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Case Report

Hepatic epithelioid angiomyolipoma with renal metastasis: radiologic-pathologic correlation

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ABSTRACT

Epithelioid angiomyolipoma (EAML) is a rare subtype of angiomyolipomas. Unlike the conventional angiomyolipomas, EAML often contains minimal fat which usually precludes prospective diagnosis on imaging. The imaging findings of EAML may overlap with other benign and malignant hepatic neoplasms. We report a hepatic epithelioid angiomyolipoma in a 47-year-old female which metastasized to the right kidney and recurred after resection in the liver. We analyze the imaging findings of EAML on ultrasound, computed tomography, positron emission tomography and magnetic resonance imaging. Correlation between the imaging and histopathologic findings is made. The estimated annual growth and doubling time of the primary hepatic EAML are calculated. To the best of our knowledge, this is the first published report of positron emission tomography–computed tomography findings and annual growth rate for hepatic EAML.

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Introduction

Angiomyolipoma (AML) is a mesenchymal neoplasm composed of adipose tissue, smooth muscle, and abnormal blood vessels in varying proportions. Epithelioid angiomyolipoma (EAML) is a rare subset composed predominantly of perivascular epithelioid cells and often contains minimal fat [1–3]. The tumor occurs most frequently in the kidneys but has also originated in either lobe of the liver. Although often benign, hepatic EAML has demonstrated rare malignant behavior and recurrence following resections [4,5], as well as several recorded instances of metastasis [2,5,6,7]. This paper will discuss a case of a hepatic EAML with metastasis to the right kidney six

years following its initial discovery. Imaging features from ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET) will be analyzed. Similarities and differences on imaging to other hepatic lesions would also be discussed. The annual growth rate of the hepatic EAML will also be estimated.

Case report

A 47-year-old female, nonsmoker with no prior surgical history apart from 2 C-sections, but has a strong family history of lung cancer, colon cancer, and other malignancies was found

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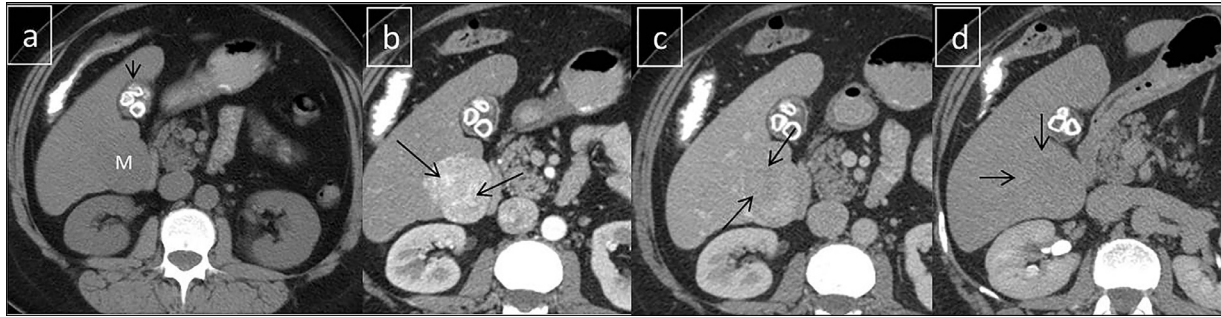


Fig. 1 – First computed tomography examination during the initial presentation (patient age 47 years): the primary lesion in the right hepatic lobe which is slightly hypoattenuating to the remainder of the liver parenchyma (M) on the nonenhanced computed tomography (a). It demonstrates heterogeneous avid enhancement on the arterial phase (b). Note the linear intralesional structures which represent prominent vessels centrally in the lesion and at the periphery (arrows in b). On the portal venous phase, the mass demonstrates mild washout, best seen in the right lateral part (arrows in c). Pseudocapsule is seen on the delayed phase (arrows in d) while the mass demonstrates mild washout (d). Incidental note is made of multiple hyperdense gallbladder stones (short arrow in a).

