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 Arık[1], Mustafa Fuat Açıkalın[1], Cavit Can[2]

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

Submitted: 24 January 2014
Accepted: 18 February 2014

Arch Med Sci 2015; 11, 3: 686–690
DOI: 10.5114/aoms.2015.52378

Corresponding author:
Deniz Arık
Department of Pathology
Faculty of Medicine
Eskisehir Osmangazi University
26480 Eskişehir, Turkey
Phone: +902222392979
E-mail: denarik@hotmail.com

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, retrocrural, 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 angiomyolipoma, 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 (Table I). There were only two previously presented cases of PRCC with CDC in the literature [9, 14]. In one of these cases, separate masses both were located at the upper pole of the kidney. The PRCC was 2.5 cm and the CDC was 1.5 cm in diameter. The PRCC was evaluated as Fuhrman grade 2, while the CDC was low-grade [9]. In the other case, the CDC was 5.3 cm in diameter and located in the medullary region. The PRCC was located in the upper pole as a 0.5 cm mass. Our case is the third in the literature showing synchronous PRCC and CDC. However, our case is different from the others due to its "tumor-in-tumor" morphology. The PRCC was a 3.5 cm cystic mass located centrally in the 10 cm solid CDC. The tumor with papillary structures extending into the cystic space consistent with type 2 PRCC was easily recognizable. The CDC component was characterized by infiltrative small tubuloglandular structures lined with highly atypical cells in a desmoplastic stroma. These two different morphologies were clearly identifiable by light microscopy and immunohistochemical studies.

Similar to our case, 5 of the 20 synchronous tumors were not entirely separate masses. Cho *et al.* [12] reported a case with two different clonal expansions in one nodule, of unclassified RCC and CDC as nodule-in-nodule morphology with different karyotypic alterations and immunohistochemical results. Two cases of the combination of chromophobe renal cell carcinoma (CRCC) and CDC in the same kidney with histologic transition have been presented in the literature [10, 15]. In the case reported by Kawano *et al.* [15] the most predominant histological component was the CRCC. The chromophobe cells also showed dedifferentiation. Besides this component, the CDC component was also noted, and the CRCC and CDC elements showed obvious transition to each other. The authors considered that their case was monoclonal in origin because of obvious histologic transition with CDC and chromophobe RCC elements. Gong *et al.* [10] reported that the CRCC component showed both CDC differentiation and sarcomatoid dedifferentiation, and concluded that the tumor was monoclonal because in metastatic focuses all three elements were seen [10]. In another case, the tumor exhibited varied cellularity with diverse architectural patterns, including solid sheets, nests, tubules, papillary formations, cords or trabeculae, and infiltrating neoplastic cells [13]. The tumor displayed intimate intermingling of histologic patterns described collectively in tumors of distal nephron derivation. There were architectural and cytologic features of oncocytoma, CRCC, and CDC, as well as sarcomatoid dedifferentiation with different karyotypic abnormalities. The authors concluded that the failure of special stains to separate one morphologic area from the other in the tumor suggests that this is a solitary, noncollision neoplasm demonstrating diverse (but closely related) morphologic differentiation of distal nephron derivation. The authors added that the karyotype of the tumor is most supportive of CRCC, but also shows the chromosomal abnormalities seen in oncocytomas and CDC. This tumor demonstrates, as is generally accepted, the ontogenetic proximity of oncocytoma, CRCC, and CDC. 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

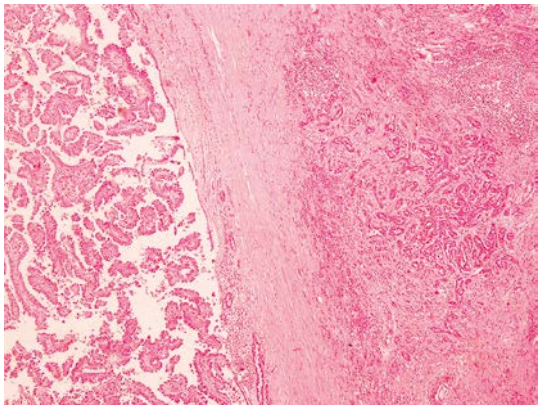

Figure 1. Papillary renal cell carcinoma (on the left) and collecting duct carcinoma (on the right) (H + E, 40×)

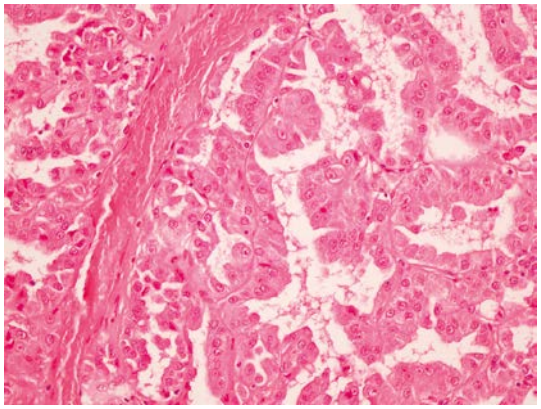

Figure 2. Papillary structures lined with columnar cells having coarse vesicular nuclei, prominent nucleoli and large eosinophilic cytoplasm (H + E, 200×)

