



Review of renal artery embolization for treatment of renal angiomyolipoma

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Abstract

Renal angiomyolipoma (AML) is a benign renal neoplasm with the exception of the rare epithelioid variant. AML may be sporadic or may be associated with tuberous sclerosis complex or pulmonary lymphangioliomyomatosis. Risk of hemorrhage is the concern for patients with AML. Renal artery embolization (RAE) is the treatment of choice for acute hemorrhage from angiomyolipoma, and also first-line prophylactic treatment for angiomyolipomas at risk of bleeding. This article reviews the prevalence of AML, factors associated with risk of hemorrhage, and the role of RAE in treatment of these patients.

Keywords: Angiomyolipoma, renal artery embolization, renal neoplasm, acute renal bleed, lymphangioliomyomatosis, tuberous sclerosis, post-embolization syndrome

Introduction

Renal Angiomyolipoma (AML) is the most common benign tumor of the kidney with a prevalence of about 0.3 to 3% worldwide, with a significant higher prevalence in females than males [1]. It is a neoplasm composed of dysmorphic tortuous vascular tissue, smooth muscle and fat. AML may be associated with Tuberous sclerosis complex (TSC) or pulmonary lymphangioliomyomatosis (LAM) or may occur sporadically. There is no histologic difference between sporadic AML and TSC-associated AML. The vascular tissues are prone to aneurysm formation and rupture. Most cases of AML are incidentally found on imaging. Approximately 10% of patients diagnosed with renal AML have tuberous sclerosis [2]. When symptomatic, AML typically presents as palpable flank mass, hematuria and flank pain.

Approximately 17 to 20 percent of patients presenting with spontaneous perinephric hemorrhage have AML [3,4]. 90% of AML cases are unilateral, solitary lesions usually seen in the sporadic AML. Multiple bilateral AML is seen in about 10% of the cases which are usually associated with TSC or LAM. TSC-associated AML is associated with loss of heterozygosity mutations of both TSC1 and TSC2 genes compared to mutations of the TSC2 gene seen in the sporadic AML [5-7]. It is hypothesized that dysregulated mammalian target or rapamycin (mTOR) signaling increases tumor cell growth, proliferation, and metabolism thus promoting progression of TSC lesions.

Angiomyolipomas associated with TSC grows more rapidly, bleeds more frequently, and more likely involve bilateral kidneys compared to sporadic form [8-12]. TSC-associated AML typically present in younger patients, within the third decade of life compared to the sporadic form seen at about the fifth decade of life. TSC-associated AML is more likely to present with atypical features such as epithelioid component or epithelial cysts [13,14]. The epithelioid variant of renal AML is a rare aggressive and malignant disease with predominantly perivascular epithelial cells [15-17]. This variant typically displays nuclei atypia and relative paucity of adipose tissue.

Renal AML greater than 4 cm in diameter have a significant risk of hemorrhage [18]. Size greater than 4 cm approaches 100% sensitivity and 40% specificity to predict rupture. Threshold size for treatment of TSC-associated AML is 3cm, and for sporadic form is 4cm [19]. Aneurysms greater than 5mm in size are more predictive for rupture than tumor size. Other factors associated with increased risk of bleeding include pregnancy and use of estrogen containing contraceptive medication [20-22].

Review

Imaging features

Thin slice non-enhanced CT images are best suited to identify macroscopic fat (attenuation of between -30 to -100 HU) within the tumor. On imaging, a renal mass with macroscopic fat in an

adult is the classical finding (**Figures 1 and 2**). Approximately 5% of AMLs may not have detectable fat on CT and may be missed by imaging. An observation of multiple AMLs on imaging usually indicate tuberous sclerosis. In large tumors greater than 4 cm, hemorrhage may be seen. On CT angiography, multiple aneurismal vessels may be noted within the tumor and its periphery.



Figure 1. Contrast enhanced axial CT shows a large right renal mass containing macroscopic fat (arrow). Presence of macroscopic fat is diagnostic of renal AML.

