



## Glomeruli Sparing Pattern of Unclassified Renal Cell Carcinoma: A Rare Neoplasm

Deepa Nagarajan<sup>1\*</sup>, Mrinal Mallya<sup>2</sup> and Mita Shah<sup>3</sup>

<sup>1</sup>Pathology Department, Lilavati Hospital and Research Centre, A-791, Bandra Reclamation, Bandra west, Mumbai 400050, Maharashtra, India

<sup>2</sup>Histopathology Department, Saifee Hospital, 15/17, Maharshi Karve Marg, Charni Road, Mumbai 400004, Maharashtra, India

<sup>3</sup>Pathology Department, Bhakti Vedanta Hospital, Srishti Complex, Bhakti Vedanta Swami Marg, Mira Road (E), Thane, Maharashtra 401107, India

### ABSTRACT

Unclassified renal cell carcinoma (URCC), an aggressive form of renal cell carcinoma (RCC), represents 0.7– 5.7% of renal tumours. Glomerular sparing in renal neoplasms (GS) is defined as a unique growth pattern in which tumour cells overrun intact glomeruli.

An elderly woman presented with symptoms of left flank pain for three months along with fullness in the abdomen. On clinical and radiological examination, a renal mass was revealed and operated upon. A diagnosis of URCC with a glomerular sparing pattern was made on histopathological examination. The pathological details of this rare neoplasm are presented in this article.

**Keywords:** *Glomeruli Sparing, Unclassified Renal Cell Carcinoma, Renal Neoplasms*

### Introduction

Kidney tumours account for two percent of all human malignancies.<sup>[1]</sup> Kidney tumour was the ninth most common cancer in men and the 14th most common in women worldwide in 2012.<sup>[2]</sup>

Renal cell carcinoma are further classified into the following subtypes: clear cell renal cell carcinoma, papillary renal cell carcinoma, clear cell papillary renal cell carcinoma, chromophobe renal cell carcinoma, renal medullary carcinoma, collecting duct carcinoma, multilocular cystic renal neoplasm of low malignant potential, hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma, MiT family translocation renal cell carcinomas, succinate dehydrogenase-deficient renal cell carcinoma, mucinous tubular and spindle cell carcinoma, tubulocystic renal cell carcinoma, acquired cystic disease-associated renal cell carcinoma and unclassified renal cell carcinoma<sup>[2]</sup>

The most common adult renal neoplasm is Clear cell renal cell carcinoma<sup>[1]</sup>. Renal cell carcinoma, unclassified (URCC) represents 0.7– 5.7% of renal tumours and is an aggressive form of renal cell carcinomas (RCC). Unclassified RCCs have histological features that do not resemble those of any of the well-characterized RCC subtypes.<sup>[2,3]</sup>

Glomerular sparing (GS) in renal tumours is defined as a tumour growth pattern in which tumour cells replace most renal tubules and overrun intact glomeruli.<sup>[4]</sup>

We report a case of a renal tumour where a myriad of histological patterns was seen and which did not fit into any of the well-characterised RCC and hence reported as RCC, unclassified.

### Case Report

An elderly woman presented with symptoms of left flank pain for three months along with fullness in the abdomen. There was no history of macroscopic haematuria or fever. On examination, a large abdominal mass with fullness in the left flank and tenderness in the left renal angle was noted. Computerized tomography showed focal enlargement of the left renal inferior pole with a heterogenous wedge-shaped hypo-enhancing area showing multiple central non-enhancing necrotic foci. Perinephric fat stranding was appreciated along the lower pole. PET-CT scan revealed hypermetabolic left renal mass consistent with primary renal neoplasm with hypermetabolic left renal hilar and para-aortic adenopathy probably suggestive of nodal metastases. CT-guided left renal mass biopsy revealed high-grade carcinoma, not further specified.

Haematological and biochemical results: Haemoglobin-11.0 g/dl, WBC count:11,200 cells/Cu.mm, Platelets:2,54,000 and serum creatinine: 1.1mg/dl.

