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Case Report

Pathology Section

Oncocytic Form of Papillary Renal Cell Carcinoma: A Rare Morphological Variant

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ABSTRACT

Oncocytic Papillary Renal Cell Carcinoma (OPRCC) is a rare variant of Papillary Renal Cell Carcinoma (PRCC), characterised by distinct morphological and immunophenotypic features. Present report is of a 75-year-old hypertensive female who presented with constipation and abdominal bloating for four months. Imaging revealed an exophytic lesion in the lower pole of the right kidney, measuring 6.1×5.8×5.4 cm, without perinephric or sinus invasion. Laboratory studies demonstrated mild haematuria, elevated Lactate Dehydrogenase (LDH), and hypercalcaemia. The patient subsequently underwent radical nephrectomy. Gross examination revealed a 6.5 cm brown-yellow tumour with haemorrhagic areas, confined to the kidney. Histopathology showed papillary structures lined predominantly by oncocytic cells with abundant granular eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli. Focal pseudostratification, nuclear atypia, haemosiderin deposition, foamy macrophages, and focal necrosis were present, with no capsular, vascular, or nodal involvement. Immunohistochemistry (IHC) demonstrated diffuse positivity for Alpha-Methylacyl-CoA Racemase (AMACR), vimentin, and CD10, with negativity for CK7, CD117, and Ki-67, confirming the diagnosis of OPRCC. Postoperative recovery was uneventful, and a structured surveillance plan was initiated. Recognition of OPRCC is crucial to prevent misdiagnosis with benign oncocytoma or more aggressive RCC subtypes, enabling appropriate prognostication and management.

Keywords: Genetic, Metastasis, Prognostic, Oncocytic variant of papillary renal cell carcinoma

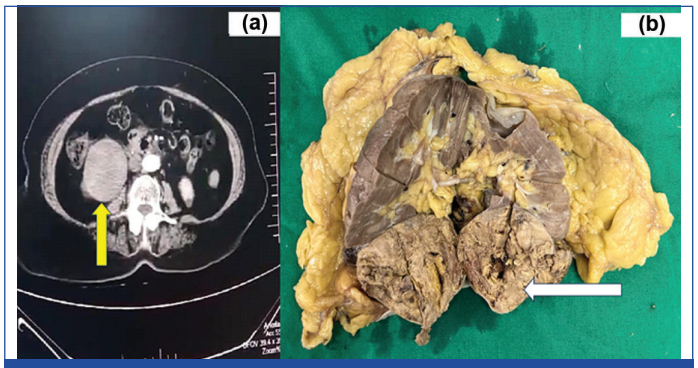
CASE REPORT

A 75-year-old hypertensive female presented to the outpatient department with complaints of severe constipation and abdominal bloating for four months. She had a history of external haemorrhoids, managed conservatively for five months, and longstanding hypertension, well controlled on medication for over 40 years. Computed Tomography (CT) colonography revealed no significant findings and excluded internal or thrombosed haemorrhoids. Further evaluation with CT of the abdomen and pelvis demonstrated a well-defined exophytic soft-tissue lesion measuring 6.1×5.8×5.4 cm arising from the lower pole of the right kidney, suggestive of a neoplastic lesion [Table/Fig-1a].

To assess possible renal pathology, renal function tests were performed, including urinalysis, serum creatinine, and creatinine clearance. Routine laboratory investigations revealed a mild increase in LDH and hypercalcaemia, with urinalysis showing microscopic haematuria. All other parameters were within normal limits. The patient was scheduled for elective surgery and underwent right radical nephrectomy under general anaesthesia. The resected specimen was sent for histopathological evaluation.

Gross examination revealed a right kidney with attached perinephric fat, easily separable, measuring 17.5×12×5.5 cm. Renal vessels were identified at the hilum, along with the ureter. External examination showed deep scars and cystic areas, the largest cyst measuring 2.5×1.8 cm. On cut section, serous fluid was seen oozing from the cysts, with loss of cortico-medullary differentiation. A tumour measuring 6.5×5.5×5 cm was located in the lower pole, appearing brown to yellow with areas of haemorrhage. The tumour did not invade the perinephric fat or renal sinus [Table/Fig-1b].

