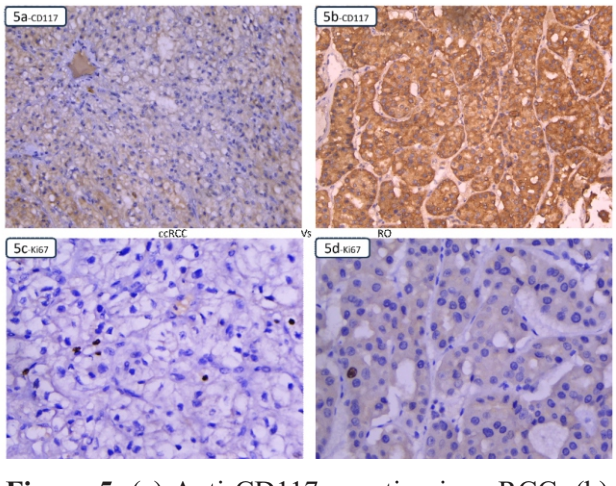

Figure 5. (a) Anti CD117 negative in ccRCC. (b) Anti Cd117 positive in RO. (c) Ki67 10% in ccRCC. (d) Ki67 low in RO.

DISCUSSION

Mixed or collision renal tumours involving multiple epithelial subtypes have been reported. The most commonly reported dual tumour in the kidney is RO with PRCC. Paschos KA et al reported such a case presenting as an emergency with rupture and hemorrhage.[1] Stempel K et al reported RO with PRCC collision tumour in 53 year old man.[2] In their review paper Mc Croskey et al discussed 8 cases of PRCC and RO collision tumour.[3] Rajen Goyal et al's report also showed this type of collision tumour.[4] Several other isolated case reports also are there in medical literature indicating that this combination is rather common. Cases of HOCT are also seen in the literature with or without associated Birt Hogg Dube syndrome.[5] A rare case of RO combined with mucinous tubular and spindle cell carcinoma (MTSCC) has been reported by Lin et al.[6] In this case report, Lin et al, claim that their case is the first known case of oncocytoma coexisting with the rare MTSCC subtype.

A thorough literature search revealed no documented case reports of synchronous tumors composed of ccRCC and oncocytoma as in our case. A poster describing this type of dual lesion of ccRCC and oncocytoma along with low-grade mucinous adenocarcinoma of appendix in a 66 year old male is seen in the internet from Moffitt Cancer Center, Tampa, Florida,[7] but peer reviewed publication of the same is not seen in English medical literature. A review study of 48 cases of renal collision tumour by Lerma et al. described different combinations of collision tumours in the kidney with a tumour-on-tumour interface and did not describe a synchronous tumour with combination of ccRCC and Oncocytoma in their study as in our case.[8] Hence, to the best of our knowledge,our report may be the first fully peer-reviewed ccRCC–oncocytoma combination of synchronous tumor in English medical literature.

The ccRCC is renal tubular epithelial origin whereas RO is a tumour originating from intercalated cell of the collecting duct. The central genetic event in the pathogenesis of ccRCC is the biallelic inactivation of Von Hippel–Lindau (VHL) gene either due to somatic mutations or promoter hypermethylation.[9] Whereas RO shows recurrent chromosomal losses (1, 14, 21, X, Y). A subgroup shows CCND1 rearrangements at the 11q13 locus.[10] How these two tumours of different histological types and different molecular landscapes occur as

combination, is still unclear.Pathogenetic theories postulated include coincidental occurrence, a common stem-cell precursor with divergent differentiation, or a collision tumour phenomenon. In the present case, the clinical and radiological diagnosis was multifocal RCC. But the RCC was a smaller lesion with a pathological stage of pT1a. Since surgical resection is the cornerstone of treatment and the pT stage in this patient was pT1a, the patient was kept on close follow-up without any chemo/radiotherapy.

Combination tumours, sometimes, cannot be assessed by clinical and radiological methods. Definitive diagnosis relies on meticulous gross examination, extensive tissue sampling, histomorphology, and immunohistochemistry.

Prognosis is primarily determined by the stage and grade of the clear cell renal cell carcinoma component in such synchronous tumours. The present case was a WHO/ISUP Grade 1, low stage tumour. Patient is on regular followup, last visit one month back. The patient is free of recurrence, metastasis and other tumour-related problems till date, 12 months after nephrectomy. He is continuing treatment for diabetes, hypertension and CVA.

CONCLUSION

The synchronous coexistence of RO with ccRCC in ipsilateral kidney is rare.Awareness of this coimbination of tumours is important for accurate diagnosis and clinical management. Clinicians should be aware of such dual tumours, as these may complicate proper imaging interpretation and directly impact surgical decision-making. Presence of RCC requires surgical management-partial or radical nephrectomy according to the tumour size/location and stage of the tumour.

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