



Renal angiomyolipomas: Typical and atypical features on computed tomography and magnetic resonance imaging

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Abstract

Angiomyolipomas (AMLs) represent the most common benign solid renal tumors. The frequency of their detection in the general population is increasing owing to advances in imaging technology. The objective of this review is to discuss computed tomography (CT) and magnetic resonance imaging findings for both typical and atypical renal AMLs, along with their associated complications. AMLs are typically defined as solid triphasic tumors composed of varying amounts of dysmorphic and tortuous blood vessels, smooth muscle components and adipose tissue. In an adult, a classical renal AML appears as a solid, heterogeneous renal cortical mass with macroscopic fat. However, up to 5% of AMLs contain minimal fat and cannot be reliably diagnosed by imaging. Fat-poor AMLs can appear as hyperattenuating masses on unenhanced CT and as hypointense masses on T2WI; other AMLs may be isodense or exhibit cystic components. Hemorrhage is the most common complication, and AMLs with hemorrhage can mimic other tumors, making their diagnosis challenging. Understanding the variable and heterogeneous nature of this neoplasm to correctly classify renal AMLs and to avoid misdiagnosis of other renal lesions is crucial.

Key Words: Kidney neoplasms; Angiomyolipoma; Classic angiomyolipoma-fat poor angiomyolipoma; Tomography; X-ray computed; Magnetic resonance imaging

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Core Tip: Angiomyolipomas can be differentiated into triphasic benign angiomyolipomas (AMLs) and potentially aggressive epithelial AMLs. Triphasic AMLs can be further subdivided into classical fat-rich AMLs and fat-poor AMLs. Fat-poor AMLs can be hyperattenuating, isoattenuating or hyperattenuating with an epithelial cystic component. Recognition of the different imaging characteristics of AML types on computed tomography and magnetic resonance imaging is fundamental for differentiating this disease from other renal neoplasms.

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INTRODUCTION

Angiomyolipomas (AMLs) are solid tumors that belong to a family of neoplasms called perivascular epithelioid cell tumors (PEComas), and they account for 1%-3% of all renal tumor cases[1]. PEComas are a family of related mesenchymal neoplasms that include AMLs (renal and extrarenal variants), lymphangiomyomatosis, clear cell tumors of the lung and clear cell myomelanocytic tumors of the falciform ligament/Ligamentum teres[1,2]. PEComas of the kidney include classic AML, microscopic AML (also known as microhamartoma), intraglomerular lesions, cystic AML, epithelioid AML, oncocyoma-like AML and lymphangiomyomatosis of the renal sinus[2]. PEComas exhibit immunoreactivity for myogenic and melanocytic markers, such as Human Melanoma Black 45, Melan-A/Mart1, smooth muscle actin and, less commonly, desmin[3]. AMLs have long been considered hamartomas rather than true neoplasms; however, reports have shown that nonrandom inactivation of the X chromosome or chromosomal aberrations occur in sporadic cases, suggesting a clonal origin consistent with neoplastic disorders[3-5].

With a prevalence of 0.3% in men and 0.6% in women, AMLs represent the most common benign solid renal tumors [6]. In most cases, they are incidentally detected during diagnostic imaging procedures performed for other medical reasons or during screening in patients with tuberous sclerosis complex (TSC). Consequently, an accurate imaging diagnosis is important[7].

The frequency of detection in the general population is increasing due to advances in imaging technology and its more widespread use. Renal AMLs are more common in women during their fifth decade and are sporadic in most cases; however, approximately 20% of AMLs are associated with the TSC[8].

AMLs are typically defined as solid “triphasic” tumors composed of varying amounts of dysmorphic and tortuous blood vessels, smooth muscle components and adipose tissue (Figure 1). A solid, heterogeneous, renal cortical mass with macroscopic fat in an adult is a reliable sign of AML, and thus, it is considered a “classic AML”, however, up to 5% of AMLs contain minimal fat, cannot be reliably diagnosed by imaging, and are considered the “fat-poor subtype”[9]. In 2014, Jinzaki *et al*[8] proposed a radiological classification classifies sporadic AML as triphasic benign AMLs (either classic or fat-poor) and epithelial AMLs, dividing the latter, with potentially malignant behavior, from the former.

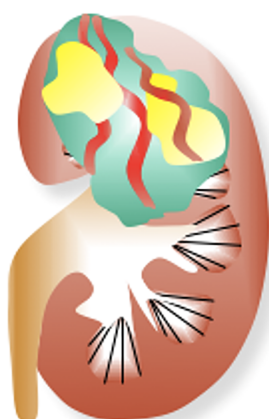


Figure 1 Schematic representation of angiomyolipomas.

The principal criteria for intervention include symptomatic lesions, a size greater than 4 cm, and a suspicion for malignancy[7].

