Collision Tumor of the Kidney Composed of Clear Cell Renal Cell Carcinoma and Papillary Renal Cell Carcinoma-A Report of a Unique Case

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ABSTRACT
A collision tumor is characterized by the coexistence of two adjacent but different tumor types with no histological admixture, forming a single lesion. The author describes a 70-year-old man, who was found to have a solitary tumor in the left kidney. Histologically, it had two distinct yet intimately associated cancer components. The first one was a conventional clear cell RCC, while the second component represented a papillary RCC. The border between them was conspicuous and corresponding cell populations did not mix together. Immunohistochemically, papillary RCC component strongly expresses cytokeratin 7 and alpha-methylacyl-CoA racemase. The final diagnosis was a collision tumor consisted of clear cell RCC and papillary RCC. Three years after surgery the patient felt well without a locoregional recurrence or distant metastasis. A collision tumor of the kidney composed of two distinct RCC subtypes is very rare finding. At the biopsy examination, a careful inspection of entire tumor lesion with precise section sampling from all areas that look grossly different is important to unveil such possible association. Further clinical outcome may be questionable, because different RCC subtypes possess distinct biological behaviour. As a general rule, a prognosis is usually determined by higher-grade cancer component.

Key words: Collision tumor, Renal cell carcinoma, Histologic subtypes

INTRODUCTION
The term collision tumor refers to the phenomenon where two different and unrelated tumor types are present within the same location, forming a single lesion. They are well demarcated and lack tissue admixture [1]. In contrast, composite tumor also comprises two morphologically and immunohistochemically distinct neoplasms coexisting in a single lesion, but they lack sharp borders, have significant cellular intermingling and a common driver mutation that results in divergent histology [1]. Various mechanisms have been proposed to explain the “collision phenomenon”. The simplest explanation is the coincidental occurrence of two primary neoplasms within a common location [1]. The second hypothesis suggests that a common carcinogenic stimulus may have altered the cellular microenvironment within the proximity of which two distinct neoplasms arise from [1]. The last hypothesis suggests that the first tumor may have altered the microenvironment within the organ and increased the likelihood of developing another primary tumor [1].

In the kidney, collision tumors represent infrequent and usually unexpected biopsy finding. Theoretically, they may occur as a combination of any of the known benign or malignant renal tumors. Among them, however, a collision of two different renal cell carcinoma (RCC) subtypes is exceedingly rare. To the best of my knowledge, only a few cases have been published until now [2-9]. Herein, I briefly report a case of a collision tumor composed of the clear cell RCC and papillary RCC presenting as a solitary mass in the kidney.

CASE PRESENTATION
A 70-year-old man was admitted to the Department of Urology in the Faculty Hospital in Žilina (Slovakia) to provide a radical nephrectomy. He was previously diagnosed to have a large tumor in the left kidney. Abdominal CT scan showed an inhomogeneously enhancing tumor mass of 5 cm in the largest diameter, arising in the middle third of the kidney. No regional lymphadenopathy was noted. The patient underwent left-sided nephrectomy. Grossly, the kidney revealed a solitary intraparenchymatous tumor measuring 45 × 45 × 40 mm. It was yellowish in color and elastic in consistency. It did not expand throughout the renal fibrous capsule, but focal tumor invasion into the hilar fat was seen. Except for this site, however, the
Lesion was well-circumscribed and surrounded by a fibrous pseudocapsule. On microscopic examination, the tumor had two distinct yet intimately associated cancer components with divergent histomorphologies and immunohistochemical profiles (Figures 1 and 2). The first one, which comprised the majority of tumor mass (over 90%) also comprised a conventional clear cell RCC. It composed of typical neoplastic cells with a clear cytoplasm that were of low to intermediate nuclear grade (Fuhrman nuclear grade 2 and 3). Mild regressive changes, such as edema, hemorrhages and deposits of hemosiderin were visible. No necrosis was present. The second component represented a papillary RCC, subtype 1, Fuhrman nuclear grade 2. It was located just beneath the tumor pseudocapsule and exhibited tubulopapillary microarchitecture. Papillae were lined by a single layer of the cells with scanty basophilic cytoplasms and low nuclear grade. Foamy macrophages and occasional psammoma bodies were found. The border between both tumors was conspicuous and corresponding cell populations did not mix together.

