Giant Epithelioid Angiomyolipoma: An Imaging-related Differential Diagnosis Among Fat-containing Renal Masses

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Clinical Practice Points

- Renal masses are a common imaging finding and include a broad spectrum of both benign and malignant histopathologic types, with pleomorphic clinical presentation and imaging features. Although differential diagnosis is often challenging, characterization is crucial for appropriate management.
- Angiomyolipomas typically occur as small and asymptomatic lesions incidentally detected while imaging the abdomen and whose radiologic criterion for diagnosis is the unequivocal presence of macroscopic fat within the lesion. Rare angiomyolipoma subtypes (such as the epithelioid variant) may reach considerable dimensions and show atypical imaging features, turning into a diagnostic conundrum.
- Multimodality imaging can guide the differential diagnosis of equivocal fat-containing renal masses and allows lesion characterization.

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Introduction

Angiomyolipomas (AMLs) are among the most common benign renal tumors, typically consisting of varying proportions of 3 components: blood vessels (angio), smooth muscle cells (myo), and fatty tissue (lipoma), and are thus called triphasic.[1] Occasionally, AMLs may present atypical histologic features consisting almost exclusively of one component (monophasic) or containing numerous epithelioid muscle cells with small amount of fat, as in the rare epithelioid variant (E-AMLs).[1-3] AMLs occur as a sporadic entity in 80% of cases; more rarely, they are related to hereditary diseases such as tuberous sclerosis complex (TSC). Hereditary AMLs can reach huge dimensions and may present unusual imaging features determining diagnostic pitfalls. Few cases of giant sporadic AMLs are reported in literature,[4,5] and even fewer regarding the epithelioid variant.[2] We present a case of a 36-year-old man suffering from anemia and fever, whose contrast-enhanced computed tomography (CT) depicted the presence of a huge (14 × 21 × 30 cm) retroperitoneal fat-containing mass.

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Case Report

A 36-year-old male was admitted to our institution to investigate fatigue and slight fever (maximum temperature, 37.5°C) that he experienced for 3 weeks. His previous medical and surgical history was unremarkable. Clinical examination showed an asymmetric distended abdomen owing to the presence of an intra-abdominal, hard, and not moveable mass that occupied the right abdominal quadrants. Moreover, edema of the lower extremities was noticed. Laboratory data showed severe anemia (red blood cells, 3.03 × 10^6/ul; hemoglobin, 7.8 g/dL; hematocrit, 25.7%) and neutrophil leucocytosis (white blood cells, 19.2 × 10^3/ul; neutrophils, 86.6%). A total body CT was performed, confirming the presence of a huge (14 × 21 × 31 mm) retroperitoneal mass extending from the right hypochondrium to the pelvis. It was indissociable from the right kidney, and it was generating mass effect on adjacent structures, compressing the inferior vena cava and the homolateral renal vena with recruitment of collateral vessels. This solid expansive lesion showed heterogeneous density

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after contrast media intravenous injection because of the presence of fatty density areas (< −20 HU) and several aneurismatic blood vessels. There was no evidence of calcification. Finally, a small amount of ascites was noticed as well (Figure 1).

In suspicion of malignancy, the patient subsequently underwent a ^{18}F-fluorodeoxyglucose positron emission tomography/CT scan that showed small heterogeneous uptake of radiotracer by lesion (maximum standardized uptake value, 5), with no detectable pathologic uptake in other districts (Figure 1).

To further characterize the huge mass, a magnetic resonance imaging (MRI) scan was performed and confirmed its renal origin and benign features. The presence of macroscopic fat was more clearly depicted on T1-weighed sequences with and without suppression of fatty tissue signal and on chemical shift images (Figure 2). Some areas of spontaneous hyperintensity on T1-weighted sequences were present, suggesting hemorrhagic areas. Despite the considerable dimensions, it was totally encapsulated and did not show any sign of local invasion. The remaining renal parenchymal was not affected, showing normal features. No pathologic lymph nodes were depicted. No significant restricted diffusion of water molecules of the mass was observed on diffusion weighed images and on the corresponding apparent diffusion coefficient map. These imaging features were highly suggestive for a benign fat-containing mass originating from the mid-inferior pole of the right kidney.

