Mixed Oncocytoma and Papillary Renal Cell Carcinoma

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Abstract

The hybrid tumors composed of oncocytoa and chromophobe renal cell carcinoma (ChRCC) are known to occur. They are seen in 3 settings, namely Birt-Hogg-Dubé Syndrome, renal oncycytosis, and as sporadic neoplasia. However, mixed renal tumors composed of a component other than ChRCC in addition to oncocytoa are extremely rare. Herein, a renal cell neoplasm consisted of two intermingled components, namely oncocytoa and papillary renal cell carcinoma were presented.

Introduction

Renal oncocytoas comprise 3–7% of all renal tumors, and are biologically benign [1,2]. They consist of uniform and round or polygonal cells that contain abundant eosinophilic granules in the cytoplasm that have been identified as mitochondria electron microscopically [3]. Neoplastic nests usually lie in a loose edematous stroma. The cell of origin of renal oncocytoa (RO) is thought to be the intercalated cells of collecting tubules [4].

Papillary renal cell carcinoma (PRCC) is the second most common subtype of renal cell carcinoma. It is believed to derive from proximal tubular epithelium [5]. This tumor exhibits papillary or tubulopapillary architecture. PRCC has been conventionally divided into two types. In type 1 carcinomas, papillae are lined by single layer of cells often with scanty pale cytoplasm. Type 2 PRCCs show cells with higher nucleolar grade and abundant eosinophilic cytoplasm, and pseudostratification.

Coexistence of PRCC and RO within the same tumoral mass is extremely unusual. There are only 7 such cases previously documented in the literature up to now. In each of these reports, an oncocytoa has been the main tumor and a smaller focus of papillary renal cell neoplasia has been found embedded within it. In this article, a unique case of intimately mixed RO and PRCC in a single tumor mass is presented.

Case Presentation

An 49-year-old man was referred to our hospital after detection of a renal mass on abdominal ultrasonography during regular medical check-up. His physical examination was unremarkable. His urinalysis and other routine blood tests were normal. Computed tomography disclosed that the mass was located at the upper pole of right kidney, was 4.2×4.0×3.4 cm in size and well circumscribed with contrast enhancement. Right partial nephrectomy was carried out.

Macroscopic examination revealed 4.5x4x3.5 cm well-circumscribed solid lesion in the renal parenchyma, yellowish/tan in color with white stellate scar in the center (Figure 1A). Light microscopy showed that the tumor was composed of two distinct elements differing both in pattern and cell morphology (Figure 1B). The first component contained nests of larger cells with dark eosinophilic cytoplasm and rounded regular nuclei, reminiscent of oncocytoa. Within this, closely blended with oncocytic nests, there was a second component made up of tubules and papillae. Tubulopapillary structures were formed by cells with different cytologic features than oncocytoa cells; they had narrower cytoplasm and oval small nuclei.

Immunohistochemical stainings demonstrated strong expression of cytokeratin 7, vimentin, α-methylacyl-CoA racemase and CD10 in the tubulopapillary areas (Figure 2 and 3). Oncocytoa component was negative for these markers but showed positivity for CD117. Based on its morphological features and immune profile, the tumor was diagnosed as mixed renal oncocytoa and type 1 PRCC.

There was no extra capsular tumor infiltration into perinephric fat tissue. Neither necrosis nor lymphovascular permeation was seen. Surgical margins were free of tumor.
Renal oncocytoma (RO) is a neoplasm of renal epithelial origin that has been thought to be derived from intercalated cells of collecting tubules [4]. On the other hand, papillary renal cell carcinoma (PRCC) is considered as proximal tubular origin [5]. ROs occasionally coexist with chromophobe renal cell carcinomas that similarly develop from intercalated cells [6]. However, coexistence of RO with papillary renal cell neoplasm is extremely rare even though PRCC is the second most frequent pathological subtype of RCC. There are only 7 such cases formerly reported in the literature [7-13] (Table 1). The age of patients in the previous reports ranged between 60 and 78, our patient was the youngest among them being 49. Clinical presentations were various, such as abdominal pain, normocytic anemia, lethargy, anorexia and hypercalcemia as well as hematuria. Three cases including ours were discovered incidentally. Total tumor size varied between 1.5 cm and 6 cm in diameter, was 4.5x4x3.5 cm in the current case. In all these lesions, the PRCC represented the smaller component and showed low grade nuclei. Our case differed from the others in that the PRCC within oncocytoma was not well delineated focus, but rather two components were intermingled closely. This is in contrast to former cases where PRCC was distinct on both gross and microscopic examination within oncocytoma.

None of the tumors had evidence of tumor recurrence or metastasis. This is consistent with low size and grade of PRCC component. In fact, according to last WHO (2016) classification of renal neoplasia, most previous lesions would be considered papillary renal tubular adenomas today instead of papillary renal cell carcinoma as the cut-off size between these two entities has been raised to 1.5 cm [14]. Only our case and the case reported by Özer et al. [12] have papillary renal cell neoplasia above this threshold diameter and can be diagnosed as PRCC today.

Renal oncocytoma has unique histologic features including an organoid and tubulocystic architecture, myxoid or hyalinized stroma, and occasionally some atypical findings including nuclear pleomorphism, prominent nucleoli, and adjacent renal parenchymal and perinephric fat involvement. By definition it lacks areas of clear cell carcinoma or conspicuous papillary arrangement. The current case demonstrating papillary formations imposes the differential diagnosis of the lesion with PRCC showing oncocytic change [15]. PRCC with oncocytic cytoplasm and oncocytoma like low-grade nuclei have been called oncocytic papillary renal cell carcinomas [16] although they are not considered as a specific subtype of RCC in the last WHO (2016) renal neoplasia classification due to their incomplete characterization yet. Our case differed from oncocytic papillary RCC in that it had two distinct components both morphologically and immunohistochemically. Areas of papillary RCC have demonstrated strongly positive staining of CK7, CD10, vimentin and alpha-methylacyl-CoA racemase (AMACR), which is characteristic of PRCC [17] whereas these markers have stained negative in oncocytic regions. Papilla formations have been limited to papillary RCC areas.
and not found in oncocytic regions. Furthermore, papillae have lining cells with pale narrow - but not copious eosinophilic - cytoplasm.

The association between oncocytoma and papillary renal cell neoplasia is hard to explain since there are only scarce previously reported cases. Since they have different genetic backgrounds, it is not possible to suggest common pathogenesis. Most likely, they are collision tumors that happen to arise together at the same site by coincidence. However their existence creates a concern thinking that when pathology is about to make a call of oncocytoma in a tumor biopsy sample, the possibility of unsampled malignant component might be needed to be brought into the consideration. These tumors pose challenges to the urologists, pathologists and oncologists who might be needed to be brought into the consideration. These tumors are benign proliferations but papillary RCC has malignant potential. Hybrid tumors containing both elements might be difficult to approach clinically. Novel cases with these types of rare tumors are needed to be reported in the literature so that additional information concerning optimal treatment policy and the prognosis of these patients can be obtained.

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### References