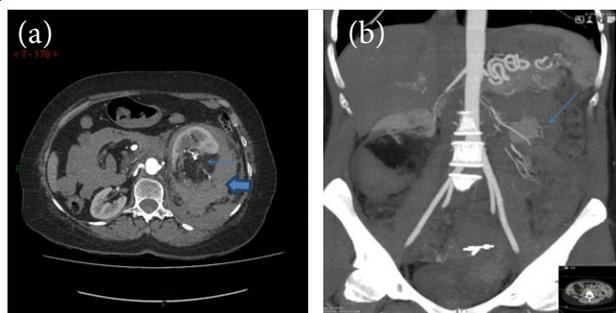


Figure 2. Contrast enhanced axial CT scan (a) shows a bleeding left renal AML (skinny arrow) with retroperitoneal hemorrhage (Big arrow). Coronal MIP reconstruction (b) demonstrates bleed around the left kidney.

MRI signal characteristic is variable depending on the amounts of fat, smooth muscle and vascular tissue. Tumors that have a high relative fat content are hyperintense on T1 weighted images. There is typically loss of signal intensity on fat suppression images. A chemical-shift artifact may also be observed.

On the contrast enhanced T1 images there is significant enhancement of the vascular portion of this lesion. On gradient recalled echo (GRE) images, there is increased signal intensity with the in-phase images, and signal drop out with the out-of-phase images depicting fat within the lesion (**Figure 3**).

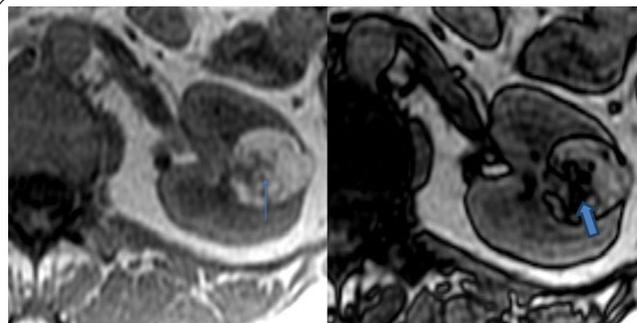


Figure 3. In-phase and out-of-phase images reveal a small left renal lesion with increased signal intensity on the in-phase images (thin arrow), and signal drop out on the out-of-phase images (thick arrow) depicting fat within the lesion.

On angiography, AMLs are a highly vascular tumor with multiple pseudoaneurysms. This gives the sunburst appearance in the capillary nephrogram phase. On the venous phase, there is an onion peel appearance of the peripheral vessels.

On ultrasound, renal AML is hyperechoic compared to normal renal parenchyma. Larger lesions may be heterogeneous and have varying vascularity (**Figures 4 and 5**). However AML is not reliably distinguished from other renal mass lesions such as renal cell carcinoma based on ultrasound findings.



Figure 4. (a) Renal ultrasound showing a large heterogenous mass (indicated by the cursors) with hyperechoic and hypoechoic regions. (b) There is slightly increased vascularity on color doppler.

Treatment

Renal artery embolization (RAE) is the treatment of choice for acute hemorrhage from angiomyolipoma [19,20,23]. It is also the first-line prophylactic treatment for angiomyolipomas at risk of bleeding [24,25]. Nephrectomy may be performed

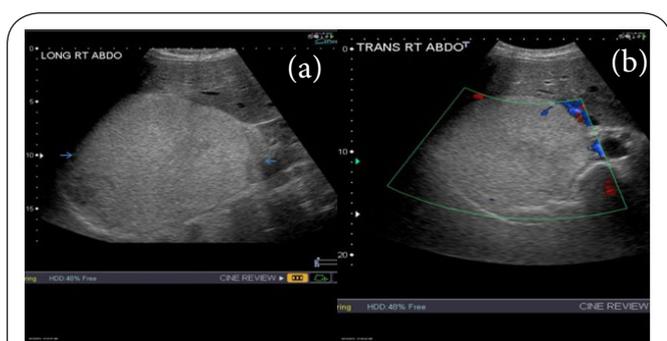


Figure 5. (a) Renal ultrasound showing a large hyperechoic mass (between arrows). (b) Mass does not reveal increase vascularity on color doppler.

if patients have refractory symptoms, complex renal artery anatomy, or in the rare instance of diagnostic uncertainty [26]. If surgery is performed, a nephron sparing approach may be followed in TSC-related AMLs, especially given propensity for recurrent lesions. Radiofrequency ablation, cryoablation and microwave ablation are other alternative treatment options. Mammalian target of rapamycin may be used to reduce the size of angiomyolipomas greater than 30mm [19].