The patient underwent a left radical nephrectomy with ureterectomy and para-aortic and hilar lymph node dissection. The specimen was sent for histopathological examination. On gross examination, the kidney was enlarged and had a smooth external surface. A large

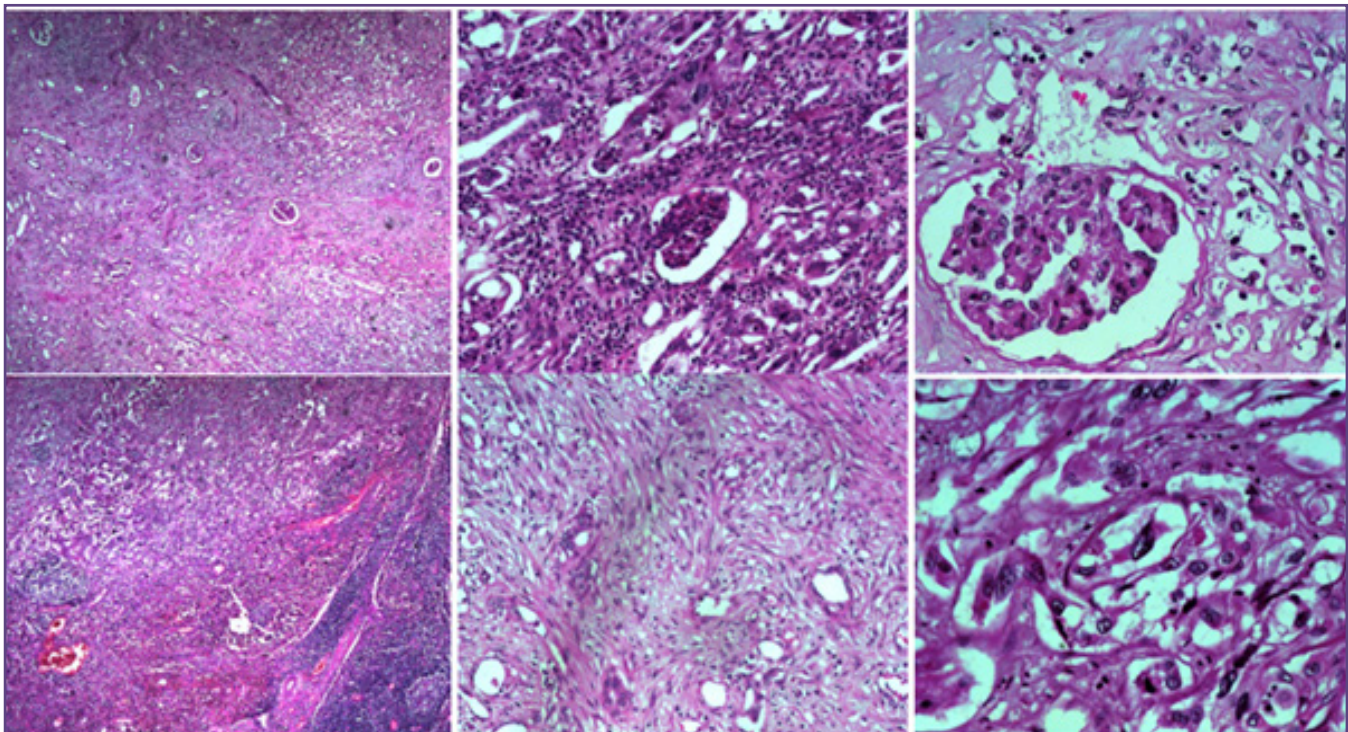


globular mass was identified, occupying almost entire kidney and measuring 8x7x6.2cm. The cut section was solid, homogenous, greyish white with focal areas of haemorrhage and necrosis. A small part of kidney at upper pole appeared to be spared. (Figure 1). Microscopic examination revealed a high -grade carcinoma. The tumour was composed of sheets, trabeculae and glands lined by atypical cells. The cells were large with clear to eosinophilic cytoplasm and irregular enlarged nucleus, few of which showed prominent nucleolus. Areas of sarcomatoid change with high grade pleomorphic nuclei and focal myxoid areas were also noted. The tumour showed a glomerulus sparing pattern (Figure 2), with involvement of stroma and tubules around the glomeruli. The calyceal system and renal sinus were infiltrated by the tumour. Three out twelve regional lymph nodes were showing metastasis with perinodal extension. On immunohistochemical analysis (IHC), tumour cell expressed pancytokeratin, EMA, vimentin, PAX8, CD10 and INI-1. They were negative for SMA, BCL2, TLE1, calponin, desmin, myogenin, ALK1, CEA and PAX2. (Figure 3).

