ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 8 | August - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

AN UNUSUAL CASE OF SYNCHRONOUS TUBULOCYSTIC RENAL CELL CARCINOMA AND CLEAR CELL RENAL CELL CARCINOMA WITH REVIEW OF LITERATURE

Pathology

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ABSTRACT

Tubulocystic renal cell carcinoma (TC-RCC) is a recently described rare subtype of renal cell carcinoma (RCC) with very few cases reported in the literature until date. Reports of concurrent papillary renal cell carcinoma (PRCC) and TC-RCC have been often documented in the literature, but the co-occurrence of clear cell RCC (CC-RCC) and TC-RCC is extremely rare. We here describe a case of an incidentally detected TC-RCC occurring with CC-RCC in the same kidney in a 45-year-old male who presented with high grade fever with chills and rigors. Grossly, there were two distinct tumors in the total nephrectomy specimen. The larger tumor displayed the histopathological features of CC-RCC and the smaller tumor revealed the features of TC-RCC. The case report highlights the importance of having an accurate knowledge of this uncommon entity and the histomorphological differentiation from the more common renal neoplasms.

KEYWORDS

Low-grade collecting duct carcinoma, renal cell carcinoma, synchronous, tubulocystic carcinoma

INTRODUCTION

Tubulocystic renal cell carcinoma (TC-RCC) is a recently described rare subtype of RCC, which has been included in the World Health Organization (WHO) 2016 classification of renal tumors.[1] It consists of a mixture of tubules and micro/macro cysts with low-grade nuclear features and appears to be derived from proximal convoluted tubule and distal nephron. Overall, less than 100 cases have been reported until date and the literature describing their clinicopathological information, biologic behavior, immunohistochemical profile, and the ultrastructural features is quite limited.[2-5] The College of American Pathologists already recognized the new entity in the protocol for invasive carcinoma of renal tubular origin.[6] The most recent International Society of Urological Pathology (ISUP) Vancouver Modification of WHO 2004 classification popularly known as the ISUP Vancouver Classification of Renal Neoplasia recommended the inclusion of TC-RCC along with four other new distinct epithelial tumors in the classification system.[3] Herein we report an unusual case of synchronously occurring TC-RCC and CC-RCC in a 45-year-old hypertensive man. To the best of our knowledge, this is the fourth such case of these two simultaneously occurring tumors, reported in the literature. [7,8]

CASE REPORT

A 45-year-old, known hypertensive, male presented with high grade fever with chills and rigors for two months. There was no significant history of weight loss, abdominal pain, hematuria or lower urinary tract symptoms during this period. On clinical examination, the patient was afebrile and showed mild tenderness in the right flank region. The results of his routine hematological and biochemical examinations were within normal limits. Ultrasonography (USG-KUB) revealed a solitary exophytic mass measuring 3.8x3.8x2.6cm arising from the lower pole of right kidney. There was no feature of associated hydronephrosis, renal calculi or hilar lymphadenopathy. On CECT-abdomen, there was a 3.5x3.2x2.5cm hypodense mass with heterogenous enhancement in the lower pole and a separate mass measuring 1.6x1.2x0.7cm in the posterior cortex at upper pole of right kidney. He underwent a right laparoscopic radical nephrectomy without any significant post-operative complication. There were no adhesions surrounding the kidney. On gross examination, two separate tumors were distinctly identified [figure 1].

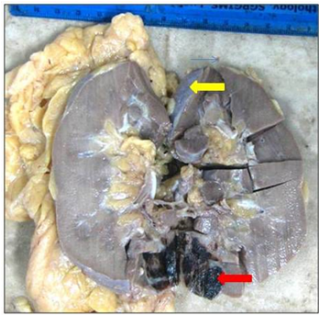

Figure 1: Gross image of the nephrectomy specimen displaying a hemorrhagic tumor at the lower pole (red arrow) and another smaller lesion at the upper pole of kidney (yellow arrow).