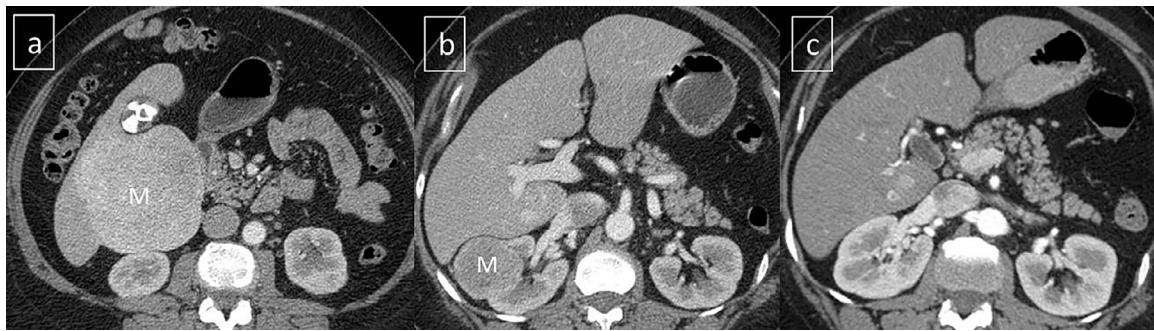


Fig. 2 – The follow-up portal venous phase computed tomography performed 6 years and 4 months after the initial presentation (patient age 53 years) (a and b); showing significant interval growth of the right hepatic lobe mass (M in a) and a new development of an interpolar partially exophytic right renal mass (M in b). The previous arterial phase computed tomography during the initial presentation at the same level of (b), is provided for comparison (c).

to have a solitary right lobe hepatic mass in outside abdominal ultrasound. The mass measured approximately 4.2 cm in longest dimension. The patient underwent a CT abdomen and pelvis with and without IV contrast according to the triphasic liver CT protocol for further evaluation of the hepatic mass. A well-defined hyperdense lesion was seen in segment VI of the liver with estimated measurements of $3.8 \times 4.6 \times 4.7$ cm (Fig. 1). It appeared solid with extension to the liver capsule and partially exophytic. There was avid arterial enhancement which filled in, appearing almost homogenous, on delayed imaging. Two additional hepatic lesions were present, one adjacent to the dominant growth and one anteriorly, measuring 6 mm and 5 mm respectively. These were thought to represent hepatic hemangiomas.

A subsequent CT was performed 6 year and 4 months after the initial presentation for evaluation of vague upper abdominal pain. The scan showed that the hepatic lesion had grown in size to an estimated $10.9 \times 9.7 \times 11.2$ cm (Fig. 2). The mass demonstrated arterial enhancement and faint washout in some areas. There was no significant necrosis, central scar, in-

tralesional fat, or calcification. The adjacent lesion had grown to 1.9 cm and the anterior lesion had grown to 2.4 cm. Incidentally, the scan revealed that a new solid, homogenous, exophytic mass had developed in the interpolar region of the right kidney (Fig. 2), measuring 4.6×5.1 cm. The mass was slightly hyperdense on the unenhanced images (34 Hounsfield units). On the contrast enhanced images, it measured up to 77 HU in the arterial phase with washout to 57 HU in the portal venous phase. This raised the possibility of an indolent malignancy and subsequently US-guided biopsies were conducted on the hepatic and renal masses after 3 months and 7 months of the later CT examination, respectively (Fig. 3). Pathologic analysis of the hepatic biopsies showed a tumor consisting of epithelioid-like cells arranged in clusters with thin interweaving vascular channels and a few spindle cells. Adipose tissue was present in one of the cores, as well as areas of inflamed fibrous macrophages, evidence of remote hemorrhage, and admixed hematopoietic cells. The sample was positive for HMB-45 and Melan A. Similar features were noted in the core samples from the renal lesion. However,

