

## Case Report

# Renal angiomyolipoma with epithelial cysts: a rare entity and review of literature

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**Abstract:** Renal angiomyolipoma (AML) with epithelial cysts (AMLEC) is a comparatively rare benign renal tumor that is recently recognized as a distinct entity and there are relatively few reported cases in the English-language literature. To date 19 cases of AMLEC have been reported in 2 case series and a few case reports. AMLEC has been described as a cystic variant of AML. Herein we reported an AMLEC in a 25-year-old female patient, and to the best of our knowledge this is the first case report of AMLEC in Chinese. She was incidentally found to have a kidney-occupying lesion during a routine medical examination for 1 month. CT examination demonstrated a multilocular cystic lesions arising from right-kidney lower pole. The patient underwent the partial nephrectomy. Histological examination of the tumor was composed of epithelial cysts, compact subepithelial mullerian-like stroma and muscle-predominant AML. Immunohistochemically, epithelial cysts were positive for CK but negative for ER, PR, CD10 and HMB-45; the subepithelial stroma and muscle-predominant AML were positive for ER, PR and HMB-45; the subepithelial stroma was negative for SMA, but muscle-predominant AML was positive for SMA. The final histopathological diagnosis was AMLEC.

**Keywords:** Kidney, angiomyolipoma with epithelial cysts, mixed epithelial and stromal tumor

## Introduction

Angiomyolipoma (AML) is well-characterized triphasic tumor, composed of varying amounts of adipose, vascular (thick-walled or dysplastic blood vessels), and smooth muscular (spindled or epithelioid with clear cytoplasm). The triphasic nature of AML has led many to consider these lesions as hamartomatous in the past, however, current evidence, based on clonality studies and rare case reports of malignancy and metastasis in AML, supports their classification as neoplastic [1]. AML share morphologic and immunohistological features with perivascular epithelioid cell, so it is considered to originate from the perivascular epithelioid cell. AML is part of a growing family of lesions that includes clear cell ("sugar") tumors of the lung and pancreas, and lymphangioliomyomatosis.

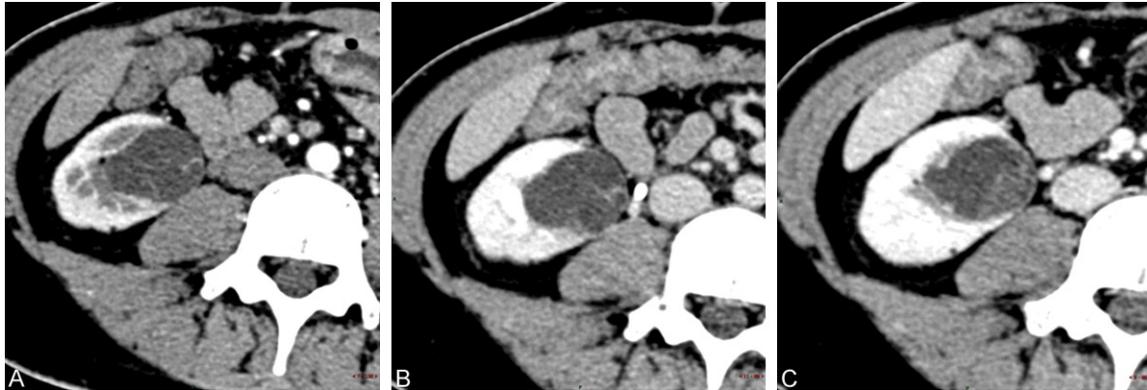
AML is generally solid mass both radio graphically and grossly, without cystic or epithelial components. Although we known that entra-

pped renal tubules may be observed in AML, presentation as a cystic mass has been reported recently in only 19 cases in six case series. An extremely rare variant of AML was first reported in two case series in 2006, termed angiomyolipoma with epithelial cysts (AMLEC) by Fine et al. [2]. And cystic AML by Davis et al. [3]. Four subsequent case reports of this entity used the designation AMLEC [4-7]. Therefore, AMLEC should be considered in the differential diagnosis of adult cystic renal neoplasms, which includes cystic nephroma (CN), mixed epithelial and stromal tumor (MEST), multilocular cystic renal cell carcinomas, cystic partially differentiated nephroblastoma, and others. Herein we report a rare case of renal AMLEC in a 25-year-old woman and present a brief review of the literature.