The larger solid tumor was hemorrhagic and grayish in colour measuring 3x2.5x1.5 cm confined to the cortical region of the lower pole of the kidney. The smaller spongy tumor measuring 1.5x1x0.8cm was restricted in the cortical region and corticomedullary junctional region of the upper pole of the kidney. No hemorrhagic or necrotic areas were identified in this part. Both the tumors were confined to the kidney with no evidence of capsular infiltration or vascular invasion macroscopically. Histopathological examination of the larger tumor displayed a well circumscribed nodule composed of multiple cystic spaces lined by tumor cells as well as solid nests of cells separated by a network of small thin walled capillaries [Figure 2A,2B]. The tumor cells were polygonal with abundant clear cytoplasm having well-demarcated distinct cell borders and hyperchromatic nuclei with irregular nuclear membrane and conspicuous nucleoli (Furhman nuclear grade 3) [Figure 2C]. The smaller nodule revealed an unencapsulated well circumscribed tumor composed of small to intermediate sized tubules with interspersed cystically dilated larger tubules, dispersed evenly in a bland hypocellular fibrotic stroma [Figure 2D]. The tubules and cysts were lined by a single layer of flat, cuboidal to columnar epithelial cells with abundant eosinophilic or amphophilic cytoplasm and conspicuous nucleoli (Fuhrman nuclear grade 3). Focal hobnail configuration was identified in the cells [Figure 2E]. Intraluminal foam cells were also seen in some of the tubules [Figure 2F]. Necrosis and mitosis were inconspicuous. There was no stratification or papillary configuration in the lining epithelial cells of the tubules and cysts. No area of solid growth was identified. Desmoplastic reaction or cellular ovarian like stroma was not appreciated in any part of the slides.

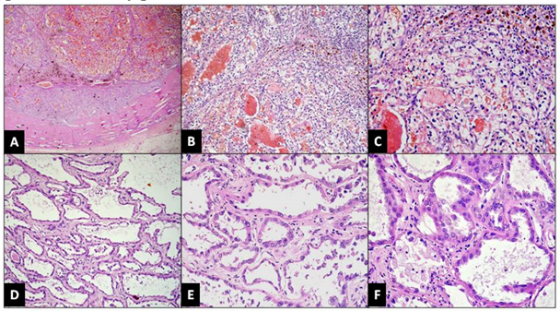

Figure 2: Microscopic findings of the tumors from lower pole (A-C) and upper pole (D-F) (Hematoxylin & Eosin). A: Well-circumscribed hemorrhagic tumor comprising of solid and cystic areas (x40), B: Multiple cystic spaces lined by tumor cells as well as solid nests of cells (x100), C: Polygonal cells with abundant clear cytoplasm, irregular nuclear borders and conspicuous nucleoli (x400), D: Well circumscribed tumor composed of small to intermediate sized tubules

with areas of cystically dilated larger tubules with intervening bland hypocellular stroma (x100), E: The tubules and cysts are lined by a single layer of cuboidal to columnar epithelial cells with abundant eosinophilic cytoplasm and with focal hobnail configuration (x400), F: Intraluminal foam cells in some of the tubules (x400).

The lesion also lacked the lymphovascular involvement, tumor necrosis, renal sinus or pelvicalyceal system involvement. On immunohistochemistry (IHC), the lower pole tumor with clear cell phenotype as well as the upper pole tumor showed positivity for CD10 and vimentin. However, epithelial membrane antigen (EMA) and cytokeratin 7 (CK7) were only expressed in upper pole tumor and were negative in the clear cell tumor [figure 3A-D]. Based on the characteristic morphological and IHC findings, the case was diagnosed as co-occurrence of TC-RCC and CC-RCC, Fuhrman nuclear grade 3, Stage T1bN0M0. On follow-up, the patient did not show any evidence of tumor recurrence in a 24 month period.

