Human Pathology (2015) **46**, 894–905

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Human PATHOLOGY

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Original contribution

Smooth muscle and adenoma-like renal tumor: a previously unreported variant of mixed epithelial stromal tumor or a distinctive renal neoplasm?☆

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Received 4 December 2014; revised 29 January 2015; accepted 4 February 2015

Keywords:
Renal neoplasm;
MEST;
Smooth muscle;
AMLEC;
RAT

Summary We describe 6 cases of a biphasic renal neoplasm, which we designate smooth muscle and adenoma-like renal tumor, which do not cleanly fit any category as currently defined. There were 4 females and 2 males (age, 27-70 years); neither male had a history of hormone exposure. All 5 neoplasms with available history were discovered incidentally on imaging studies with sizes ranging from 4 to 20 cm. The stroma was composed of smooth muscle fascicles alternating with looser, edematous areas; none of the cases contained ovarian-like stroma. The complex but cytologically benign epithelial component consisted of tubulopapillary nodules, branching tubules, clefts, and large cysts. The stroma of all of the cases labeled diffusely for desmin. Estrogen receptor labeling was absent in 4 cases with only minimal (<10%) weak labeling in the remaining 2. The epithelial component of each case labeled diffusely for cytokeratin 7 and was patchy for α-methyl-CoA racemase (P504S). Carbonic anhydrase IX, HMB45, WT-1, and inhibin were negative. None of the 5 cases tested demonstrated trisomies of chromosome 7 or 17 by fluorescence in situ hybridization. Two patients with significant follow-up are disease free at 18.5 and 2.5 years. Smooth muscle and adenoma-like renal tumor could potentially represent a variant of mixed epithelial stromal tumor, which would expand its reported spectrum. However, the absence of clinical history of hormone exposure, predominance of smooth muscle with lack of ovarian-like stroma, prominence of epithelial nodules, and typical absence of estrogen receptor labeling suggest that it may represent a distinct entity.

☆ Disclosures: The authors have no conflicts of interest or relevant funding to disclose.

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http://dx.doi.org/10.1016/j.humpath.2015.02.003
0046-8177/

1. Introduction

In the past 15 years, a variety of renal neoplasms featuring both smooth muscle stromal and epithelial components have been described. One entity is mixed epithelial stromal tumor (MEST) [1-12], a complicated biphasic solid and cystic lesion previously reported under the terms *cystic hamartoma of the renal pelvis* or *adult mesoblastic nephroma*. MEST features a variety of stromal patterns including ovarian-like stroma and a variety of complex epithelial patterns. Over time, cases of highly cystic MEST, which overlap with adult cystic nephroma (CN), have been described [13-18], leading to the proposal that these 2 lesions form the spectrum of a single entity for which some authors have proposed the term *renal epithelial stromal tumor* [19]. A second proposed entity is renal cell carcinoma (RCC) with angioleiomyomatous-like proliferation, which was considered in its initial description to be a clear cell RCC with a dissecting, sometimes infiltrative, bland smooth muscle stroma resembling angioleiomyoma [20]. A third entity is renal angiomyoadenomatous tumor (RAT), which, after some initial debate, is now considered by most to be a clear cell papillary RCC with prominent smooth muscle stroma [21-26]. Finally, a fourth entity, angiomyolipoma with epithelial cysts (AMLEC), is essentially a smooth muscle–predominant angiomyolipoma with prominent cysts composed of entrapped renal tubular epithelium and subepithelial, müllerian-like stroma [27].

Over the past few years, we have encountered 6 cases of a biphasic renal neoplasm, which does not cleanly fit any of the above accepted categories, as currently described. This neoplasm is variably solid and cystic and features a prominent smooth muscle stroma, which alternates with looser more edematous areas, along with complex epithelial patterns, including tubulopapillary nodules, branching tubules, clefts, and cysts. We have designated this lesion "smooth muscle and adenoma-like renal tumor" (SMART), and the features of these neoplasms are described herein.

