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Should Cytologists Diagnose Clear Cell Papillary Renal Cell Carcinoma on Cytologic Material?

Andrew A. Renshaw, MD 

In this issue of *Cancer Cytopathology*, Griffin and Lin¹ describe the cytologic features of a large series of clear cell papillary renal cell carcinomas (CCPRCCs) on fine needle aspiration and core needle biopsy material. While at least some of the cytologic features have been noted previously,^{2,3} this is the largest series to date, and it provides a sense of both how frequent and how accurate these cytologic features can be at distinguishing CCPRCC from other tumors. While the authors define criteria for distinguishing CCPRCC from both clear cell renal cell carcinoma (CCRCC) and papillary renal cell carcinoma—and while both sets of criteria are useful—in our experience, papillary carcinomas are usually much easier to distinguish based on the relative cellularity of the specimen, the more rigid architecture of the papillae, the larger size of the papillae, and the slightly more abundant and slightly more granular nature of the cytoplasm. In contrast, paucicellular specimens from CCRCC are not at all uncommon due to their extensive fibrous stroma, and these may be extremely difficult to distinguish from CCPRCC. For the patient, the identification of this type of renal cell carcinoma can be extremely important, since clinical progression has not yet been identified in any patient with this lesion.⁴ These data also expand the list of benign renal lesions (oncocytoma, cystic nephroma, angiomyolipoma, and papillary adenoma [given the appropriate size]) that in at least some cases can be recognized on cytologic material alone. In many cases, these lesions can be confirmed with immunohistochemistry (IHC) performed on core needle biopsy, though large core needle biopsy of renal lesions has its drawbacks (most notably bleeding and needle track seeding⁵).

How, then, should cytologists use this information in daily practice? Clinicians are always hoping that cytologists will be willing to make a definitive benign diagnosis—not only because it is better for their patient, but also because it gives them more options for managing the patient. However, CCPRCC and CCRCC can vary considerably from case to case and from region to region, and tumors with overlapping features (including CCRCC with the “picket fence” arrangement of nuclei) are well described.^{6,7} In addition, the pathology community has been cautious about making a definitive diagnosis of a benign renal tumor on limited material; many genitourinary pathology specialists refuse to make a definitive diagnosis of oncocytoma on large core needle biopsy.⁸ However, there is an important difference between making a diagnosis of oncocytoma and CCPRCC: unlike oncocytoma, there are highly specific immunohistochemical markers to distinguish CCPRCC from its most common mimics. So, if one can perform IHC, one should be making a definitive diagnosis of CCPRCC on cytologic material, and the criteria defined here are an excellent way to determine whether these markers should be obtained.

Nevertheless, there are situations where IHC is not available, including rapid evaluation and cases where the risk of performing a core biopsy are too high. In these settings, being able to provide a differential diagnosis that includes CCPRCC may also be of value. Just as a diagnosis of “oncocytic lesion, oncocytoma versus chromophobe renal cell carcinoma” in the appropriate setting may be sufficient to direct patient management,

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a diagnosis of “low-grade renal cell carcinoma, clear cell papillary versus clear cell renal cell carcinoma” may also be enough to direct patient management in the appropriate setting. The criteria outlined by Griffin and Lin³ provide an excellent way to reach this differential diagnosis and should be part of the armamentarium of every cytologist who interprets fine needle aspirations of renal masses.

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