Renal artery embolization

Renal artery embolization was first developed in the 1970s and is used to treat conditions such as renal malignancies, renal aneurysms, and other vascular pathologies as well as complications from renal transplant [27,28]. Compared to surgical nephrectomy, RAE has less renal parenchymal volume loss, a shorter recovery time and generally fewer complications. However up to 5% of initial embolization may require a repeat embolization. In less than 7% of cases there is subsequent nephrectomy after RAE [8,29,30-35]. Lesions with a higher rate for subsequent re-embolization and potentially nephrectomy include larger lesions, hypervascular lesions, multiple lesions, bilateral lesions, and patients with tuberous sclerosis which have a higher tumor recurrence [8]. The use of larger particle size embolization agents have been shown to decrease the rate of repeat embolization [28].

The goal of renal artery embolization is selective devascularization of the AML with microparticles and coils to prevent growth of the mass or spontaneous aneurysmal rupture, as well as to preserve normal renal parenchyma. In 90-100% of cases after RAE, there is decrease in the AML volume by about 20-70% of the initial volume depending on the relative proportion of vascular and fatty components [8,29,30,32-41]. Reduction of volume is more noticeable in the vascular component compared to the fat component of AML.

Preparation prior to procedure

A thorough medical history is obtained including information concerning allergies. Recent laboratory evaluation of coagulation factors and renal function is obtained. Patient

should have no oral intake for at least 6-8 hours prior to the procedure. Intravenous access is obtained. Some interventional radiologists prescribe prophylactic antibiotics to avoid subsequent infection within the infarcted areas. Prior to this procedure moderate sedation is given. General anesthesia is usually not required unless concentrated alcohol is used as a sclerosing agent, due to patient discomfort [42-44].

Before renal artery embolization, a detailed evaluation for variant anatomy of the renal arteries is recommended. This could be evaluated by CT, MRI or during angiography. A unilateral accessory renal artery is present in up to 30 percent of patients, and can be seen bilaterally in approximately 10% of patients. Knowledge of accessory renal arteries is needed to prevent incomplete embolization. The renal arteries arise from the abdominal aorta at the level of L1-L2. At the hilum of the kidney, the renal artery divides first into an anterior and a posterior branch which is subsequently divided into upper, middle, and lower segmental arteries. Segmental arteries give rise to the lobar arteries, which in turn give rise to the interlobar arteries after penetrating the renal parenchyma. Interlobar arteries give rise to the arcuate arteries which give rise to the interlobular arteries. Interlobular arteries become the afferent and efferent arterioles which cannot be distinguished by angiography.

RAE procedure

Vascular access is obtained commonly through a common femoral artery approach with an 18- or 19-gauge puncture needle via a modified Seldinger technique. A 4-6 French sized sheath is used. Axillary and brachial artery access, though rarely performed, may be necessary if there is iliac artery occlusion, significant tortuosity within the iliac artery, or other anatomic reasons [42].

Abdominal aortography is performed. It evaluates for renal ostial disease and offers information regarding possibility of accessory renal arteries. AML may receive vascular supply from other arteries such as adrenal, gonadal, and lumbar arteries. The main renal artery is selectively accessed with a 4-5 French size Cobra, visceral hook or Shepherd hook shaped catheter with coaxial microcatheter. For super-selective embolization, 3Fr micro catheters are used. This decreases the degree of renal infarction and morbidity [43]. Renal artery digital subtraction angiography (DSA) is performed to assess renal artery anatomy and to locate the AML (Figure 6). A guidewire is advanced to the artery supplying the AML (Figure 7). A catheter is advanced over the guidewire. Embolization particles or alcohol is then released at the target vessel. There should be stasis of contrast in the feeding artery upon completion of administration of the embolic agent. After embolization, DSA is performed to evaluate for proper treatment, assess for degree of renal parenchymal loss and assess for complications (Figure 8).

Embolic agents

The most commonly used embolic agents are absolute alco-



Figure 6. A right renal artery Digital subtraction angiogram (DSA) image shows selection of the right renal artery (straight arrow) with a 5 french selective catheter (curved arrow).

