A 16 Year Follow Up of Interventional Radiology Treatment And Management of A Renal Angiomyolipoma

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Not relevant

ABSTRACT

Renal angiomyolipoma are benign vascular tumours that can lead to life threatening haemorrhage. This paper describes a case of further growth of a previously coil embolised renal angiomyolipoma in a patient on warfarin requiring reembolisation. A literature review of the different types of embolization material, their associated complications, current recommendations and comparison between each technique was performed. The rate of recurrence of angiomyolipoma post embolization was also reviewed.

CASE REPORT

BACKGROUND

This case report is unique in that it demonstrates long term (16 year) follow up of an embolized renal angiomyolipoma and discusses current embolization techniques. We also discuss the long term and short term complications of embolization.

CASE REPORT

A 68-year-old lady, who 16 years earlier was first referred for an abdominal ultrasound on the initial presentation of right groin pain. On ultrasound, she was found to have a right renal mass (Figure 1) and two small angiomyolipoma (AML) in the left kidney. Her previous medical history includes mitral valve replacement 5 years earlier for mitral regurgitation for which she is currently on Warfarin.

CT kidneys was performed which confirmed the presence of fat component in the 5.8 x 4.4 cm right renal mass in keeping with AML with some areas of higher density suggestive of prior associated haemorrhage (Figure 2a). Small AMLs were again demonstrated in the left kidney.

The patient underwent embolization with platinum microcoils a few months after with incomplete embolization noted on post embolization angiogram due to extensive blood supply of the AML (Figure 3a,3b). The post embolization follow up CT kidneys 6 months post procedure demonstrated decrease in size of the right renal AML to 5.3 x 2.7 cm (Figure 2b).

The patient was followed up with CT kidneys every two years for the next 16 years following embolization monitoring for changes in size and looking for complications. It was noted on ultrasound and CT kidneys performed 6 years post embolization that the right renal AML had started increasing in size measuring 6.5 x 4.4 x 8.6 cm (Figure 4a,4b). The patient was not keen for any invasive treatments since she was asymptomatic, thus she was followed up for a further 10 years which showed gradual increase in size to 8.8 x 6.1 x 11.7 cm (Figure 4c,4d), with calculated rate of growth of 0.31 cm/year.

Over the course of follow up, the patient continued to be asymptomatic from the large AML. Following episodes of spontaneous bruising secondary to warfarin use, the patient eventually consented for further embolization of the AML, given the risk of life threatening haemorrhage.

The control fluoroscopic image of the right kidney showed some of the previously inserted coils in the right renal lower pole had migrated distally. Of note, the embolised vessels did not demonstrate any significant supply to the enlarged AML (Figure 5a), suggestive of new vascular supply recruitment by the AML.

Dedicated microcatheter angiograms demonstrated main supply to the AML arises off the (likely ureteric) arterial branch coming off the main renal artery (Figure 5b) which was not clearly demonstrated on the previous completion angiogram (Figure 3b), as well as a lower pole branch which does not supply any normal renal parenchyma (Figure 5c).These were selectively embolised with 355-500um PVA particles with complete occlusion of the vessels feeding the AML while maintaining the normal parenchymal perfusion in the right lower pole.

Further angiogram also demonstrates supply of the upper and interpolar regions of AML by the right lumbar 1 artery which also supplied the pelvic side wall (Figure 5d). The recruited branches supplying the AML were too small and distal for super selective cannulation. Coil embolization was performed as distal as possible with 3 x 80mm detachable coils.

Post procedure angiogram demonstrated good angiographic result with preservation of the renal parenchyma. The patient was discharged the next day and Warfarin restarted 24 hours after the procedure. The patient was subsequently reviewed in clinic a week later with no procedural complications noted.

DISCUSSION

Etiology and Demographics

Renal angiomyolipomas (AML) are the most common benign renal neoplasms composed of varying proportions of adipose, vascular, and muscular tissue [1]. A retrospective analysis of 61,389 patients demonstrated overall prevalence of 0.44%, with stronger female predisposition for AMLs than males [2]. AMLs are associated with genetic conditions such as Tuberous Sclerosis Complex (TSC) and lymphangioleiomyomatosis but up to 80% of AMLs are sporadic [3].

