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Original Article

Clear cell papillary renal cell carcinoma − An indolent subtype of renal tumor

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Abstract

Background: Clear cell papillary renal cell carcinoma (CCPRCC) is a new but rare tumor entity as listed in the World Health Organization 2016 renal tumor classification. Around 360 cases have been reported in the English literature to date, and only one tumor with sarcomatoid change was reported to develop distant metastasis. In the present study, we aim to review the clinical course and analyze the treatment outcome of CCPRCC in our institution.

Methods: We retrospectively collected patients diagnosed with CCPRCC between January 2008 and September 2016 in our institute. The clinical features, pathology slides, and clinical outcomes were reviewed.

Results: Twenty-five patients were collected during the study period, with a mean age at diagnosis of 62.8 years (range 35−85 years). Three patients developed the tumor in their native kidney following a kidney transplant, and three patients were diagnosed by needle biopsy before cryoablation therapy due to high surgical risk. The mean follow-up time was 49.7 months (range 12−119 months). During the follow-up period, all patients were alive without local recurrence or distant metastasis. All tumor specimens in our series expressed cytokeratin 7 (CK7) diffusely in immunohistochemistry staining. One patient was diagnosed with pT3a cN0M1, Fuhrman grade 3 CCPRCC with renal vein invasion and lung metastasis in 2010 on the basis of the histologic pattern and immunoreactivity for CK7. The clinical course was not compatible with any of the reported cases in the literature, so the kidney specimen was re-examined using whole-exome sequencing. The diagnosis was then revised to clear cell renal cell carcinoma.

Conclusion: Our series confirmed that CCPRCC has an indolent clinical behavior. When the diagnosis is made in a high-grade renal tumor, it should be carefully re-confirmed using cytogenetic or genomic methods.

Keywords: Clear cell papillary renal cell carcinoma; Cytokeratin 7 immunoreactivity; Whole-exome sequencing

1. Introduction

Clear cell papillary renal cell carcinoma (CCPRCC) is a new entity as listed in the World Health Organization 2016 renal tumor classification.[1] It was first reported in patients with end-stage renal disease (ESRD) in 2006[2], and was named "clear-cell papillary renal cell carcinoma of end-stage kidneys" according to its

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pathological features and the patient's renal disease background. However, the majority of cases subsequently reported were in normal kidneys. These tumors have distinct pathological immunohistochemical staining features. Morphologically, CCPRCC exhibits a clear cytoplasm with variable tubular/acinar, papillary, and cystic architecture, and the tumors show strong positive staining for cytokeratin 7 (CK7).[3−8]

The published literature to date indicates that CCPRCC has an indolent clinical behavior with low-grade cytology, no lymph node metastasis, no local recurrence, and no distant metastasis, except for one case reported by Diolombi et al. who was diagnosed with sarcomatoid pT3 CCPRCC with skeletal and lung metastasis in 2015.[9]

In this study, we aim to review the clinical course and analyze the treatment outcome of CCPRCC patients in our hospital.

2. Methods

The first case of CCPRCC in our hospital was diagnosed in 2008. From January 2008 to December 2016, 765 patients were newly diagnosed with primary renal cell carcinoma (RCC), of whom 25 (3.3%) had CCPRCC. The medical charts, imaging studies, and pathology slides were retrospectively reviewed under patient agreement. All of the patients were regularly followed for at least 12 months. Among them, 22 patients received nephrectomy (including: radical nephrectomy in five patients and partial nephrectomy in 17 patients), and the other three patients were diagnosed by biopsy before cryoablation therapy. All of the pathology slides were reviewed by the same pathologist (C.C. Pan). Tumor size was evaluated by assessing the tumor diameter of the nephrectomy specimen or by computed tomography (CT) in the patient who received cryoablation therapy. All tumors were staged according to the American Joint Committee on Cancer (AJCC) Staging Manual 8th edition.

3. Results

3.1. Clinical findings and outcomes

The clinical characteristics of our patients with CCPRCC are summarized in Table 1. There were 11 men and 14 women, with a median age at diagnosis of 62.8 years (range 35−85 years). The mean tumor size was 2.6 cm (range 0.5−6.2 cm). Three patients received cryotherapy after a biopsy confirmed CCPRCC due to a poor general condition. In the other 22 patients who received surgical resection, four had end-stage

Table 1
Patient characteristics.

Case	Age (year)	Gender (Male/Female)	Operation	If ESRD status at diagnosis (Yes/No)	Tumor laterality	Tumor number	Size (cm)	Fuhrman grade	Stage	Follow-up time	Other tumor in the resected kidney
1	39	F	ORN, bilateral	LDKT[b]	Bilateral	3[a]	2	2	pT1a	119m	
2	67	F	RAPN	No	Left	1	3.1	2	pT1a	76m	
3	35	M	OPN	No	Right	1	5	2	pT1b	76m	
4	60	F	LRN	Yes	Right	1	0.6	2	pT1a	74m	ACKD-RCC
5	68	F	LPN	No	Right	1	2.1	2	pT1a	70m	Renomedullary interstitial cell tumor
6	71	M	RAPN	No	Right	1	2.8	2	pT1a	67m	
7	61	M	RAPN	No	Left	1	1.2	2	pT1a	62m	
8	56	F	ORN, bilateral	DDKT[c]	Right	1	3.3	2	pT1a	57m	
9	60	F	RAPN	No	Left	1	2.4	2	pT1a	56m	
10	61	M	RAPN	No	Right	1	1.5	2	pT1a	53m	ccRCC
11	72	M	OPN	No	Right	1	1.1	2	pT1a	52m	Papillary adenoma
12	35	F	OPN	No	Left	1	3.5	2	pT1a	51m	
13	67	M	ORN, bilateral	LDKT[d]	Right	1	1.5	2	pT1a	47m	
14	77	F	Bx + cryo	No	Left	1	3.7	2	cT1a	64m	
15	42	F	OPN	No	Right	1	2.3	3	pT1a	32m	
16	57	F	OPN	No	Left	1	1.8	2	pT1a	24m	
17	72	M	RAPN	No	Left	1	3.5	2	pT1a	44m	
18	68	M	Bx + cryo	No	Left	1	2.2	2	cT1a	42m	
19	51	M	RARN	Yes	Left	2	0.5	2	pT1a	32m	ccRCC
20	75	F	RAPN	No	Left	1	6.2	2	pT1b	32m	
21	84	F	Bx + cryo	No	Left	1	2.8	2	cT1a	31m	
22	64	M	RAPN	No	Right	1	2.1	2	pT1a	24m	
23	63	M	OPN	No	Right	1	3.1	2	pT1a	23m	
24	85	F	OPN	No	Right	1	1.5	2	pT1a	22m	
25	81	F	OPN	No	Left	1	6	2	pT1b	12m	

ESRD = end stage renal disease; ACKD-RCC = acquired cystic kidney disease-associated renal cell carcinoma; ORN = open radical nephrectomy; OPN = open partial nephrectomy; RAPN = robot-assisted partial nephrectomy; Bx + cryo = biopsy then cryoablation; LDKT = living donor kidney transplant; DDKT = deceased donor kidney transplant.

[a] One tumor (1.2 cm) was at left kidney; Two tumors (2 cm, 1.5 cm) were at right kidney. The above three tumors were all CCPRCCs.

[b] Case 1: diagnosed 29 months after living donor kidney transplant. The graft kidney function was normal.

[c] Case 8: diagnosed 55 months after deceased donor kidney transplant. The graft kidney function was normal.

[d] Case 13: diagnosed 30 months after living donor kidney transplant. The graft kidney function was normal.

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