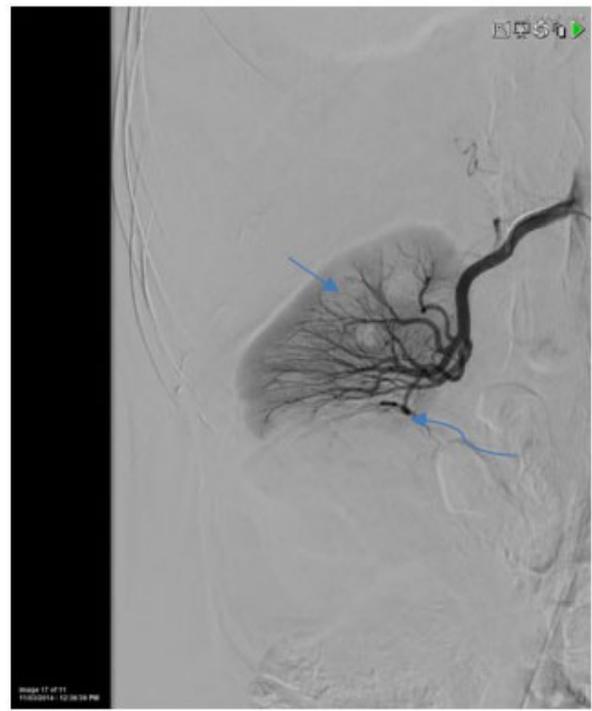


Figure 8. Post embolization renal angiogram shows little to no flow to renal AML (curved arrow) and preserved flow to the remaining normal renal parenchyma (straight arrow).



Figure 7. Subselective lower pole angiogram through a microcatheter (arrow). Subselective release of embolization material at the target artery perfusing the AML is performed.

hol and microspheres. Absolute alcohol provides permanent occlusion at the arteriolar and capillary level distal to the level of collateral inflow. This subsequently causes necrosis of the tumor. There is a higher theoretical risk of nontarget embolization compared to microspheres due to reflux of alcohol from the vessels [45]. Therefore, an occlusion balloon may be advanced selectively to the renal arteries distal to the origin of the adrenal and ureteral branches to decrease this risk. The balloon remains inflated for several minutes after alcohol injection into the renal artery.

Inert microparticles such as Trisacryl-gelatin microspheres (Embosphere™, Guerbet, France) and Non-spherical polyvinyl alcohol particles, Ivalon (Ivalon™, Medsorb Dominicana, USA) also provide permanent distal occlusion of capillaries leading to tissue necrosis. Embospheres are typically the most common used microparticle for distal embolization of renal arteries. Embosphere can be calibrated in different sizes (100–1,000µm) to suit targeted vessels and hence produces a more consistent outcome [46]. A calibrated polyvinyl alcohol-based microsphere is also available (Contour SE™, Boston Scientific, USA; Bead Block™, Biocompatibles, UK).

Coils can also be used for renal artery embolization. They thrombose vessels by causing vascular stasis at the destination site. Once a vessel is coiled, further access cannot be obtained for retreatment. Therefore vessels distal to the lesion are first coiled before more proximal vessels which also

prevents bleeding from retrograde collaterals.

Contraindications

Relative contraindications to renal artery embolization include a solitary kidney, or acute or chronic infection to the kidney due to concern for contrast induced renal damage. Patients with pre-existing renal disease are at a higher risk for contrast-induced nephrotoxicity. Adequate hydration is the most important factor in protecting renal function [47]. Radiation dose to the fetus is always of concern in pregnant patients [48-50]. Intravenous iodinated contrast is a US Food and Drug Administration Class B agent, and can be given in pregnancy [51]. Animal studies have not shown a risk to the fetus, and there is not sufficient data evaluating risk of contrast dose in pregnant women.

Microparticles are contraindicated in patients with arteriovenous fistula due to concern for particle migration causing pulmonary embolism. Coils may not be employed if there is concern for subsequent intervention at that arterial bed. When coils are used, subsequent intervention in the event of re-bleeding from collateral vessels may be compromised since the main feeding vessel has been occluded.

Complications

Renal artery embolization is generally associated with lower rate of complications compared to surgical procedures [27,52-55]. The most feared but rare complication is peri-procedural aneurysm rupture. Post-embolization syndrome comprising of abdominal pain, cramping, fever, nausea and vomiting may occur due to release of inflammatory modulators by the infarcted tissues within 72 hours after embolization. This was seen in up to 62% of cases [56]. Larger lesions have a higher incidence of post embolization syndrome. Treatment is symptomatic relief with analgesia and IV fluids.