Pathologically, AMLs are divided into a classic type and an epithelioid variant with the latter having a higher probability of malignant transformation [4].

Clinical and Imaging Findings

AML classically presents with symptoms of flank pain, palpable mass and hematuria [5]. Due to the heterogenicity of its various tissue components, AMLs may have mixed appearance seen on imaging depending on the amount of macroscopic fat present [6]. A typical AML displays fatty attenuation on Computed Tomography (CT) and hyper-intensity on T1 and T2-weighted images seen on Magnetic Resonance Imaging (MRI) with signal loss on fat-suppression sequence [3]. In contrast, a fat-poor AML can appear heterogeneously hyperdense on unenhanced CT and display a hypo-intense signal on T2-weighted MRI [7].

Treatment and Prognosis

Most AMLs are asymptomatic and several studies are in concordance with the continuous monitoring of asymptomatic AMLs <4 cm in diameter [8,9]. The 2012 International Tuberous Sclerosis Complex Consensus Conference suggested a combination of surveillance modalities utilizing follow-up imaging and repeated measurement of glomerular filtrate rate to evaluate kidney function [10]. The recommended interval for imaging surveillance is proposed to be annually [11].

The main worrisome complication of AMLs is intra-tumoral and retroperitoneal haemorrhage [12]. There are multiple factors attributing to the risk of AML rupture and haemorrhage, including tumour size (diameter of >4 cm), presence of genetic abnormalities such as TSC, formation of intra-tumoral aneurysm >5 mm and AML growth rate of >0.25cm per year [13,14]. Prophylactic treatment with embolization of high-risk AMLs can be considered, taking into careful consideration a proposed 65% over-treatment rate should all AMLs >4 cm be prophylactically embolised [8,14].

The 2023 Japanese clinical practice guidelines for TSC-associated AML proposed Everolimus (an mTOR inhibitor) as first-line therapy for asymptomatic AML given that it has been shown to decrease the size and prevent rupture of AMLs [15]. For cases of TSC-associated AML rupture, urgent renal artery embolization is strongly recommended, with surgery reserved for patients where embolization is not accessible [8].

Conversely, the 2020 Canadian Urological Association best practice report on the diagnosis and management of sporadic angiomyolipomas recommended both minimally invasive nephron-sparing surgery and embolization to be acceptable

first-line treatments [16]. While embolization might be safer and less invasive, the guidelines stated a high re-treatment rate of 41% associated with embolization [16].

Different Types of Embolization

Embolization of the renal arterial supply has been shown to downsize AMLs and prevent recurring major bleeding episodes [17, 18]. Embolization of AMLs is associated with low complication rates and preservation of renal function [8]. Different embolization methods include insertion of coils, injection of microparticles, and usage of onyx [19]. Deliberate selection of the embolization agent should be based on the size and calibre of target vessels [20].

Coils

Coils used in embolization contain bio-inert metallic cores, such as steel or platinum, and can be deployed easily through a catheter to provide mechanical occlusion to aneurysms or to occlude larger bleeding vessels [21]. It provides a thrombogenic surface for clot formation [22, 21326511) and is currently being used in clinical practice for proximal embolization [22- 24]. Complications of using coils include occlusion of non-target vessels and coil migration [22].

Polyvinyl Alcohol (PVA) particles

PVA is a synthetic polymer derived from polyvinyl acetate and its irregularly- shaped particles are obtained by rasping vacuum-dried foam sheets of PVA and sieving them based on size [22, 25]. PVAs adhere to blood vessel walls resulting in inflammatory reactions and thrombus formation [26]. Instead of targeting proximal embolization like coils, PVA particles are designed to embolize tissue at the arteriole and capillary levels, targeting distal embolization.

A comparative study by Jacqueline et. al suggested that small-sized microparticles <150u seemed less effective with a sixfold higher risk of re-embolization as compared to the larger-sized microparticles >150u [27]. Complications of respiratory distress together with pulmonary hypertension with microparticles less than 500u have been reported [27].