## Case report

A 25-year-old Chinese female had a right kidney tumor incidentally discovered during routine medical examination. Physical examina-

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**Figure 1.** CT findings revealed a polycystic low density shadow measuring 34 mm × 28 mm in the lower lobe of the right kidney (arterial phase A, venous phase B and delay phase C).

tion: There was no abdominal tenderness, rebound tenderness and palpable abdominal mass. Murphy sign was negative; there was no percussion pain under the kidney area, and no tenderness under the bilateral ureteral traveling area. Routine laboratory investigations were normal, including complete blood count and serum urea and electrolyte levels. Tumor markers, including  $\alpha$ -fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9, were all within normal limits. The liver and kidney function tests were normal. CT findings revealed a polycystic low density shadow measuring 34 mm × 28 mm in the lower lobe of the right kidney, the boundary was clear, dynamic enhanced scanning the mass with an moderate enhancement in the edge nodes and segmentation, and the effect was weakened in the delay phase (**Figure 1A-C**). Imaging reminded multilocular cystic renal cell carcinoma. She had no personal or family history of tuberous sclerosis (TSC), renal cyst, renal malignancy or lymphangiomyomatosis. The patient underwent a lower-pole partial right nephrectomy. Our patient has been free from tumor recurrence and metastasis in the 18 months since surgery.

