Original Study

Multilocular Cystic Renal Cell Neoplasm of Low Malignant Potential: A Series of 76 Cases

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Abstract

Multilocular cystic renal cell carcinoma (MCRCC) is a rare and distinct subtype of clear cell renal cell carcinoma (RCC). The incidence of MCRCC in patients with RCC is low. MCRCC has distinct pathologic features, and its nuclear grade is unrelated to the tumor size and TNM stage. Thus, the follow-up interval after surgery can be longer to minimize unnecessary examinations.

Introduction: Multilocular cystic clear cell renal cell neoplasm of low malignant potential or multilocular cystic renal cell carcinoma (MCRCC) is a rare distinct subtype of clear cell renal cell carcinoma (RCC). No large series of cases have been reported to date. The present study aimed to characterize the clinical and pathologic features of MCRCC. **Patients and Methods:** From January 2006 to December 2014, 76 cases were identified as MCRCC among 4345 patients with RCC at our institution. Their clinical and characteristics, surgical management, pathologic features, and outcomes were retrospectively reviewed. **Results:** The incidence of MCRCC in our patients with RCC was 1.7%. The mean age at diagnosis was 46.7 ± 10.5 years (range, 18 to 80 years). Most cases showed no symptoms. Nuclear grade was unrelated to the tumor size ($P = .112$) and TNM stage ($P = .451$). Of these 76 patients, 66 (86.8%) were followed up for a median of 52 months, and no tumor recurrence or metastasis was found. **Conclusion:** The incidence of MCRCC in patients with RCC is low. The nuclear grade of MCRCC cases was unrelated to the tumor size and TNM stage, suggesting that the current stage criteria might not suitable for this lesion. Patients with MCRCC have an excellent prognosis; thus, the follow-up interval after surgery can be longer to minimize unnecessary examinations.

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Introduction

Multilocular cystic renal cell carcinoma (MCRCC), also known as multilocular clear cell renal cell carcinoma or multicystic clear cell carcinoma, is a rare type of renal cell carcinoma (RCC) with a relatively better outcome.[1] In the 2004 World Health Organization (WHO) classification of kidney tumors, MCRCC was classified as a distinct subtype of clear cell RCC and defined as a tumor composed of numerous cysts, the septa between cysts contain groups of clear cells indistinguishable from grade 1 clear cell carcinoma.[2] The diagnostic criteria for MCRCC are relatively strict, limited to RCCs with a malignant clear cell lining and small collections of cells without formation of a malignant and expansive nodule. Histologic examination of MCRCC will reveal cysts lined by occasionally flattened cuboidal clear cells and septa containing aggregates of epithelial cells with clear cytoplasm.[2] Multiple reports of > 200 patients with follow-up periods of > 5 years concluded that no recurrence or metastasis developed in patients with MCRCC.[3] Owing to the consistently reported indolent behavior of MCRCC, this tumor has been designated by a new term of *multilocular cystic clear cell renal cell neoplasm of low malignant potential* at the 2012 International Society of Urological Pathology (ISUP) consensus meeting on adult renal neoplasia. Cells displaying nuclear grade 2 are also acceptable in the diagnosis of MCRCC.[4]

As a rare subtype of clear cell RCC, MCRCC has usually been reported in published studies as a series of several cases. The real incidence of MCRCC diagnosed using the new diagnostic criteria is still unclear, and whether MCRCC should be further classified by the TNM stage remains unsettled. In the present study, we report the clinical and pathologic features of 76 MCRCC cases diagnosed using the 2004 WHO diagnostic criteria in our institute to increase our understanding of MCRCC. To our knowledge, the

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present study represents the largest series of MCRCC cases from a single center.

Patients and Methods

From January 2006 to December 2014, 4345 patients were pathologically diagnosed as having RCC in our institute. All cystic RCCs in the pathologic files of surgical samples were reviewed, and 76 cases were identified as MCRCC in accordance with the 2004 WHO diagnostic criteria (nuclear grade 2 was accepted based on the suggestion from the ISUP). Their clinical and radiographic characteristics, surgical management, pathologic features, and outcomes were retrospectively reviewed. An analysis of the patient data was approved by the Medical Ethics Committee of Peking University First Hospital. All the patients provided written informed consent.

