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Adult renal cell carcinoma with rhabdoid differentiation: incidence and clinicopathologic features in Chinese patients

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ABSTRACT

Renal cell carcinoma (RCC) with rhabdoid differentiation is a recently described variant of RCC, which has seldom been reported in China. This form of differentiation has been generally associated with a poor prognosis and is often present in tumors with a poorly differentiated morphology. The development of a rhabdoid morphology appears to represent a common dedifferentiation pathway for renal parenchymal malignancies. The aim of this study is to evaluate the incidence and clinicopathologic features of RCC rhabdoid differentiation in Chinese adult patients and to further investigate its origin. We reviewed 723 cases of RCC obtained between January 2012 and March 2014 in Peking University First Hospital. From these cases, 10 (1.4%) were found to have areas of classic rhabdoid morphology. Immunohistochemistry for vimentin, cytokeratin (CK) (pan-cytokeratin (AE1/AE3), CK20, CK5/6, CK7, and CK8/18), RCC, CD10, Pax-2, Pax-8, CD117, desmin, muscle-specific actin, CD68, p53, and Ki-67 was performed in each case using the labeled streptavidin-biotin method. Rhabdoid differentiation was identified in association with clear cell RCC, papillary RCC (II type), and sarcomatoid RCC. We compared the morphologic and immunohistochemical features between rhabdoid and nonrhabdoid components. In our cases, rhabdoid differentiation was characterized by the presence of cohesive large epithelioid cells with abundant pink cytoplasm and central eosinophilic intracytoplasmic inclusions and 1 or more large, oval, eccentric, or irregular nuclei containing prominent nucleoli. Most of the rhabdoid areas showed a solid growth pattern. In our series, RCC with rhabdoid differentiation had an aggressive biological behavior, and rhabdoid components were most likely associated with high-grade tumors of advanced stage. In all cases, the rhabdoid and nonrhabdoid tumoral areas without sarcomatoid differentiation exhibited the very similar immunophenotype as follows: vimentin (+/−), AE1/AE3 (+), CK8/18(+), CK7(+/−), CK5/6 (−), CK20 (−), RCC (focal +), CD10 (focal +), Pax-2 (+), Pax-8 (+), CD117 (+/−), desmin (−), muscle-specific actin (−), and CD68 (−). On p53 and Ki-67 immunohistochemistry, the positive rate of rhabdoid cells for both p53 and Ki-67, similar to sarcomatoid cells, was higher than that of nonrhabdoid tumor cells without sarcomatoid differentiation. Our results indicate that the incidence rate of rhabdoid differentiation in Chinese adult RCC patients is lower than that of foreign reports. We support that the rhabdoid and nonrhabdoid tumor cells originate from the same clone, and the rhabdoid components present high proliferative activity and indicate a poor prognosis.

1. Introduction

Renal cell carcinoma (RCC) with rhabdoid morphology is a recently described variant of RCC, which has an aggressive biologic behavior and poor prognosis, akin to sarcomatoid RCC [1-3]. In the adult kidney, the histomorphology of the rhabdoid cell was initially described by Gokden et al [1] as variably cohesive epithelioid cells with eccentrically located vesicular nuclei with prominent nucleoli. The presence of large intracytoplasmic eosinophilic hyaline globules is the characteristic feature. Rhabdoid differentiation in adult RCC is usually found in association with a conventional-type (clear cell and chromophobe cell) RCC, from which it is thought to evolve [3-8], and current World Health Organization classification of RCC does not include the rhabdoid phenotype as a distinct histologic entity. At present, there are approximately 75 reported cases of adult RCC with rhabdoid morphology in the English literatures [8], whereas only 1 case has been reported in China [9]. Despite the limited reports of rhabdoid differentiation in adult RCC, it is generally accepted that this feature is associated with more aggressive RCC and poorer prognosis. The International Society of Urological Pathology (ISUP) 2012 Consensus Conference has identified rhabdoid differentiation as a prognostic parameter for adult RCC, which indicates an aggressive clinical behavior and a poor prognosis and has recommended some therapeutic regimen that may be effective [8]. But there

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is still little information on the prevalence of rhabdoid morphotype in adult RCC, especially in Asia.

This study reports the incidence and clinicopathologic features of adult RCCs with rhabdoid differentiation identified from a large series and further investigates the origin of these tumors.

2. Materials and methods

We reviewed a consecutive series of 723 RCCs submitted to Uropath, Institute of Urology, Peking University First Hospital, Peking University, China, for routine pathologic examination between January 2012 and March 2014 to identify rhabdoid features.

For the selection, we used the microscopic criteria described by Gokden et al [1]. We identified 10 tumors with rhabdoid differentiation, representing 1.4% of RCCs in this series. For each case, the percentage of rhabdoid area was determined. All cases were reviewed by the identical pathologist to confirm the comparability of tumor grading and immunohistochemistry revealing between all cases, and Fuhrman nuclear grading was applied in all cases.

