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Transarterial embolization for renal angiomyolipomas: A single centre experience in 79 patients

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Abstract

Objective: To evaluate the long-term efficacy and safety of selective arterial embolization (SAE) in the treatment of renal angiomyolipomas (AMLs).

Methods: This was a retrospective review of medical records and imaging findings from patients with renal AMLs who attended our clinic and received SAE between January 2007 and January 2014. Only patents with complete medical records, preoperative computed tomography scans using typical imaging and follow-up data were included.

Results: A total of 79 patients were enrolled in the study. Technical and clinical success rates were 100% and 91% ($n = 72$), respectively. Only two patients experienced major complications. Post-embolization syndrome (i.e. fever, abdominal pain, nausea or vomiting) was reported in 68 (86%) patients, but all symptoms were mild and resolved with conservative measures. Mean radiological and clinical follow-up periods were 16.8 and 35.9 months, respectively. In 75 (95%) patients, tumours decreased in size; mean $\pm$ SD tumour size significantly decreased from 8.4 ± 3.5 cm pre-embolization to 6.7 ± 3.0 cm post-embolization.

Conclusions: This study provides long-term evidence that SAE is a safe and effective method in the treatment of patients with renal AMLs.

Keywords

Angiomyolipoma, renal, tuberous sclerosis, embolization, polyvinyl alcohol, bleomycin-lipiodol emulsion

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Introduction

Renal angiomyolipomas (AMLs) are uncommon benign masses composed of varying amounts of abnormal blood

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vessels, smooth muscle and adipose tissue.[1] The blood vessels within AMLs are abnormal with no internal elastic lamina and the smooth muscle is replaced by fibrous tissue making the vessels rigid, tortuous and prone to aneurysm formation and rupture.[2] Indeed, it has been documented that AMLs show a high likelihood of rupture during their clinical course, with the presentation of haematuria, retroperitoneal bleeding and haemorrhagic shock.[3]

The tumours are classically identified by the characteristic presence of fat on computed tomography (CT), magnetic resonance imaging or ultrasonography of the kidneys. They are found in <0.3% of the general population and account for about 3% of all tumours in the kidneys.[4] The majority of AMLs occur sporadically whilst the remaining cases are associated with tuberous sclerosis complex (TSC), an autosomal dominant disorder.[5] Although some renal AMLs are asymptomatic, they have a propensity to increase in size and may cause local complications.[6] Common symptoms of AMLs include flank pain, palpable mass, gross haematuria, anaemia and symptoms related to a mass effect, such as abdominal pain, abdominal fullness, abdominal visceral compression and anorexia.[7] Management recommendations are based on tumour size and symptoms,[8] and treatment goals focus on preventing acute events, preserving renal parenchyma and maintaining long-term kidney function.[9] While selective arterial embolization (SAE) for AMLs has gained popularity in recent years, few large studies are available with long-term follow-up data.[10,11] The objective of this retrospective study was to evaluate the long-term efficacy and safety of SAE in the treatment of AMLs in patients treated at our institution over a 7-year period (2007 to 2014).

Patients and methods

Patient population

This was a retrospective review of the medical records and imaging findings from patients with renal AMLs who attended the Department of Interventional Radiology and Vascular Surgery, Peking University First Hospital, Beijing, China and received SAE between January 2007 and January 2014. Only patents with complete medical records, preoperative CT scans using typical imaging and follow-up data were included. Demographic data, type of AMLs (sporadic or TSC-related), clinical symptoms, tumour size and location, technical success, clinical success, complications and tumour relapse were recorded by one of three investigators (G.N., Z.Y. or B.Z.). The primary indications for SAE were acute haemorrhage, haematuria, pain or asymptomatic size greater than 4 cm. Indications for unplanned repeat embolization included uncontrolled symptoms, re-bleeding and subsequent increase in the size of the mass.

This study received institutional review board approval from the Ethics Committee of Peking University First Hospital, Beijing, China before commencement and because it was a retrospective study, patient informed consent was not required.