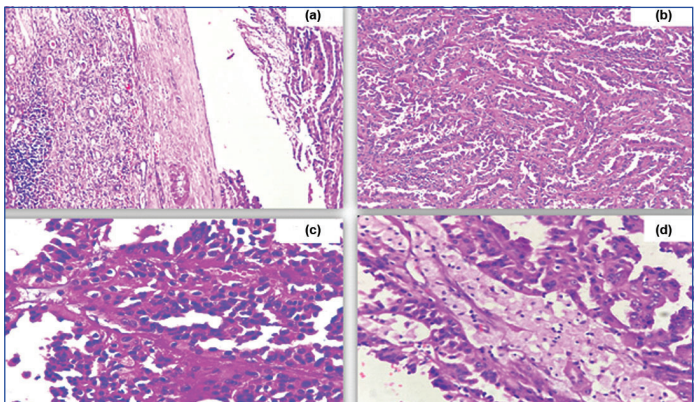
Histopathological analysis revealed the tumour arising in normal kidney tissue [Table/Fig-2a]. It was composed of papillae formed by fibrovascular cores. The papillae were predominantly lined by a single layer of oncocytic cells with hyperchromatic, pleomorphic nuclei and abundant granular eosinophilic cytoplasm. Focal areas showed pseudostratification and nuclear atypia [Table/Fig-2b,c]. Foamy macrophages were present within the fibrovascular cores



[Table/Fig-1]: (a) CT scan revealing the soft-tissue mass in the lower pole of the right kidney measuring 6.1×5.8×5.4 cm (yellow arrow). (b) Gross showing exophytic soft-tissue lesion in the lower pole of the right kidney (white arrow).

of some papillae [Table/Fig-2d]. Haemosiderin-laden macrophages and focal necrosis were also noted.

The tumour was confined to the kidney, with no involvement of the renal vein, renal sinus fat, perinephric fat, Gerota's fascia, renal



[Table/Fig-2]: (a) Shows tumour with normal kidney (H & E 40x). (b) Tumour is arranged in the papillary architecture (H&E 10x). (c) Tumour cells show abundant granular eosinophilic cytoplasm with variable sized nuclei (H&E 40x). (d) Papillary architecture of tumour showing foamy macrophages (H&E 40x).

capsule, or pelvicalyceal system. All surgical margins were clear. There was no evidence of lymphovascular invasion, and all examined lymph nodes were free of metastatic disease.

Pathological stage (AJCC Cancer Staging Manual, 8th Edition): pT1b pNx pMx [1].

IHC performed externally, showed diffuse positivity for AMACR, vimentin, and CD10, and negativity for CK117, CK7, and Ki-67. Based on the histopathology and IHC findings, a diagnosis of OPRCC was confirmed.

The procedure was uneventful, and postoperative recovery was smooth, allowing discharge on the sixth day. Follow-up demonstrated no short-term or long-term complications. A structured surveillance plan was implemented, consisting of weekly follow-up during the first two months, monthly reviews over the subsequent six months, and annual assessments for the next five years to facilitate early detection of recurrence or delayed complications.

The patient provided informed consent for the use of clinical images in research publications, with assurance of anonymity.

DISCUSSION

Renal Cell Carcinoma (RCC) is the most common renal malignancy in adults, accounting for approximately 85% of malignant kidney tumours and nearly 3% of all human cancers. PRCC comprises 10-15% of RCCs and is characterised by distinctive pathological and molecular features. Historically, PRCC has been subclassified into type 1 and type 2 [2]. According to the International Society of Urological Pathologists/World Health Organisation classification, type 1 tumours are composed of a single layer of low-grade (nuclear grade 1 or 2) tumour cells with scant amphophilic cytoplasm, whereas type 2 tumours demonstrate stratified or pseudostratified high-grade (nuclear grade 3 or 4) tumour cells with abundant eosinophilic cytoplasm [3]. This morphological distinction holds prognostic relevance, as type 2 PRCC is associated with a less favourable clinical outcome [4].

The OPRCC is a rare subtype that demonstrates overlapping features of both type 1 and type 2 PRCC [5]. This classification remains clinically significant as it reflects meaningful differences in morphology, underlying molecular alterations, and prognostic behaviour [6]. OPRCC is defined by unique pathological features and generally exhibits a less aggressive clinical course [5]. Tumour sizes reported in the literature range from 0.8 cm to 27 cm. Grossly, these lesions are well-circumscribed and often exhibit a brown cut surface, with intratumoural haemorrhage being a common finding even in relatively small tumours [7]. Most cases occur in patients between 40 and 80 years of age, with a male predominance, mirroring the distribution seen among other RCC subtypes [2]. Importantly, the oncocytic variant is distinct from both conventional PRCC subtypes and benign renal oncocytomas, based on its imaging and microscopic characteristics [4].

OPRCC usually lacks specific clinical manifestations. In most cases, it is incidentally detected as a renal mass during routine physical examinations [2,8]. Some patients may present with haematuria or flank pain; therefore, definitive diagnosis relies on histopathological evaluation [2].

One reported case involved a middle-aged male who presented with left flank pain and reduced urine output. Contrast-enhanced CT of the abdomen demonstrated a well-defined solid-cystic mass arising from the inferior pole cortex of the left kidney. On gross examination, the cut surface revealed a haemorrhagic, encapsulated tumour in the lower pole, measuring 10×9×6 cm. Microscopy showed predominantly papillary architecture, with tumour cells exhibiting abundant granular eosinophilic cytoplasm and round vesicular nuclei with small nucleoli. The fibrovascular cores contained foamy histiocytes and areas of hemosiderin deposition [5].