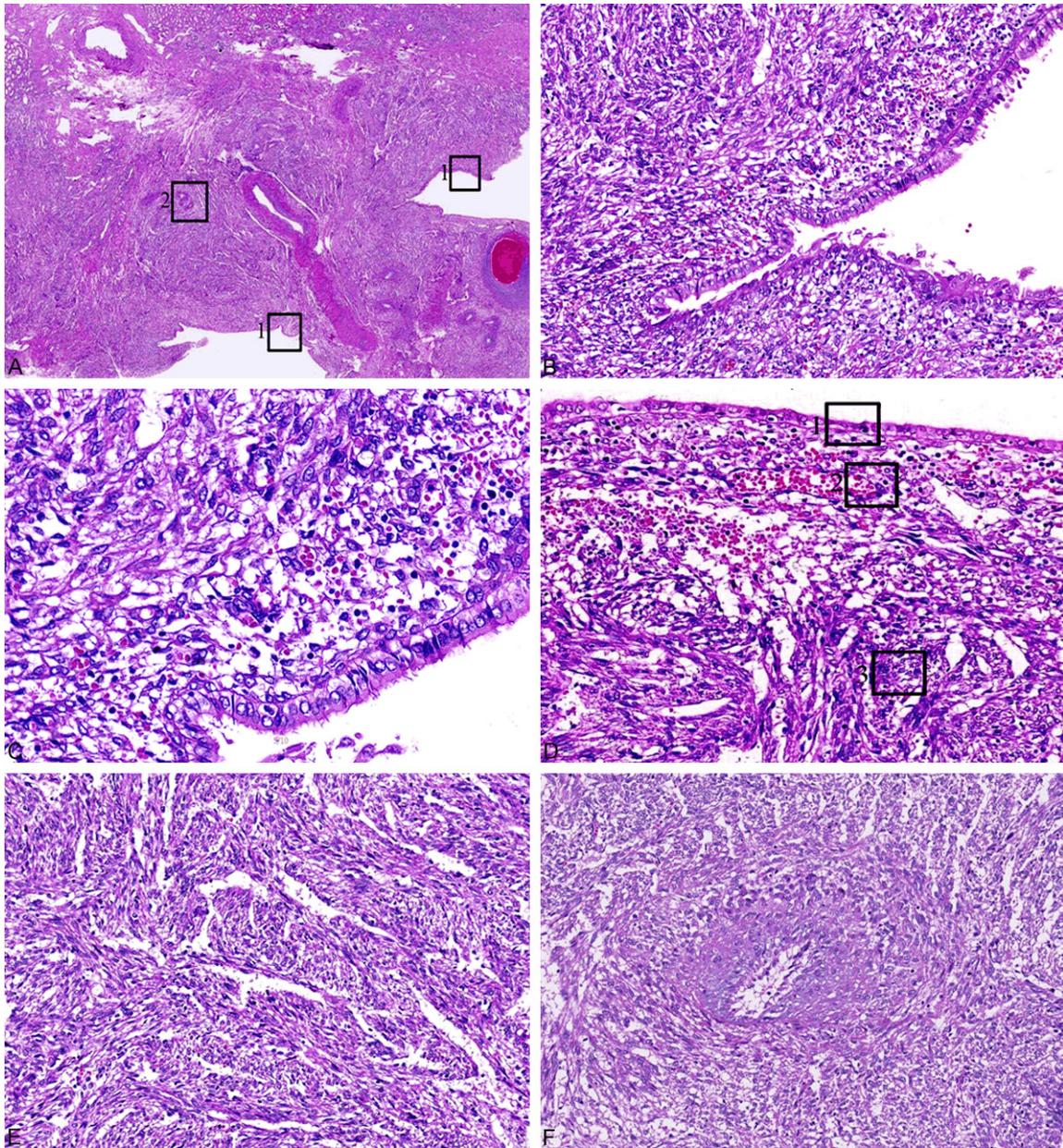
### Pathological examination

Grossly, the size of the surgical specimen was 4.0 cm × 3.0 cm × 2.0 cm, and tumor was 2.5 cm in largest diameter. On cross-sections the tumor was yellowish-white with a cyst measuring up to 0.8 cm, inner surface was smooth, with clear liquid, wall thickness was about 0.1 cm. Microscopically, there was no capsule between the tumor and the surrounding normal

tissue, and revealed three components (**Figure 2A**). The first component was cystic spaces lined by epithelium which ranged from flat to cuboidal to columnar and hobnail cells, whereas the flat cells had abundant eosinophilic cytoplasm with nuclei, the cuboidal to columnar cells had unremarkable clear cytoplasm (**Figure 2B**). The second component was a subepithelial “cambium-like” stroma immediately subjacent to the cyst epithelium, this subepithelial stroma showed mullerian-like stroma with admixed lymphoplasmacytic infiltrate and red blood cells extravasation (**Figure 2B, 2C**). The third component was exterior to the subepithelial stroma and was typical muscle-predominant AML, which was a thick exterior wall of spindle shaped smooth muscle cells in formed fascicles, often appearing to emanate from irregular thick-walled or dysplastic blood vessels, and prominent lymphatic spaces (**Figure 2D-F**).

Immunohistochemically, HMB45 was positive in the subepithelial “cambium-like” stroma and exterior muscle-predominant AML (**Figure 3A**). SMA was positive in the exterior muscle-predominant AML, but negative in the compact subepithelial stroma (**Figure 3B**). CD10 was positive in the compact subepithelial stroma, but it was negative in the muscle-predominant AML (**Figure 3C**). The subepithelial stroma and exterior muscle-predominant AML were strong and diffuse positive for ER (**Figure 3D**) and PR (**Figure 3E**). The cyst lining epithelia was positive for pancytokeratin (CK) (**Figure 3F**), but was negative for HMB-45, SMA, CD10, ER and PR. Ki-67 nuclear proliferation index was positive less than 2% of neoplastic cells.

