# *Selective arterial embolization of angiomyolipoma leading to pulmonary hypertension*

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***Objectives:*** *To report two cases of secondary pulmonary hypertension resulting from microsphere extravasation following selective arterial embolization of renal angiomyolipoma, its diagnosis, and management.*
***Methods:*** *We reviewed the cases of two patients at the University of California, San Francisco, treated with selective arterial embolization for management of their angiomyolipoma (AML) using Tris-Acryl Gelatin Microspheres.*
***Results:*** *Both patients were women, ages 51 and 77. Indications for treatment were the following: Patient 1 was treated for a large asymptomatic AML. Patient 2 was treated for a symptomatic, bleeding AML. Both patients developed progressive hypoxia following selective arterial embolization using Tris-Acryl Gelatin Microspheres. Each patient underwent a subsequent work up including a CT chest, echocardiogram, and chest x-ray. Both demonstrated significant pulmonary hypertension following their procedure and were discharged with supplemental oxygen.*
***Conclusions:*** *Selective arterial embolization of AML with microsphere extravasation into the pulmonary vasculature can lead to pulmonary hypertension and hypoxemia.*

**Key Words:** foreign body pulmonary hypertension, microsphere embolization, angiomyolipoma

## Introduction

Angiomyolipoma (AML) is a benign renal mass, without the propensity to metastasize or invade adjacent tissue. However, its capacity to cause significant hemorrhage and other clinical symptoms warrants treatment in select cases. Options for treatment include surgical removal and selective arterial embolization (SAE).[1] The benefits of embolization include preservation of renal function, selective embolization of bleeding vessels, relatively low complication rate, and negating the need for a surgical incision.[1]

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While the majority (87%) of complications from SAE are minor and managed with supportive care alone, other more serious and potentially fatal complications can arise.[1] For example, there have been reports of embolization material (microspheres) occluding the pulmonary vasculature leading to pulmonary hypertension and subsequent death in the setting of SAE for hepatocellular carcinoma.[2] Autopsy of these patients demonstrated SAE material in lung alveoli.[2]

The following case series details for the first time, two patients who developed symptomatic pulmonary hypertension following SAE of AML. The aim of this case series is threefold: 1) to describe the clinical signs and symptoms of pulmonary compromise due to migration of microspheres; 2) to describe the clinical management of this complication; and 3) to reconsider which patients undergo SAE for AML.

## Case series

Our first patient is a 51-year-old woman with a large (10 cm x 9 cm x 13 cm) incidental AML diagnosed by computed tomography (CT) scan for work up of severe, refractory gastroesophageal reflux disease, Figure 1. The patient was otherwise healthy and took no medications. In fact, she had recently completed an exercise treadmill test with no sign of ischemic changes or symptoms of cardiac distress.

AML embolization was carried out due to risk of hemorrhage using highly concentrated ethanol and microspheres with sizes ranging from 40-120 microns, 300-500 microns, and 700-900 microns. The patient tolerated the procedure well and was discharged from the hospital without any difficulties.

Follow up CT scan at 3 and 9 months demonstrated residual AML and a second embolization was performed again using high concentration ethanol and microspheres with sizes ranging from 40-120 microns to 700-900 microns. During the second procedure she was noted to have an arterio-venous fistula from the AML to the IVC, Figure 2.

While in the recovery room she was noted to have room air saturations around 80% and supplemental oxygen (2-4 liters nasal canula) was initiated to keep her oxygen saturation above 90%. Physical exam was significant for signs of right heart failure.

High resolution chest CT did not show pulmonary embolus, or other etiologies for hypoxemia. Echocardiogram showed moderate right ventricular enlargement and an increased pulmonary arterial pressure elevated to 40 mmHg. Cardiology and pulmonary services were consulted and she was ultimately discharged on post-embolization day 5 with home oxygen and the diagnosis of acquired right ventricular hypertrophy.