**Figure 1:** Two distinct carcinoma subtypes in a single lesion: Papillary RCC (black arrow) at the periphery and clear cell RCC (blue arrow) in the centre. (hematoxylin & eosin; magnification: 150X)

**Figure 2:** Detail on interface between papillary RCC component (upper part) and clear cell RCC component (lower part). (hematoxylin & eosin; magnification: 200X)

Immunohistochemically, the papillary RCC component strongly express cytokeratin 7 (Figure 3) and alpha-methylacyl-CoA racemase (Figure 4). In the clear cell RCC component, cytokeratin 7 was negative, while alpha-methylacyl-CoA racemase was slightly expressed in some areas (<10% of tumor tissue). The final diagnosis was a collision tumor of the kidney consisted of the clear cell RCC and papillary RCC with hilar fat infiltration (stage pT3a). After receiving a biopsy report, the patient was referred to oncodispensary care and underwent further clinical examinations. None of the clinical and imaging investigations confirmed metastatic deposits. The patient underwent periodic clinical exams several times a year. Three years after surgery he felt well without a locoregional tumor recurrence or distant metastasis.

**Figure 3:** Strong expression of cytokeratin 7 in papillary RCC component (upper part), while clear cell RCC component (lower part) is negative. (Clone OV-TL 12/30, DAKO; magnification: 150X)

**Figure 4:** Strong expression of alpha-methylacyl-CoA racemase in papillary RCC component (upper part), while clear cell RCC component shows only slight focal positivity (black arrow). (Clone 13H4, DAKO; magnification: 150X)

**DISCUSSION**

RCC is very heterogeneous neoplasia that comprises different histological subtypes. Despite advances in molecular pathology, an accurate diagnosis and subclassification continue to be based primarily on histomorphology. The two most common histological subtypes include clear cell RCC and papillary RCC [10]. The first one represents approximately 75% of the cases. It may show solid, alveolar, or papillary microarchitecture and typically consists of cell population with a clear cytoplasm due to the accumulation of lipid and glycogen [10]. The second one comprises about 10% of the cases. It commonly shows well-developed fibrovascular cores expanded by foamy macrophages and microcalcifications that are lined by neoplastic cells with eosinophilic (type 2) or basophilic (type 1) cytoplasm [10]. These two subtypes exhibit some immunophenotypic differences [10,11]. While the papillary RCC is typically strongly positive for cytokeratin 7 and alpha-methylacyl-CoA racemase, they are usually negative in the clear cell RCC, although it may
sometimes show focal reactivity for both markers [11]. In general, the clear cell RCC carries a worse prognosis than the papillary RCC [10,11]. In a routine biopsy practice, a distinction between these histologic subtypes is usually not difficult. However, the cases of RCCs that show composite and overlapping histomorphology, such as tumors with mixed clear cell and papillary features, are increasingly seen in contemporary practice and present a great diagnostic challenge [10,11].

In the current case, as both tumor components were sharply demarcated from one another within a single lesion, keeping their own histomorphological identities and immunoprofiles, it allowed us to use the term collision tumor. As far as I know, only a few case reports addressing collision tumors of the kidney consisting of two different RCC subtypes have been documented in the literature. I have reviewed eight cases, which are briefly summarized in Table 1 [2-9], including the present case. The mean age of the patients was 63.4 years (range 24-72 years) with no apparent gender predominance. A combination of five histologic subtypes has been found in the individual tumor lesions, of which the papillary RCC was the most common.

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F=Female; M=Male; RCC=Renal Cell Carcinoma

Table 1: Summary of clinicopathologic findings of the patients extracted from published case reports

CONCLUSION

A collision tumor of the kidney composed of two distinct RCC subtypes is very rare and usually incidental finding. At the biopsy examination, a careful inspection of entire tumor lesion with precise section sampling from all areas that look grossly different is important to unveil such possible association. Further clinical outcome may be questionable, because different RCC subtypes possess distinct biological behaviour. As a general rule, a prognosis is usually determined by higher-grade cancer component.

ACKNOWLEDGEMENT

The author would like to thank all physicians, who participated on treatment and clinical management of this patient.

REFERENCES