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Tubulocystic renal cell carcinoma: Case report and literature review

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ABSTRACT

To optimize the diagnosis and treatment of Tubulocystic renal cell carcinoma, we present our experience with a case of it and review the literature. Tubulocystic renal cell carcinoma (TRCC) is a rare subtype of renal carcinoma with distinctive histological and molecular characteristics. This study provides a comprehensive analysis of TRCC, focusing on its pathological features, diagnostic criteria, and potential molecular mechanisms. The findings highlight the unique histological architecture and biological behavior of TRCC, distinguishing it from other renal cell carcinomas. Advanced imaging techniques and molecular biomarkers play a pivotal role in its accurate diagnosis.

1. Introduction

Tubulocystic renal cell carcinoma (TCRCC) is a rare histological subtype of renal cancer. TCRCC was first identified as a novel subtype of renal cell carcinoma in the 2012 Vancouver Classification of Renal Cancer by the International Society of Urological Pathology.[1]. In 2016, the World Health Organization separately classified it as a new histological type, defining tubulocystic renal cell carcinoma as a new entity primarily composed of cystic renal epithelial tumors.[2].Through the analysis of this case and a review of related literature, we aim to enhance the understanding of this disease.

2. Case

A case of a 52-year-old male patient admitted due to the discovery of a space-occupying lesion in the left kidney during a routine examination. The patient had no obvious discomfort symptoms, and no hematuria, flank pain, or other urinary symptoms.There was no significant family history of tumors or other systemic diseases.Ultrasonography showed a multicystic lesion with a relatively clear internal septum and no obvious blood flow signal. CT(Figure A) examination indicated a slightly low-density, predominantly multilocular cystic lesion in the left kidney, measuring 2.8*1.2 cm, consistent with a Bosniak III renal cyst, in addition to significant hepatic cysts. MRI **(**Figure B**)** showed that the lesion presented as a high signal on T2-weighted imaging, containing multiple small cystic cavities with slight septal thickening.Considering renal cancer, the patient underwent laparoscopic left partial nephrectomy, and postoperative pathology showed a tumor composed of multiple cystic cavities of varying sizes, with a "spongy" appearance **(**Figure C**)**. Microscopically, the lesion exhibited a mixed pattern of tubular and cystic structures, with enlarged nuclei and nucleoli.Immunohistochemical analysis showed positive reactions of the tumor cells for PAX8, AMACR, and CD10.Postoperatively, no biological or chemical therapy was given, and no signs of metastasis were found during 37 months of follow-up**(**Figure D**)**.

3. Discussion

TC-RCC is a newly identified rare renal cancer, characterized by less aggressiveness compared to other urological tumors. Initially thought to be a variant of collecting duct carcinoma, it was later identified based on its distinct histopathological characteristics, setting it apart from other renal cancers.

As early as 2009, Amin et al. first reported a tumor called tubulocystic carcinoma, but it was not included in the WHO classification of genitourinary tumors.[3]. Currently, fewer than 200 cases of tubulocystic renal cell carcinoma have been reported in the literature, with fewer than 6 % showing high aggressiveness or metastasis.[4,5]. Clinically, it predominantly affects middle-aged males aged 50–60, with a male-to-female ratio of 7:1.[6].Most cases are asymptomatic, with only a few showing symptoms like flank pain or hematuria[5]。

The prognosis for most patients is favorable, with a low metastasis rate; metastasis has been observed in less than 10 % of the reported cases[7]。In a review of larger study cohorts comprising 89 cases, only 3

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showed metastasis[8,9]。Among these, 2 cases were pure TCRCC, and 1 case involved metastasis mixed with high-grade papillary carcinoma[10]。Statistics from our hospital from January 2016 to June 2024 show a total of 10,770 cases of renal cancer, with 1 case of tubulocystic renal cell carcinoma, accounting for 0.01 % of all renal cancers, indicating its rarity.

Cornelis et al. reported that the ultrasound characteristics of TC-RCC are multicystic, containing multiple thin septa. CEUS demonstrates significant advantages in differentiating TC-RCC from other renal cystic lesions, as it offers real-time visualization of tumor vascularity and microvascular architecture.CT typically shows a multilocular cystic lesion with septal enhancement, composed of numerous small cysts or tubular structures and clear serous fluid, consistent with Bosniak classification II-IV. MRI examination aids in the accurate diagnosis of cystic masses based on the Bosniak classification system[11]。Hindman et al. observed that higher Bosniak grades in multilocular cystic renal cell carcinoma correlate with a larger volume of vascularized fibrous tissue, appearing as significant enhancement on imaging[12]。Cornelis et al. argued that TCRCC could display a very low vascular count.[2]. Differences in enhancement may assist in differentiating TC-RCC from multilocular cystic RCC. Distinguishing TC-RCC from other cystic renal tumors (e.g., multicystic renal cell carcinoma, mixed epithelial and stromal tumor [MEST], adult cystic nephroma) solely through imaging remains challenging.[8]. In this case, TCRCC was accompanied by hepatic cysts; therefore, the possibility of TCRCC should be considered in cases of complex renal cysts with hepatic cysts.

