Papillary renal cell carcinoma and collecting duct carcinoma combination. A case report and review of synchronous renal cell carcinoma subtypes in the same kidney

Deniz Arık1, Mustafa Fuat Açıkalın1, Cavit Can2

1Department of Pathology, Faculty of Medicine, Eskisehir Osmangazi University, Eskisehir, Turkey
2Department of Urology, Faculty of Medicine, Eskisehir Osmangazi University, Eskisehir, Turkey

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Collecting duct carcinoma (CDC), also known as Bellini duct carcinoma, is a rare neoplasm comprising less than 1% of renal epithelial tumors [1]. Collecting duct carcinoma is an aggressive neoplasm and is thought to arise from the collecting ducts of renal medulla [2]. Papillary renal cell carcinoma (PRCC) comprises 10% of renal cell carcinomas (RCC) and has distinct cytogenetic and molecular features [3].

Concurrent primary neoplasms of the kidney have been rarely reported in the literature as an association of RCC and transitional cell carcinoma (TCC) or oncocytoma [4–6]. But coexistence of the RCC subtypes in the same kidney is exceptional.

To the best of our knowledge, 20 cases have been reported to date as synchronous RCC subtypes in the same kidney [7–21]. Among them there have been only two cases of synchronous CDC and PRCC. In these cases, the tumors were usually seen as separate masses. In contrast, in some reports tumor components were seen as a single mass or “tumor in tumor” or with obvious histological transition [10, 12, 13, 15, 16].

Here we present the third case of CDC and PRCC association and the first one of this association as a “tumor-in-tumor” morphology.

A 42-year-old man initially presented with flank pain and hematuria. His personal or family histories were not contributory. In ultrasonography, soft tissue density was detected at the lower pole of the right kidney. An abdominal computed tomographic scan demonstrated a 38 mm cystic lesion and 35 mm mass with equal density in the renal cortex. A right radical nephrectomy with lymph node dissection was performed. Macroscopic examination showed a 10 cm, solid, gray-white mass containing a 3.5 cm cystic area with papillary features in the renal parenchyma extending to the pelvis. Microscopically, the solid part of the mass revealed infiltrative tubuloglandular formations in a desmoplastic stroma. Tumor cells had large hyperchromatic and pleomorphic nuclei and relatively scant cytoplasm. The cystic part of the tumor showed entirely different histology consisting of papillary structures lined with columnar cells having coarse vesicular nuclei, prominent nucleoli and large eosinophilic cytoplasm. Dysplastic features were seen in the epithelium of the distal collecting ducts too. The tumor invaded the renal capsule and extended into the perirenal fat. Gerota’s fascia, renal vein, ureter, and adrenal gland were free of
tumor. In the perirenal fat, four metastatic lymph nodes were detected. At the renal hilus, perineural invasion and tumor cell emboli were seen. In the perirenal fat, 7 lymph nodes were detected and 4 of them showed CDC component involvement. Lymph node dissection material from the right hilar, paracaval and right common iliac region revealed 13 lymph nodes with reactive hyperplasia. The adrenal gland was intact.

Immunohistochemistry showed different features in the two components. The solid component showed reactivity with CK-AE1 and CK19. Histochemically the mucicarmine and alcian blue stains were negative. At the cystic component, the tumor cells were focally positive for 34BE12 but not for CK-AE1 and CK19. Uroplakin, AMACR, CK7 and CD10 were negative for both tumor components (Figures 1–6).

The solid component was diagnosed as CDC with nodal metastasis, renal capsular and pelvic invasion. The cystic component was diagnosed as type 2 PRCC.

At this time no distant metastasis was detected by abdominal or thoracic computed tomographic scan. After 18 months, a millimetric hypodense nodule in the liver and a 13 mm lymph node in the upper paraaortic region were observed and immunotherapy was planned. After 3 months multiple metastatic nodules were detected in the liver, retrocaval, paraaortic and paratracheal regions, and vertebral bones. External radiotherapy to the vertebral region was planned. After 30 months multiple bone, liver, upper and lower paraaortic metastatic nodules were in progression.

Synchronous tumors in the same kidney is a rare occurrence. The RCC cases associated with angiomylolipoma, oncocytoma and TCC were presented as a small series in the literature [4–6]. However, combination of the subtypes of RCC (clear cell, chromophobe, papillary, collecting duct) in the same kidney is very rare. To the best of our knowledge, only 20 cases with different RCC subtypes in the same kidney have been reported [9, 14]. Table I shows the clinical and histological characteristics of these cases. The following is a summary of the cases.

Roehrl et al. [16] reported another unique case of RCC that exhibited the features of both chromophobe and papillary carcinoma within the same tumor [16]. By light microscopy the two admixed tumor types could be readily distinguished from each other. Based on surface area estimates of representative tissue sections, approximately
70% of the tumor was composed of chromophobe and 30% of papillary carcinoma. Immunohistochemical, electron microscopic and cytogenetic analysis of the tumor revealed distinct patterns too. According to the authors it was conceivable that their particular RCC may have arisen from a pluripotent cancer stem cell that was capable of recapitulating both proximal and distal nephron histogenesis, either by acquiring dichotomous additional genetic alterations along the way of the two different morphogenic pathways (chromophobe vs. papillary) or by undergoing microenvironment-specific differentiation within the tumor.

