Histological tumour type (Required)

Reason/Evidentiary Support

Many of the various sub-types of renal epithelial neoplasia exhibit differing clinical behaviour and prognosis.[1,2,9-14] This has been confirmed in large single and multicentre studies for the main tumour sub-types. Several series have also clearly demonstrated that many of the newly described entities of renal malignancy have a prognosis that differs from that of clear cell renal cell carcinoma.[14] In addition to this protocols for the various types of adjuvant anti-angiogenic therapy relate to specific tumour sub-types.[15]

The 2013 International Society of Urological Pathology (ISUP) Vancouver Classification of adult renal tumours identified an emerging/provisional category of renal cell carcinoma (RCC).[8] While appearing distinctive, these rare tumours had not been fully characterized by morphology, immunohistochemistry and molecular studies. This category was also included in the fourth edition of the World Health Organisation (WHO) classification of renal neoplasia. In the WHO classification oncocytoid RCC post-neuroblastoma, thyroid-like follicular RCC, anaplastic lymphoma kinase (ALK) rearrangement-associated RCC and RCC with (angio) leiomyomatous stroma are included in this category. These entities should be classified under 'other' with the name specified.

Papillary RCC has traditionally been subdivided into Type 1 and Type 2.[16] Recent studies have shown these tumours to be clinically and biologically distinct. Type 1 tumours are associated with alterations in the MET pathway while type 2 tumours are associated with activation of the NRF2-ARE pathway. On the basis of molecular features type 2 tumours may be sub-divided into at least 3 subtypes.[17] Type 1 and type 2 tumours show differing immunohistochemical staining with type 1 tumours more frequently expressing cytokeratin 7 in comparison to type 2.[1,8,16,17]

Oncocytic papillary renal cell carcinoma is a category included in the fourth edition of the WHO renal tumour classification.[1] While not fully characterized, this tumour is best included in the broader papillary category.

Papillary RCC is associated with a more favourable outcome than clear cell renal cell carcinoma (ccRCC), collecting duct carcinoma and hereditary leiomyomatosis and renal cell carcinoma (HLRCC)[1,14] Papillary subtyping is also of prognostic significance with type 1 tumours having a more favourable prognosis then those with type 2 morphology.[14,16,17]

On occasion it may be difficult to accurately classify tumours with deeply eosinophilic cytoplasm on renal biopsy. Here the differential diagnosis includes oncocytoma, chromophobe renal cell carcinoma, oncocytic papillary renal cell carcinoma and post-neuroblastoma renal cell carcinoma. Immunohistochemical assessment may be helpful but due to the limited tissue available in a needle biopsy this may be inconclusive. In such instances the term oncocytic neoplasm may be used with a note emphasising that this is not a diagnostic category but a descriptor that includes both benign and malignant entities.[18,19]

The benign entities of renal neoplasia commonly encountered in renal biopsies such as oncocytoma, angiomyolipoma, papillary adenoma, metanephric adenoma and other forms of adenoma should be classified under 'other' with the diagnosis specified.

References

1. World Health Organization (WHO) Classification of tumours. Pathology and genetics of the urinary system and male genital organs. Humphrey PA, Moch H, Reuter VE, Ulbright TM, editors. Lyon, France: IARC Press. 2016

2. Amin MB, Edge SB, Greene FL, *et al, eds. (2017)* AJCC Cancer Staging Manual. 8th ed. New York*: Springer*

8. Srigley JR, Delahunt B, Eble JN, et al. The International Society of Urological Pathology (ISUP) Vancouver classification of renal neoplasia. Am J Surg Pathol 2013; 37: 1469-1489.

9. Murphy WM, Grignon DJ, Perlman EJ, editors. Tumours of the Kidney, Bladder, and Related Urinary Structures. AFIP Atlas of Tumour Pathology Series 4. American Registry of Pathology. Washington DC; 2004.

10. Kim H, Cho NH, Kim D et al. Renal cell carcinoma in South Korea: A multicenter study. Hum Pathol 2004; 35: 1556-1563.

11. Ljungberg B, Alamdri FI, Stenling R et al. Prognostic significance of the Heidelberg Classification of renal cell carcinoma. Eur Urol 1999; 36: 565-569.

12. Moch H, Grasser T, Amin MB. Prognostic utility of the recently recommended histologic classification and revised TNM staging system of renal cell carcinoma. A Swiss experience with 588 tumours. Cancer 2000;89:604-614.

13. Srigley JR, Delahunt B. Uncommon and recently described renal carcinomas. Modern Pathology 2009;22:S2-S23.

14. Delahunt B, Cheville JC, Martignoni G, et al. The International Society of Urological Pathology (ISUP) Grading System for Renal Cell Carcinoma and Other Prognostic Parameters. 2013; 37:1490-1504.

15. O'Brien MF, Russo P, Motzer RJ. Sunitinib therapy in renal cell carcinoma. BJU International 2008;101:1339-1342.

16. Delahunt B, Eble JN, McCredie MR, et al. Morphologic typing of papillary renal cell carcinoma: comparison of growth kinetics and patient survival in 66 cases. Hum Pathol 2002; 32: 590-595.

17. The Cancer Genome Atlas Research Network. Comprehensive molecular characterization of papillary renal-cell carcinoma. NEJM 2015; 1-10. November 4, 2015DOI: 10.1056/NEJMoa1505917

18. Delahunt B, Samaratunga H, Martignoni G, Srigley JR, Evans AJ, Brunelli M. Percutaneous renal tumour biopsy. Histopathology 2014; 65: 295-308.

19. Evans AJ, Delahunt B, Srigley JR. Issues and challenges associated with classifying neoplasms in percutaneous needle biopsies of incidentally found small renal masses. Semin diagn Pathol 2015; 32: 184-195.