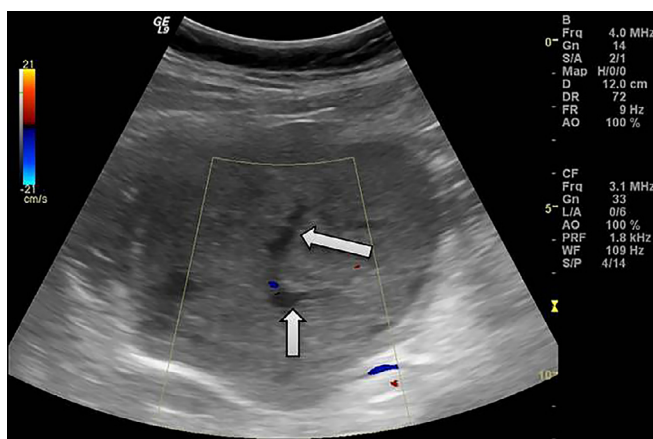


Fig. 3 – The ultrasound image with Doppler Interrogation (7 years after the initial presentation, patient age 55 years): showing a large relatively hyperechoic partially exophytic right hepatic lobe mass with internal vascularity. Note the dilated vessels within the mass (thick arrows).

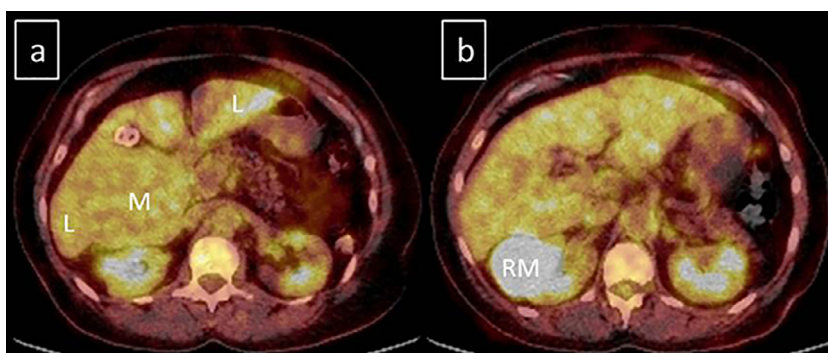


Fig. 4 – Fused fluorodeoxyglucose positron emission tomography-computed tomography images (7 years after the initial presentation, patient age 54 years) showing similar fluorodeoxyglucose uptake of the right hepatic lobe epithelioid angiomyolipoma (M in a) to the remainder of the liver parenchyma (L in a). The renal epithelioid angiomyolipoma, however, demonstrates more avid uptake in comparison to both the renal parenchyma and the hepatic mass (renal mass (RM) in d).

cells were primarily oncocyctic with abundant eosinophilic cytoplasm, and bland-looking nuclei. The sample was positive for HMB-45, Melanoma cocktail, and vimentin. Both lesions were diagnosed as epithelioid angiomyolipoma.

The patient underwent a staging CT of the chest after 1 month of the later CT abdomen and pelvis which showed a 3 cm ground glass opacity with eccentric solid component in the posterior segment of the right upper pole. The patient underwent a CT-guided biopsy and the lesion was confirmed to represent a non-small cell adenocarcinoma. A PET-CT scan was performed 6 months later to the CT chest for staging which showed no evidence of metastasis. However, the scan showed fluorodeoxyglucose (FDG) uptake in both the hepatic and renal EAML (Fig. 4). The tumor in the liver demonstrated tracer uptake equal to that in surrounding liver parenchyma. Interestingly, the mass in the kidney demonstrated intense FDG uptake, with a standard uptake value of 14.3. A subsequent MRI exam 8 months later to the PET-CT (Fig. 5) showed that the dominant liver EAML had grown to 12 × 11 cm. It demonstrated hypointense signal on T1-WI and heterogeneous hyperintense signal on T2-WI. The renal EAML

had grown to 6.2 × 5.6 cm. There was no evidence of microscopic or macroscopic fat in either lesion. Following this examination, it was suggested that an elective surgical resection would be of benefit.

