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Original contribution

# Tubulocystic carcinoma of the kidney with poorly differentiated foci: a series of 3 cases with fluorescence in situ hybridization analysis

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**Summary** We identified 3 consult cases of tubulocystic renal cell carcinoma with poorly differentiated areas. Two lesions measuring 9.5 and 3.8 cm were described as partly solid and cystic. One case was grossly a 14.0-cm cyst with a granular lining. Microscopically, all had classic areas of circumscribed tubulocystic renal cell carcinoma occupying 30%, 80%, and 90% of the tumor; 2 cases had small components of papillary renal cell carcinoma, and 1 case had a central large cystic component. In 2 cases, proliferations of small tubules infiltrated away from the main mass with typical features of collecting duct carcinoma. In the third case, a focus of poorly differentiated carcinoma was seen adjacent to the tubulocystic renal cell carcinoma. In 2 cases, tumor invaded perirenal tissue. The third case was organ confined with vascular invasion. One patient died 9 months postoperatively with metastases to the abdominal wall and femur. The second case developed a recurrence in the renal bed 3 years postoperatively. The third patient was lost to follow-up. Fluorescence in situ hybridization studies results showed some features overlapping with papillary renal cell carcinoma in both the tubulocystic and collecting duct–like components and with 1 exception showed identical cytogenetic findings between the 2 components. Morphologically, in 2 cases, the collecting duct–like areas were also indistinguishable from collecting duct carcinoma suggesting a relationship between the 2 entities. This is the first series and only the second report of tubulocystic renal cell carcinoma with poorly differentiated components and documents the increased the risk of aggressive behavior above that of usual tubulocystic renal cell carcinoma.


## 1. Introduction

Tubulocystic carcinoma of the kidney is a recently described variant of renal cell carcinoma (RCC) and was not included in the last World Health Organization 2004

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classification [1]. It only received its current name in 2004 in a series of 29 cases presented in an abstract at the United State and Canadian Academy of Pathology meeting by Amin et al [2]. Initially, it was described as a favorable prognosis variant of collecting duct carcinoma with only a few cases in the reported series of metastases to lymph node, bone, pleura, and liver [3-6]. Its relationship to collecting duct carcinoma is controversial, and recent studies have linked it with papillary RCC [6,7]. Only 1 case of tubulocystic carcinoma with sarcomatoid features has been reported where the patient developed multiple peritoneal metastases and died 14 months after diagnosis [8]. In this study, we identified 3 consult cases of tubulocystic RCC with poorly differentiated areas and fluorescence in situ hybridization (FISH) analysis was performed.

## 2. Materials and methods

Three consult cases of tubulocystic RCC with poorly differentiated areas were identified at The Johns Hopkins Hospital. Hematoxylin and eosin (H&E)–stained slides were available for all cases, and paraffin blocks were available for 2 cases. FISH studies were performed on 2 cases with available material looking for trisomies of chromosomes 7 and 17 and loss of chromosome Y.

FISH was performed as previously described [9]. Five-micrometer-thick sections were cut from paraffin-embedded blocks. α-Satellite centromeric DNA probes for chromosomes 7, 17, and Y were obtained from Vysis (Downers Grove, IL). The CEP 7 and Y probe labeled with spectrum green and CEP 17 probe labeled with spectrum orange were diluted with tDenHyb1 (Insitus, Alburquerque, NM) in a ratio of 1:100. Five microliters of diluted probes was added to the slide in the reduced light condition. The slides were counterstained with 10 μL of 4′,6-diamidino-2-phenylindole/Antifade (4′,6-diamidino-2-phenylindole in Fluorguard, 0.5 μg/mL, Insitus) for 2 minutes and covered with a 50 × 22 mm coverslip and were sealed. The slides were examined (L. C.) using a MetaSystem Axioplan 2 System (Metasystem Group, Belmont, MA).

Fifty to 200 nuclei were scored for α-satellite signals observed with the fluorescence microscope at original magnification ×400 (L. C.). As much as possible, signals from solitary nuclei were counted, but groups of 2 or 3 adjacent but not overlapping nuclei were occasionally included in the counts. Nuclei were counted when the entire nuclear circumference had a round to oval contour and showed no evidence of fragmentation. Two signals of the same size in close proximity, not connected by a link, were counted as 2 signals. A diffuse (splatter) signal was regarded as a signal if it was contiguous and within an acceptable boundary. Two small signals connected by a visible link were counted as 1 signal. Overlapping nuclei and nuclei with uncertain signals were not counted. There was no significant variation in hybridization efficiency when different areas of the slides were examined. The number of signals visualized in nuclei was tabulated from areas of the slides in which nuclear overlap was minimal. Cells bearing 1, 2, and 3 signals were counted separately. Normal tissue on the same slides was also counted as a control.

## 3. Results

### 3.1. Case 1 (68-year-old man)

Macroscopically, the lesion measured 9.5 cm in greatest dimension and was described as yellow-tan, partly solid, and cystic. Microscopically, the lesion had a classic area of circumscribed tubulocystic RCC occupying 30% of the tumor (Fig. 1A). Proliferation of small tubules infiltrating away from the main mass with typical features of collecting duct carcinoma was also identified (Fig. 1B and C). The poorly differentiated area measured 1.0 cm and was composed of small tubules with markedly enlarged vesicular nuclei with very prominent eosinophilic nucleoli identical to that seen in the tubulocystic component. Mitotic figures were scant, and necrosis was absent. FISH study revealed trisomy of chromosome 17 in both tubulocystic and collecting duct–like areas. Trisomy of chromosome 7 or loss of chromosome Y was not detected (Table).

The tumor was organ confined with invasion of a medium-sized intrarenal artery by the poorly differentiated tumor. Three years postoperatively, the patient developed a clinical local recurrence in the renal bed, which was not biopsied.

### 3.2. Case 2 (58-year-old man)

Macroscopically, the lesion measured 3.8 cm in greatest dimension and was described as partly solid and cystic. Microscopically, the lesion had classic areas of circumscribed tubulocystic RCC occupying 80% of the tumor (Fig. 1D). Focally, a component of papillary RCC was noted. The lesion had a central large cystic component (Fig. 1E). A focus of poorly differentiated carcinoma with marked nuclear atypia and prominent nucleoli (Fig. 1F) was seen adjacent to the tubulocystic RCC. This focus measured 7 mm and consisted of predominantly sheets of cells with slight spindling and markedly enlarged round to oval nuclei with very prominent eosinophilic nucleoli. Focally, the tumor exhibited cords and tubules. Mitotic figures were scant, and necrosis was absent. FISH study was not performed. The poorly differentiated tumor invaded perirenal tissue, and no follow-up was available.

### 3.3. Case 3 (73-year-old man)

Macroscopically, the lesion measured 14.0 cm in greatest dimension and was described as a cyst with a granular lining. Microscopically, the lesion had classic areas of circumscribed