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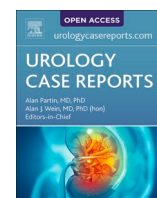
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# Nephrolithiasis associated with embolization material, Lipiodol®, following embolization of large renal angiomyolipoma

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## ABSTRACT

Angiomyolipoma (AML) is a benign renal mass that can be treated with nephron sparing surgery or transarterial embolization. Embolization has been favored due to efficacy and safety profile. This case demonstrates a previously undocumented phenomenon of AML treated with transarterial embolization using Lipiodol® (Guerbet LLC, Princeton, NJ) resulting in nephrolithiasis and retention of Lipiodol® two years after original embolization. Although Lipiodol®-based embolization has not been shown to cause nephrolithiasis, it may have been the nidus for stone formation, and this is an important potential complication worthy of further study.

## 1. Introduction

Renal angiomyolipomas (AMLs) are the most common benign solid tumors of the kidney, and are comprised of dysmorphic blood vessels, adipose tissue and smooth muscle.<sup>1</sup> AMLs carry a high risk of aneurysm formation and spontaneous hemorrhage especially with increasing AML size. Four centimeters is a common size cut-off, above which intervention if often recommended given the elevated risk of spontaneous severe retroperitoneal bleeding.<sup>1</sup> Most AMLs are diagnosed incidentally on CT imaging where they can be identified with the classic finding of a renal mass with macroscopic fat. Treatment of symptomatic or large AMLs originally included nephron sparing surgery (NSS); however, renal artery embolization has become a more popular option due to its safety profile, preservation of renal parenchyma, and shorter convalescence period.

Renal AML angioembolization is associated with certain complications, some expected and others rare, but severe. Most commonly, patients can experience post-embolization syndrome comprised of abdominal pain, cramping, fever, nausea, and vomiting due to release of inflammatory modulators in response to the infarcted tissue, occurring within 72 hours after embolization.<sup>1</sup> Although exceedingly rare, embolic events following transcatheter arterial chemoembolization (such as done for liver tumors) have been reported, including cerebral Lipiodol® embolism, which proved fatal.<sup>2</sup>

We report a case of a patient with no prior nephrolithiasis history

who underwent successful transarterial embolization of a renal AML with an admixture of Lipiodol® and 98% dehydrated ethanol. Two years later the patient was found to have developed new renal stones and found to have evidence of original embolization agent, Lipiodol® present in renal collecting system.

## 2. Case presentation

A 58-year-old female with past medical history of hypothyroidism and hyperlipidemia presented to the urology clinic in April 2018 after intermittent episodes of gross hematuria and right flank pain over the span of 6 months. Social history included 20 pack-year smoking history with last use 25 years ago. Renal ultrasound was performed which showed a large echogenic mass in the right kidney, concerning for neoplasm. Subsequent contrast-enhanced CT confirmed a 7.6cm × 7.2cm × 10.4cm macroscopic-fat containing mass consistent with an AML (Fig. 1). Renal function was normal and there was no proteinuria. Due to the symptomatic presentation and size of the AML, treatment was recommended. The patient was referred to Interventional Radiology and transarterial embolization was successfully performed using 4mL of 3:1 alcohol to Lipiodol® mixture in May 2018.

The patient had two years of unremarkable follow-up until summer 2020 when she developed gross hematuria. Upon presentation a CT was obtained and showed progressive involution of the right AML with new stone development including an obstructing 1.1cm stone at the right

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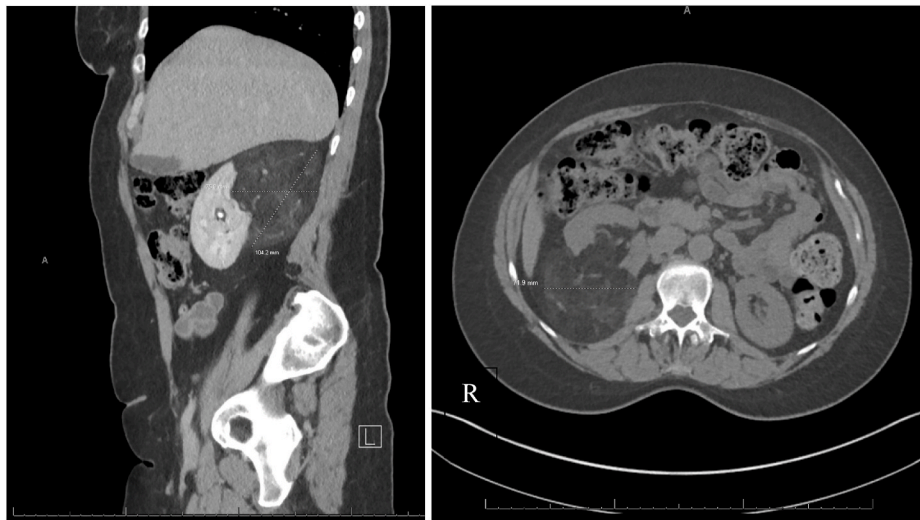


Fig. 1. Right AML measuring 7.4cm × 7.2cm x 10.4cm found on initial CT scan.



Fig. 2. CT scan obtained 2 years after successful transarterial embolization showing new 1.5 cm calculi in the superior pole of the right kidney as well as 1.1 cm calcification in the right proximal ureter with mild hydronephrosis.

ureteropelvic junction, and a 1.5cm curvilinear right upper pole stone (Fig. 2). The patient then underwent ureteroscopy, laser lithotripsy and stone basketing. Intraoperative findings included two “shell” shaped stones with floating pale yellow lipid-like material around them that appeared to have surrounding small calcifications (Fig. 3). In addition, the same lipid-like material was seen actively extruding into the collecting system. The stones were sent for chemical analysis, revealing 60% calcium oxalate monohydrate, 33% calcium oxalate dihydrate, 7% calcium magnesium phosphate. The lipid-like material was sent for fluid analysis but results were inconclusive. The patient has been symptom-, stone-, and hematuria-free since the ureteroscopy and is currently scheduled for a follow-up renal ultrasound.

