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# Case Report

## Oncocytic variant of papillary renal cell carcinoma – should it be classified as a distinct subtype?

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**Abstract**

Renal tumor classification has evolved during the last several decades based on different microscopic and molecular patterns. We present a case of a renal mass which on evaluation revealed a radiologically, histologically and immunologically distinct pattern from the currently described subtypes. Evaluation of the histology of our patient revealed it to have features of papillary renal cell carcinoma with atypical features not conforming to either category of the two currently described subtypes. This atypical pattern consisted of oncocytic cells with malignant features organized in papillary architecture. Analogous oncocytic tumors have been described in tumours in other organs including thyroid and parotid gland. This oncocytic variant is distinct from the two subtypes of papillary renal cell carcinoma as well as the commonly described benign oncocytoma both microscopically and radiologically. Establishing this as a separate subtype may help in better treatment and prognostication.

**Key words:** Renal cancer, papillary renal cell carcinoma, oncocyte, tumor classification

### Introduction

Papillary variant is the second commonest type of renal cell carcinoma (RCC) constituting 15-18% of RCC. Papillary renal cell carcinoma (pRCC) is traditionally subdivided into two types (type 1 and 2) with different morphological and prognostic characteristics. We present a case of an oncocytic papillary RCC, a variant of renal carcinoma with morphological and immunological features relating to papillary RCC (pRCC) although sufficiently distinct from above two subtypes. Oncocytic pRCC is rare and only a small number of cases are reported in literature since the initial coining of the term by Lefèvre in 2005 (1). We review the existing literature on oncocytic pRCC to help identify characteristic morphological, histological and immunohistochemical features for accurate diagnosis which would increase awareness of it as a distinct entity.

### Case history

A 40-year-old man presented with left flank and abdominal pain of eight months duration. He had no haematuria or any systemic symptoms. He was a smoker of five pack-years. His BMI was 28 and the rest of his physical examination was unremarkable. Abdominal ultrasonography revealed a lesion with a diameter of 4.5 cm in the upper pole of left kidney. A CT urogram showed a well-defined rounded lesion in the posterior aspect of upper pole of left kidney measuring 5.7 cm x 5.4 cm x 4.8 cm. It was heterogenous with a star shaped lucent area in the Centre after

contrast enhancement (Figure1). Nephrometry (RENAL) score of the lesion was 9. The liver and lungs were free of metastases. He underwent left radical nephrectomy and had an uneventful recovery.

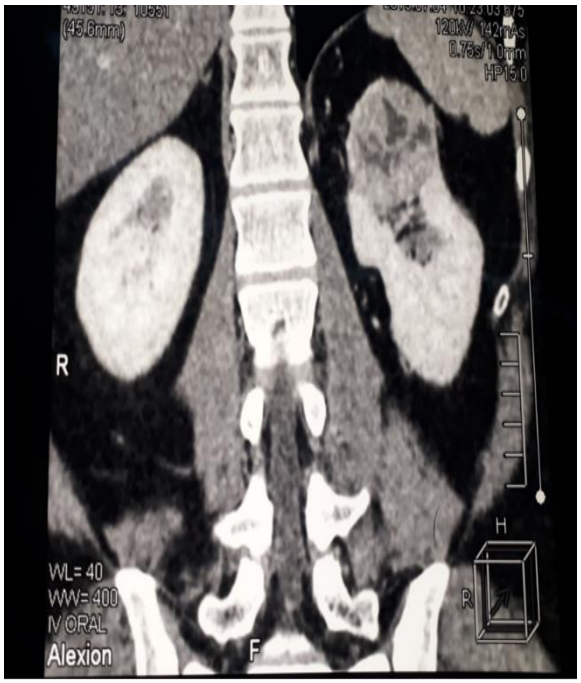


**Figure 1**. *CT Urogram image of the tumor in the upper pole of left kidney*

The macroscopy of the cut surface showed a tan-coloured, irregular and firm tumour in the upper pole of left kidney. The histological assessment showed papillae lined by polygonal cells with abundant eosinophilic granular cytoplasm and hyperchromatic nuclei (Figure 2). The microscopic features favoured a diagnosis of oncocytic variant of papillary RCC. The tumor stage was T1a and ISUP grade was 1. After three years of follow-up, he is asymptomatic with normal imaging and renal functions.

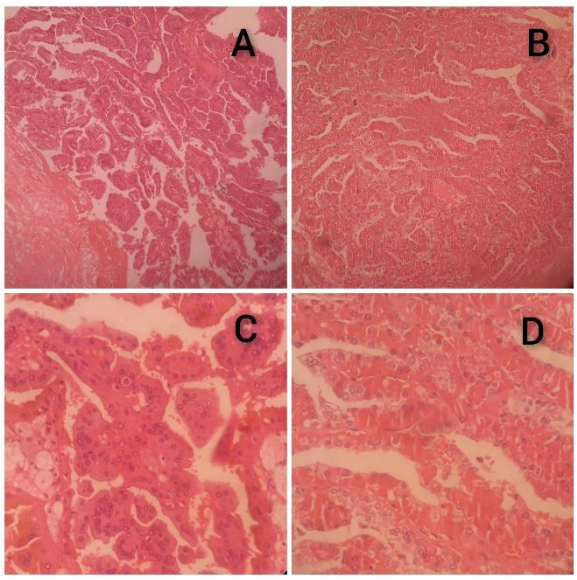


**Figure 2**. *Microscopic images of the tumor: A – papillae lined by oncocytic tumour cells (H&E stain, X 10); B – Oncocytic tumor cells with abundant eosinophilic cytoplasm (H&E stain, X 10); C – Oncocytic tumor cells with abundant cytoplasm (H&E stain, X 40); D – Oncocytic tumor cells (H&E stain, X 40)*

## Discussion

Evaluation and initial surgical management of renal masses are based on findings of contrast imaging studies without a tissue diagnosis. However, presence of histopathological features like sarcomatoid and rhabdoid differentiation may preclude nephron sparing surgery. Furthermore, prognostication and follow-up depend on the histological subtype.

