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A Rare Case of Synchronous Oncocytoma and Angiomyolipoma of the Kidney

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Conflict of interest: None declared

Patient: Female, 75-year-old
Final Diagnosis: Oncocytoma and angiomyolipoma
Symptoms: Epigastric discomfort
Medication: —
Clinical Procedure: —
Specialty: Pathology

Objective: Rare disease

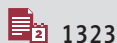
Background: The co-occurrence of renal oncocytoma and angiomyolipoma is exceedingly rare. To date, 17 such cases have been reported in the literature. This report describes a unique case of that association that presented as a single renal mass on imaging.

Case Report: A 75-year-old woman presented with epigastric discomfort. A CT scan of the abdomen revealed a 6.6×5.7×4.7 cm enhancing right renal mass. Gross examination revealed a nodular, well-circumscribed, tan-brown mass located in the lower pole of the kidney that was abutting the renal capsule. Interestingly, superior to this mass, there was an adjacent, pale tan-white, firm, well-circumscribed nodule in the mid-pole, which was not detected on the CT scan and grossly extended to 1.1 cm of the overlying renal capsule. Histologically, the larger tumor showed characteristic features of oncocytoma. The smaller tumor had an admixture of mature adipose tissue, smooth muscle, and vessels, consistent with a renal angiomyolipoma.

Conclusions: We present a new case of synchronous renal angiomyolipoma and oncocytoma, which were uniquely adjacent and coexisted with minimal intermingling renal parenchyma. Other "eosinophilic renal tumors" are significant differential diagnosis considerations. Due to the close proximity of these lesions, this association can present clinically and radiologically as a single renal mass. Careful examination of the nephrectomy specimen is essential for the proper detection of small-sized tumors.

Keywords: Angiomyolipoma • Kidney Neoplasms • Oncocytoma, Renal

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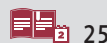
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Background

Renal oncocytomas and angiomyolipomas are benign renal neoplasms that usually present as incidental findings on imaging [1]. Of all resected renal tumors, renal oncocytomas account for 3% to 7%, and angiomyolipomas constitute about 1% [2,3]. To the best of our knowledge, the co-occurrence of angiomyolipoma with oncocytoma is infrequent and has been reported in only 17 cases, with 3 cases in the context of tuberous sclerosis [4,5]. This paper presents a case report of that association.

Case Report

A 75-year-old woman presented with epigastric discomfort, without pain, hematuria, or weight loss. She had no significant past medical history or family history of cancer. Creatinine, electrolytes, and hemoglobin levels were within normal ranges. A CT scan of the abdomen, with and without IV contrast, revealed a 6.6×5.7×4.7 cm enhancing right renal mass (Figure 1A). No retroperitoneal lymphadenopathy or masses in the contralateral kidney were noted. The left kidney was radiographically unremarkable.

Subsequently, the patient underwent immediate right total nephrectomy. The 298-g nephrectomy specimen displayed a 6.8×5.4×4.9 cm brown, nodular, well-circumscribed mass with a central stellate scar. No evidence of necrosis, perirenal fat, or renal vein involvement was noted. Interestingly, a 0.8×0.7×0.7 cm, pale tan-white, firm, well-circumscribed nodule was found 0.2 cm superior to the mass. These tumors were separated by a small amount of parenchyma (Figure 1B).

Microscopic examination revealed 2 adjoining lesions separated by a thin area of renal parenchyma (2 mm in thickness) (Figure 2A). The larger tumor consisted predominantly of nests of cells with abundant granular eosinophilic cytoplasm, uniform round nuclei, and regular centrally-located nucleolus. Localized collections of degenerative cells with nuclear atypia were also present (Figure 2B). In contrast, the smaller tumor was triphasic, well-circumscribed, and composed of spindled myoid cells admixed with thick hyalinized blood vessels and adipose tissue. Aggregates of more epithelioid tumor cells were focally present surrounding the vessel walls. Scattered hyperchromatic nuclei were present (Figure 2C). The absence of mitosis was noted on both tumors.

The larger tumor showed diffuse nuclear expression with PAX-8 and cytoplasmic/membranous positivity for CD117 by immunohistochemistry, consistent with oncocytoma (Figure 2D, 2E). However, the smaller tumor was focally positive for HMB45, and positive for SMA and melan-A, with diffuse cytoplasmic expression (Figure 2F). In addition, both tumors were negative for CK7. A recent follow-up of the patient using CT scan showed no evidence of local recurrence or metastatic tumors.