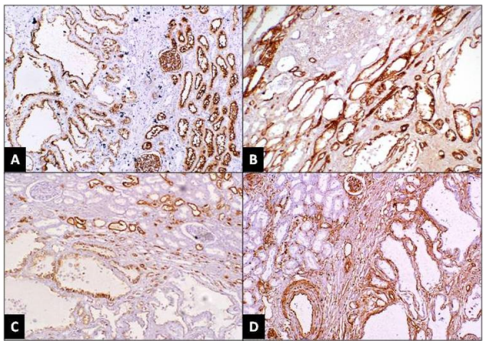

Figure 3: Immunohistochemical findings in Tubulocystic Renal Cell Carcinoma (X200, DAB). Tumor cells are positive for A: CD10, B: Cytokeratin-7, C: Epithelial membrane antigen (focal) and D: Vimentin

DISCUSSION

The histological features of the high-grade collecting duct carcinoma (CDC) of the kidney with hobnail cells occurring in the central region of the kidney were described for the first time in 1956 by Pierre Masson as “bellinian epithelioma” or “carcinoma of Bellini (collecting) duct.”[1] The neoplasm which is distinctly different from classic CDC in many ways, was described as “low-grade CDC” by MacLennan et al.in 1997.[9] In 2004, Amin et al. coined the term “tubulocytic carcinoma of the kidney” based on its characteristic morphology.[2] The tumor has now been considered as a distinct entity in the 2016 WHO classification of renal tumors, with the typical macroscopic and microscopic features. [1] According to the ISUP, the use of this term should be refrained in cases where there is a tubulocystic pattern admixed with the elements of P-RCC or CDC.[3,10] TC-RCC is an indolent tumor with a characteristically male predilection and a mean age of 54 years. [2,3] The patient in our case was a 45 year old male. More than 90% of the tumors are aymptomatic and are usually detected incidentally. [2,4,5] Grossly these tumors are well-circumscribed and unencapsulated with a mean size of 4cm. Cut surface of the tumor resembles a 'swiss cheese' or 'bubble-wrap' appearance due to presence of multiple cysts. Ares of hemorrhage and necrosis are usually not present. [2,4]

Microscopically, these tumors demonstrate a mixture of closely packed tubules and variable sized cysts separated by fibrous septae. The tumors cells display uniform round nuclei with distinct nucleoli (Fuhrman grade 3) and moderate to abundant eosinophilic cytoplasm with hobnailing, similar to our findings.[4,5] These tumors are not uncommonly associated with papillary neoplasms, though no such finding was evident in our case. [2,10]

Though there are no discriminating IHC markers specific for TC-RCC, these tumors are usually immunopositive for CK-7, AMACR, EMA, vimentin and PAX-8 with variable CD10 positivity. [2,4,5] In our case, the tumor cells expressed CK-7, CD10, Vimentin and EMA. Ultrastructurally, the tumor cells display short microvilli with brush border organisation, resembling features of both the proximal tubular and collecting duct cells. [4] Recent studies have demonstrated the signature molecular markers of the tumor which include gain of chromosome 7 and 17 and loss of Y, which distinguish it from other common renal tumors.[3,5]

The major differential diagnosis of TC-RCC includes adult and pediatric cystic nephromas, multilocular cystic renal neoplasm of low malignant potentitial , hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome associated renal cancer with tubulocystic carcinoma like areas, mucinous tubular and spindle cell carcinoma and lastly the CDC which is characterized by aggressive behavior and highly infiltrative growth pattern.[2,4,5,11] However, the distinctive clinico-radiological features along with the typical gross and microscopic features of TC-RCC are usually sufficient to distinguish this entity from its close differentials, as in the present case. TC-RCC appears to have a favorable prognosis and presents at the lower stage with very few reports of local recurrence or metastatic disease.[4] However, the rare occurrence of these tumors have precluded accurate evaluation of the biological behavior of these tumors and mandates further studies including more number of cases for better understanding this neoplasm and to ascertain its prognosis.

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