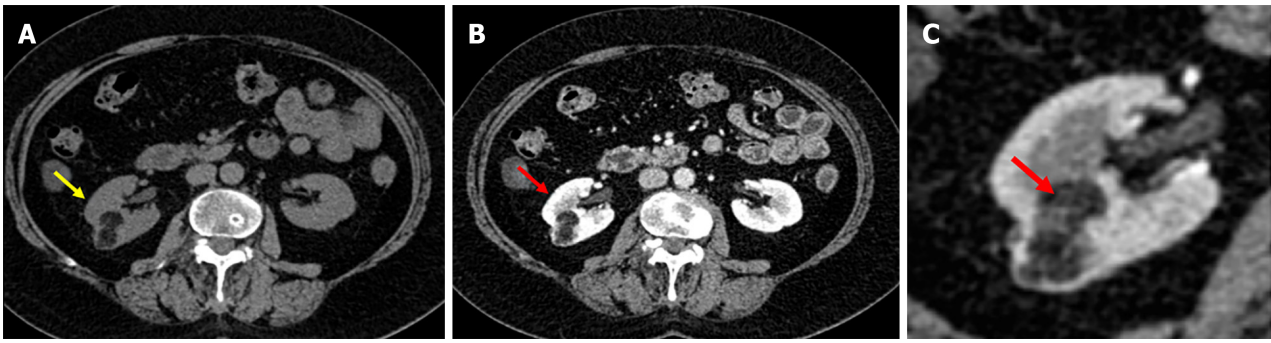


Figure 2 Classic angiomyolipoma containing macroscopic fat on computed tomography. A: Well-circumscribed, hypodense lesion in the right kidney containing macroscopic fat (yellow arrow) on non-enhanced computed tomography (CT); B and C: A heterogeneously enhanced lesion (red arrows) with central blood vessels on contrast-enhanced CT.

Surgical reports indicate that 6%-7% of partially resected tumors that are initially presumed to be renal carcinomas are identified as AMLs. Consequently, a preoperative diagnosis supported by imaging findings remains a significant challenge and is crucial in guiding clinical decision-making.

Retroperitoneal hemorrhage is the most severe complication of AML that occurs in 15% of cases and potentially leads to shock in 20%-30% of cases[10]. It is well established that the tumor size is a significant risk factor and predictor of the development of complications. Therefore, early diagnosis and monitoring of AMLs with imaging techniques are critical [7].

The objective of this review is to demonstrate the imaging findings from computed tomography (CT) and magnetic resonance imaging (MRI) of both typical and atypical renal AMLs, along with their associated complications.

IMAGING CHARACTERISTICS OF CLASSIC RENAL AMLS ON CT

The CT findings of classic AMLs vary according to the amount of fat and vascular and smooth muscle components.

On nonenhanced CT (NECT), thin sections are best for detecting subtle fat components within the tumor. The presence of regions containing attenuation values under -10 Hounsfield units (HU) allows for the confident identification of adipose tissue (Figure 2).

However, sometimes, the presence of adipose tissue cannot be demonstrated by CT because it is heterogeneous and mixed with other components or because of its small amount or a small size of the AML. Calcification rarely occurs in AMLs but may be present after hemorrhage; if calcification is detected, renal cell carcinoma (RCC) should be considered [11]. Additionally, when AMLs bleed, the hemorrhage may obscure their fat content and increase the density of the lesion on images, resulting in a homogeneous hyperattenuating lesion or being confused with liposarcoma because of its size and the combination of adipose and intermediate- to high-attenuation regions.

Contrast-enhanced CT (CECT) enhancement patterns vary on the basis of tumor composition. In lesions without evidence of macroscopic fat, enhancement alone does not differentiate AMLs from other renal tumors[12].

In terms of morphology, eighty percent of tumors are mostly intraparenchymal. Only approximately 25% are exophytic (Figure 3).

IMAGING CHARACTERISTICS OF RENAL AML ON MRI

AMLs have heterogeneous signal intensities due to the varying proportions of vessels, muscle, and fat. Macroscopic fat has high signal intensity on T1- and T2-weighted images, showing loss of signal with fat-suppression techniques[12]. In opposed-phase imaging, the signal decreases in out-of-phase images of tissues containing intracellular lipids. However, this finding is not specific, as it can also occur in various benign and malignant renal cortical tumors. Another important imaging characteristic is the “India ink artifact”, which refers to signal suppression at fat-water interfaces in opposed-phase images (Figure 4)[13].

Contrast-enhanced images show heterogeneous signals due to the tumor composition and are usually hypointense compared to the renal parenchyma. Fat-poor AMLs cannot be reliably differentiated from hypovascular RCCs or other lesions.

To date, diffusion-weighted imaging has not proven to be reliably useful for differentiating AML from other renal lesions, particularly RCC[14].