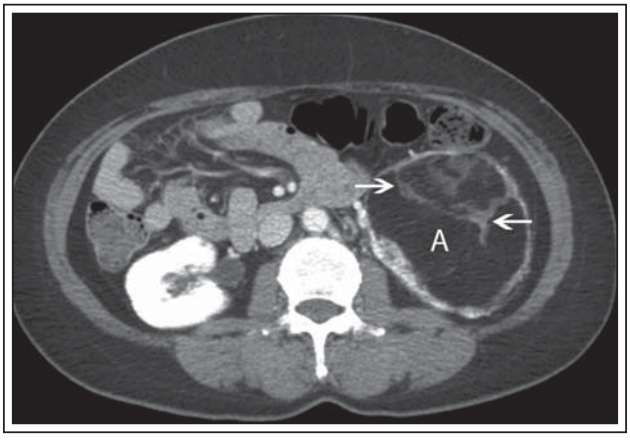


**Figure 1.** Non-contrast axial CT (computerized tomography) scan demonstrating 10 cm x 9 cm x13 cm AML (A) with visible lipid components (arrows).

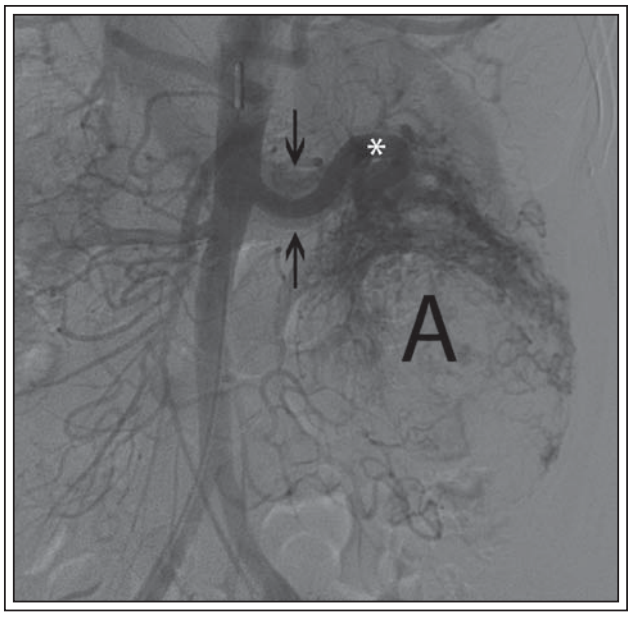


**Figure 2.** Selective posterioanterior (PA) arteriogram of the left kidney demonstrating large AML (A), renal artery (asterix), and renal vein (arrows).

Our second patient is a 77-year-old woman with tuberous sclerosis, bilateral renal AMLs, lymphangioleiomatosis, and hypertension. She presented with significant abdominal pain and was found to have a ruptured left renal AML.

She underwent SAE with microspheres that ranged in size from 40-120 microns to 700-900 microns. During the procedure the patient's oxygen requirements increased from 2 to 4 liters in order to maintain oxygen saturations above 95%.

Following her procedure, the patient had oxygen saturations around 70% on room air. On 2 liters nasal cannula, her oxygen saturation was 92%-97%. She denied any dyspnea with supplemental oxygen and appeared without distress. CT scan demonstrated no pulmonary embolism. CXR was negative for pulmonary edema, evidence of consolidation, or atelectasis. Echocardiogram demonstrated new, significant pulmonary hypertension with pulmonary systolic pressure of 52 as well as a mild increase in pulmonary vascular resistance.

## Discussion

Since SAE was first described, it has become the first line treatment in the management of AMLs both

in the acute and non-acute phase.[3] The benefits of SAE include the preservation of renal function while utilizing minimally invasive techniques. Furthermore, SAE has a low overall complication rate reported to be near 10%.[1] Most complications are minor and managed conservatively, the most common of which is post-embolization syndrome.[4] However, we wish to report the potentially lethal complication of pulmonary hypertension after SAE which, to our knowledge, has not been previously reported.

This complication may be particularly likely to occur in individuals with a prior history of pulmonary or cardiac disease, or in those undergoing repeat embolization as these patients may already have suffered an undiagnosed pulmonary insult. The later relative contraindication to SAE might be the most salient as repeat embolization procedures for complete treatment of AML ranges from 0% to 80%.[5,6] Overall repeat embolization rates are reported to be 14%.[1]

Our first patient required re-embolization of her AML. The medical consultants believed that a diagnosis of acquired pulmonary hypertension due to pulmonary embolization of microspheres was the most likely etiology of this patient's symptoms. In addition, the cardiology consults thought that the right ventricular hypertrophy demonstrated on echocardiogram was likely the result of pulmonary embolization of microspheres during her initial SAE. In fact, it was felt that the resultant right ventricular hypertrophy might have been protective during the second SAE as the patient had compensatory reserve cardiac function during her second pulmonary insult.