Before surgery, the patients underwent abdominal ultrasonography, computed tomography (CT), and/or magnetic resonance imaging (MRI) for the evaluation of bilateral kidneys and overall status. The surgical samples were reassessed and confirmed by 2 urologic pathologists, including 1 pathologist with extensive expertise in urologic pathology. A third specialist was consulted when the 2 pathologists disagreed regarding the pathologic diagnosis. The nuclear grade was determined using the Fuhrman nuclear grading system,[5] and the tumor stage was determined according to the 2010 TNM classification of the American Joint Committee on Cancer. The tumor size was expressed as the longest diameter. Using the largest diameter, the tumors were stratified into 4 groups: $\leq$ 4.0 cm, 4.1 to 7 cm, 7.1 to 10 cm, and $>$ 10 cm. Follow-up examinations of the patients were performed every 3 to 6 months, including physical examination, routine laboratory evaluation, and imaging studies (abdominal ultrasonography, CT/MRI scan, or chest radiography). The data were analyzed using Student's t test or χ^2 test. Spearman's correlation analysis was performed to evaluate the association between nuclear grade and tumor size/TNM stage. Statistical analysis was performed using Statistics SPSS, version 19.0, software, with $P < .05$ considered statistically significant.

Results

In the present study, 76 MCRCC cases were identified, for an incidence of 1.7% (76 of 4345) in our patients with RCC (Table 1). The mean age at diagnosis was 46.7 $\pm$ 10.5 years (range, 18-80 years). Of the 76 patients, 48 were men, with a mean age of 47.0 $\pm$ 8.9 years (range, 30-72 years), and 28 were women, with a mean age of 46.1 $\pm$ 12.9 years (range, 18-80 years), with no significant difference in age between the men and women ($P = .483$). In contrast, the average age of the 4345 patients with RCC was 54.3 $\pm$ 7.0 years, older than the age of the patients with MCRCC ($P < .01$). The male-to-female ratio for the patients with MCRCC and RCC was 1.7:1 and 2.3:1, respectively ($P = .104$).

Before surgery, none of the 76 patients had metastatic foci at diagnosis, and none had presented with the classic triad of RCC (palpable mass, flank pain, and painless gross hematuria). Of the 76 patients, 58 asymptomatic patients (76.3%) were detected by regular physical examinations, 8 (10.5%) because of flank pain, and 10 because of abdominal pain, hematuria, and/or hypertension. One patient was misdiagnosed as having a simple renal cyst, and the tumor in 1 case was found during routine examinations before rectal cancer surgery.

Table 1 Clinical Features of 76 Patients With Multilocular Cystic Renal Cell Carcinoma

Feature	n (%)
Age at diagnosis (years)	
Mean	46.7
Range	18-80
Gender	
Male	48 (63.2)
Female	28 (36.8)
Symptoms	
None	58 (76.3)
Flank pain	8 (10.5)
Abdominal pain	4 (5.3)
Hematuria	4 (5.3)
Hypertension	3 (3.9)
Treatment	
Open radical nephrectomy	18 (23.7)
Open partial nephrectomy	22 (28.9)
Laparoscopic radical nephrectomy	18 (23.7)
Laparoscopic partial nephrectomy	18 (23.7)
Side	
Left	36 (47.4)
Right	40 (52.6)
Tumor size[a] (cm)	
Mean	3.9
Range	0.6-15
Fuhrman nuclear grade	
I	65 (85.5)
I-II	5 (6.6)
II	6 (7.9)
TNM stage	
T1aN0M0	56 (73.7)
T1bN0M0	13 (17.1)
T2aN0M0	5 (6.6)
T2bN0M0	1 (1.3)
T3aN0M0	1 (1.3)

[a]Measured by longest diameter.

Most tumors were solitary and unilateral, except for in 5 patients (Table 2), 3 of whom had multiple tumors in a unilateral kidney, including 1 patient genetically diagnosed with von Hippel-Lindau syndrome, and 2 had multiple tumors in bilateral kidney. Radical nephrectomy was performed in 36 cases (open surgery in 18 and laparoscopically in 18) and nephron-sparing nephrectomy in 40 cases (open surgery in 22 and laparoscopically in 18).

The tumors were located in the left kidney in 36 patients (47.4%) and in the right kidney in 40 patients (52.6%). The mean tumor size was 3.9 $\pm$ 2.3 cm (range, 0.6-15 cm). The TNM stage and Fuhrman grade are listed in Table 1. The nuclear grade was unrelated to the tumor size ($P = .112$) and TNM stage ($P = .451$).