Discussion

Renal oncocytomas are benign renal tumors within the so-called “pink” renal neoplasms, composed of mitochondria-rich cells with a specific metabolic pathway to eliminate ATP consumption. Therefore, tumor cells manage to accumulate mitochondria and energy carrier molecules such as NAD⁺, NADH, NADP, ATP, and ADP in their cytoplasm [6]. Classic oncocytomas

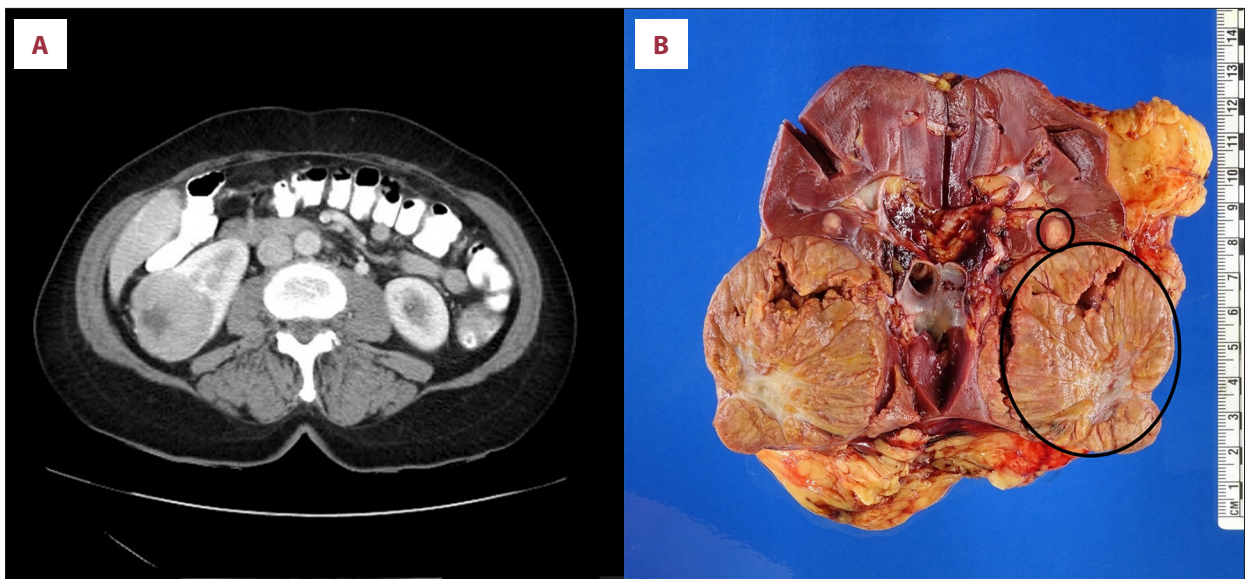


Figure 1. (A) CT imaging shows right renal mass (6.6 cm in diameter). (B) Photograph of the gross surgical specimen of the right kidney (bivalved coronally) shows the presence of 2 renal masses.