Calibrated microspheres had been developed to circumvent the problem of unpredictable embolization secondary to irregularly shaped particles [21]. Microspheres have also been shown to be effective for embolization of unruptured sporadic AMLs [28, 29].

Ethanol-lipiodol emulsion

Ethanol in high concentrations can result in tissue necrosis, acting as a sclerosing agent [21]. With the addition of lipiodol, ethanol-lipiodol emulsion becomes radio-opaque aiding in the visibility of delivery of this embolization agent [30]. However, ethanol-lipiodol emulsion can be associated with non-target embolization, rarely pleural effusion, and rise in pulmonary artery pressure requiring close monitoring intra-procedurally [31,32]. Usage of a micro-balloon catheter for the injection of ethanol-lipiodol emulsion has allowed for the selective embolization of tumour-feeding vessels and prevention of systemic effects but yielded little evidence with regards to tumour shrinkage rate compared to non-balloon occlusion group [33,34].

Onyx injection

Onyx, also known as ethylene vinyl alcohol copolymer, is a liquid embolic agent favoured for its slow and controlled administration and its non-adhesive characteristics [35]. Onyx is available in two formulations Onyx-18 (6% EVOH) and Onyx-34 (8 % EVOH) with some users preferring Onyx-18 for its reduced viscosity allowing it to penetrate deeper into the microvasculature [35].

Few publications on the successful use of Onyx embolization for AMLs can be found with the first successful embolization reported in 2008 achieving complete devascularisation of a sporadic AML [36]. Another 2016 study followed ten AMLs embolized with onyx in seven patients, with results showing no subsequent haemorrhage within the follow-up period and a mean decrease in AML size of 22 mm [35]. The latest 2023 single-centre study showed that usage of Onyx for embolization resulted in signification post-embolization tumour size reduction. However, this single-centre study also reported minor complications from the use of Onyx such as poor visibility of Onyx resulting in non-targeted embolization, pseudoaneurysm of the femoral artery, and major complications such as renal artery dissection [37]. However, due to its high cost, Onyx is not commonly used as a first line embolic agent in many centres.

Complications of embolisation

The most common complication of embolization of AML is post-embolization syndrome (PES) which comprises a myriad of symptoms like fever, nausea, vomiting, and pain can occur in 35.9% of procedures [38]. Severe complications post-embolization include the formation of renal abscesses and renal artery thrombosis which could ultimately lead to irreversible loss in kidney function [39].

Comparison between techniques

Currently, there is no established consensus on the superiority of any embolic agent used in symptomatic treatment of AML, prophylactic bleeding prevention, and the treatment of active bleeds [38].

Publication by J Lenton et al. advocates for a combination of particulate material and coils for AML embolization, given that a higher incidence of acute bleeding is associated with embolization with particulate material alone while O. Rouviere et al. recommend the use of microparticles for distal embolization of the tumour-bed in conjunction with the use of coils for proximal embolization of vessels and aneurysms [8, 40].

On the contrary, a single-centre retrospective analysis performed to evaluate treatment outcomes in AML patients across 13 years, compared patients who underwent embolization with solely particles versus patients who received both particle and proximal coil embolization, concluded no added benefit

from proximal embolization with coils in terms of bleeding and complication rates [32].

Another study conducted in 2023 by Long Jin et al. also showed no significant difference in the tumour-shrinkage rate in AMLs and the occurrence of post-embolization syndrome between patients who underwent ethanol-lipiodol emulsion embolization compared to patients who received PVA particle embolization [41].

Likewise, findings by Schwartz et al. reported that the type of embolization agent used did not affect the incidence of post-embolization syndrome [42].

However, it is essential to note that most of the current literature comparing embolization methods is retrospective and limited by small cohort size.

Recurrence of AML after each embolization method

Generally, the recurrence rate of TSC-associated AML is higher compared to that of sporadic AMLs even after embolization [43,44]. A 2015 literature review by S. Kumar et al quoted a recurrence rate as high as 60% in TSC-associated AMLs post embolization [45].