We assessed paraffin-embedded sections from the 10 rhabdoid RCCs with routine stains and immunostains for vimentin, cytokeratin (CK) (pan-cytokeratin (AE1/AE3), CK20, CK5/6, CK7, and CK8/18), RCC, CD10, Pax-2, Pax-8, CD117, desmin, muscle-specific actin (MSA), CD68, p53, and Ki-67. Immunohistochemical stains were performed on 4-μm-thick sections from the formalin-fixed embedded tissues of the 10 specimens using the labeled streptavidin-biotin method after antigen retrieval. Blocks were selected for each case representing rhabdoid and nonrhabdoid areas. Sections from appropriate tissue recommended by the manufacturer served as positive control.

3. Results

A total of 723 cases of RCC were identified, 10 (1.4%) of which were found to have areas of classic rhabdoid morphology. The mean age of all the 723 patients and the 10 patients with rhabdoid features was 54.6 and 57.8 (range, 46-72) years, respectively. Of the 10 cases with rhabdoid differentiation, 3 occurred in left kidney, whereas the other 7 occurred in right kidney. The clinical features were flank pain, fever, hematuria, or no complaints. Imaging manifestation was renal masses (Table 1).

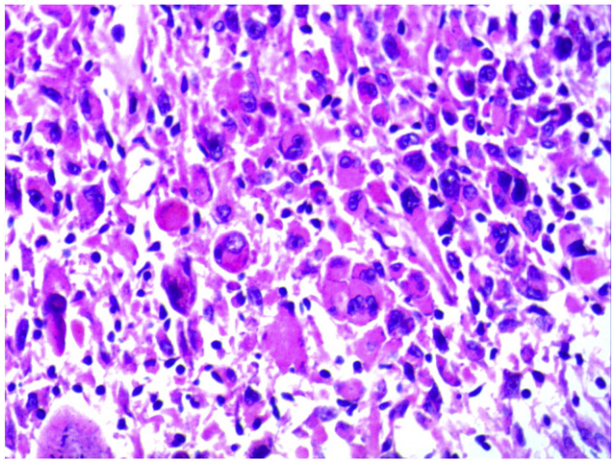

Fig. 1. Renal cell carcinoma with rhabdoid differentiation. Rhabdoid cells are cohesive large epithelioid cells with abundant pink cytoplasm and eosinophilic intracytoplasmic inclusions.

In our series, all the 10 cases with rhabdoid differentiation were "composite" tumors; in other words, none was pure rhabdoid tumor. In 8 cases, the rhabdoid tumor was found adjacent to a clear cell tumor (Fig. 2). In the remaining 2 cases, the rhabdoid tumor was associated with papillary RCC (II type) (Fig. 3). The largest dimension of tumor ranged from 4.4 to 9.8 cm. Macroscopically, the tumors were mostly hard moderate, solid with a mixed color, gray white, or gray brown cut surface. Hemorrhage and cystic change was also observed in some cases. Only 2 cases (case 3 and 4 in Table 2) showed regular edge, and the individual tumor masses were separated by dense fibrous tissue; whereas the other 8 cases showed edge of infiltration. Microscopically, 8 cases showed tumoral necrosis, representing 5% to 70% of the tumor volume, whereas the other 2 cases showed no necrosis. Six cases exhibited microvascular invasion. In 5 cases (case 4, 6, 7, 8, and 10), there was a sarcomatoid area composed of highly atypical spindle

Table 1
Cliinical features (when available)

Patient	Age (y)	Sex	Presentation	Metastasis at diagnosis	Metastasis	Outcome	Surgery	Follow-up time
1	64	M	5 y before admission, physical examination revealed 3-cm right renal tumor, no complaints, untreated. 6 mo before admission, right lumbar pain, getting worse progressively, CT showed the huge mass of right kidney	No	Intercostal soft tissue	Survival	Right RNE and adrenalectomy	28
2	62	M	Right lumbar pain, fever on and off, B ultrasound showed right renal tumor	Lymph node	Lymph node	Deceased	Right RN and lymphadenectomy	2
3	72	M	B ultrasound showed left renal tumor when gallstones review	No	Lost of follow-up		Left RN	
4[a]	46	F	B ultrasound showed right renal tumor during a routine check-up	No	No	Survival	Right partial nephrectomy	25
5	48	M	Intermittent back blunt pain, CT showed the huge mass of left kidney	No	No	Survival	Left RN	23
6[a]	60	M	Painless gross hematuria, frequent micturition, urgent urination, B ultrasound showed right renal tumor	No	Lung	Survival	Right RN	18
7[a]	52	M	Lumbosacral pain and numbness of lower limb, CT showed right renal tumor with bone metastasis	Lymph node and bone	Lymph node, bone, and pleura	Survival	Right RN with excision of RVT, partial sacrectomy and lymphadenectomy	17
8[a]	61	M	Total painless gross hematuria, B ultrasound showed right renal tumor	No	No	Survival	Right RNE	12
9	62	M	Fever, weak, bilateral waist rib discomfort, CT showed left renal tumor	No	Lung	Deceased	Left RNE, adrenalectomy, and lymphadenectomy	9
10[a]	51	M	Right lumbar dull pain, CT showed right renal tumor	No	No	Survival	Right RNE	9

Abbreviations: *CT*, computed tomography; *RNE*, radical nephrectomy with excision of renal vein and inferior vena cava thrombus; *RN*, radical nephrectomy; *RVT*, renal vein thrombus.
[a] With sarcomatoid differentiation.