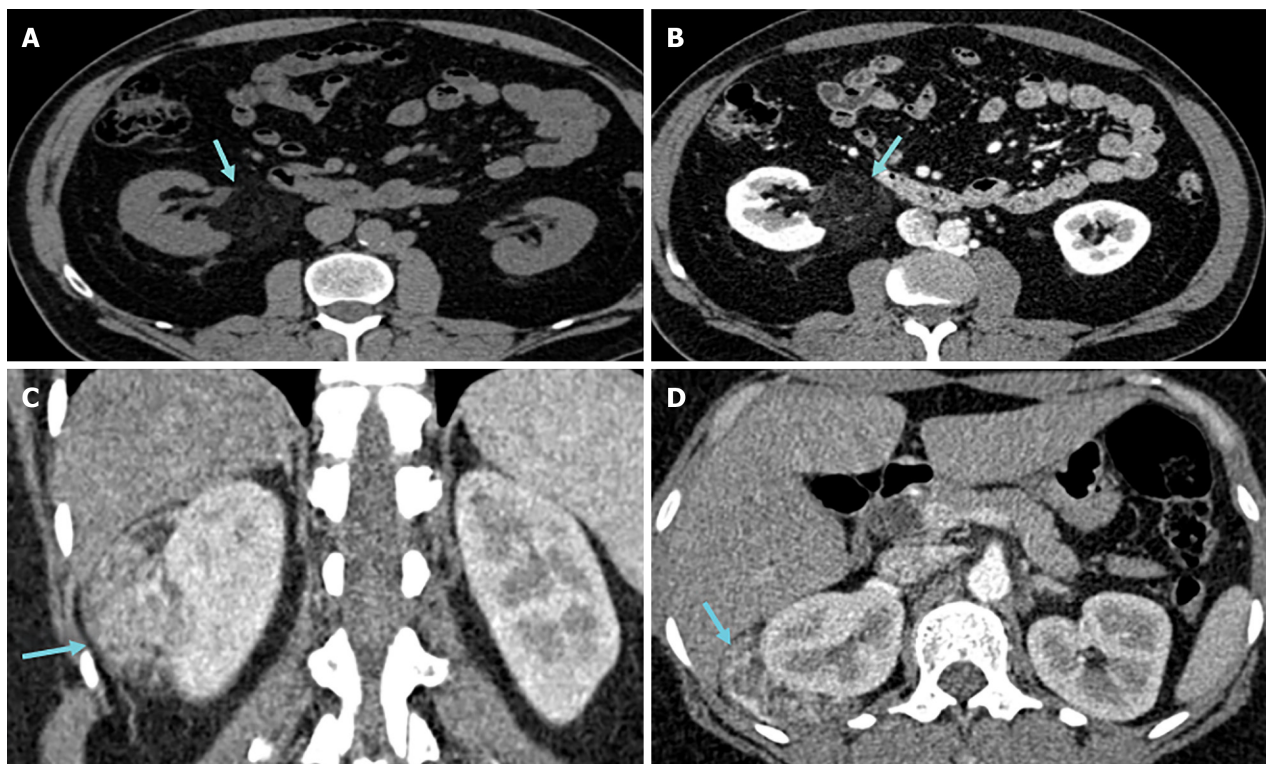


Figure 3 Exophytic angiomyolipoma on computed tomography. A and B: Non-enhanced computed tomography (CT) (A) and contrast-enhanced CT (B) in one patient; C and D: Contrast-enhanced CT in another patient, both with an exophytic mass in the right kidney with macroscopic fat and some vessels (blue arrows).

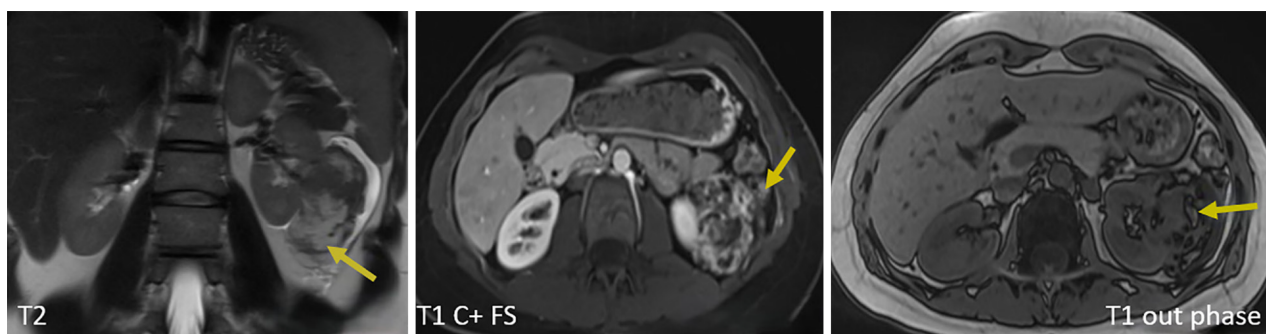


Figure 4 Exophytic angiomyolipomas on magnetic resonance imaging. Abdominal magnetic resonance imaging image showing a single lesion localized in the lower third of the left kidney (yellow arrows), with macroscopic fat. Presents heterogeneous signal intensity in T2WI, chemical shift artifacts in the T1 out phase and heterogeneous enhancement in T1WI with fat saturation and intravenous contrast (T1 C+ FS).

IMAGING FEATURES OF FAT-POOR RENAL AMLS

Approximately 5% of AMLs contain less than 25% fat and cannot be reliably diagnosed by CT. Fat-poor AMLs are also commonly small in size, with most measuring under 3 cm in diameter, further complicating differentiation. Fat-poor AMLs can be classified as hyperattenuating (approximately 4.5% of cases), isoattenuating, or AML with epithelial cysts, all of which are rare.