Angiography methods

Angiography was performed in all patients under local anaesthesia via the femoral artery. Abdominal aortography had been taken to identify renal arteries and exclude alternative feeding vessels. In addition, selective renal arteriography was performed through a standard 5-F catheter (Figure 1). Once the feeding vessels to the targeted AML were identified, they were catheterized supra-selectively using a coaxial microcatheter. Based on the size and number of the feeding vessels of the tumour,

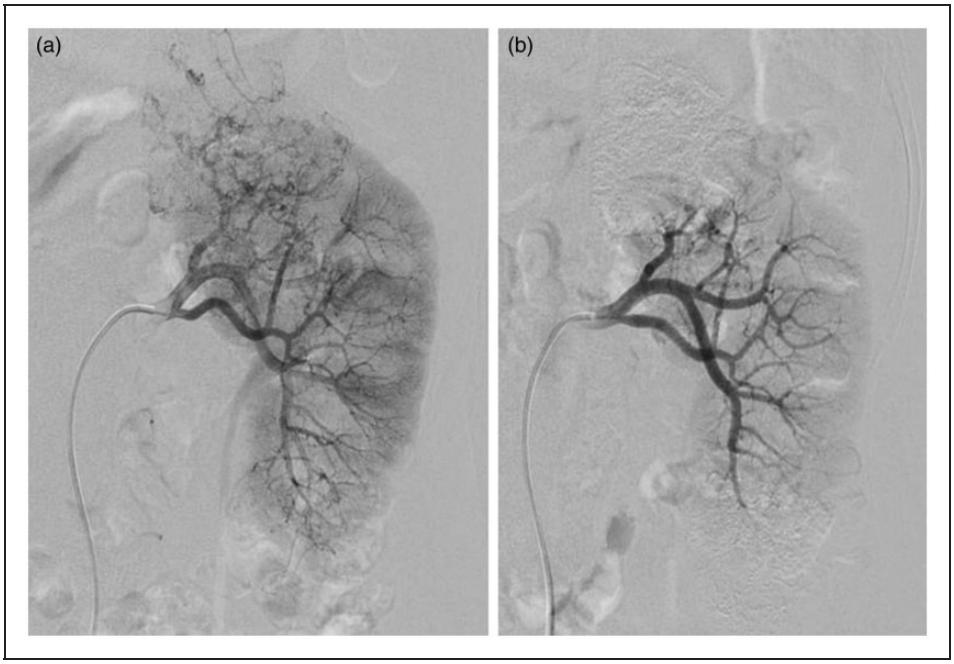

Figure 1. Arteriogram from a patient showing marked vascularity of the angiomyolipomas in the superior and inferior pole of the left kidney (a). Post-embolization angiogram from a patient demonstrating complete obliteration of the angiomyolipomas and stasis of flow to the lesions (b).

an appropriate amount of embolic material had been injected under continuous fluoroscopic guidance to prevent reflux and non-target embolization. Bleomycin-lipiodol emulsion and 300–500 μm nonspherical polyvinyl alcohol (PVA) particles were used as embolic agents to interrupt the blood flow of the AMLs. Coils were also applied to seal feeding vessels when aneurysms were found on the angiograms. Coils are increasingly used to treat aneurysms and provide satisfactory proximal occlusion as a complement to distal occlusion to maximize the embolic effect and so facilitate the rapid cessation of blood flow in a targeted inflow artery.[12] If the lesion was large or had multiple feeding vessels, embolization was staged to keep complication rates low.[6]

Tumour size was measured as the maximal diameter on axial CT images and the shrinkage rate was calculated by comparing the change in the cross-sectional diameter of the lesion with previous imaging. Technical success was defined as tumour vascular occlusion characterized by cessation of flow in the target vessels and lack of tumour staining. Clinical success was defined as no worsening of symptoms, no evidence of severe complications attributed to SAE and/or a re-bleeding episode after SAE. Post-embolization syndrome was defined as fever, abdominal pain, nausea or vomiting after SAE that the patient experienced during hospitalization. Tumour relapse after SAE was defined as recurrent symptoms (i.e. flank pain, tumour bleeding, or tumour rupture) requiring further treatment or tumour growth larger than 2.0 cm measured according to follow-up images. However, if a repeat embolization was used

to control persisting symptoms or tumour growth this was considered a failure of initial treatment. Tumours selected for staged treatment at initial presentation were not deemed failures due to repeat embolization as part of this treatment plan.

Statistical analyses

Nominal variables were summarized as counts and percentages whereas continuous variables were reported as mean ± SD. To compare groups, χ^2-test and Student's *t*-test were used for nominal data and continuous variables, respectively. Data analyses were performed using IBM SPSS software (version 19.0 for Windows®; IBM Corp, Armonk, NY, USA). A P-value < 0.05 (2-sided) was considered to indicate statistical significance.