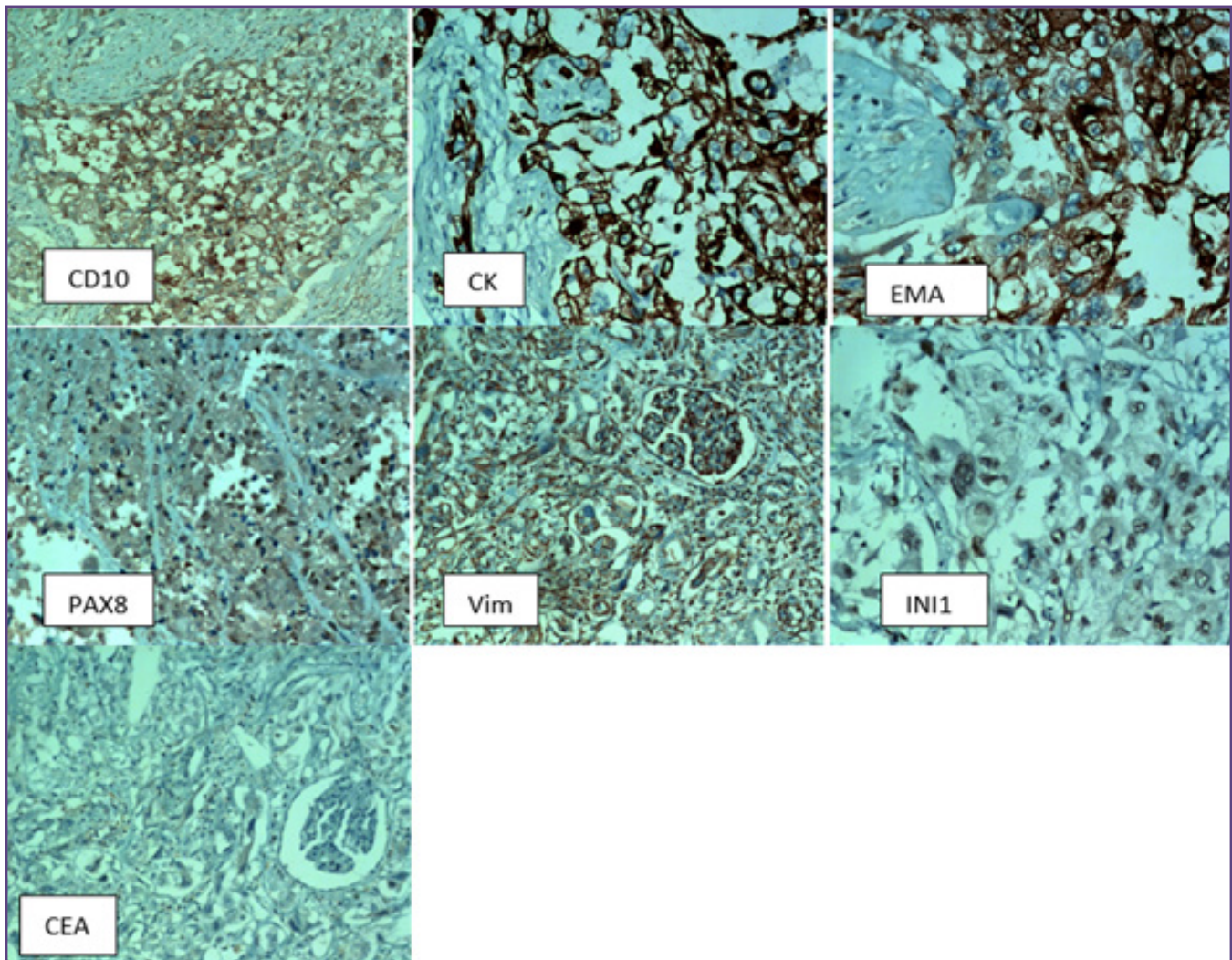
A final diagnosis of renal cell carcinoma, unclassified with glomerulus sparing pattern was arrived upon. Pathological staging of pT<sub>2a</sub> N<sub>1</sub> M<sub>x</sub> was given.



**Fig. 1: Gross photograph of left kidney showing solid white tumour involving almost entire kidney.**



**Fig. 2: Microscopic picture of glomeruli sparing pattern and sarcomatoid areas, haematoxylin and eosin (H&E). (a) H&E, (×4) glomerular sparing pattern and focal myxoid areas. (b) H&E, (×20) tumor infiltrating stroma and tubules (c) H&E, (×40) glomeruli sparing pattern. (d) H&E, (×4) different areas. (e) H&E, (x40), sarcomatoid areas. (f) H&E, (x40) pleomorphic cells with clear to eosinophilic cytoplasm.**



**Fig. 3: Immunohistochemistry markers. (x40). On IHC, tumour cells express (a) CD10 (b) CK (c) EMA, (d) PAX8, (e) vimentin, (f) tumour cells retain INI1 stain, (g) tumour cells negative for CEA.**

### Discussion

According to the 2016, WHO classification of urological tumours, the features that might prompt assignment of a tumour to this category include combination of features of more than one recognized subtype, low/ high grade unclassified oncocyctic neoplasms, mucin production, pure sarcomatoid morphology without recognizable epithelial elements, and unrecognizable cell types.<sup>[2]</sup>