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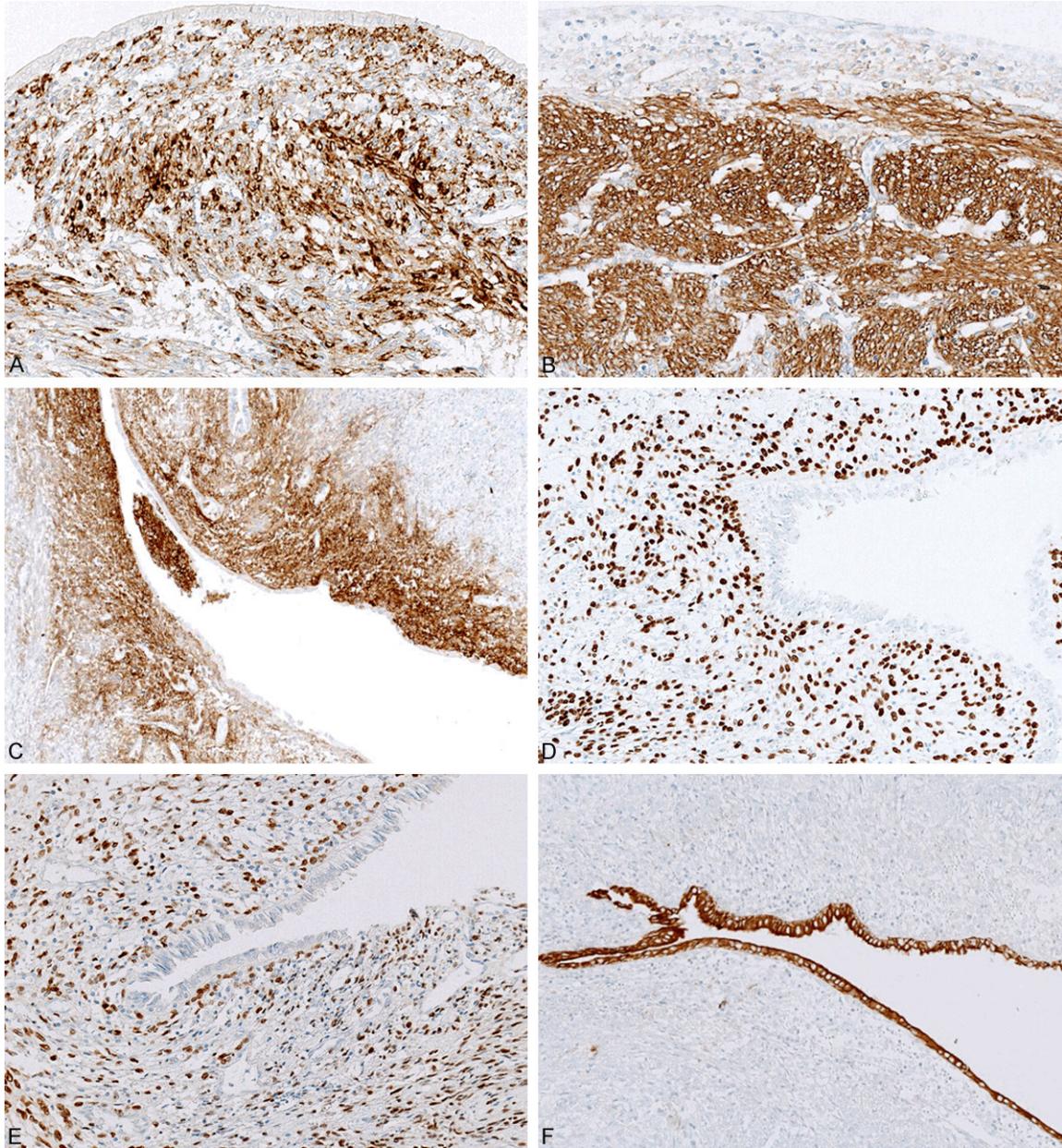
**Figure 2.** Microscopically, histological findings of three components of AMLEC. There was no capsule between the tumor and the surrounding normal tissue, at low magnification, epithelial cysts (boxed area 1) and typical AML regions (boxed area 2) was easy to be identified (A); epithelial cysts lined by columnar to hobnail cells, and a sub-epithelial “cambium-like” stroma with admixed lymphoplasmacytic infiltrate and red blood cells extravasation (B and C); epithelial cysts lined by cuboidal cells (boxed area 1), and was typical muscle-predominant AML component (boxed area 3) which was exterior to the subepithelial stroma (boxed area 2) (D); muscle-predominant AML with associated prominent lymphatic spaces (E) and dysmorphic thick-walled blood vessels (F).

### Discussion

Angiomyolipoma with epithelial cysts (AMLEC) is a rare variant of angiomyolipoma with minimal fat that contains epithelial-lined cysts. The 19 reported cases of AMLEC demonstrated similar demographic and clinical features as

conventional AML [2-7]. Patient age ranged from 20 to 76 years (mean age 44, median age 45). The female:Male ratio was 11:8. The left:right side location ratio was 10:9. All patients did not have a history of hormonal therapy. Only one of the 20 patients (including our cases) had TSC, suggesting that AMLEC

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**Figure 3.** Immunohistochemically, a subepithelial “cambium-like” stroma and muscle-predominant AML showed HMB45 staining (A); SMA was positive in the exterior muscle-predominant AML, but was negative in the compact subepithelial stroma (B); CD10 was positive in the compact subepithelial stroma, but it was negative in the muscle-predominant AML (C); The subepithelial stroma and exterior muscle-predominant AML were strong and diffuse positive for ER (D) and PR (E); The cyst lining epithelia was positive for CK (F).

may not be related to TSC [2]. Clinical manifestations included incidental finding, flank pain, hematuria, proteinuria, hypertension, and retroperitoneal hemorrhage et al. [2-7]. Our patient was found to have kidney-occupying lesion incidentally when undergoing an abdominal B ultrasound examination during a routine medical examination.

There are no tumor markers or imaging characteristics that allow a preoperative diagnosis for AMLEC, the diagnosis is based entirely on histopathological and immunohistochemical findings. Grossly, the tumor was well demarcated and partially cystic, measured between 1.3 and 7.0 cm in greatest dimension. Microscopically, AMLEC was composed of three components: 1)

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epithelial cysts lined by flat, cuboidal, columnar or hobnail cells; 2) a compact subepithelial “cambium-like” layer of cellular, mullerian-like stroma with prominent admixed chronic inflammation; and 3) muscle-predominant AML exterior to the cellular subepithelial stroma. Immunohistochemically, the compact subepithelial stroma was positive for HMB-45, ER, PR and CD10, but muscle-predominant AML was mainly positive for SMA and HMB-45. Epithelial cysts were positive for CK. Based on the pathological morphology and immunohistochemical result that subepithelial compact stroma and muscle-predominant AML were positive for HMB-45, the final diagnosis was AMLEC.