The presence of genetic conditions like TSC, patient age, and pre-embolization tumour volume are suggested to be risk factors for AML recurrence post-embolization [46].

While Murray et al. reported a post-embolization 20.9% reintervention rate, at an average follow-up of around 3 years, quoting enlarging AMLs, revascularization of AMLs, and acute bleeding as reasons for reintervention [38]. The current literature has yet to provide an in-depth evaluation of AML recurrence rates status post various embolization methods respectively and could be a potential area for future analysis.

Differential Diagnoses

Macroscopic fat on CT points towards an AML unless presence of calcification is seen for which suspicion for renal cell carcinoma should be raised [47].

Microscopic fat on the other hand such as demonstrated though MRI drop-signal (chemical-shift) in out-of-phase sequence is not as specific to AML and can also be demonstrated in renal cell carcinoma (RCC) [48].

In solid renal lesions without macroscopic fat, the differentials include RCC and oncocytoma. Contrast enhancement pattern of the lesion assists in differentiating with oncocytoma demonstrating central scar and inversion pattern of enhancement where a hyperenhanced tumor segment on the corticomedullary phase reverts to hypoenhancing on the excretory phase [49, 50]. Lesions with size more than 4cm and heterogenous enhancement are more suspicious for RCC [51].

TEACHING POINT

Embolization remains a great option for the prophylactic treatment of high risk AML considering it is safer and less invasive than surgical management though carries the risk of recurrence and therefore the need for reintervention. There is no established consensus on the superiority of any embolic agent compared to another but patient should be made aware of the most common complication of embolization, post-embolization syndrome.

QUESTIONS

Question 1: AMLs are associated with which genetic condition?

a. Tuberous Sclerosis Complex
b. Cystic fibrosis
c. Marfan syndrome
d. Huntington's disease

Answer: a

Explanation: Tuberous sclerosis complex is characterised by development of multiple benign tumours including AML. It is caused by genetic mutations in the TSC1 and TSC2 genes.

Question 2: Which of the following is the most significant factor associated with an increased risk of rupture in renal angiomyolipomas?

a. Tumour location in the renal cortex
b. Presence of cysts within the angiomyolipoma
c. Male gender
d. Large tumour size (> 4cm)
e. Presence of fat poor angiomyolipoma

Answer: d

Explanation: Larger tumours are more prone to rupture

Question 3: What is the most common complication of embolization?

a. Acute kidney failure
b. Haematuria
c. Pulmonary embolism
d. pseudoaneurysm formation
e. Post-embolization syndrome

Answer: e

Explanation: Post embolization syndrome (fever, pain, nausea) is the most common complication but is self-limiting.

Question 4: What is the primary goal of prophylactic embolization in the management of renal angiomyolipomas

a. Complete tumour eradication
b. Reduce the risk of rupture and haemorrhage.
c. Improve renal function
d. Prevent tumour recurrence
e. Shrink the tumour to <1 cm

Answer: b

Explanation: Prophylactic embolization aims to control bleeding and prevent rupture, especially in larger or symptomatic tumours. It is not intended for complete tumour removal.

Question 5: Which embolic agents can be used for embolization or renal angiomyolipomas?

a. Coils
b. Balloon catheters
c. Polyvinyl Alcohol (PVA) Particles
d. Onyx injection
e. Ethanol-lipiodol emulsion

Answer: a, c, d, e

Explanation: Balloon catheters are used to assist with embolization but are not an embolic agent themselves.

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FIGURES

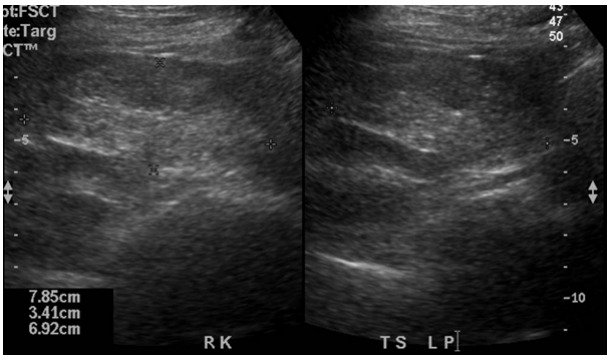


Figure 1: Ultrasound of the right kidney

Echogenic mass in the lower pole of the right kidney.