Non-target embolization is a less common complication which could lead to extensive infarction of the kidneys (Figure 9), adrenal glands, ureters, lower limbs, small and large intestines, and testicles. Damage to normal renal parenchyma can occur due to a lack of significant intrarenal collaterals.

Other complications include bleeding, infection, groin hematoma, arterial dissection, arterial spasm (Figure 10), contrast induced nephropathy, renal abscess (Figure 11), emphysematous pyelonephritis, and anaphylaxis [57,58].

Conclusion

Renal AML is a renal neoplasm which is benign with the exception of the rare epithelioid variant. AML may be sporadic or may be associated with tuberous sclerosis complex or pulmonary lymphangiomyomatosis. Patients with tuberous sclerosis have a higher rate for subsequent re-embolization, should be followed more closely clinically and with imaging and as warranted. Presence of macroscopic fat on imaging is classic for diagnosis. Aneurysm greater than 5mm and tumor size greater than 4cm are associated with a higher risk of rupture.

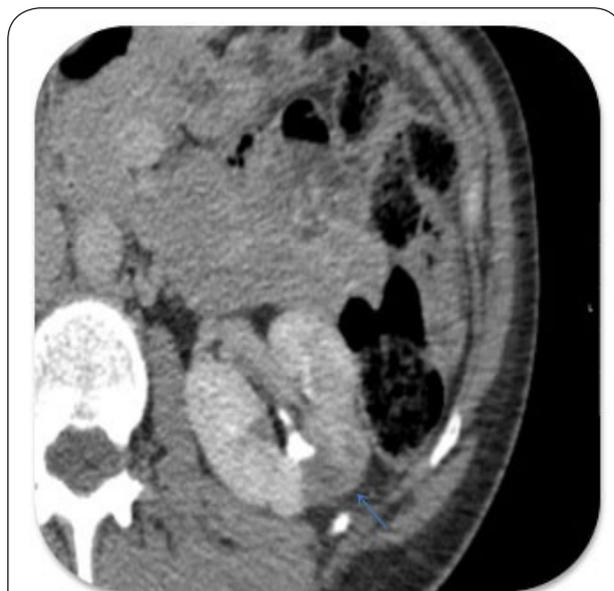


Figure 9. Contrast enhanced axial CT depicting a wedged shaped small left renal infarct caused by nontarget embolization of normal renal parenchyma.



Figure 10. Left renal artery angiogram depicting spasm (arrow) of the left renal artery as a result of catheter and wire manipulation.

RAE is the treatment of choice for acute hemorrhage from angiomyolipoma, and also first-line prophylactic treatment for angiomyolipomas at risk of bleeding. Up to 5% of initial embolization may require a repeat embolization, and in a few cases post RAE nephrectomy may be necessary. Post embolization syndrome comprised of abdominal pain, cramping, fever, nausea and vomiting, is a relatively common complication especially in large tumors. Treatment is with symptom relief.

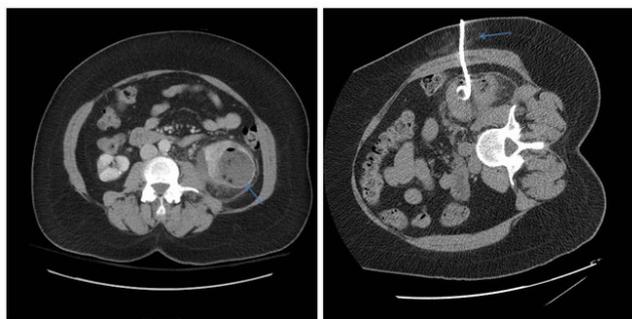


Figure 11. Contrast enhanced axial CT depicts a left renal abscess (arrow) in a patient who presented with a UTI post renal artery embolization for AML. This required CT guided drainage (arrow) (8B).

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	MO	GA	IJP
Research concept and design	✓	--	✓
Collection and/or assembly of data	✓	✓	✓
Data analysis and interpretation	--	--	--
Writing the article	✓	✓	✓
Critical revision of the article	✓	✓	✓
Final approval of article	✓	✓	✓
Statistical analysis	--	--	--

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