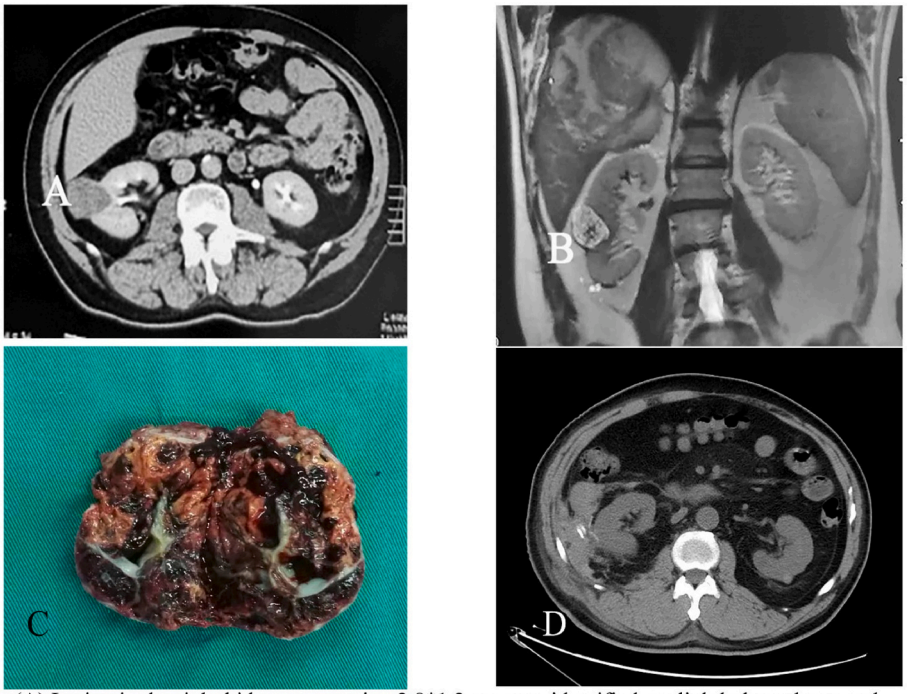
From a histological perspective, gross pathology demonstrates TC-RCC as a localized multicystic lesion, typically appearing "bubble-like" or "spongy".[8]. Microscopically, the typical histological features of TC-RCC include tubular and cystic spaces lined by a single layer of cuboidal to hobnail epithelial cells, characterized by enlarged nuclei and prominent nucleoli (WHO/ISUP grade 3 nucleoli).[13].Immunohistochemically, TC-RCC shows positive expression of PAX8, AMACR (alpha-methylacyl-CoA racemase), and CD10. Fumarate hydratase (FH) deficiency is not a typical feature of TC-RCC; instead, FH expression is usually retained, further supporting its classification as a distinct subtype.[14,15].

Given the frequent reports of TC-RCC coexisting with papillary renal cell carcinoma, many researchers seek to uncover a strong relationship between the two.Nonetheless, genomic studies have been instrumental in confirming TC-RCC as an independent entity. Studies have shown that TC-RCC harbors consistent genetic alterations, such as the loss of chromosomes 9 and Y and the gain of chromosome 17, which differ from the molecular characteristics of other RCC subtypes, such as clear cell RCC and chromophobe RCC. Furthermore, recurrent mutations in chromatin-modifying genes such as KMT2C and KDM5C have been reported in some cases, indicating its unique genetic features.[16].

The prognosis of TC-RCC is generally favorable, with most patients achieving long-term survival after surgical resection, such as radical or partial nephrectomy.TC-RCC seldom shows invasive tendencies or the potential for metastasis, although poorly differentiated regions may suggest a more aggressive clinical trajectory. Adjuvant therapy is generally not required for TC-RCC unless the tumor exhibits aggressive features or invades local structures.[17]. Targeted therapies, like tyrosine kinase inhibitors, are being explored for advanced or metastatic TC-RCC, though their effectiveness is yet to be established.[7,18,19].

4. Conclusion

TC-RCC represents a rare subtype of RCC, distinguished by its distinct clinical, radiologic, histopathologic, and molecular characteristics. Despite the typically favorable prognosis of TC-RCC, distinguishing it from other cystic renal tumors is critically important. Future studies are required to investigate the molecular mechanisms of TC-RCC and identify the most effective treatment approaches to enhance the prognosis of patients with this rare renal tumor.。



(A) Lesion in the right kidney, measuring 2.8*1.2 cm, was identified as slightly hypodense and predominantly multilocular cystic in nature.(B)The T2-weighted MRI revealed a high signal intensity lesion with multiple small cystic cavities and mild septal thickening.(C)Several cystic spaces of different sizes are visible within the tumor. (D) No signs of metastasis were found during 37 months of follow-up.

Fig. 1.

CRediT authorship contribution statement

Yun-Shen Ding: Writing – original draft. **Yi-Han Wang:** Writing – review & editing. **Feng Liu:** Writing – review & editing.

Disclosure

The authors report no conflicts of interest in this work.

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