In contrast, we hypothesize that our second patient suffered rapid pulmonary deterioration following a single embolization due to her preexisting medical condition: lymphangioleiomyomatosis and hypertension. These preexisting conditions suggest worse initial cardiopulmonary reserve, leading to pulmonary decline following a single procedure.

Common to both of these cases was the use of tris-acryl gelatin coated microspheres that were as small as 40-120 microns. This small size theoretically allows for better terminal vessel occlusion. Unlike polyvinyl alcohol particles which vary in size and rarely are under 50 microns, microspheres are uniform and are available in a variety of sizes (40-120 microns; 100-300 microns; and 700-900 microns).[7] The use of smaller microspheres may predispose patients to particle embolization.

Microsphere embolization has never been reported in the AML literature, yet it has been reported that three fatal pulmonary complications occurred after SAE of hepatocellular carcinoma using tris-acryl gelatin coated microspheres.[2] It was also theorized that the use of these microspheres, especially the smallest 40-120 micron microspheres, may predispose patients to embolic events.[2] The extremely small size of these beads creates a variety of problems: 1) the beads are difficult to visualize under fluoroscopic vision due to their small size and 2) the small size may allow passage through unseen arterio-venous shunts leading to embolic events.

Our first patient had a visible shunt from the AML to the IVC seen during her SAE procedure. This shunt may have allowed for embolization of the microspheres to the lungs. Although during the case this shunt was thought to be successfully embolized with ethanol, it is possible that a small shunt may have persisted, allowing access of microspheres to the venous vasculature.

Diagnosis of pulmonary embolization of SAE material must be made in clinical context after other causes of decreased oxygenation have been excluded. Onset of symptoms in the form of decreased oxygenation will be sudden and temporally related to a recent SAE procedure. CT and other radiographic images are typically unable to demonstrate embolization of SAE microspheres due to small particle size. An echocardiogram will frequently show acute pulmonary hypertension and, as in the case of our first patient, may demonstrate right ventricular hypertrophy.

Clinical management of patients with pulmonary embolization of SAE particles requires supportive care and supplemental oxygen as there is no nonsurgical way to remove microspheres from the alveoli. Both of our patients were sent home with oxygen and were carefully weaned off supplemental oxygen over several weeks. It is unclear whether they will suffer long term adverse effects, as there is no long term data regarding chronic pulmonary hypertension secondary to pulmonary embolization of foreign material. The data on chronic thromboembolic pulmonary hypertension, however, shows a 5 year survival of only 10% with little treatment options other than surgical removal of foreign material.[8]

While our current manuscript focuses on microsphere embolization in the setting of SAE of AML, it is our belief that a risk of foreign body embolism exists in any setting where SAE is attempted on a tumor with increased vascularity: i.e. AML and renal cell carcinoma (RCC). Several recent studies with sizable samples sizes have analyzed preoperative embolization in the management of RCC, with no report of foreign body embolus. None of these studies however, utilized the newer microspheres outlined in this case series. May et al (n = 227) utilized a combination of gelfoam and

wire coils while Subramanlan et al (n = 135) utilized ethanol embolization.[9,10] We believe that as the new smaller microspheres become more widely used, the incidence of clinical and subclinical foreign body embolus may increase.

## Conclusion

While most adverse sequelae of AML embolization are minor, we have presented two cases of respiratory compromise and acute pulmonary hypertension that we hypothesize was due to microsphere migration to the lungs. We posit that smaller microspheres may be more likely to migrate to the lungs than larger sized embolization particles. Patients with pre-existing pulmonary or cardiac disease as well as those patients undergoing re-embolization for AML may require more caution when performing SAE. Additional thought should also be given when choosing to use microspheres, especially those measuring 40-120 microns in size. □

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