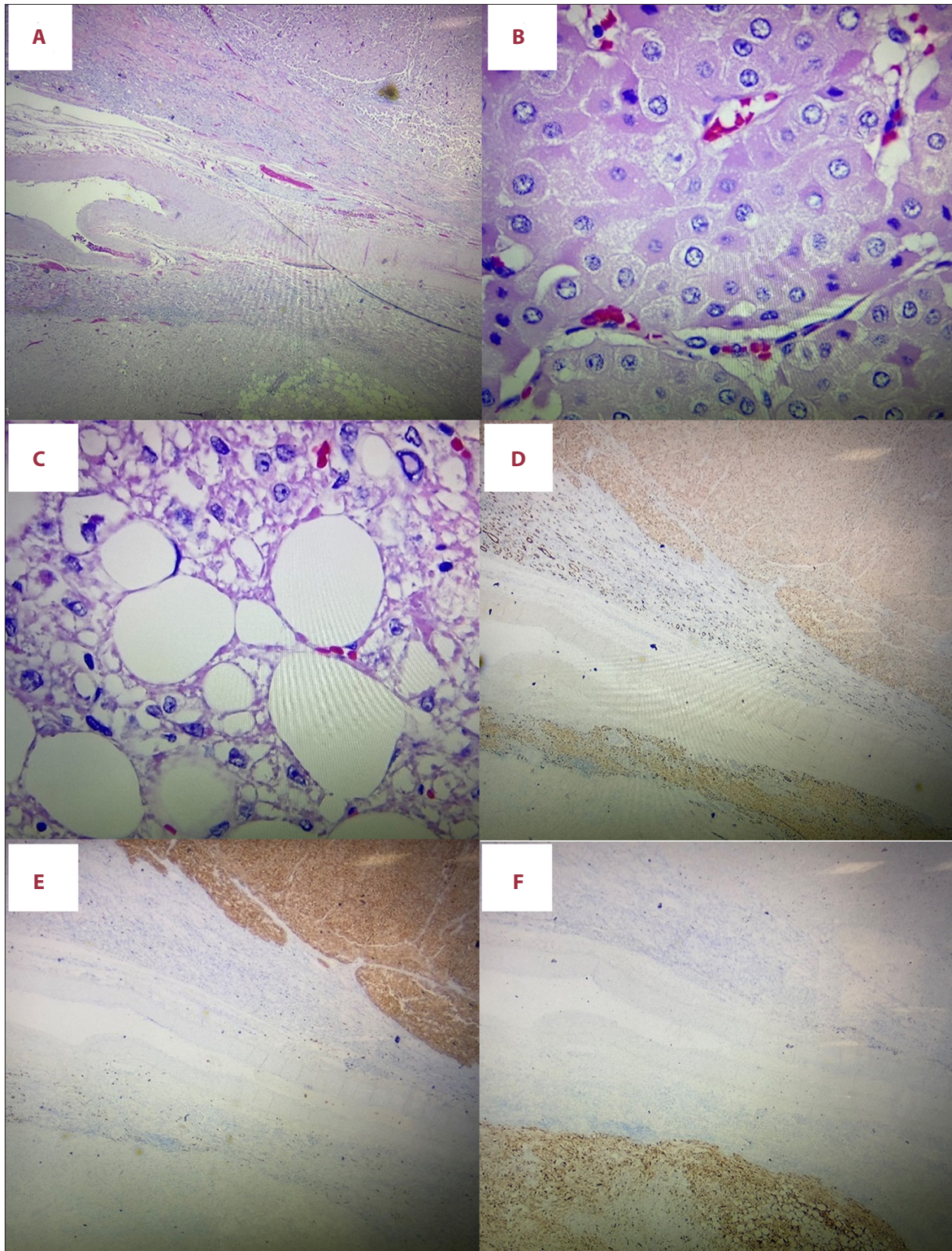


Figure 2. (A) H&E-stained section shows the relationship between the 2 masses. The oncocytoma is present in the upper field separated from AML, which is present in the lower field, showing as a thin area of renal parenchyma (40×). (B) H&E-stained section of the larger tumor shows tumor cells with dense eosinophilic cytoplasm and round regular nuclei (400×). (C) H&E-stained section of the smaller tumor shows admixture of mature adipose tissue formation and aggregate of epithelioid tumor cells (400×). The oncocytoma is positive for PAX-8 (D) and CD117 (E), while the AML is positive for melan-A (F) (40×).

are well-circumscribed tumors with a tan or mahogany-colored cut surface and frequently display a central satellite scar. Microscopically, oncocytomas are composed of islands of tumor cells with dense eosinophilic cytoplasm in loose hypocellular connective tissue [7].