Tumors that are separate masses in the same kidney are considered as synchronous tumors. If the tumors with different morphology are seen as a single mass or with histologic transition in the kidney, their pathogenesis should be peculiar. Re-
Table I. Documented cases of synchronous RCC subtypes in the same kidney

| Study            | Age/sex | RCC subtype            | Location       | Dimension [cm] | With                                      |
|------------------|---------|------------------------|----------------|----------------|-------------------------------------------|
| Renshaw et al.   | 70/F    | Papillary              | NS             | 3              | Radiologic evidence of lung metastases   |
|                  | 62/M    | Papillary              | NS             | 4              | Radiologic evidence of lung metastases   |
| Auget et al.     | 73/M    | Clear cell             | Right upper pole | 1.3           |                                           |
|                  |         | Collecting duct        | Right lower pole | 6             |                                           |
| Daniel et al.    | 75/M    | Papillary              | Right upper pole | 2.5           |                                           |
|                  |         | Collecting duct (low grade) | Right upper pole | 1.5           |                                           |
| Gong et al.*     | 72/M    | Chromophobe            | Left lower pole | NS            | Transition with sarcomatoid component    |
| Jun et al.       | 62/M    | Chromophobe            | Lower pole     | 1.7           | Epithelioid angiomylipoma                |
| Cho et al.*      | 24/M    | Clear cell (unclassified) | Left inner nodule | 1.5         | Nodule-in-nodule pattern                 |
| Lindgren et al.* | 47/M    | Chromophobe            | Right lower pole | 8.5 cm as a single mass | Oncocytoma and sarcomatoid differentiation |
| Matei et al.     | 70/M    | Papillary              | Left upper pole | 0.5           | Obvious transition to each other with dedifferentiation |
|                  |         | Collecting duct        | Left medulla   | 5.3           |                                           |
| Kawano et al.*   | 64/F    | Chromophobe            | Left middle to the lower portions | 4.3         | 0.2 cm subcapsular tubulopapillary adenoma |
| Roeffl et al.*   | 65/M    | Papillary              | Left superior pole | 5.4 cm as a single mass |                                           |
| Tyritzis et al.  | 57/M    | Chromophobe            | Lower pole     | 12.5          |                                           |
|                  |         | Papillary              | Upper pole     | 5             |                                           |
| Tsai et al.      | 57/F    | Clear cell             | NS             | NS            | TCC of renal pelvis and acute pyelonephritis |
| Capaccio et al.  | NS      | Papillary              | Left upper pole | 6             |                                           |
|                  |         | Clear cell             | Left lower pole | 1             |                                           |
|                  | NS      | Papillary              | Left lower pole | 4             |                                           |
|                  |         | Clear cell             | Left lower pole | 3             |                                           |
|                  | NS      | Papillary              | Right upper pole | 3.4         |                                           |
|                  |         | Clear cell             | Right upper pole | 1             |                                           |
|                  | NS      | Clear cell             | Right upper pole | 5.7         |                                           |
|                  | NS      | Chromophobe            | Right lower pole | 1             |                                           |
|                  |         | Chromophobe            | Right lower pole | 12            |                                           |
|                  |         | Papillary              | Right upper pole | 4             |                                           |
| Lee et al.       | 79/M    | Clear cell             | Right mid portion | 2            |                                           |
|                 |         | Chromophobe            | Right lower pole | 3.5         |                                           |
| Quiroga-Garza et al. | 67/M | Clear cell             | Right upper pole | 4.1          |                                           |
|                 |         | Tubulocystic           | Right mid lateral | 2           |                                           |
| Current case*    | 42/M    | Papillary              | Right lower pole | 10            | Tumor-in-tumor morphology                |
|                  |         | Collecting duct        | Right lower pole | 3.5         |                                           |

*Cases with single mass, or tumor-in-tumor morphology or histologic transition. RCC – renal cell carcinoma, CRCC – chromophobe renal cell carcinoma, PRCC – papillary renal cell carcinoma, CDC – collecting duct carcinoma, NS – not stated.
cently, the concept of cancer stem cells has become a focus of investigation in cancer biology. It is conceivable that these particular tumors may have arisen from a cancer stem cell. Consequently, combination of the masses that are thought to arise from distal and proximal tubules may be developed from a pluripotent stem cell that has capability of both proximal and distal nephron histogenesis.

Our case is unique because this is the first case of synchronous PRCC and CDC seen as a single mass. Previously reported PRCC and CDC combinations were completely separate tumors at different locations in the same kidney. In such tumors, the possibility of collision tumor should also be considered. We speculate that in a case with separate tumors located close to each other in the same kidney, the more aggressive one may invade the other and may present an image like a single mass, or “tumor-in-tumor” morphology or histologic transition. In our case, the CDC is expected to behave in an aggressive way. Infiltration and encircling of the PRCC by the CDC may form the morphology we have described.

Conflict of interest

The authors declare no conflict of interest.

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