Hyperattenuating AML

Hyperattenuating AML is predominantly composed of smooth muscle cells and contains approximately 4% fat; these cells hyperattenuate on NECT (> 45 HU) and enhance homogeneously with intravenous contrast[10,15]. On MRI, they behave like smooth muscle, are T1-hypointense, are T2-hypointense, and enhance homogeneously with contrast. In fat-suppressed pulse sequences or in- and out-of-phase images, they typically do not show signal loss (Figure 5). The differential diagnosis of hyperattenuating, homogeneously enhancing renal masses is broad and includes RCC (papillary type), lymphoma, oncocytoma, leiomyoma, and metastasis. Thus, these results do not provide enough evidence for a confident diagnosis of AML, as they overlap with those of RCC, and a confirmatory percutaneous biopsy is recommended in most cases. Calcification and necrosis are not common but, if present, should increase concern for RCC[16].

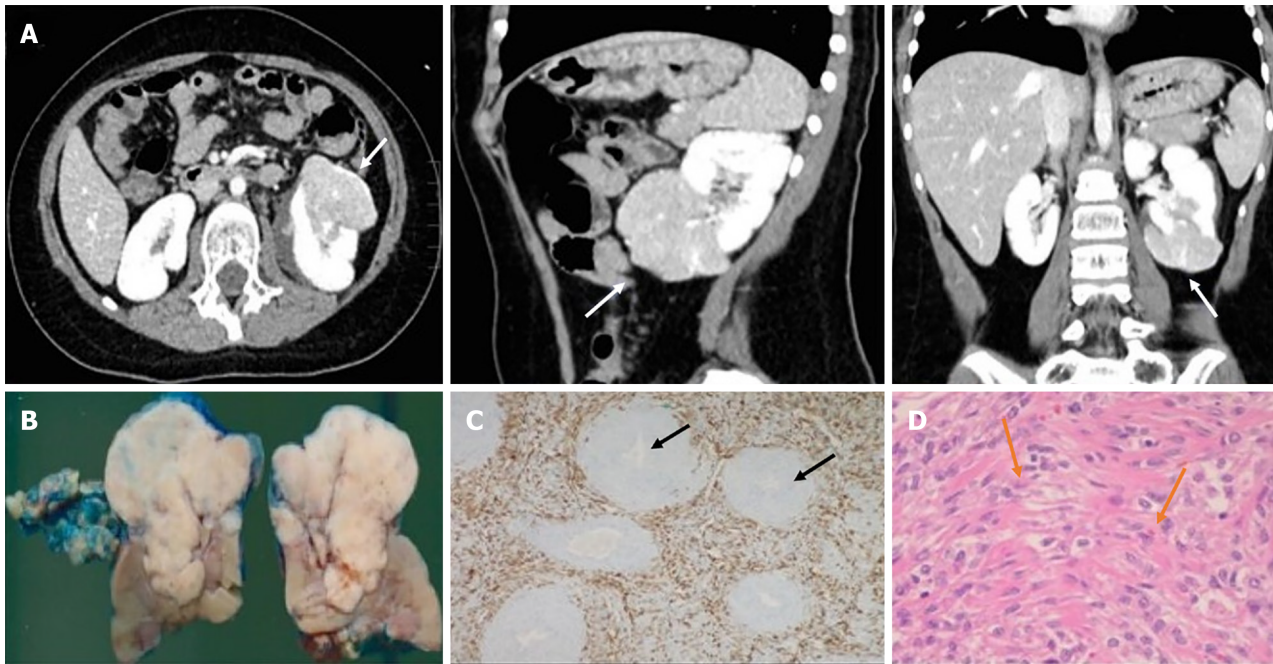


Figure 5 Hyperattenuating angiomyolipoma. A 9-year-old girl with a left renal mass suggesting Wilms' tumor, and biopsy demonstrated angiomyolipoma. A: Axial, sagittal and coronal planes of a contrast-enhanced computed tomography image with a hyperattenuating renal mass without a recognizable fat component (white arrows); B: Macroscopic appearance of the tumor; C: Positive Human Melanoma Black 45 (HMB-45) staining in the cytoplasm of perivascular cells of large vessels was also observed (black arrows). The anti-HMB-45 antibody is a monoclonal antibody that reacts with an antigen present in melanocytic tumors and is nonreactive to most nonmelanoma human malignancies, with some notable exceptions, among which are perivascular epithelioid cell tumors; D: Hematoxylin-eosin staining showing mostly spindle-shaped perivascular cells (orange arrows).

Isoattenuating AML

Isoattenuating fat-poor AMLs are rare and composed of diffusely scattered fat cells, containing up to 25% of fat components. Typically, signals in the -10 to 45 HU range are T2 hypointense and may or may not present signal loss on fat-suppressed MRI. They usually exhibit some enhancement on CECT (Figure 6). Different enhancement patterns have been described in the literature. Reports suggest that progressive enhancement is a characteristic pattern of AMLs with minimal fat[16]. However, other studies did not find significant differences in the enhancement patterns between AMLs without visible fat and RCC[17]. Thus, without macroscopic fat, contrast enhancement alone does not differentiate AMLs from other renal tumors, particularly from RCC.

