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Original contribution

Clear cell papillary renal cell carcinoma is the fourth most common histologic type of renal cell carcinoma in 290 consecutive nephrectomies for renal cell carcinoma☆

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Summary Clear cell papillary renal cell carcinoma (CCP-RCC) has recently been recognized as a distinct subtype of renal cell carcinoma (RCC) due to its unique morphologic, immunohistochemical, and genetic features and indolent clinical behavior. However, the incidence of this tumor in a nephrectomy series for renal mass has not been fully investigated. Twelve cases of CCP-RCC were identified from a total of 290 consecutive partial (n = 137) or radical nephrectomies (n = 153) for RCC from 2010 to 2012 in our hospital. In this series, CCP-RCC was the fourth most common (4.1%) kidney tumor following clear cell (conventional) (70%), papillary (16.6%), and chromophobe (5.9%) RCCs. The average age of the CCP-RCC patients was 58.2 years (range, 18-81 years), with an equal sex distribution. Four cases (33.3%) were associated with end-stage renal disease. Of the 12 CCP-RCCs, 9 presented as solitary tumors; 2 coexisted with clear cell RCC; and 1 with papillary RCC. The average size of tumors was 2.5 cm (range, 0.8-6.0 cm). All tumors were pT1 (10 pT1a and 2 pT1b). Two cases were initially misclassified as clear cell RCC. Strong positive cytokeratin 7 stain and negative stains with α-methylacyl-CoA racemase and RCC marker differentiate CCP-RCC from low-grade clear cell RCC with similar histologic features. We conclude that CCP-RCC is a common renal neoplastic entity, representing the fourth most common (4.1%) RCC. It can be easily misclassified due to its overlapping features with low-grade clear cell RCC. In equivocal cases, immunohistochemical stains with a small panel of markers (cytokeratin 7, α-methylacyl-CoA racemase, RCC marker, or CD10) are warranted in making the correct histologic classification.

1. Introduction

Clear cell papillary renal cell carcinoma (CCP-RCC) is a distinctive histologic entity of renal tumor [1-11], which was initially recognized as a benign angioadenomatous tumor [2], and later shown to be associated with end-stage

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renal disease (ESRD) [1]. With the increasing awareness of this entity, published studies of CCP-RCC have demonstrated a better clinical depiction of CCP-RCC. Recent findings indicate that CCP-RCC also occurs in patients without ESRD [3,4,6,7,10,11], often presents as a solitary mass, and may coexist with other renal tumors. Patients with CCP-RCC have very good prognosis, and no tumors of the reported cases have metastasized. It seems that CCP-RCC is relatively common; however, the true incidence of this entity has not been fully investigated.

The histologic features of CCP-RCC [3,5,9] are not exclusive [11], as they may overlap with other renal tumors, especially those that contain clear cells [12]. Therefore, in this study, we report the incidence of CCP-RCC in a consecutive nephrectomy series for renal cell carcinoma (RCC) at our institution, emphasize the overlapping histologic features of CCP-RCC with other clear cell–containing RCCs, and review its immunohistochemical expression for correct classification.

2. Materials and methods

2.1. Cases

We undertook a systematic review of all RCCs with a total of 290 patients who underwent partial (n = 137) or radical (n = 153) nephrectomies from 2010 to 2011 at Houston Methodist Hospital in Houston, TX. All cases with a diagnosis of CCP-RCC as well as those cases with features that resemble CCP-RCC were retrieved. Twelve CCP-RCC cases were identified. Four cases of clear cell RCC (CC-RCC) with features of CCP-RCC were also collected. All slides from each case were evaluated by 2 pathologists (S. Z. and S. S.). Clinicopathologic data of these 12 CCP-RCCs were reviewed.

2.2. Immunohistochemistry

Immunohistochemical studies were conducted with the following panel of markers: cytokeratin 7 (CK7), RCC marker (RCCm), and α-methylacyl-CoA racemase (AMACR). The staining was performed using automatic stainers from Ventana (Ventana Medical Systems, Tucson, AZ) with an enzyme-conjugated polymer complex. The dilution and sources of antibodies are CK7 (1:50; Dako, Carpinteria, CA), CD10 (1:10; Vector, Burlingame, CA), AMACR (1:100; Dako), RCCm (1:10; Novo Castra, Newcastle upon Tyne, UK), and transcription factor E3 (TFE3) (1:100; Cell Marque, Rocklin, CA).

3. Results

3.1. Incidence of CCP-RCC

Among the 290 RCCs, 12 cases (4.1%) of CCP-RCC were identified. Clear cell (conventional), papillary, chromophobe, and unclassified RCC accounted for 70%, 16.6%, 5.9%, and 1.7%, respectively. The remaining 5 tumors (1.7%) were tubulocystic RCC, mucinous tubular and spindle cell RCC, Xp11 translocation RCC, and 2 ESRD-associated RCCs.

3.2. Clinical and pathologic characteristics of the CCP-RCC patients

The clinical and pathologic characteristics of the CCP-RCC patients can be found in Table 1. The patients included 6 men and 6 women with a mean age of 58.2 years (range, 18-81 years). Clinically, 4 cases (33.3%) were associated with ESRD, and 1 patient with von Hippel-Lindau syndrome (VHL) was diagnosed with multiple CC-RCCs. The tumors

Table 1 Clinicopathologic characteristics of the 12 CCP-RCC patients

Case no.	Sex	Age (y)	Clinical presentation	Tumor size (cm)	Stage	Follow-up (mo)	Disease progression	Operation	Comments
1	M	66	No symptom	0.8	T1a	6	No	RN	Coexist with papillary RCC, Type 1
2	M	62	Right flank pain	2	T1a	9	No	PN	Initial Dx with CC-RCC
3	F	74	No symptom	4.5	T1b	10	No	RN	Coexist with CC-RCC
4	F	68	No symptom	2.5	T1a	11	No	PN	
5	M	69	No symptom	1.6	T1a	15	No	PN	
6	F	36	Abdominal pain	2	T1a	17	No	PN	
7	F	58	No symptom	2.7	T1a	22	No	PN	
8	F	63	ESRD	1.3	T1a	22	No	RN	
9	F	81	ESRD	6	T1b	24	No	RN	Initial Dx with CC-RCC
10	M	18	VHL	3	T1a	27	No	PN	Coexist with multiple CC-RCC
11	M	58	ESRD	2.5	T1a	30	No	RN	
12	M	45	ESRD	1.2	T1a	35	No	RN	

Abbreviations: M, male; F, female; ESRD, end-stage renal disease; VHL, von Hippel-Landau syndrome; RN, radical nephrectomy; PN, partial nephrectomy; Dx, diagnosis.