At times, the sarcomatoid elements overgrow the antecedent carcinoma to the extent that it cannot be recognized; such tumours were assigned to renal cell carcinoma, unclassified.<sup>[3]</sup>

One of the unique histopathological features of kidney neoplasms is glomerular sparing (GS) pattern. GS is defined as a characteristic tumour growth pattern in which

tumour cells replace most renal tubules but overrun intact glomeruli, thus sparing them. This pattern is recognized, and images are present in the literature.<sup>[4]</sup>

These GS cases need to be recognized as they are associated with high grade, high stage, large tumour size, and worse prognosis.<sup>[4]</sup> One of the reasons for absence of haematuria could be the GS pattern of this large high-grade tumour.

The exact mechanism of glomerular sparing pattern in kidney neoplasms is still unclear. Ronny et al supported hypothesis of glomeruli being more tolerable for neoplastic stress due to rich blood supply. On the other hand, renal tubules which lack blood supply are more vulnerable for neoplastic stress. In their study, the most GS pattern was associated with high grade/fast growing neoplasm and was found at the edge of neoplasm.<sup>[4]</sup>

However, in our study the GS pattern is seen all over the tumour. Ronny et al also concluded that GS was a rare morphology associated with heterogenous malignant entities and significant morphological overlapping with no specificity for any tumour type. The primary kidney tumours with glomerular sparing pattern are rare and incidence in their study was less than four percent (7/204).<sup>[4]</sup>

In the study by A L Beltran et al of 56 U RCC cases, nuclear grade, TNM classification, tumour coagulative necrosis, tumour size, microvascular invasion and 2004 WHO histotype were independent predictors of disease-free and cancer-specific survival. Also, sarcomatoid morphology portended a dismal prognosis in their series.<sup>[5]</sup>

In our case study, tumour cells showed unusual morphology and areas of sarcomatoid change. This histologically unrecognizable high-grade tumour showed a glomerulus sparing pattern, with involvement of stroma and tubules around the glomeruli. The IHC profile has confirmed the primary renal origin of this tumour and has ruled out medullary RCC, urothelial carcinoma, Alk+ RCC, synovial sarcoma and carcinosarcoma with heterologous elements, this in concordance with published literature.<sup>[6]</sup>

## Conclusion

Careful histomorphological examination and appropriate immunohistochemistry stains are necessary for an accurate diagnosis of renal neoplasms. GS pattern if observed in the tumour should always be documented, since it is associated with high grade, high stage, large tumour size, and presumably bad prognosis.

## Acknowledgements

I would like to acknowledge the histopathology department and management of Saifee hospital, Mumbai.

## Funding

None

## Competing Interests

None

## References

1. Chander B, Preet K, Bharti R, Deb P. Renal cell carcinoma, unclassified with unique features. *J Cancer Res Ther.* 2015;11(4):1027.
2. Moch H., Humphrey PA, Ulbright TM, Reuter V. WHO Classification of Tumours of the Urinary System and Male Genital Organs (4th edition). Lyon, France: International Agency for Research on Cancer; 2016.
3. Eble J N, Sauter G, Epstein J I, Sesterhenn I A. WHO classifications of tumor. Pathology and Genetics of Tumors of the Urinary System and Male Genital Organs. Lyon, France: International Agency for Research on Cancer Press; 2004.
4. Ronny FMH, Sarungbam J, Zhong X, Yusuf Y, Yang X, Zhong M. Glomerular sparing pattern in primary kidney neoplasms: clinical, morphological and immunohistochemical study. *Am J Clin Exp Urol.* 2014;2(1):76–81.
5. Lopez-Beltran A, Kirkali Z, Montironi R, Blanca A, Algaba F, Scarpelli M, et al. Unclassified renal cell carcinoma: a report of 56 cases: UNCLASSIFIED RCC. *BJU Int.* 2012;110(6):786–93.
6. Truong LD, Shen SS. Immunohistochemical diagnosis of renal neoplasms. *Arch Pathol Lab Med.* 2011;135(1):92-109.

### \*Corresponding author:

**Dr Deepa Nagarajan**, A/2 Om Eash Kripa, Sant Janabai Rd, Vileparle east, Mumbai 400057 Maharashtra, India.

**Phone:** +91 8828689462

**Email:** renad4@gmail.com

**Date of Submission** : 24/01/2020

**Date of Final Revision** : 04/03/2021

**Date of Acceptance** : 11/03/2021

**Date of Publication** : 30/03/2021

**Financial or other Competing Interests:** None.