Characteristic Enhancement Patterns of Renal Epithelioid Angiomyolipoma: a case report and literature review

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ABSTRACT

We present a case of renal epithelioid angiomyolipoma in a 42-year-old woman with diabetic nephropathy for two years. Ultrasonography revealed a right renal mass in the patient. Further imaging could not confirm the nature of the mass, which grew noticeably over the course of 4 months. The mass was treated with right radical nephrectomy and diagnosed as renal epithelioid angiomyolipoma. Characteristic enhancement patterns of renal epithelioid angiomyolipoma were observed and supported by a review of the literature.

CASE REPORT

A 42-year-old woman had diabetic nephropathy with nephrotic syndrome for two years. The patient’s renal function deteriorated progressively, and she experienced several episodes of general edema and oliguria. In addition, initial renal ultrasonography revealed two hyperechoic nodules at the upper pole of the right kidney, with sizes of 4 mm and 1.7 cm in diameter. Further examination by using computed tomography (CT) demonstrated these nodules to be well-defined lipomatous lesions. These lesions were diagnosed as renal AMLs and monitored annually by using ultrasonography. Two years later, a new lesion with a diameter of approximately 3 cm was identified in the right kidney. This mass had a hypoechoic texture and contained few color Doppler signals (Fig. 1). Further evaluation with non-contrast enhanced MRI revealed that this mass was exophytic in the middle pole of the right kidney and had homogeneous isointensity on both T1- and T2-weighted images (T1WI and T2WI, respectively) (Fig. 2). As RCC could not be excluded, biopsy of the mass was recommended but the patient refused. Over the next 4 months, there was clear evidence of expansion of the mass. Repeated MRI with and without contrast enhancement revealed that the growth pattern of this mass, with a diameter of 3.5 cm, was more exophytic and still had homogeneous isointensity on both T1WI and T2WI (Fig. 2). Dynamic contrast-enhanced imaging was also performed with a manual contrast injection rate of approximately 1.5 to 2 cc/s and phase interval of approximately 20 to 22 s. The mass appeared to be homogeneously enhanced. Compared to the renal parenchyma, it was enhanced at the same level in the corticomedullary phase and less enhanced in the subsequent early nephrogenic phase (Fig. 3). Because the possibility of...
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RCC still could not be excluded, right radical nephrectomy was performed. Histopathology with immunohistochemical staining revealed that the mass was predominantly composed of large epithelioid cells. Most cells stained intensely for HMB-45 (Fig. 4). According to these findings, the tumor was confirmed to be an EAML.

**DISCUSSION**

AML is the most common mesenchymal renal neoplasm, composed of variable proportions of adipose tissue, spindled or epithelioid smooth muscle cells, and abnormally thick-walled blood vessels [1]. It has been classified as a perivascular epithelioid cell tumor (PEComa), which also includes lymphangioleiomyomatosis, clear cell "sugar" tumor, and clear cell myomelanocytic tumor. In addition to the common classic/triphasic subtype, several morphological variants of AML have been reported, including EAML, oncocytoma-like, leiomyoma-like, and liposarcoma-like, vascular predominant AML, as well as AML with epithelial cysts [2]. Among these variants, EAML is particularly noteworthy because it has been regarded as a potentially malignant mesenchymal neoplasm by the World Health Organization [3].

EAML was first described in 1995 by Martignoni et al. as a distinct clinicopathological variant of AML characterized mainly by a predominance of epithelioid cells [4]. However, there is no definite pathological criterion regarding the required percentage of epithelioid component to define EAML. The percentage of epithelioid component used for pathological analysis varies and ranges from 5% to 100% [5, 6]. EAML can also pose significant diagnostic challenges as it morphologically mimics a variety of neoplasms, including RCC, renal oncocytoma, adrenal cortical neoplasm, epithelioid smooth muscle tumor, epithelioid peripheral nerve sheath tumor, epithelioid gastrointestinal stromal tumor, epithelioid melanoma, hepatoblastoma, and hepatocellular carcinoma [4]. Therefore, a prudent use of immunohistochemistry and occasional complementation with electron microscopy is necessary to establish the correct diagnosis. As EAML belongs to the PEComa family, it also shares characteristic pathological features of PEComa, such as epithelial cell-like morphology with clear eosinophilic cytoplasm, expression of HM B-45, microphthalmia transcription factor, and melan-A [7, 8]. In our case, pure EAML was confirmed based on the demonstration of a predominant epithelioid component in the tumor, with strong staining for HM B-45.

Renal EAML usually occur sporadically but may be associated with tuberous sclerosis complex (TSC) in approximately a quarter of cases. According to a report by Aydin et al., who classified EAMLS by using an epithelioid component ranging from 10% to 100%, women are predominantly affected, with a female to male ratio of approximately 6.5:1 [5]. The mean age of patients with renal EAML

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**Figure 1.**

1a. A gray-scale ultrasonography image showing a hypoechoic mass in the right kidney (arrow) without apparent posterior acoustic enhancement.

1b. A color Doppler ultrasonography image showing only few color signals in the mass.
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Figure 2. Initial MRI demonstrates the right renal mass to be exophytic (short arrow). Besides, the mass revealed isointensity on T2WI a. and T1WI b. Follow-up MRI 4 months later still demonstrates the mass to be isointense on T2WI c. and T1WI d.. However, decreased angle between the mass and adjacent renal surface is observed, indicating interval growth of the mass (long arrow).