A right liver resection and partial right nephrectomy were performed 2 months after the MRI examination, in addition to a cholecystectomy to facilitate the hepatic resection. On gross examination, the resected segment of the liver showed an exophytic, subcapsular, cystic mass measuring 10.0 × 7.0 × 6.0 cm. The central area of the tumor contained extensive necrotic material, dark brown in color. The cut segment of the kidney showed a well-circumscribed, subcapsular mass with dimensions 5.8 × 5.4 × 4.8 cm. Cystic necrosis was present to a lesser extent. Microscopic examination of the hepatic tumor showed epithelioid cells and rare adipocytes. The lesion was well-vascularized, containing both delicate vessels around nests of cells and large, thick-walled, occasionally irregular, vessels at the periphery. The renal tumor cells appeared to be more epithelioid and oncocyctic. Both tumors tested positive for Melan-A and MelCT and patchy positivity for HMB-45. The hepatic tumor tested patchy positive for smooth muscle actin while the

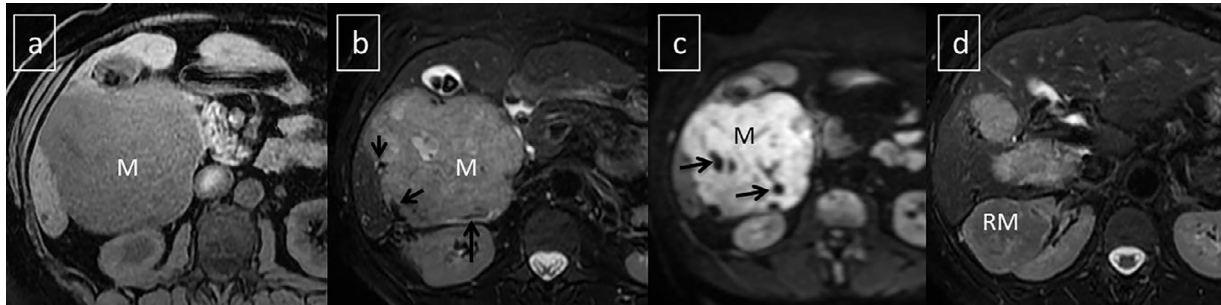


Fig. 5 – Nonenhanced magnetic resonance imaging of the liver (8 years after the initial presentation, patient age 55 years) showing the large hepatic epithelioid angiomyolipoma which demonstrates hypointense signal on T1-WI (M in a), heterogeneous signal on T2-WI (M in b) and hyperintense signal on the diffusion weighted imaging (DWI) (M in c). Note the linear flow void vessels in the T2-WI and DWI (arrows in b and c). T2-WI with fat saturation, at the level of the right renal mass which demonstrates heterogeneous signal on T2-WI but predominantly hyperintense (RM in d).

$SGR = \frac{\ln (V_2/V_1)}{t_2 - t_1}$ $DT = \frac{\ln (2)}{SGR}$
V2: 10.9 x 9.7 x 11.2 x 0.52 = 616 cc
V1: 3.8 x 4.6 x 4.7 x 0.52 = 43 cc
t2: Follow up CT after 6 years and 4 months of the initial CT
t1: Date of the CT at initial presentation
t2 - t1 = 6 years and 4 months

Fig. 6 – The formula and the values used to calculate the tumor growth rate of the right hepatic lobe epithelioid angiomyolipoma. (SGR, specific growth rate; t, time; ln, natural log; V, tumor volume in centimeter cube).

renal tumor tested negative. These results were concordant with the preoperative diagnosis of EAML.

A postoperative MRI examination 6 months after resection found that there was a 2.5 × 2.1 cm arterially enhancing lesion with mild T2 hyperintensity and no microscopic or macroscopic fat along the resection line. Additionally, there was a 2.3 × 1.6 lesion in the peripheral medial aspect of liver segment II. It was mildly hyperintense on T2-WI, enhanced avidly in the arterial phase, and slightly retained contrast in the portal venous phase. The lesions were suspicious for a recurrent EAML. There was no solid recurrent kidney mass or elsewhere in the abdomen. Using specific growth rate (Fig. 6), the dominant hepatic tumor is estimated to have increased in size by approximately 44% each year, with a doubling time of approximately 1.5 years. The initial presentation CT and the CT done 6 years and 4 months later are used in the calculations.