Unfortunately, these classic features are not always present, and the diagnosis of oncocytoma frequently overlaps with chromophobe renal cell carcinoma (ChRCC) [8]. Unlike oncocytomas, typical ChRCCs have a higher nuclear grade, prominent cell borders, perinuclear halos with irregular “raisinoid” nuclei, and mitotic activity [9]. Immunohistochemistry shows oncocytomas are positive for CD117 like ChRCC but are negative or only have patchy positivity toward cytokeratin 7 (CK7). One of the most challenging differential diagnoses is with low-grade oncocytic tumors (LOT), which do not fit the diagnostic criteria of these 2 entities. Such “difficult to classify” tumors may not have the classic features of ChRCC, but demonstrate a variety of atypical features such as nuclear size variability and nuclear membrane irregularity in a diffuse or focal distribution. Various diagnostic terms have been used when referring to such borderline tumors that do not strictly fit the criteria for either oncocytoma or ChRCC. Low-grade oncocytic renal tumor (LOT) has been identified as a provisional entity that morphologically shows eosinophilic cells in solid and nested patterns admixed with sharply demarcated edematous areas and has demonstrated an indolent clinical course [10]. They show a characteristic immunoprofile with a diffuse expression of CK7 and a negative expression of CD117. Studies have demonstrated LOTs harbor *TSC/MTOR* mutations [11], but more studies are necessary to characterize them further.

In addition, oncocytomas can mimic other renal cell tumors such as clear cell RCC eosinophilic variant, succinate dehydrogenase (SDH)-deficient RCC, low-grade FH-deficient RCC, MiT family translocation, and eosinophilic vacuolated tumors (EVTs) [12]. The absence of vacuolated cytoplasm and neuroendocrine-like nuclei rules out SDH-deficient RCC and EVT [13,14]. Likewise, the lack of psammomatous calcification, biphasic changes with basement membrane formation, hyaline globules, and CMV/Cytomegalovirus-like nucleoli excludes fumarate hydratase (FH)-deficient and MiT family translocation RCCs [15,16]. Moreover, useful IHC markers such as CD117, PAX-8, Hale colloidal iron, CAIX, TFE3, SDH, and CK7 can help differentiate oncocytoma from these tumors, as oncocytoma will be positive for CK7 and CD117, but negative for other markers [17]. The oncocytoma tumor cells in our patients were positive for CD117 and PAX-8 and negative for CK7.

Angiomyolipomas belong to a family of neoplasms called perivascular epithelioid cell tumors (“PEComas”), which are identified by the proliferation of unique epithelioid cells distributed around blood vessels [18]. Angiomyolipomas can occur

sporadically (50-70% of cases) or as inherited neoplasms in patients with tuberous sclerosis (30-50%) [19]. Angiomyolipomas, with or without associated tuberous sclerosis, tend to occur in females. Microscopically, they are composed of a variable mixture of mature adipose tissue, blood vessels, and smooth muscle [20]. In the present patient, the classic morphology of the smaller tumor on H&E and co-expression of 2 different IHC markers that confirm the myelomelanocytic lineage (SMA and melan-A) was sufficient to establish the diagnosis of angiomyolipoma for the smaller tumor.

Surgical excision with thorough follow-up was the treatment of choice because there is no definite method to identify these tumors or target them with medications preoperatively [21]. Since these tumors are derived from the perivascular epithelioid cell, they are characteristically positive for melan-A [22]. Interestingly, angiomyolipoma can have oncocytoma-like patterns, known as oncocytoma-like epithelioid PEComa [23]. In these cases, the tumors consist of uniform epithelioid and plump spindle cells, with no fascicles of smooth muscle, blood vessels, or fat cells. Also, these tumors tend to have characteristic diffuse growth and lack of atypia. Three cases have been reported with no signs of tuberous sclerosis found [23,24].

Finally, the size of the angiomyolipoma observed highlights that these tumors can be small, and a careful examination of the nephrectomy specimen is required for proper detection. On imaging, angiomyolipoma can appear as hypoattenuating areas, particularly if the tumor has high fat content [25]. Although a correlation between the morphology, immunohistochemistry, and molecular analysis is sometimes required to confirm eosinophilic tumors, histological assessment using H&E remains the criterion standard to differentiate these tumors.

Conclusions

In conclusion, we present a case of synchronous renal angiomyolipoma and oncocytoma, which were uniquely adjacent to one another and coexisted with minimal intermingling renal parenchyma in between. Seventeen cases have been described in the literature and an association with tuberous sclerosis complex is not always present. Microscopic examination using H&E followed by confirmatory immunohistochemistry is required for diagnosis. Surgical excision provides a definitive cure for cases with this association. Other “eosinophilic renal tumors” that mimic oncocytomas are the primary differential diagnosis that must be considered. A thorough examination of the nephrectomy specimen is essential for the proper detection of small tumors that can be missed on radiological examination, particularly with the close proximity of lesions.

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