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ScienceDirect
Annals of Diagnostic Pathology 11 (2007) 13–21
Annals of DIAGNOSTIC PATHOLOGY

Mucinous tubular and spindle cell carcinoma of kidney is probably a variant of papillary renal cell carcinoma with spindle cell features

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Abstract Mucinous tubular and spindle cell carcinoma is a rare and newly described type of renal cell carcinoma (RCC) with a relatively indolent behavior. However, its histogenetic origin or line of differentiation remains unclear. Twelve cases of mucinous tubular and spindle cell carcinoma were identified and retrieved from the files of 3 institutions. Detailed morphological features, as well as their immunohistochemical profile established with markers of proximal renal tubules (RCC marker antigen, CD15, and α-methylacyl-CoA racemase) and of distal renal tubules (kidney-specific cadherin and cytokeratin 7), were studied. The age range of the patients was 35 to 73 years with a median of 56 years. The male to female ratio was 1:3. All of the patients were alive with follow-up between 4 and 38 months. All the tumors were confined to the kidney with a mean tumor size of 6.9 cm (range, 1.8-17 cm). The tumors were composed of variable proportions of tubular and spindle cell areas with focal to prominent mucinous or myxoid stroma. Foamy macrophages were seen in 10 cases and were prominent in 4 cases. A focal compressed tubulopapillary growth pattern was seen in 10 cases. The tumor cells were uniformly cuboidal with ovoid to round nuclei and inconspicuous nucleoli (Furhman nuclear grade 3 in 6 cases). Focal necrosis was seen in 3 cases. Immunostains showed that tumors were positive for RCC marker antigen (11/12), α-methylacyl-CoA racemase (11/12), CD15 (8/12), CD10 (2/12), kidney-specific cadherin (1/12), and cytokeratin 7 (11/12). Its morphological features as well as a strong preferential expression of proximal tubule markers suggest that this tumor is a type of RCC with proximal tubular differentiation, which appears closely related to or represents a morphological variant of papillary RCC.

Keywords: Renal cell carcinoma; Mucinous tubular and spindle cell carcinoma; Papillary renal cell carcinoma; Immunohistochemical markers

1. Introduction

A rare and unusual morphological variant of renal cell carcinoma (RCC) composed of tubular and spindle areas within a myxoid and/or mucinous stroma was recently described and designated as mucinous tubular and spindle cell carcinoma (MTSCC) [1]. It had previously been referred to as an RCC with unusual differentiation [2], unusual RCC with prominent spindle cell change, RCC with loop of Henle's differentiation [3], low-grade myxoid tumor, and low-grade collecting duct carcinoma [4-7]. Although a number of small series of MTSCC have been reported, neither the morphological spectrum nor the histogenesis of this tumor has been fully assessed. Immunohistochemical (IHC) studies with a variety of markers have been performed on these cases, but the results were inconsistent or even contradictory, because of either the heterogeneity of the tumor or an insufficient

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doi:10.1016/j.anndiagpath.2006.09.005

Table 1
Antibodies used in the current study

Marker	Source	Clone	Dilution	Antigen retrieval
RCC Ma	Novo Castra (Newcastle Upon Tyne, UK)	66.4.C2	1:10	Yes (citrate)
AMACR (P504S)	Dako (Carpinteria, CA)	13H4	1:100	Yes (tris-EDTA)
CD10	Vector (Burlingame, CA)	56C6	1:10	Yes (citrate)
Ksp cadherin	Zymed (South San Francisco, CA)	4H6/F9	1:75	Yes (citrate)
CD15	Becton-Dickinson (Mountain View, CA)	Leu-M1	1:10	Yes (citrate)
Cytokeratin 7	Dako	OV-TL 12/30	1:50	Yes (citrate)

number of cases. The results of the ultrastructural studies published on this tumor have also been inconsistent [2,4,8]. These tumors have been shown to have fairly characteristic loss of multiple chromosomes in the limited number of cytogenetic studies that have been published [9-12], but gains of chromosomes have also been reported in some series [10,12]. The chromosomal 3p deletion, which is typical of clear RCC, however, has not been identified in any study. Therefore, the line of differentiation or histogenetic origin of MTSCC remains unclear. Interestingly, a recent study by Paner et al [13] using a tissue microarray of 27 MTSCCs has shown striking similarities between MTSCC and papillary RCC. The purpose of this study is to provide a detailed description of the morphological features and the IHC profile of 12 cases of MTSCC with particular attention to the shared features with papillary RCC. These features are compared with those of previously published cases.