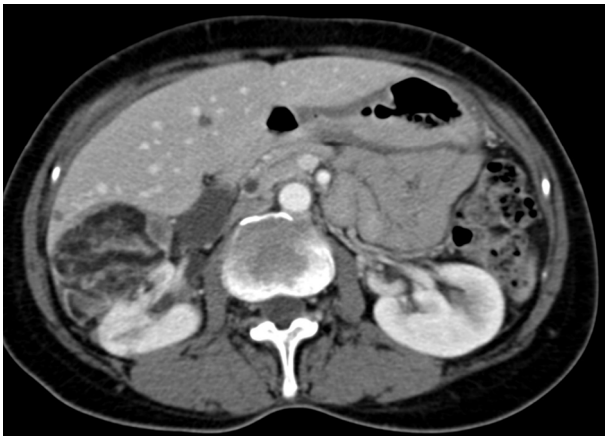


Figure 2a: Axial section of CT abdomen

Right renal lower pole mass containing macroscopic fat in keeping with angiomyolipoma (white arrow)

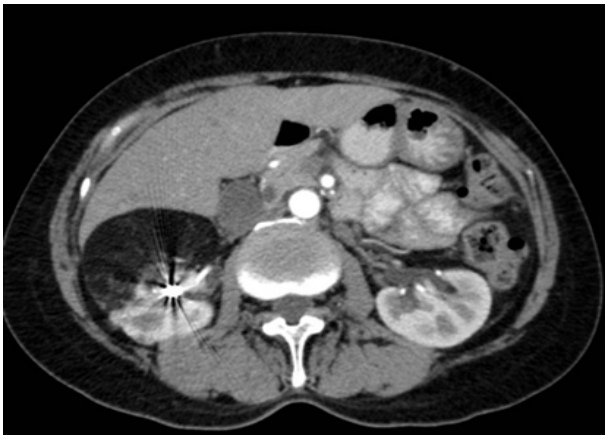
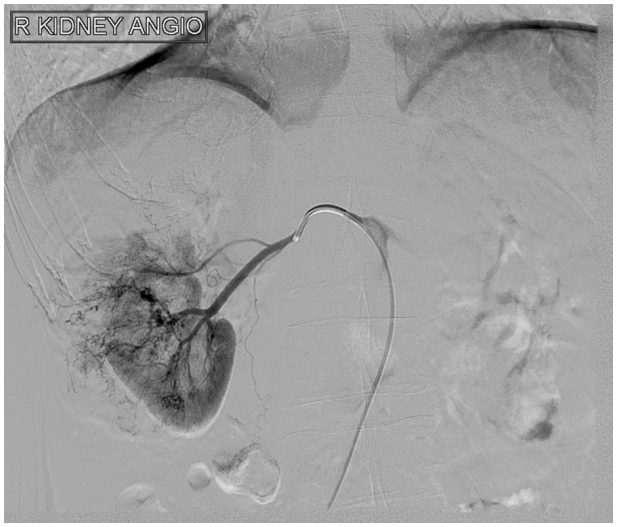


Figure 2b: Axial section of CT abdomen

Post embolization of the right renal lower pole angiomyolipoma demonstrating decrease in size



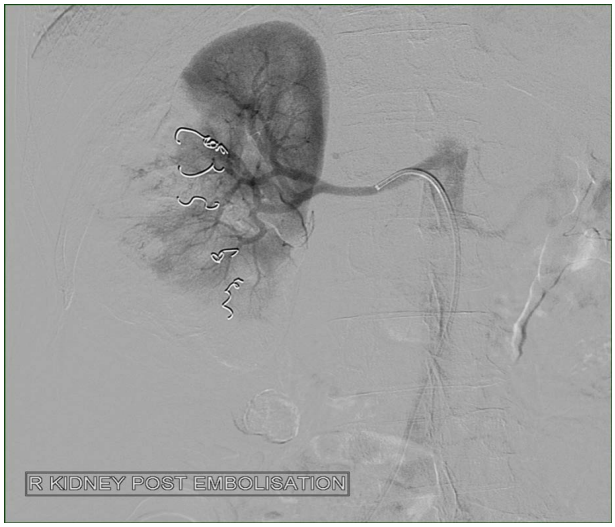


Figure 3a: Pre-embolisation angiogram of the right kidney demonstrating vascular supply to the angiomyolipoma.