A right nephrectomy was deemed necessary and was performed after right renal artery embolization without any complications. The specimen measured 15 × 22 × 30 mm and weighed 6 kg (Figure 3). Histologic exams revealed an epithelioid variant of AML (Figure 4). Finally, the patient underwent a brain CT scan that showed no abnormalities associated with TSC.

Discussion

Renal AMLs are benign lesions commonly encountered in clinical practice, originating from perivascular epithelioid cells (PEC), and therefore also referred to as PEComa.[6] These pleomorphic lesions are mostly sporadic, with the tendency to be single, small, and asymptomatic, often representing an incidental finding in patients undergoing abdominal imaging for other reasons.[7] Less frequently, AMLs occur as hereditary lesions in association with TSC or, less commonly, with other PEComas such as pulmonary lymphangioleiomyomatosis. Compared with the sporadic form, these hereditary lesions can be multiple, large, bilateral, and even aggressive.[1] When AMLs reach dimensions larger than 4 cm, they may become symptomatic. Abdominal pain is the most frequent symptom, followed by hematuria and retroperitoneal bleeding or rupture (Wunderlich syndrome).[8] In our case, the patient only suffered from deep asthenia owing to severe anemia, a sign of bleeding of an aneurysmatic vessel within the mass. The huge (14 × 21 × 30 mm) dimensions reached are unusual for a sporadic form; in fact, we could consider this lesion one of the largest sporadic AMLs ever reported in literature.[4,5] The epithelioid type observed on histologic exams is unusual as well.[2] The specimen microscopically consisted of 80% of epithelioid cells and immunologically expressed

Figure 1 **Craniocaudal Computed Tomography Axial Scans (A-F) After Contrast Media Intravenous Injection (Arterial Phase) and ^{18}F-fluorodeoxyglucose Unenhanced Positron Emission Tomography/Computed Tomography Images (G-H). The Huge Mass Showed Heterogeneous Enhancement Owing to the Presence of Fatty Areas (Asterisks in B and E) and Dilatated Blood Vessels (Arrows in C and D); There Was no Evidence of Calcifications. Owing to Compression of the Inferior Vena Cava and Right Renal Vena, Collateral Vessels Were Recruited (Arrowhead in E). A Small Amount of Ascites Was Noticed (Star in A). The Mass Was Arising From the Mid-inferior Pole of the Right Kidney and Was Extending From the Right Hypochondrium (A) to the Pelvis (F). The Giant Lesion (Maximum Diameter, 30 mm) Showed a Mild and Non-focal Uptake of Radiotracer With no Pathologic Uptake in the Whole Body (G-H)**

