Diagnostic Biomarkers in Eosinophilic Renal Neoplasms

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KEYWORDS

• Renal cell carcinoma • Biopsy • Eosinophilic • Biomarkers

KEY POINTS

- CK7, S100A1, vimentin/c-KIT, and Claudin 7/8 can help to differentiate renal oncocytoma and chromophobe renal cell carcinoma (RCC).
- CAIX, CK7, racemase, CD117, and CD10 can help to differentiate oncocytoma, chromophobe RCC, clear cell RCC, and papillary RCC.
- "High-grade" nuclear features are seen in renal neoplasms with wide-ranging clinical behavior. Immunomarkers are useful in differentiating these entities.
- Unique markers and molecular tests are helpful to diagnose certain neoplasms, such as translocation-associated RCC and hereditary leiomyomatosis-related RCC.

INTRODUCTION

Immunohistochemical biomarkers are useful when diagnosing renal cell carcinomas (RCC) with less than straightforward morphology or for confirming the presence of metastatic carcinoma of renal origin.[1] They have been proven to increase the accuracy of diagnosis in limited biopsy material.[2] Incidental small renal masses identified on imaging are increasingly investigated via needle core or fine needle aspiration biopsies with limited material provided for rendering a diagnosis. These lesions are amenable to treatment by noninvasive techniques, such as ablation, instead of resection. Consequently, the readily available immunohistochemical stains take on a more significant role in current practice.

RCC with distinct morphologies do not pose much difficulty in daily diagnostic practice. Moreover, many of these have well-described immunoprofiles (**Fig. 1**, **Table 1**). The challenge lies in lesions with a prominent eosinophilic or oncocytic cell presence and where there is morphologic overlap between the well-known eosinophilic neoplasms. Additionally, with only limited biopsy material, the onus is on the pathologist to rule out an eosinophilic neoplasm with potentially aggressive behavior without the reassurance of subsequent confirmation by nephrectomy. The impact on patient care of missing such a diagnosis is not inconsequential. As such, we review the range of known benign and aggressive eosinophilic renal neoplasms and their immunoprofiles to elucidate a

Conflicts of Interest: None.

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Urol Clin N Am 43 (2016) 87–94
http://dx.doi.org/10.1016/j.ucl.2015.08.008

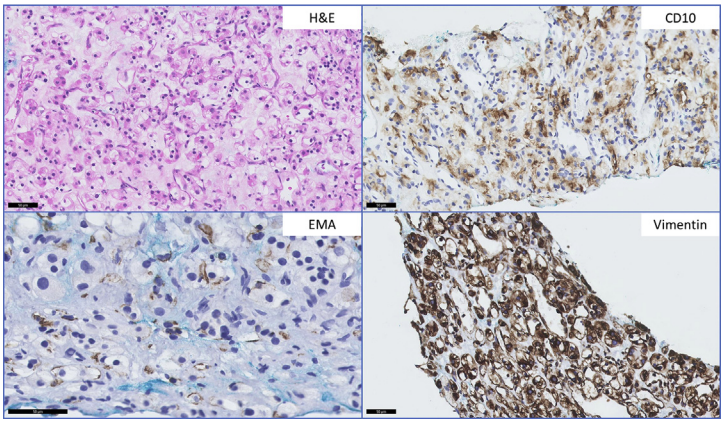

Fig. 1. A clear cell renal carcinoma with low-grade cytologic features and eosinophilic cytoplasm, showing CD10, EMA (patchy), and vimentin positivity.

useful panel of stains that could be used in this scenario.

Renal Oncocytoma Versus Chromophobe Renal Cell Carcinoma

The most commonly encountered diagnostic dilemma of a low-grade nonpapillary oncocytic renal neoplasm is between renal oncocytoma and a chromophobe RCC (ChRCC), eosinophilic type.[3] Morphologic heterogeneity can be seen in ChRCC with foci exhibiting features virtually indistinguishable from oncocytoma. Although the majority of ChRCC are regarded to have favorable prognosis, a small subset of patients show disease progression.[4] Many well-established and novel biomarkers have been tested for use in this context. However, few have been validated in more than 1 series. CK7 positivity in ChRCC is well-described and considered to be useful in differentiating ChRCC from benign renal oncocytoma, although some studies have shown similar expression in both entities[5] (**Fig. 2**). Liu and colleagues,[6] in determining a practical panel to distinguish clear cell RCC (CCRCC), ChRCC, and oncocytoma, confirmed the usefulness of CK7

Table 1
Helpful markers in the differential diagnosis of eosinophilic renal tumors

Renal Tumors	Positive Markers	Negative Markers
Clear cell RCC	Vimentin, keratin, EMA, CD10, RCCm, Pax2/8, CAIX	CK7, ksp-cadherin, parvalbumin
Papillary RCC	Keratin, CK7, AMACR, RCCm	c-KIT/CD117, ksp-cadherin, parvalbumin, WT-1
Chromophobe RCC	e-Cadherin, ksp-cadherin, c-KIT/CD117, EMA, CK, CK7	Vimentin, CAIX, AMACR
Oncocytoma	ksp-Cadherin, c-kit/CD117, parvalbumin, S100A1	CK7, moc31, EP-CAM
Translocation RCC	TFE3/TFEB, CD10, RCCm	CK
Collecting duct RCC	EMA, p63, CK7, HMWCK, Pax2/8	CD10, RCCm, CK20
Angiomyolipoma	HMB45, Melan-A, SMA	CK, CD10, RCCm, Pax2/8
Tumors with papillary architecture		
Papillary RCC	Type 1: CK7	CK20, 34BE12, ULEX-1, Type2: CK7
Collecting duct carcinoma	CK7, CK20(focal+), 34BE12, ULEX-1	CK20
Urothelial carcinoma	CK7, CK20, 34BE12, ULEX-1	—

Abbreviation: RCC, renal cell carcinoma.