Figure 3b: Post embolization angiogram of the right kidney demonstrating the deployed coils.

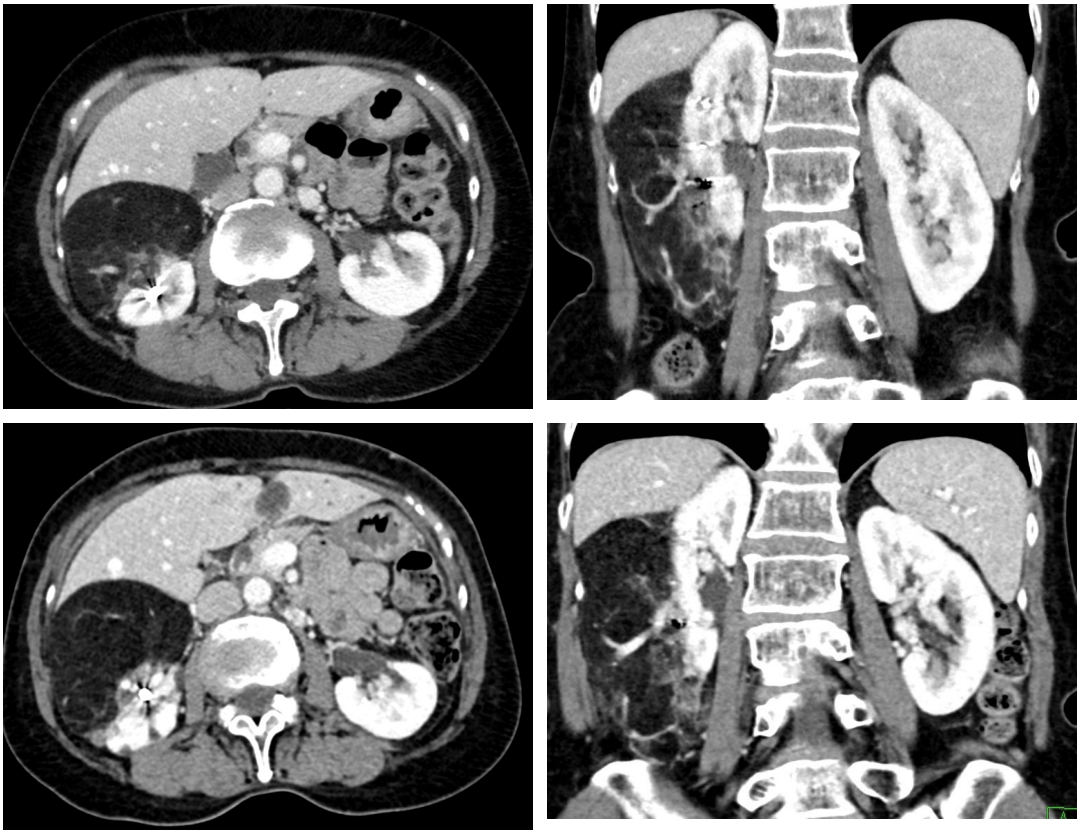


Figure 4: Axial and coronal sections of CT kidneys

The images 4a and 4b demonstrate CT kidneys performed 9 years post coil embolization of right angiomyolipoma.

The images 4c and 4d, CT kidneys performed 16 years post coil embolization demonstrating increase in size of the right renal angiomyolipoma.