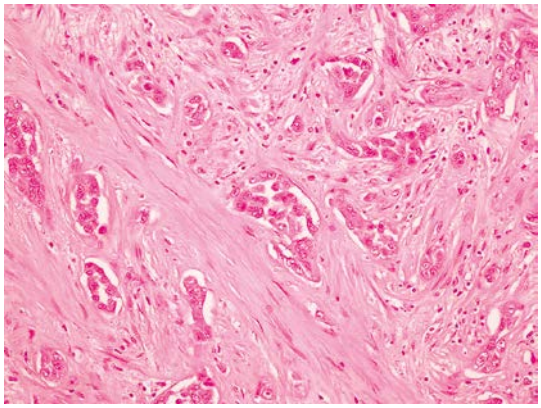

Figure 3. Infiltrative tubuloglandular formations in a desmoplastic stroma (H + E, 200×)

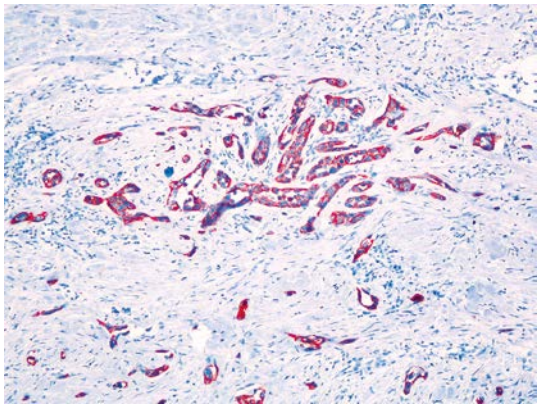

Figure 4. Collecting duct carcinoma component is positive with low molecular weight keratin (A + E1, 100×)

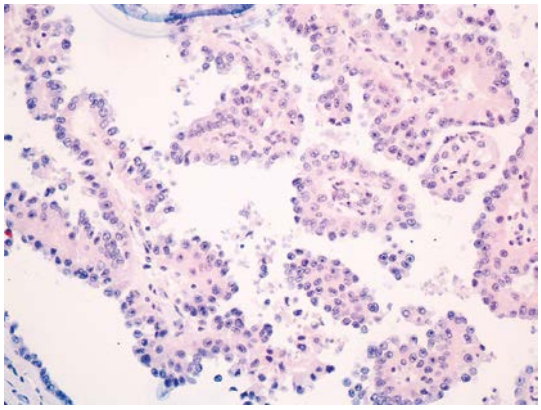

Figure 5. Papillary renal cell carcinoma component is negative with cytokeratin 19 (CK19, 200×)

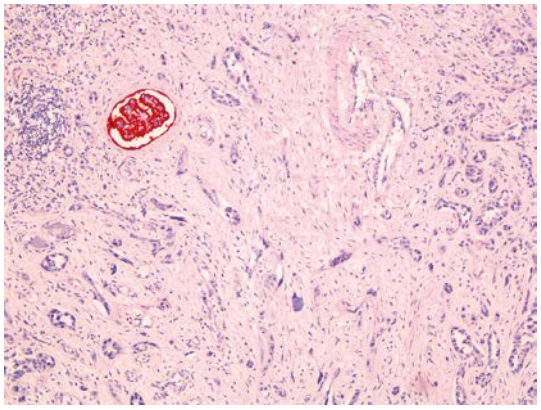

Figure 6. Collecting duct carcinoma component is positive with CD10. On the upper left renal glomerulus seems to be positive (CD10, 100×)

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
		Chromophobe	NS	3	
	62/M	Papillary	NS	4	Radiologic evidence of lung metastases
		Chromophobe	NS	5.5	
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
		Collecting duct			
Jun *et al.*	62/M	Chromophobe	Lower pole	1.7	Epithelioid angiomyolipoma
		Clear cell	Lower pole	0.6	
Cho *et al.**	24/M	Clear cell (unclassified)	Left inner nodule	1.5	Nodule-in-nodule pattern
		Collecting duct	Left outer nodule	14	
Lindgren *et al.**	47/M	Chromophobe	Right lower pole	8.5 cm as a single mass	Oncocytoma and sarcomatoid differentiation
		Collecting duct			
Matei *et al.*	70/M	Papillary	Left upper pole	0.5	
		Collecting duct	Left medulla	5.3	
Kawano *et al.**	64/F	Chromophobe	Left middle to the lower portions	4.3	Obvious transition to each other with dedifferentiation
		Collecting duct			
Roehrl *et al.**	65/M	Papillary	Left superior pole	5.4 cm as a single mass	
		Chromophobe			
Tyritzis *et al.*	57/M	Chromophobe	Lower pole	12.5	0.2 cm subcapsular tubulopapillary adenoma
		Papillary	Upper pole	5	
Tsai *et al.*	57/F	Clear cell	NS	NS	TCC of renal pelvis and acute pyelonephritis
		Collecting duct			
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	
		Chromophobe	Right lower pole	1	
	NS	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 what we have described.

Conflict of interest

The authors declare no conflict of interest.

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