In most cases, a low T2 signal can help distinguish them from clear cell RCC because the latter frequently exhibits high T2 signal areas. However, as they cannot be confidently differentiated, a biopsy of a small, solid, fat-poor lesion should be considered[16].

AML with epithelial cysts

AMLs with epithelial cysts present as hyperattenuating masses (> 45 HU) and exhibit homogenous enhancement, accompanied by cystic areas or multilocular cysts. On MRI, they are T2 hypointense with hyperintense cystic components and, except for the cystic component, show homogenous enhancement with contrast (Figure 7). The differential diagnosis differs from that of other types of AMLs and includes multilocular cystic RCC, multilocular cysts, cystic nephroma, and mixed epithelial and stromal tumors. However, it is often difficult to rule out malignancy in this scenario, and in most cases, biopsy or surgery is preferred.

IMAGING FEATURES OF EPITHELIOID AMLS

Epithelioid AMLs are considered different from triphasic benign AMLs; they are typically large masses that average 7 cm in diameter and frequently present as an aggressive tumor with intratumoral hemorrhage and necrosis. On NECT, they are hyperattenuated, with variable enhancement due to intratumoral hemorrhage and necrosis. On MRI, they are T2-hypointense secondary to the epithelioid muscle component (Figure 8)[18]. The hyperattenuating appearance due to its hemorrhagic content can mimic other hyperattenuating masses and appear mainly solid on NECT. Considering its aggressive behavior and necrotic areas, sarcoma and cystic RCC need to be considered as differential diagnoses.



Figure 6 Isoattenuating fat-poor angiomyolipoma. A: Non-enhanced computed tomography (CT) - no macroscopic fat is shown, and the lesion is isoattenuating to the renal parenchyma (yellow arrow). Contrast-enhanced CT: The renal mass shows some enhancement (white arrow); B: Magnetic resonance imaging - exophytic lesion without macroscopic fat (red arrow) and low signal intensity on T2WI.