2. Materials and methods

2.1. Institutional review board approval

This study was approved by the Institutional Review Board of the Johns Hopkins Hospital.

2.2. Cases

Cases 1, 2, and 6 were resected at The Johns Hopkins Hospital. Case 1 was resected almost 20 years earlier in 1995 but was identified during a recent review of cases originally characterized as adult mesoblastic nephroma or MEST [28]. Three of the cases in these series were consultations to The Johns Hopkins Hospital and reviewed by the senior author (P. A.).

2.3. Immunohistochemistry method

Immunohistochemical labeling was performed on the Benchmark XT autostainer (Ventana Medical Systems, Tucson, AZ) using the I-View detection kit. The standard antibodies used, vendors, pretreatments, and dilutions were as follows: cytokeratin 7 (clone ov-tl12/30, protease, 1:500; Dako, Carpinteria, CA), RCC marker antigen (steam, 1:50; Leica, Buffalo Grove, IL), desmin (Dako M0760, clone D33, steam, 1:100), CD10 (org-8941, steam, prediluted; Leica), α-methyacyl-CoA racemase (P504S, steam, 1:100; Zeta, Arcadia, CA), inhibin (steam, 1:25; Serotec, Raleigh, NC), PAX8 (steam, 1:100; ProteinTech Group, Chicago, IL), carbonic anhydrase IX (CA-IX) (NCL-L-CAIX, steam, 1:100; Novacastra, Buffalo Grove, IL), WT-1 (C-19, steam, 1:100; Santa Cruz, Dallas, TX), HMB45 (catalog no. ncl-hmb45, steam, 1:100; Novacastra), progesterone receptor (org-8721, steam, prediluted; Lecia), and estrogen receptor (ER) (6 F11, 1 μg/mL; Novacastra).

2.4. Fluorescence in situ hybridization method

Formalin-fixed, paraffin-embedded tissue blocks were serially sectioned at 5-μm intervals. Hematoxylin and eosin sections were used to determine the area of the tissue to be targeted for analysis. Fluorescence in situ hybridization method (FISH) slides were deparaffinized in xylene twice for 10 minutes, dehydrated twice with 100% ethanol, and then pretreated using the Vysis Paraffin Pretreatment Kit (Abbott Molecular, Des Plaines, IL). Slides were digested for 36 minutes in protease solution (0.5 mg/mL) at 37°C. FISH was performed using CEP7 (7p11.1q11.1) and CEP17 (17p11.1q11.1) centromere probes labeled using Spectrum Green (Abbott Molecular). The target slide was denatured in 70% formamide at 75°C for 5 minutes and dehydrated in 70%, 85%, and 100% ethanol. Slides were incubated with probe overnight at 42°C in a humidified chamber. Posthybridization washes were performed using 0.4X SSC/0.3% Igepal (Sigma, St Louis, MO) at 72°C for 2 minutes, followed by a room temperature 2XSSC/0.1% Igepal wash for 30 seconds. Slides were air dried in the dark and counterstained with 4′, 6-Diamidino-2-Phenylindole (DAPI)/antifade (Abbott Molecular). Analysis was performed using a Leica DM5500 B fluorescence microscope (Leica Microsystems) and CytoVision Workstation (Applied Imaging, Santa Clara, CA) equipped with Chroma Technology 83000 filter set with single- and dual-band excitors for Spectrum Orange, Spectrum Green, and DAPI (uv 360 nm) (Abbott Molecular). Only individual and well-delineated cells were scored. Overlapping cells were excluded from the analysis. Approximately 60 tumor cells were analyzed in the targeted region. Using established criteria [29], chromosomal gains were considered significant if present in greater than 20% of cells. Gains were considered artifactual if seen in less than 20% of cells. We used normal kidney to determine the cutoffs. None of the control kidneys in our study demonstrated trisomic cells.