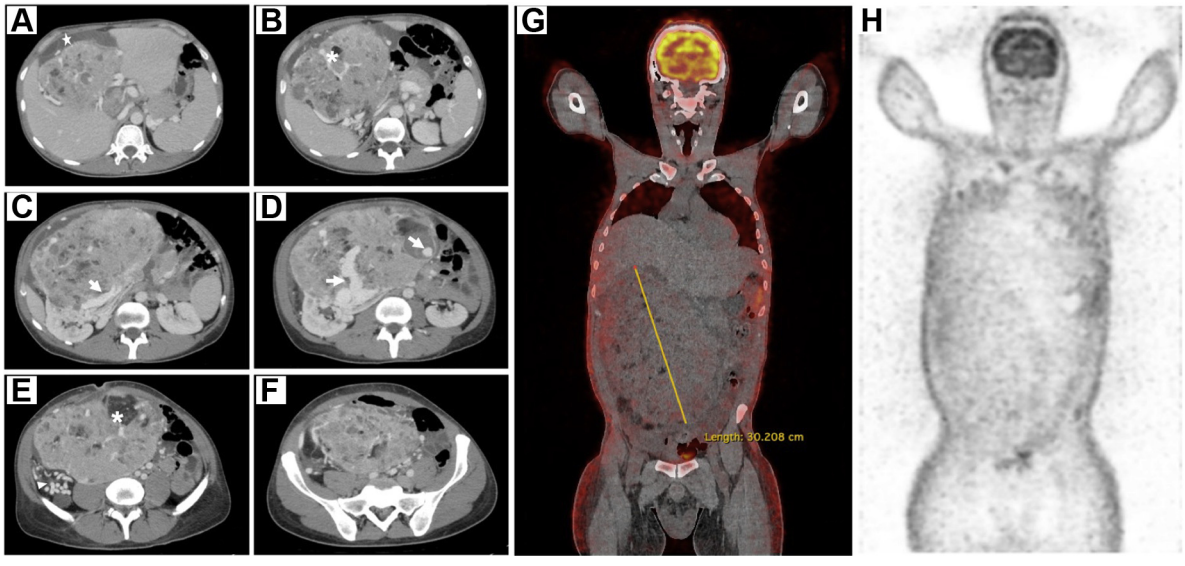


Figure 2 Multiple Magnetic Resonance Imaging Sequences (A-D). The Presence of Macroscopic Fat Was Clearly Noted as Areas of High Signal Intensity to Renal Parenchyma in the T1-weighed Image Without Fat Suppression (A) Corresponding to a Loss of Signal on the T1-Weighed Fat-suppressed Image (B) (White Arrow). On in- (C) and Out-of Phase (D) Chemical Shift Images, the India Ink Artefact Will Appear on "Out-of-phase" Images (D) at the Interface of Fatty and Non-fatty Portions of the Mass (White Arrowhead)

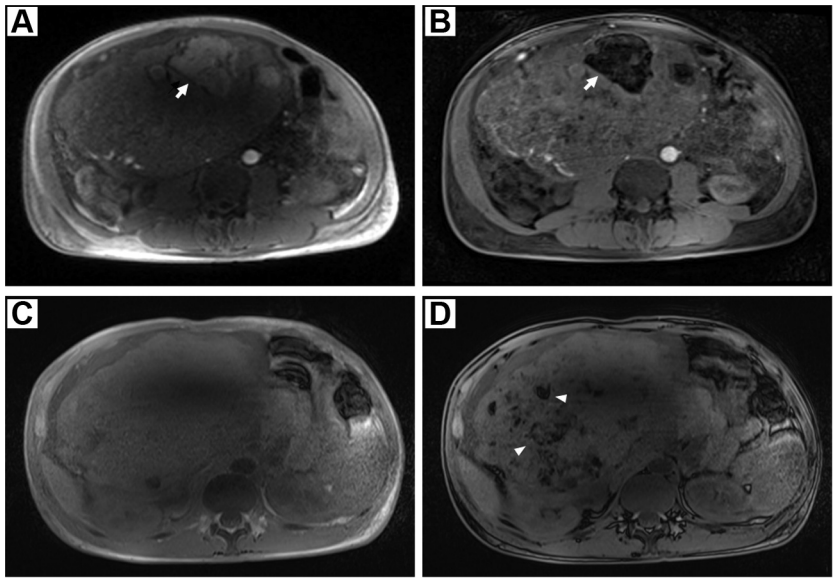


Figure 3 Macroscopically, the Mass Measured More than 30 cm in Maximum Diameter (A), and the Cut Section Was Variegated, Showing Whitish, Yellowish, and Hemorrhagic Aspects (B)