With regard to the differential diagnosis, AMLEC are notably distinct from most adult cystic renal tumors. When considering a grossly cystic lesion, one must always exclude cystic nephroma (CN), mixed epithelial and stromal tumor (MEST), multilocular cystic renal cell carcinomas (MCRCC), cystic partially differentiated nephroblastoma (CPDN) et al. CN and MEST represent opposite ends of the same entity [8, 9]. CN is characterized by thin septa with paucicellular ovarian-type stroma and may possess flat, cuboidal or hobnail epithelium, but they lack a compact subepithelial “cambium-like” layer, dysplastic vessels and smooth muscle which the characteristic features observed in AMLEC. There are a lot of overlaps between AMLEC and MEST on the morphology. Cysts lined by cuboidal or hobnail epithelia and smooth muscle walls are their common features, MEST stroma may be hypocellular and fibrous, but are often composed of well-formed smooth-muscle fascicles. Furthermore, the stromal cells of AMLEC and MEST are immunoreactive for ER, PR and CD10. However, 90% cases of MEST predominantly occur in women and male patients have long-term history of hormone therapy, but AMLEC occur in men without a history of exogenous hormone exposure. The vessels of AMLEC have dysplastic features, which are not observed in MEST [8-10]. And the biggest distinguishing point is that AMLEC is positive for melanocytic markers HMB45 and Melan A, but MEST is negative for the two markers. In the MCRCC, the cysts are lined by single layers of clear epithelial cells with grade 1 nuclear, there are no thick-walled blood vessels and smooth muscle walls, also the stromal cells are negative for ER, PR and

CD10 [11]. CPDN are usually presented before the age of 2 years, which having immature to maturing nephroblastomatous epithelial and stromal elements, along with characteristic blastema [12].

The histogenesis of AMLEC is unclear. Filho et al. [4] found that diffuse and strong expression of Melan A and focal expression of HMB45 in the cyst lining epithelia in a renal epithelioid AMLEC, which likely represents the stromal-epithelial interaction, strongly suggests that those cysts were derived from AML, rather than entrapped native collecting duct epithelium. Also Davis and his colleagues [3] supported the view that the epithelial component of AMLEC represented true epithelial differentiation towards the AML, but Fine and colleagues [2] favored the view that it mainly represented entrapped native renal collecting duct epithelium. Both views seem to be rational. In addition the strong HMB-45, ER, PR, and CD10 positivity of the “cambium-like” layer of compact subepithelial cells, not only supports the viewpoint that they are a variant of AML, but also suggests mullerian differentiation, although their morphology is distinctly different from the exterior muscle-predominant AML.

The behavior of AMLEC appears to be no different from other AML. AML are generally considered benign with an indolent clinical course, only a few reports have described AML was malignant and could be metastasis [13]. There is no standard treatment for renal AMLEC with particularly rare cases, complete surgical excision of the tumor may be the only potentially curative treatment. 11 of 20 (including our cases) patients had partial nephrectomy, and the other 9 had radical nephrectomy. None of them received radiotherapy and chemotherapy. 11 of 20 patients were no evidence of disease by follow-up ranging from 6 months to 108 months (median: 24 months; mean: 43.6 months), one patient died of unrelated disease at 3 years, 8 patients were lost follow-up. It seems feasible that a partial nephrectomy is performed for renal AMLEC < 5 cm in size, but larger (> 5 cm) may be treated by radical surgery. Chemotherapy or radiation therapy is unnecessary, although the timing and frequency of follow-up is essential.

In conclusion, this is the first reported case of AMLEC in Chinese which presenting as a

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radiographically and grossly cystic renal lesion, so we must differentiate it from other cystic renal neoplasms. A unique feature of this case was with three unique kinds of morphological and three different immune phenotypes. AMLEC may be confused with MEST, the most distinctive feature is that AMLEC is immuno reactive not only to ER, PR, and CD10, but also to melanocytic markers (Melan-A and HMB45). AMLEC is extremely rare benign tumor of the kidney, partial nephrectomy or radical nephrectomy is the main treatment method.

### Disclosure of conflict of interest

None.

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