Discussion

The imaging features of hepatic EAML are generally nonspecific, making the tumors difficult to differentially diagnose without immunohistochemical analysis [2,5,6]. On MRI, the tumor generally appears hypointense or isointense on T1-weighted images and hyperintense on T2-weighted images [2,8], as seen in this case. Depending on the amount of intralesional microscopic and macroscopic fat, signal drop on the T1-out-of-phase sequence or in the T1-fat saturated sequence may be observed, respectively. However, most of the lesions contain minimal adipose tissue if any which makes it hard to detect on imaging. In addition, the distinction from other malignancies which may contain adipose tissue cannot be made based on the presence of intralesional fat. On contrast-enhanced CT, the lesion generally shows enhancement in the arterial phase with wash out in the portal venous and delayed phases [2,5,6,9]. However, variations can exist. Of 5 hepatic EAML samples analyzed in one study, 3 had a fat component, 2 had portal phase enhancement, and 3 had delayed phase enhancement [10]. In this case, the hepatic EAML appeared to demonstrate enhancement on both the arterial and portal venous phases.

One of the distinct imaging features which are thought to be useful in the diagnosis is the presence of intralesional punctiform or filiform vessels [2]. This particular imaging feature was present in our case in all different imaging modalities; US, CT, and MRI (Figs. 1, 3 and 5). The presence of these vessels has been confirmed on the histopathologic examination. The washout on the portal venous and delayed phases has also been described in this entity which is more frequently seen in lesions with punctiform or filiform vessels [2], which is similar to our case. The hepatic EAML in our case demonstrated an enhancing capsule on the delayed phase (Fig. 1), a feature which has been described in the literature and is not a true capsule but, in fact, a pseudocapsule due to compressed surrounding hepatic parenchyma [2]. In a study analyzing US findings of 6 hepatic EAML cases, it was observed that 3 were hypoechoic while 3 were mixed echoic. On contrast-enhanced

US, it was observed that all 6 displayed homogeneous hyperenhancement in the arterial phase and 4 showed hypoenhancement in the late phase [9]. While there have been no prior reports on the PET-CT findings of hepatic EAML, one past study described FDG uptake by classical AML in the liver. It found that a hepatic AML with intratumoral hemorrhage demonstrated FDG uptake equivalent to that seen in the liver parenchyma, while another hepatic AML without hemorrhage experienced no uptake [11]. The hepatic EAML in this case report demonstrated similar properties: containing remote hemorrhage and tracer uptake similar to hepatic background. The hypermetabolic activity in the renal EAML is likely due to the oncocytic composition of the lesion.

The formation of renal EAML in our patient is likely a result of metastasis from the hepatic tumor. A review of 97 prior cases, and a subsequent review of 81, found that recurrence or metastasis occurred in 9.3% and 10% of patients, respectively [5,6]. Hepatic EAML has been reported to have metastasized into the lungs 7 years following its initial appearance in the liver [7]. This timeframe is similar to the 6 years and 4 months between the initial discovery of the hepatic EAML and the formation of the new mass in our patient's right kidney.

In summary, this paper presents a case of EAML which originated in the liver, grew significantly in size over 6 years, metastasized as an oncocytic lesion to the kidney, and demonstrated recurrence following resection. The lesions demonstrate imaging features congruent to the past reported cases of hepatic EAML. PET-CT findings observed in this case are similar to those seen in classical hepatic AML, with FDG uptake equivalent to that of liver parenchyma. Observing distinct imaging features of EAML like punctiform or filiform vessels may help in raising the possibility of the diagnosis on imaging. However, these imaging findings may not be specific and are not seen in all cases and hence biopsy is needed for confirmation of the diagnosis. The estimated growth rate of the dominant hepatic tumor was approximately 44% per year with a doubling time of approximately 1.5 years. Primary hepatic EAML is a rare but possibly aggressive neoplasm and careful follow-up is recommended when the tumor is diagnosed.

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