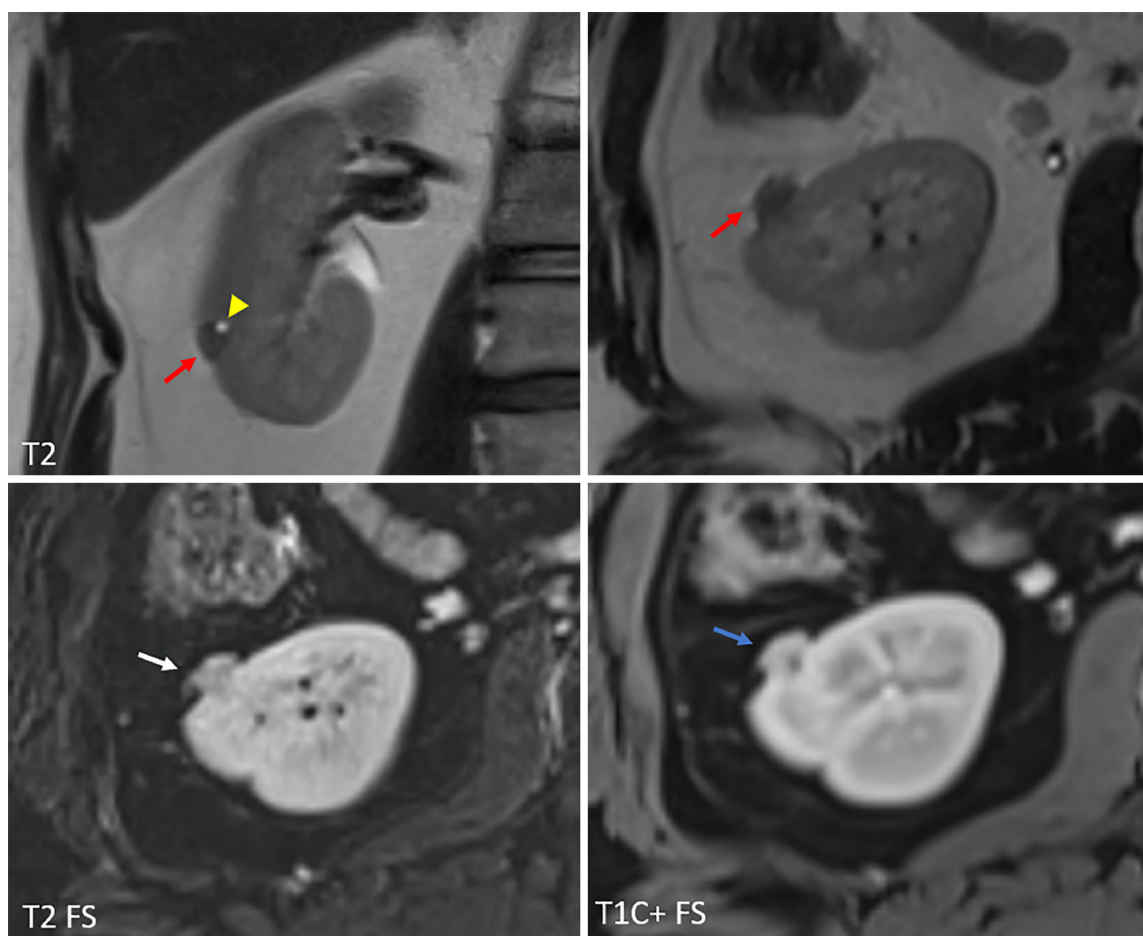


Figure 7 Angiomyolipoma with epithelial cysts. T2WI hypointense exophytic lesion (red arrows) containing an epithelial cyst (yellow arrowhead) is shown. The lesion shows no significant signal drop on the fat-saturated T2 sequence (white arrow) and is homogeneously enhanced with contrast medium (blue arrow).

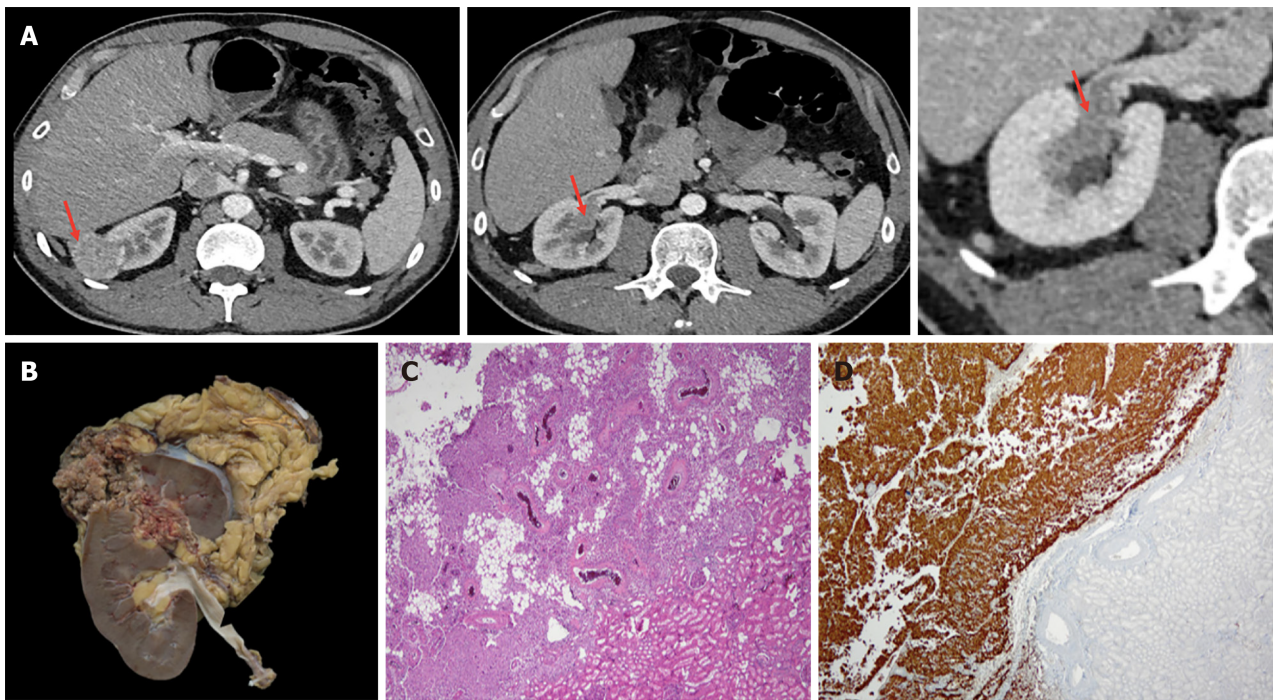


Figure 8 Epithelioid angiomyolipoma. A: Contrast-enhanced computed tomography image showing an aggressive epithelioid angiomyolipoma with a carcinoma-like growth pattern invading the right renal vein (red arrows); B: Macroscopic appearance of the tumor; C and D: Epithelioid smooth muscle cells around blood vessels shown by hematoxylin and eosin staining (C) and focal nuclear atypia CK-7 (+) by immunohistochemistry (D).



Figure 9 Angiomyolipoma associated with lymphangioleiomyomatosis and tuberous sclerosis. A and B: Giant angiomyolipoma with macroscopic fat in the left kidney; C: It is associated with a pulmonary cyst as an expression of lymphangioleiomyomatosis in a patient with tuberous sclerosis.

AMLS IN TUBEROUS SCLEROSIS AND LYMPHANGIOLEIOMYOMATOSIS

Approximately 10% of AMLs occur in association with the TSC or pulmonary lymphangioleiomyomatosis (LAM). The relationship between AML and TSC is well known. Between 50% and 80% of patients with TSC present with AMLs, but only 20% of patients with AML have tuberous sclerosis. In these cases, the AMLs are often multiple and bilateral. When renal AMLs are bilateral, patients have an 80%-90% chance of having tuberous sclerosis.