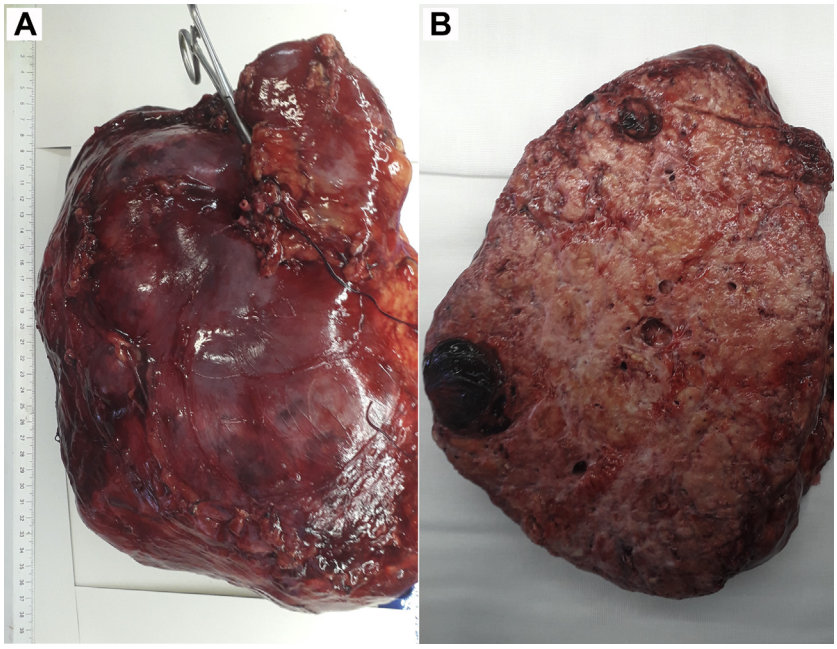
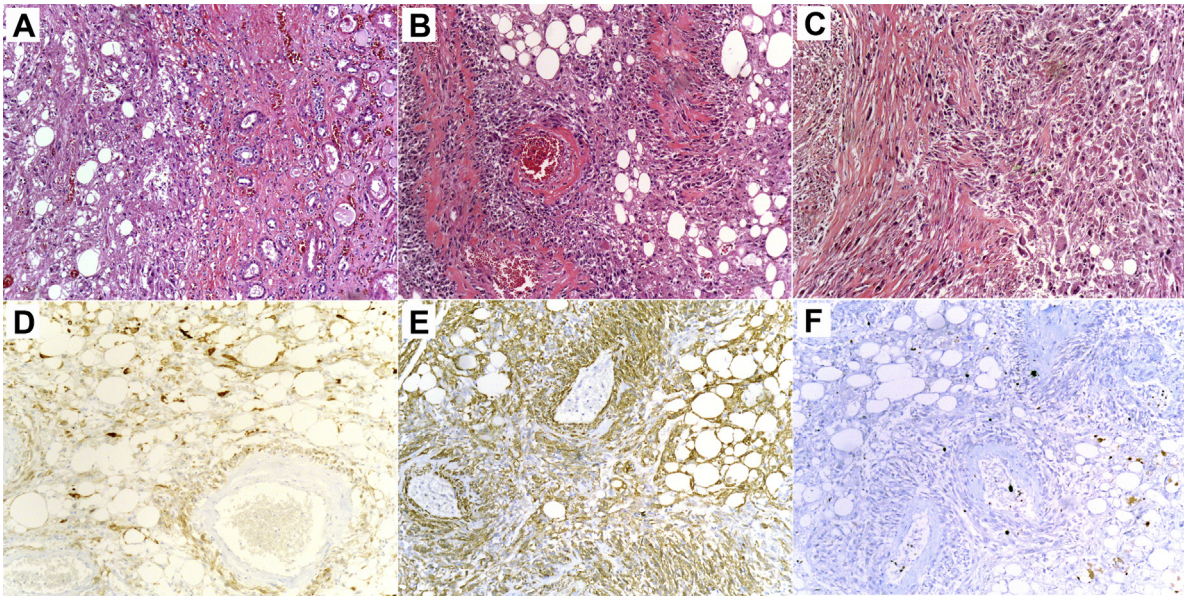