A series of 34 cases of pRCC was first published in 1976 and the papillary variant of RCC was accepted as a separate entity after its inclusion in the Heidelberg classification. It has distinct features such as a higher risk of spontaneous hemorrhage, multifocality and calcification. Cytogenetic aberrations with trisomies, tetrasomies and loss of Y chromosome are frequently associated with pRCC (2).Subsequently,

pRCC was divided into two subtypes (type 1 and type 2) according to microscopic, immonotypical and genotypic features which correlate well with distinct prognostic patterns.

Recently another subtype of RCC was described in literature that has morphological and immunological profile similar to pRCC, but consisting of oncocytes. Hence it is termed as oncocytic variant of pRCC (1). Oncocytic lesions may be found in almost any organ but the common sites are thyroid (Hurthle cell carcinoma), kidney, salivary glands (Warthin's tumour) and liver (fibrolamellarcarcinoma)(3).

Microscopically oncocytes are cells with finely granular eosinophilic cytoplasm with a swollen appearance and containing an increased number of mitochondria. Oncocytic pRCCs commonly show histological features overlapping those of both type 1 (low nuclear grade and single layer arrangement) and type 2 (abundant eosinophilic cytoplasm) pRCC.

Differentiation of oncocytic pRCC from other mimicries like renal oncocytoma and typical pRCC can be done with morphological characteristics as well as the immunohistochemical profile (4). Oncocytoma of the kidney is a benign tumor with an indolent course. It is mainly a solid tumour with minimal papillary structures and contains large, round, eosinophilic cells with densely granular cytoplasm. The nuclei are round and regular with small nucleoli and no visible mitoses. Foamy macrophages and foci of necrosis are rarer in oncocytoma compared to oncocytic pRCC. Oncocytomas do not metastasise while oncocytic pRCC may develop lymph node and systemic metastases rarely (5).The rate of metastases during follow-up among reported cases of oncocytic pRCC had been low (5.5%). Rarely, kidney can be affected by numerous oncocytomas or oncocytic lesions. This is called oncocytosis or oncocytomatosis and may show clusters of oncocytic cells within interstitium and cysts lined by oncocytic cells (6).

The majority of reported cases of oncocytic pRCC shows a male preponderance and the median age is about 65 years (range: 40 – 80 years) (4, 7). This index patient was 40 years old at the time of diagnosis. It is interesting to note that average age of patients with RCC in Sri Lanka has been much lower than in the West (8).

There are no distinct imaging or macroscopic features that would suggest a diagnosis of oncocytic pRCC. The appearance of a central area in the renal lesion mimicking a cart-wheel in the CT urogram of this patient could be purely incidental (Figure 1). However, this finding is unusual as pRCC is known to show lower mean attenuation values and homogenous appearance on the corticomedullary and nephrographic phases of CT urogram. Most cases of oncocytic pRCC have been T1 stage and ISUP grade I. Rarely, cases with sarcomatoid changes and higher ISUP grades have been reported (4). Immunohistochemically oncocytic pRCC has strong, diffuse expression of racemase, vimentin, CD10, and MET, but is negative for CK7 in most cases (4). However, there is heterogeneity in the limited cases reported. The common differentials such as oncocytoma and typical pRCC can be excluded with morphological characteristics as well as the immune profile. Type 1 pRCC is often uniformly positive for Valentin, AE1/AE3 keratins, CK7, AMACR, and RCC marker. It is usually negative for CD117, kidney-specific cadherin, and parvalbumin. However, type 2 pRCC displays a variable immunoprofile.The immunoprofile of

benign oncocytoma is usually quite distinct from those of clear cell and papillary RCCs but similar to chromophobe RCC and is positive for kidney-specific cadherin, parvalbumin, CD117, epithelial membrane antigen, AE1/AE3 keratin, and CK7. It is usually negative for vimentin, carbonic anhydrase IX, and AMACR (9).

This entity of oncocytic pRCC has been recognized and discussed at the International Society of Urological Pathology (ISUP) consensus conference held in Vancouver in 2013. The majority of the pathologists attending the conference declined to classify oncocytic pRCC as a distinct group (2). This entity was further highlighted in the most recent ISUP consensus conference which suggested that reversed nuclear polarity and KRAS mutation in addition to oncoctytic cells and papillary architecture may distinguish these tumors as an emerging entity in future schemes (10). However, identifying oncocytic RCC as a distinct entity may have diagnostic, prognostic and potential therapeutic implications. Recognizing its long-term behavior may lead to more appropriate follow-up strategies. Identification of molecular patterns may help to determine the subtypes accurately as well as identifying potential targets for more accurate targeted therapy in the future. Therefore, documentation of these cases is important to determine its characteristics and behavior which may pave the way to identification of oncocytic pRCC as a distinct subtype of pRCC.

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