Results

In total, 79 patients (60 [76%] women and 19 [24%] men) received SAE for AMLs in the 7-year study period (Table 1). Of these patients, 22 (28%) had a background of TSC and 57 (72%) had sporadic AMLs. Overall, the mean ± SD age for the patient population at diagnosis was 40.3 ± 14.8 years (range, 12–75 years). The subgroup of patients with TSC were significantly younger than those with sporadic AMLs (Table 1; $P < 0.001$). Common presenting symptoms were flank pain (45 [57%] patients) and haematuria (10 [13%] patients). AMLs were discovered incidentally in 31 (39%) patients who were examined for other reasons.

With regard to the location of the AMLs, 19 (24%) patients had involvement of in the left kidney only, 14 (18%) patients the right kidney only and 46 (58%) patients had bilateral involvement (Table 1). The lesions were multifocal in 56 (71%) patients. Among the 22 patients with TSC, all had multifocal lesions and 21 (95%) had bilateral AMLs. There was also a trend towards bilateral and multiple masses in the TSC subgroup (Table 1; $P < 0.001$). Pre-embolization, the largest lesion detected was 18.0 cm and only one lesion was less than 4 cm. Single or multiple aneurysms were found in 10 (13%) patients and retroperitoneal haematomas in 22 (28%) patients.

In total, 48 (61%) patients underwent SAE to treat bleeding/symptomatic AMLs and in 31 (39%) patients SAE was used as a prophylactic treatment against high-risk AMLs (i.e. size >4 cm, abnormal vasculature on CT). All patients received the bleomycin/lipiodol emulsion with PVA and 10 (13%) patients also had coiling of aneurysms. Embolization was technically successful in all cases, with de-vascularization of the embolized feeding vessels at angiography.

Mean radiological and clinical follow-up periods were 16.8 and 35.9 months, respectively. During the 3-year clinical follow-up period, 34 (43%) patients had planned repeat embolization and five (6%) patients needed unplanned repeat embolization due to tumour relapse. There was no statistically significant difference between the TSC and sporadic subgroups in the proportion of patients requiring repeat embolization.

Computed tomography scans of patients showed that in 75 (95%) patients tumours decreased in size, in four (5%) patients they were stable and no patients had tumours that increased in size. At the end of the radiographic follow-up period (16.8 months), mean ± SD tumour size for all patients was statistically significantly smaller post-embolization compared with pre-embolization (mean ± SD: 6.7 ± 3.0 cm versus 8.4 ± 3.5 cm, respectively; $P < 0.001$).

All measured tumours were reduced by a mean ± SD of 1.7 ± 1.3 cm (20.7% ± 16.0%) following SAE and there was a similar decrease in size for the TSC group (17.9% ± 10.8%) and the sporadic group (21.7% ± 17.6%) (Table 1).

Table 1. Demographic details, angiomyolipoma (AML) characteristics and clinical outcomes following selective arterial embolization in all patients, those with tuberous sclerosis complex (TSC) and those in whom the tumours were sporadic.

Variable	All patients $n = 79$	TSC $n = 22$	Sporadic $n = 57$	Statistical significance[a]
Age, years	40.3 ± 14.8	29.6 ± 13.6	44.4 ± 13.1	$P < 0.001$
Sex				
Female	60	19	41	NS
Male	19	3	16	
Location of AMLs				$P < 0.001$
Left	19	0	19	
Right	14	1	13	
Bilateral	46	21	25	
Masses				$P < 0.001$
Single	23	0	23	
Multiple	56	22	34	
Symptoms				NS
Yes	48	11	37	
No	31	11	20	
Haemorrhage				NS
Yes	22	5	17	
No	57	17	40	
Tumour size, cm				
Pre-embolization	8.4 ± 3.5	9.1 ± 3.5	8.2 ± 3.5	NS
Post-embolization	6.7 ± 3.0	7.4 ± 3.0	6.4 ± 3.0	NS
Decrease in size, cm	1.7 ± 1.3	1.7 ± 1.2	1.8 ± 1.4	NS
Decrease in size, %	20.7 ± 16.0	17.9 ± 10.8	21.7 ± 17.6	NS
PES				NS
Yes	68	21	47	
No	11	1	10	
Repeat embolization				NS
Planned	34	10	24	
Unplanned	5	0	5	

Data presented as mean $\pm$ SD or *n* of patients.

[a]Comparison between TSC and sporadic groups; χ^2-test and Student's *t*-test were used for nominal data and continuous variables, respectively.

TSC, tuberous sclerosis complex; PES, post-embolization syndrome (i.e. fever, pain or nausea after embolization); NS, no significant between-group difference ($P \geq 0.05$).

