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Tubulocystic carcinoma of the kidney

ABSTRACT

Tubulocystic carcinoma of the kidney is a recently described unique entity. Initially, it has been described as a low-grade variant of collecting duct carcinoma. However, recent studies have demonstrated close relation to papillary renal cell carcinoma. It has a male preponderance. Macroscopically, it consists of a well-circumscribed tumor composed of multilocular small cystic spaces with spongy cut surface. Microscopically, it composed of well-formed tubules and cysts separated by thin fibrous septa and lined by a single layer of flat, hobnail, or cuboidal epithelial cells with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli. Tubulocystic carcinoma of the kidney has an indolent behavior with a low potential for metastasis. This review highlights clinical, pathological, immunohistochemical and molecular features of tubulocystic carcinoma of the kidney and discusses the differential diagnosis and prognosis.

INTRODUCTION

Tubulocystic carcinoma of the kidney is a recently described entity that was not included in the latest WHO 2004 classification [1]. Initially, it was described as a low-grade variant of collecting duct carcinoma and 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 (USCAP) meeting [2]. Tubulocystic carcinoma has been found to express markers of proximal nephron and distal nephron by immunohistochemistry [5]. Recent studies have shown that tubulocystic carcinoma is closely related to papillary renal cell carcinoma [4,7]. Tubulocystic carcinoma has an indolent behavior with a low potential for metastasis.

CLINICAL FEATURES

The mean patient age is 58 years with a range from 34 to 94 years and a male preponderance of 4-7:1 [3–5]. Patients may present with abdominal distension, pain or hematuria. However, in some of the reported cases tumor was incidentally discovered [5]. The tumor tends to involve left more than right kidney.

PATHOLOGIC FEATURES

On macroscopic examination, tubulocystic carcinoma is a well circumscribed tumor, it involves mainly renal cortex with or without renal medulla, and it ranges in size from 0.5 to 17 cm in greatest dimension. The tumor presents as solitary mass in most of the reported cases [4,7]. Multicentric tumors arising within the same kidney are uncommon. Cut surface of the tumor reveals multilocular small cystic spaces with a spongy ‘‘Swiss cheese’’ or ‘‘bubble wrap’’ appearance. The cysts are variable in size and containing clear serous fluid [3–5, 7, 8]. No necrosis or hemorrhage has been reported.

On microscopic examination, tubulocystic carcinoma is nonencapsulated but well-demarcated and composed of well-formed tubules and cysts separated by thin fibrous septa and lined by a single layer of flat, hobnail, or cuboidal to columnar epithelial cells with abundant eosinophilic cytoplasm (Figure 1). Amin et al reported 2 cases showing focal to patchy clear cell change within tubules and cysts in addition to the abundant eosinophilic cytoplasm [5]. The lining cells contain round nuclei with irregular nuclear membranes and fine but unevenly dispersed chromatin with prominent nucleoli equivalent of Fuhrman nuclear grade 3 (Figure 2).

The tumor lacks necrosis, solid growth pattern, desmoplasia, and ovarian type stroma. Yang et al reported that 3 of their 13 cases coexisted with papillary renal cell carcinoma and 2 with papillary adenoma [4]. Zhou et al also reported that 10 of 20 cases had associated papillary renal neoplasms within the same kidney [7]. Mitotic activity is usually sparse or absent. Only 1 case of tubulocystic carcinoma with sarcomatoid features has been reported [9].

On ultrastructural examination, the tumor reveals abundant mitochondria and microvilli with brush border similar to proximal convoluted tubules. Few cells have shorter and sparse microvilli with cytoplasmic interdigitation analogous to intercalated cells of the collecting ducts [5].

IMMUNOHISTOCHEMICAL FEATURES

Previous studies have shown that tubulocystic carcinoma is strongly positive for AMACR (racemase), CD10, CK8, CK18 and CK19, Parvalbumin, Carbonic Anhydrase-IX, and Kidney-Specific Cadherin. CK7 immunoreactivity is usually focal or weak. Tumor may also be positive for PAX2 and CK34βE12. Table 1 summarizes expression of different immunohistochemical stains in percentage based on large published series.

MOLECULAR FEATURES

Tubulocystic carcinoma is closely related to papillary renal cell carcinoma than to any other subtypes of renal neoplasms. Zhou et al reported that 10 of 12 tubulocystic carcinoma cases had a gain of chromosomes 7, 8 of 12 cases had a gain of chromosome 17, and 8 of 9 cases had a loss of the Y chromosome [7]. Also, Yang et al reported that tubulocystic carcinoma showed gains of chromosome 17 but not chromosome 7 [4]. By gene expression profiling, tubulocystic carcinomas are characterized by relative overexpresion of vimentin, p53, and AMACR, compared with collecting duct carcinomas [6].

DIFFERENTIAL DIAGNOSIS

The main differential diagnosis of tubulocystic carcinoma includes cystic nephroma, mixed epithelial stromal tumor, and multilocular cystic renal cell carcinoma. Cystic nephroma is characterized by larger cysts with hyalinized or fibrotic stroma. The cysts are lined by flat to attenuated cells with occasional hobnailing. However, unlike tubulocystic carcinoma the nuclei are typically benign with absent or inconspicuous nucleoli. Also, cystic nephroma occurs almost always in females whereas tubulocystic carcinoma is more frequent in males. Mixed epithelial stromal tumor is similar to cystic nephroma in addition to characteristic ovarian-like stroma that separates cystic spaces and often positivity for estrogen and progesterone receptors. Multilocular cystic renal cell carcinoma is characterized by variably-sized cystic spaces lined by flattened to cuboidal clear cells separated by fibrous stroma containing small groups of clear cells of low Fuhrman nuclear grade.

PROGNOSIS

Studies have shown that the majority of patients with tubulocystic carcinoma have stage pT1 [3–5]. Approximately 12 % (5/41) of the reported cases with follow-up in four series developed metastases into lymph node, bone, pleura, and liver [3–5, 8]. Bhullar et al reported a case of tubulocystic carcinoma with sarcomatoid features that developed multiple peritoneal metastases; the patient died after 14 months of diagnosis [9].

CONCLUSION

Tubulocystic carcinoma of the kidney is a unique renal neoplasm with distinctive morphologic features. On the basis of molecular features, it is closely related to papillary renal cell carcinoma. Recognition of this entity is important since it can mimic benign tumors such as cystic nephroma. It has an indolent behavior with low potential for metastasis.

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