2. Materials and methods

The 12 cases of MTSCC in the current study were identified from a review of approximately 1800 cases of RCC from the Methodist Hospital, Houston, TX; the University of Texas MD Anderson Cancer Center at Houston, TX; and the Inje University College of Medicine, Busan, Korea. Glass slides of all cases were reviewed, and archival formalin-fixed paraffin-embedded tissue sections of each case were subjected to IHC analysis. The diagnosis of MTSCC was made according to the 2004 World Health Organization consensus pathologic definition criteria [1].

In all 12 cases, paraffin blocks of the nephrectomy specimen were available. Five-micrometer-thick sections were cut and stained with hematoxylin and eosin stain (H&E). Immunohistochemical studies were carried out on consecutive tissue sections using the avidin-biotin-peroxidase complex method in a Dako AutoStainer (Dako, Carpinteria, Calif). The primary antibodies used are listed in Table 1. The immunostaining was performed using the LSAB2 peroxidase kit (Dako). To enhance the immunostaining, we performed a heat epitope retrieval procedure using a Black-and-Decker vegetable steamer (Shelton,

Table 2
Summary of clinicopathologic features of 12 cases MTSCC of the kidney

Case no.	Age (y)	Sex	Tumor size (cm)	Stage	Follow-up (mo)
1	48	Female	4.5	T1b NX	18
2	59	Female	4	T1a NX	12
3	58	Female	2.5	T1a NX	8
4	73	Female	13.8	T2 NX	14
5	50	Female	1.8	T1a N1	2
6	46	Female	2	T1a N0	38
7	62	Female	10.5	T2 N0	17
8	35	Female	2	T1a NX	25
9	71	Female	17	T2 NX	14
10	59	Male	6.2	T1b NX	NA
11	61	Male	14.5	T2 NX	8
12	47	Male	3.5	T1a NX	4

NA indicates not applicable.

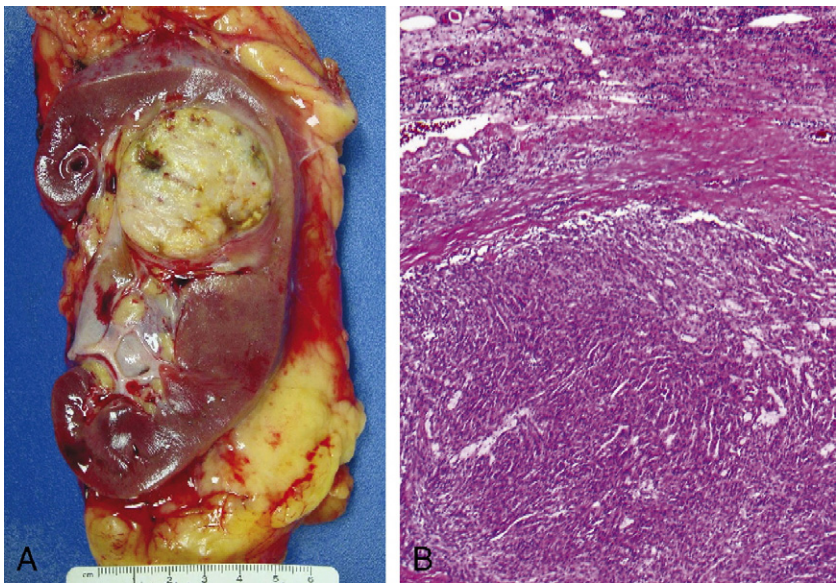

Fig. 1. Gross and microscopic image (original magnification ×40) of MTSCC showing the sharp circumscription of tumor from surrounding fibrous capsule.