Figure 3. Dynamic contrast-enhanced magnetic resonance imaging with a time interval of approximately 20 s showing the sequential precontrast (a), arterial (b), corticomedullary (c), early nephrogenic (d) and late nephrogenic phases (e). c. The mass was equally enhanced to renal parenchyma in corticomedullary phase. The inferior vena cava was not well enhanced at that time. d. The mass was less enhanced than renal parenchyma soon in early nephrogenic phase.
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Figure 4. a. The tumor is predominantly composed of large epithelioid cells with abundant pinkish granular cytoplasm, pleomorphic nuclei, and prominent nucleoli. Only some fatty and vesicular components are visible (hematoxylin and eosin staining, magnification, ×400). b. Most tumor cells are strongly positive for HMB-45 (immunohistochemical staining for HMB-45, magnification, ×400).

Figure 5. A graph showing enhancing kinetics of the tumor (red line, T) and renal parenchyma away from the tumor (blue line, K). The percentage enhancement is calculated for the different phases as follows: [(SIpost - SIpre)/SIpre] × 100, where SIpost is the signal intensity(SI) of the region of interest (ROI) on the contrast-enhanced phase images and SIpre is the SI of the ROI on the image obtained before contrast injection.

is significantly less than that of patients with non-epithelioid AML (38.6 vs. 52.3 years). However, in a study of pure EAMLs (epithelioid component greater than 95%) by Nese et al., the mean age is 40 years, and there is no predominance considering the sex [8]. Half of the patients with pure EAMLs are symptomatic and may present flank pain, fever, weight loss or have a palpable abdominal mass [9]. EAML is potentially malignant and may present with perirenal or hilar invasion, renal vein invasion, regional lymph node involvement, local recurrence, and metastasis. In a study by Brimo et al. on renal EAML with atypia, 9 of 34 follow-up patients (26%) showed local recurrence or distal metastases [6]. The authors developed a predictive model based on four atypical pathological features: ≥70% atypical epithelioid cells, ≥2 mitotic figures per 10 high-power field, atypical mitotic figures, and necrosis. The presence of at least three features was highly predictive of malignant behavior. Nese et al. reported metastases at the initial examination or follow-up in 50% of the included 41 pure EAMLs [8]. They also propose adverse prognostic factors, including patients with associated TSC or concurrent AMLs, necrosis, lesion size >7 cm, extrarenal extension and/or renal vein involvement, and a carcinoma-like growth pattern. According to these data, pure EAMLs appear to have more malignant potential than non-pure EAMLs.

Compared to histopathological features, there are very few reports on the visual features of renal EAMLs in imaging. To our knowledge, the most extensive report on CT or MRI imaging characteristics of renal EAMLs is currently that by Froemming et al., in which 9 renal EAMLs, with an epithelioid composition of 80% or greater, were examined [10]. The size of the lesions ranged from 1.4 cm to 22 cm, with a mean size of 7.8 cm. As demonstrated in other smaller studies, renal EAMLs generally tend to be exophytic in growth, hyperattenuating on unenhanced CT images and heterogeneously enhanced after contrast injection [11-13]. Heterogeneous texture of renal EAMLs may result from significant fat component, hemorrhage, cystic degeneration, or hyalinization within the tumor. In addition, renal EAMLs may display early contrast washout,
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as shown in the triphasic studies [11, 14, 15]. In our case, the tumor measured approximately 3 cm in diameter at the initial examination but grew up rapidly to 3.5 cm within 4 months. This growth rate is faster compared to the reported growth rates of RCC [16]. In both the initial and follow-up MRI studies, the tumor revealed homogeneous isointensity in the T1WI and T2WI. This homogeneous intensity corresponds to pathological findings of tumor components that are exclusively epithelioid cells without obvious hemorrhage, cystic change, or hyalinization. The tumor was homogeneously well enhanced. The enhancement kinetic curves of the tumor and normal renal parenchyma (Fig. 5) also show that, compared to the renal parenchyma, tumor enhancement was similar in the corticomedullary phase (40 s after contrast injection) but lower in the early nephrogenic phase (60 s after contrast injection). In addition, contrast washout of the tumor was also shown in early nephrogenic phase (60 s after contrast injection). These characteristic enhancement patterns are similar to the findings in case reports of renal EAML [11, 14, 15]. Although hypervascular RCCs have been reported to show contrast washout in the nephrogenic phase (80–120 s after contrast injection) [17-19], they are increasingly enhanced in the early nephrogenic phase (60 s after contrast injection) [20, 21]. Therefore, renal EAMLs appear to demonstrate contrast washout slightly earlier than hypervascular RCCs do. This means that renal EAMLs may reach peak enhancement earlier than hypervascular RCCs do. Although lipid-poor AMLs and EAMLs have been reported to demonstrate contrast washout in nephrogenic phase (90 s after contrast injection), or early excretory phase (3 min after contrast injection) [22, 23], tumor enhancement is not evaluated in the early nephrogenic phase (60 s after contrast injection). Therefore, this is to our knowledge, the first study on the enhancement kinetic curve of renal EAML with inclusion of the early nephrogenic phase (60 s after injection).

In conclusion, EAML should be included in the differential diagnosis while a renal tumor presents hyperattenuation on unenhanced CT image or low signal intensity on T2WI [13]. Besides, we think that the characteristic early contrast washout, observed in this study and demonstrated in case reports, may help in differentiating renal EAMLs from RCCs, although larger studies using dynamic contrast-enhanced MRI studies with short time intervals or triphasic CT studies are necessary to define its sensitivity and specificity.

REFERENCES

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