In terms of complications, 68 (86%) patients experienced post-embolization syndrome (i.e. fever, pain or nausea after SAE). Most of these patients had mild symptoms that lasted < 5 days and resolved with conservative treatment. Only two (3%) patients experienced major complications. One 12-year old girl with TSC and bilateral AMLs developed a urinary tract infection and subsequent acute renal insufficiency and was treated with a course of antibiotics and dialysis. The other patient had pleural effusion after SAE but the condition resolved after thoracic drainage. Therefore, of the 79 cases, 72 patients (91%) achieved a clinical success: two patients experienced

major complications and five patients experienced worsening of symptoms (i.e. flank pain, haematuria).

Discussion

Haemorrhage from AMLs can be life-threatening, and so treating symptomatic patients or patients with lesions of >4 cm has become widespread practice.[7] Due to the current availability of microcatheters and superior image quality of diagnostic equipment, SAE has gained favour as a treatment option for AMLs in both the elective and emergency settings over the past decade. Bleomycin-lipiodol emulsion and PVA were successfully used as the main embolic agents in this present study. Bleomycin, a complex of 11 glycopeptide antitumour antibiotics,[13] acts by intercalation of DNA and RNA.[14] Lipiodol has the advantage over other embolic agents of causing permanent occlusion at a capillary level and hence inducing tissue necrosis.[15] Lipiodol also aids in the visualization of the embolic mixture, which helps prevent reflux and non-target embolization. PVA is available with different particle sizes and is considered a permanent embolic agent.[16] At a particle size of 300–500 μm, PVA facilitates occlusion of the distal vascular bed of the tumour.[17] Only a small proportion of patients (13%) in this study required additional coiling of aneurysms.

In this present study of 79 patients at a single centre in China, SAE for renal AMLs achieved a technical success of 100%, clinical success of 91% and tumour shrinkage was significant. The present findings of a mean ± SD reduction in axial dimension of the tumours of 20.7% ± 16.0% agree with a previous report[18] and demonstrate the efficacy of SAE on renal AMLs. In addition, the present results were similar to the conclusions of a systematic review of 31 studies that involved 524 AML cases treated with transarterial embolization, which found a mean technical success rate of 93.3% and no procedural mortality.[19] However, the authors reported that among 263 AML patients with a mean follow-up of 39 months, angiomyolipoma was reduced by a mean of 3.4 cm (38.3%), a value higher than the present result (mean ± SD decrease: 1.7 ± 1.3 cm). A possible explanation for the discrepancy may be the difference in the radiological follow-up period; the mean follow-up period for the present study was only 16.8 months.

This present study found no differences in pre-embolization mass size, decrease in mass size with embolization, complications, requirement for repeat embolization or haemorrhage between patients with and without TSC. Treatment options for AMLs are often complicated by the presence of bilateral and multiple lesions, which particularly affect the TSC subgroup.[20] In the present study, 71% of patients had multiple lesions, rendering traditional surgical techniques for preserving renal function, such as partial or total nephrectomy, a less favourable option.[6] TSC is an autosomal dominant disease affecting approximately 2 million people globally.[21] Mutations in the *TSC1* and *TSC2* genes, important regulators of the mammalian target of rapamycin (mTOR) signalling pathway, result in the development of tumours involving multiple organ systems.[22] As many as 80% of patients with TSC develop renal AMLs and the tumours are frequently bilateral and multiple.[23]

As observed in this present study, several patients may have multiple, large or re-growing AMLs that require re-embolization. However, repeated embolizations may cause loss of normal renal parenchyma and renal function. Therefore, an effective pharmacological treatment is required to address this problem. A recent study suggests that the mTOR inhibitor, everolimus, may become an effective treatment option for AMLs in TSC patients.[24]

Moreover, everolimus is currently licenced in Europe and USA for the treatment of AMLs in adult patients with TSC. As more data from large clinical trials becomes available, mTOR inhibitors may be approved for the treatment of TSC-AMLs worldwide.

A main limitation of the present study was its retrospective design. In addition, the sample size was small; several patients had to be excluded from the study because they lacked complete radiological follow-up data. Prospective studies are required to confirm these findings and better evaluate the characteristics of AMLs and clinical outcomes.

In conclusion, this present study provides long-term evidence that SAE using bleomycin-lipiodol emulsion and PVA is a safe and effective method in controlling haemorrhage, improving clinical symptoms and preventing tumour progression in patients with renal AMLs.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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