LAM occurs sporadically or in association with TSC, affecting mostly women (Figure 9)[19].

COMPLICATIONS OF AMLS

Among the most common complications are hemorrhage caused by vessel abnormalities, such as deficiency of elastic tissue, wall thickening, macro- or microaneurysms and tortuous venous invasion. While the risk of bleeding is related to vascularity and tumor size, the incidence of major bleeding is high in sporadic AMLs, surpassing 4 cm in size[20]. Hemorrhage from ruptured AMLs can extend into the perinephric space and renal hilum (Figure 10). Extensive hemorrhage may obscure AMLs on initial CT[5].

The high attenuation of blood may mask fat, especially if fat is present in small amounts. It can be difficult to make the distinction from a classic AML with hemorrhage. Depending on the time of the scan, the blood may be hyperdense, thus mimicking an RCC (clear cell variant) or a hyperattenuating AML variant. If the lesion presents calcifications, it is highly suggestive of RCC. This is a key feature; although it can be present in AML, it is rare. If the scan is delayed by days or

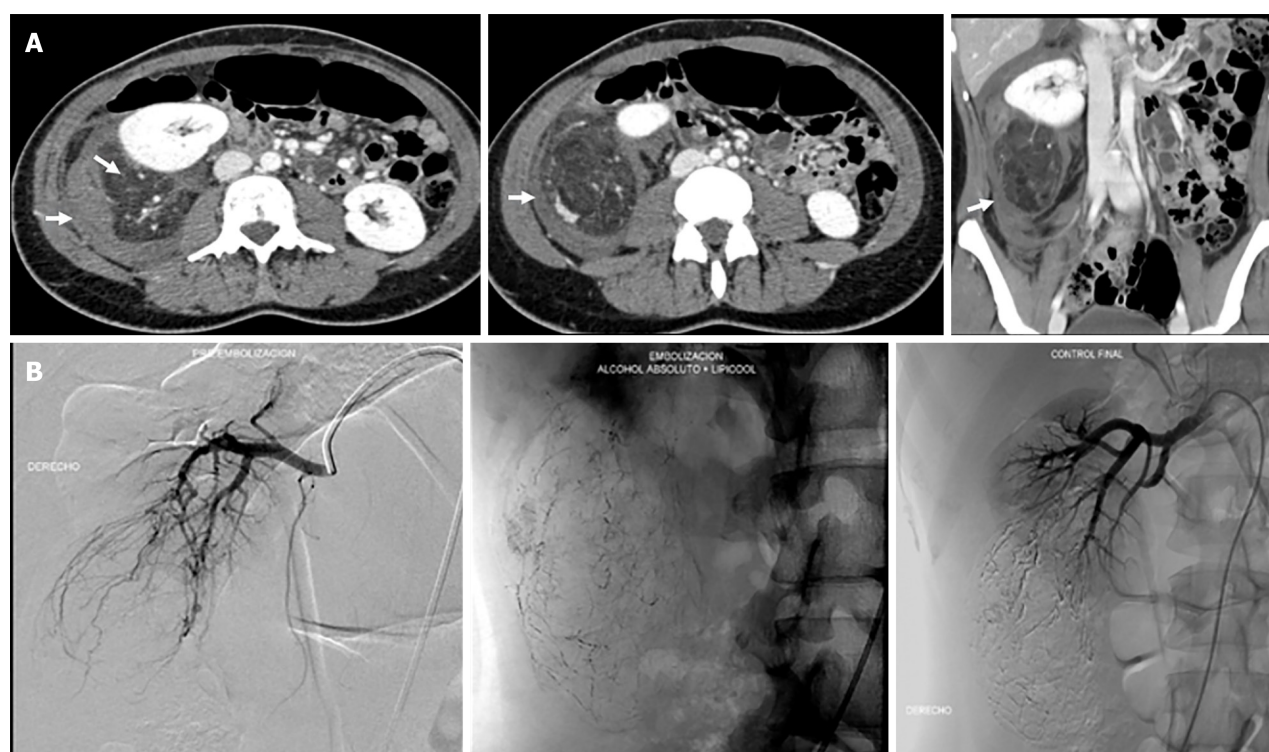


Figure 10 Angiomyolipoma complicated with hemorrhage. A: Contrast-enhanced computed tomography image showing a perirenal hematoma caused by bleeding from an angiomyolipoma; B: Percutaneous treatment with embolization using a Lipiodol-ethanol mixture.

weeks after hemorrhage, the blood can become iso- or hypodense, respectively. In the case of an isodense appearance, a hyperattenuating AML or an RCC (clear cell type) need to be included in the differential diagnosis. In the subacute stage, the clot begins to form and can present hypodense areas that simulate a complex cystic lesion; thus, a cystic RCC or another cystic lesion must be considered.

If a fat component remains visible after hemorrhage, the AML can be confused with a liposarcoma. The key is to recognize the renal location of the tumor because liposarcomas are frequently retroperitoneal lesions rather than renal lesions.