A similar presentation was reported in a 47-year-old male with haematuria, passage of blood clots, occasional dysuria, and urinary tract irritation without systemic symptoms. Ultrasonography revealed a lesion in the upper pole of the left kidney, while CT demonstrated an enhancing mass. The patient underwent laparoscopic radical nephrectomy. Histopathology supported by IHC confirmed OPRCC. The tumour measured 3.8×3×3 cm, invaded the renal pelvis but spared the capsule (pT3aNxMx). Immunohistochemistry was positive for Vimentin, PAX8, RCC, P504S, CD10, and EMA, with a Ki-67 index of 10% [2].

An instance of a tumour mimicking an oncocytic renal tumour was reported in a 30-year-old woman who presented with an incidental left renal mass detected during a physical examination. She was asymptomatic with an unremarkable history and clinical findings. Ultrasound revealed a well-defined 2.6×2.3 cm mass in the upper-middle pole of the left kidney. CT confirmed a renal lesion, initially suspected to be clear cell carcinoma. Laparoscopic partial nephrectomy was performed. Grossly, the tumour was encapsulated and brown. Histology showed complex papillae lined by oncocytic cuboidal to columnar cells with apically located nuclei. IHC was positive for GATA3, CK7, PAX2/8, EMA, and AMACR, and negative for vimentin, CD10, and CD117, leading to a diagnosis of papillary renal neoplasm with reverse polarity [9].

In a study by Xia QY et al., six cases of OPRCC were analysed in detail. All tumours showed strong and diffuse immunoreactivity for MET protein, indicating consistent overexpression. To further explore the molecular basis, direct sequencing of exons 14-21 of the MET gene, which encode the tyrosine kinase domain, was performed; no pathogenic mutations were identified in any case. Cytogenetic evaluation by FISH demonstrated chromosomal abnormalities similar to those described in conventional papillary RCC, including trisomy 7 in three cases, trisomy 17 in two cases, and loss of chromosome Y in one of four male patients. These findings suggest that while MET protein overexpression is a reproducible feature of OPRCC, it does not arise from activating MET mutations. Instead, chromosomal gains—particularly trisomy 7, where the MET gene resides—or other transcriptional and post-transcriptional regulatory mechanisms may account for the increased MET expression observed [10]. Han G et al., similarly reported recurrent trisomy 7 and 17, and Y-loss in male patients, along with consistent AMACR, CD10, and vimentin expression. Clinically, most patients had favourable outcomes; only one developed bone metastasis, while the remaining cases were recurrence-free [11].

The histological classification of renal neoplasms has expanded due to advances in radiology, cytogenetics, IHC, and molecular diagnostics. Recently, additional subtypes have been described and defined by recurrent molecular alterations [12]. Colloidal iron staining is often positive in oncocytic and chromophobe RCC [13]. In the present case, strong diffuse colloidal iron expression further supported the diagnosis of OPRCC [13].

Differentiating OPRCC from other eosinophilic/oncocytic renal tumours is crucial. OPRCC is characterised by papillary structures lined with oncocytic cells, foamy histiocytes, and eosinophilic cytoplasm. It typically shows AMACR, CD10, vimentin, and MET positivity; variable CK7/EMA; absence of CD117; and cytogenetic alterations such as trisomy 7/17 and Y-loss [10,11,14]. Papillary renal neoplasm with reverse polarity shows nuclei with apical misorientation, CK7 and GATA3 positivity, and KRAS mutations [15]. Chromophobe RCC (eosinophilic variant) exhibits sheets of cells with perinuclear halos and raisinoid nuclei, and is CK7/CD117 positive, unlike OPRCC [16]. Hybrid oncocytic/chromophobe tumours combine oncocytoma and chromophobe features with multiple chromosomal losses [14]. SDH-deficient RCC shows nests of eosinophilic cells with cytoplasmic vacuoles and SDHB loss, while OPRCC retains SDHB expression [17]. Translocation

RCCs (TFE3/TFEB) occur in younger patients, demonstrate papillary or nested growth, and are confirmed by nuclear TFE3/TFEB positivity [18]. Renal oncocytoma, a benign tumour, is predominantly solid, lacks foamy histiocytes and necrosis, and shows CD117/progesterone receptor positivity but is negative for AMACR, vimentin, and CD10 [2].

CONCLUSION(S)

OPRCC is regarded as a distinct subtype of PRCC owing to its characteristic pathological features and relatively favourable clinical course. Accurate identification of this uncommon variant is important, as it can significantly influence diagnostic interpretation and therapeutic decisions. Recognising OPRCC helps avoid confusion with benign oncocytic tumours or more aggressive RCC subtypes, thereby ensuring appropriate prognostication and management.

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