Figure 4 Microscopically, Renal Parenchyma Was Involved by a Neoplasm Composed of 3 Mixed Components (A, Hematoxylin and Eosin Stain, 10× Magnification). The Majority Was Characterized by Spindle and Epithelioid Cells, Immerged in a Stroma Made of Adipose Tissue With a Rich Vascular Network, Thick-wall Vessels, and Hyaline Changes, Mixed With Bundles of Smooth Muscle Cells (B, Hematoxylin and Eosin Stain, 20× Magnification). Pleomorphism Was Moderate (C, Hematoxylin and Eosin Stain, 20× Magnification). Immunohistochemistry Displayed Reactivity to MelanA in Spindle Cells (D, 40× Magnification), to Actin in Muscular Cells (E, 20× Magnification) and a Low Ki67 Proliferative Index (F, 20× Magnification)



melanocytic markers, vimentin, and smooth muscle actin. Conversely, the markers of epithelial or neural cells were negative. Relative to the benign prognosis of typical AMLs, E-AMLs may potentially undergo malignant transformation and metastasize.[9]

Both CT and MRI allow accurate diagnostic evaluation of renal masses for lesion identification and characterization as benign or malignant.[10] To identify a mass as arising from the kidney, 2 imaging findings can be helpful: the "claw sign" relates to the sharp angles of kidney at the edge of its interface with an adjacent mass, whereas the "feeding vessel sign" refers to the presence of interlobar or interlobular feeding arteries arising from the kidney and supplying the mass.[11] To characterize a mass, the demonstration of macroscopic fat within a lesion is the hallmark feature of AML, even if AMLs without visible amount of fat can exist.[12] In particular, E-AML has a distinctive feature owing to its abundant epithelioid muscle component that determines hyperattentuation on CT and low signal intensity on T2-weighted MRI relative to renal parenchyma.[2] Moreover, the expansive growth without any sign of local and distant invasion were highly suggestive of a benign pathologic process, shown by small standardized uptake value on ^{18}F-fluorodeoxyglucose positron emission tomography/CT. These radiologic findings were helpful in the differential diagnosis of fat-containing renal masses. Between malignant lesions, liposarcomas of kidney were ruled in, even if they are rare entities with only a few cases reported in literature.[13] Renal liposarcomas usually are large (average diameter $>$ 20 cm) slow-growing tumors with various imaging appearances depending on the tumor grade. A cross-sectional imaging demonstrating a lipomatous lesion with pushing borders and enhancing septa, with or without solid nodules, is highly suggestive of liposarcoma. Calcification is seen in 30% of cases and is an important sign of dedifferentiation.[14] Calcification within AML is extremely rare, although has also been described.[15] Conversely, fat-containing renal cell carcinoma (RCC) was ruled out. The presence of fat within an RCC is a rare phenomenon, mostly in the clear-cell type, and consists of small fat foci scattered within a soft-tissue mass with calcifications in close proximity to fat foci. RCCs that contain fat without calcifications are extremely rare.[16] Leiomyoma and leiomyosarcoma of the kidney were ruled out because these entities usually show extensive necrosis and hemorrhage, can present myxoid or cystic degeneration, and have contiguous involvement of a vessel. Moreover, they do not contain macroscopic fat.[14,17] Finally, mixed epithelial and stromal tumour (MEST) of the kidney was also ruled in. MEST is a recently defined entity that predominantly affects perimenopausal women. Typically, it is a benign lesion having a typical appearance of a well-circumscribed multiloculated cystic mass with a variable proportion of solid and cystic components and enhancing intratumoral septa. Rarely, MEST may have atypical imaging features, consisting of a predominantly fatty lesion with no appreciable cystic component.[18]

Conclusions

AMLs can be identified using various imaging modalities thanks to their typical imaging features. However, rare histologic variants and large lesions can pose a diagnostic challenge. In these cases, even if histopathologic analysis is required for a definitive diagnosis,

imaging findings play a crucial role in guiding the differential diagnosis and characterizing the lesion.

Disclosure

The authors have stated that they have no conflicts of interest.

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