On rare occasions, the tumor may extend into venous structures, indicating aggressive local invasion. Intravascular extension of the lesion into the renal vein or IVC indicates aggressive behavior[15,18]. CT with reformatted images and MRI not only confirm the diagnosis but also clearly demonstrate the cephalic extension of the tumor thrombus (Figure 11).

SUMMARY

Knowledge of the pathology, imaging, and clinical behavior of AMLs has evolved well beyond the original “classic” descriptions.

Although the detection of macroscopic hypoattenuating fat is a well-established diagnostic imaging feature of classic AMLs, a hyperattenuating appearance on unenhanced CT and a hypointense appearance on T2WI may correspond to the predominant smooth muscle component of a fat-poor AML; they may also contain between 10% and 25% fat, resulting in isoattenuating fat-poor AML, or exhibit cystic components characteristic of AMLs with epithelial cysts. All these characteristics constitute important diagnostic clues for AMLs with very little or practically no fat.

CONCLUSION

It is very important to understand the variable and heterogeneous nature of this neoplasm to correctly classify renal AMLs. Recognition of the different image patterns and clues presented is crucial for making the correct diagnosis and avoiding misdiagnosis of other renal lesions, such as RCCs. This is highly relevant and has a direct impact on clinical decision-making and management of patients.

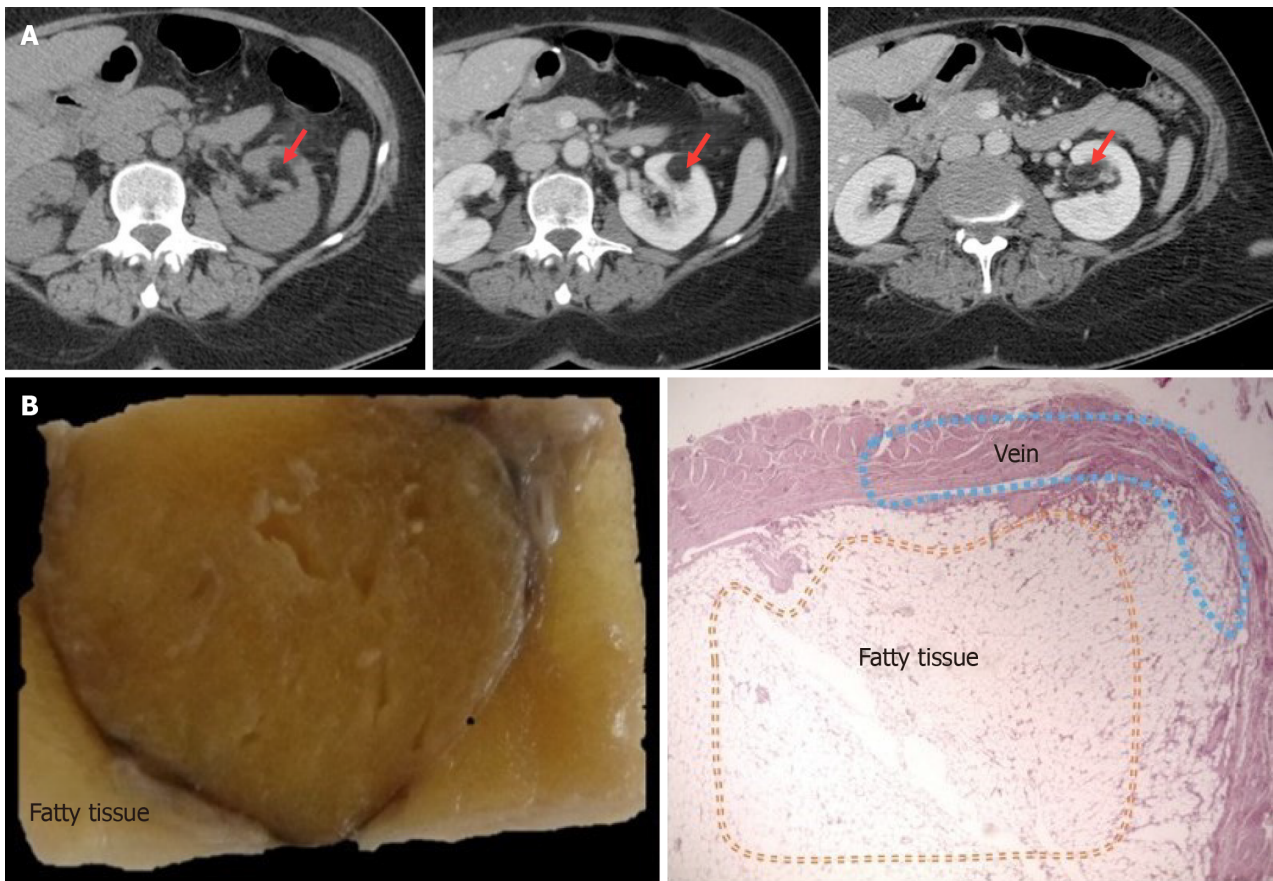


Figure 11 Angiomyolipoma complicated with vein invasion. A: Aggressive angiomyolipoma invading the left renal vein on non-enhanced computed tomography (CT) and contrast-enhanced CT (red arrows); B: Histopathological correlation.

FOOTNOTES

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