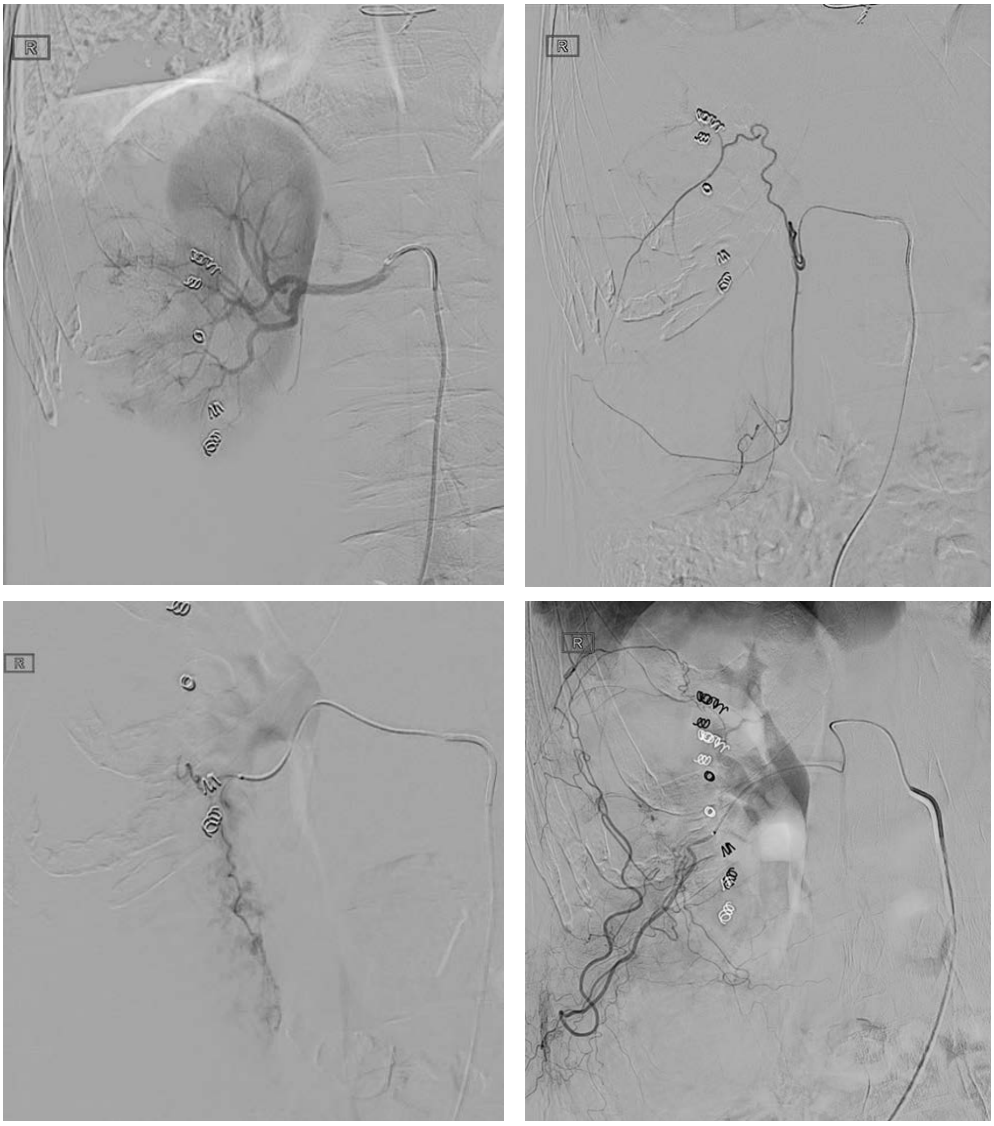


Figure 5a: No significant supply to the enlarged AML from the previously embolised vessels.

Figure 5b: Moderate supply to the mid and lower pole of the AML, likely recruited from the branch supplying the proximal ureter.

Figure 5c: Branch arising off the lower pole of the kidney with no supply to the renal parenchyma but supplies the medial aspect of the lower pole of the AML.

Figure5d: Right lumbar artery branches supplying the interpolar and upper pole of the enlarged AML.

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