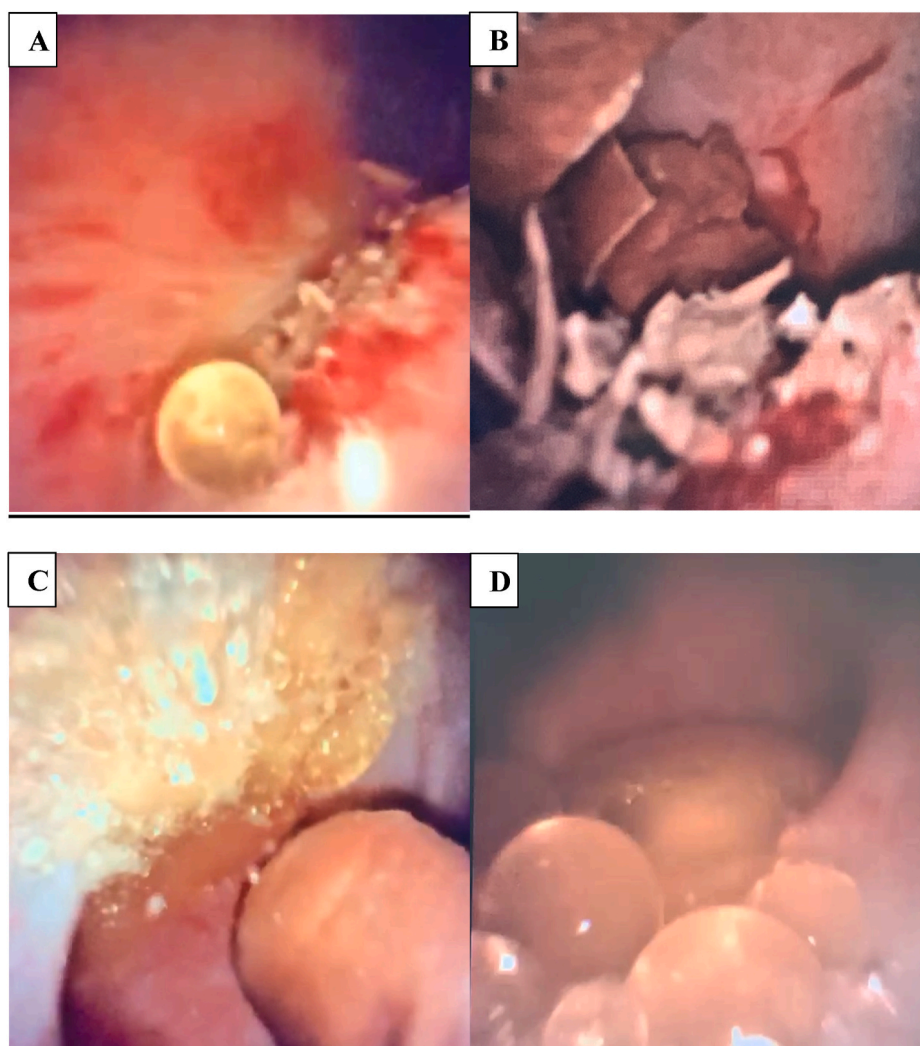
### 3. Discussion

First-line treatment for asymptomatic small AMLs is usually active surveillance. However, if they become symptomatic or large (>4cm), proactive treatment is recommended to reduce the risk of severe, spontaneous hemorrhage. Treatment in this setting often involves minimally invasive NSS or selective arterial embolization. NSS has been shown to preserve renal functioning over nephrectomy, while selective arterial embolization has been associated with renal functional preservation and minimal blood loss.<sup>1</sup> The ultimate treatment decision is one of shared-decision making and depends on many factors including renal

and AML anatomy and multiplicity, and renal function. In the presented patient, the size, location of the AML, and patient preference led to the decision to pursue renal angioembolization.

Lipiodol® is composed of iodine and ethyl esters of fatty acids from poppyseed oil. It was developed in the early 1900s to assist in diagnostic imaging for liver, lung, and lymphatic disease.<sup>3</sup> Lipiodol® has been used as a contrast agent during hysterosalpingography in adults, lymphography in adults and pediatrics, and selective hepatic intra-arterial use for imaging tumors with known hepatocellular carcinoma.<sup>3</sup> Lipiodol® was first used for transarterial catheter embolization in the 1980s. Since then, there have been case reports of pulmonary and cerebral embolism resulting from inadvertent non-target injection or intravasation of Lipiodol®.<sup>3</sup>

Although there have not been case reports of Lipiodol® transferring to and remaining within the renal collecting system, Lipiodol® residue has mimicked a calcified biliary stone following transarterial embolization for hepatocellular carcinoma and caused occlusion of the common bile duct.<sup>4</sup> There have also been inflammatory complications when Lipiodol® was used for galactography where it mimicked intraductal microcalcifications seen on mammography even up to 6 years after the procedure.<sup>5</sup> Lipiodol® residues also persisted in duct ectasia 1 year after galactography.<sup>5</sup> Lipiodol® is known to remain in tissue for long periods of time, but to our knowledge, there have not been prior reports of Lipiodol® eroding or migrating into the renal collecting system. Since



**Fig. 3.** Intraoperative findings of Lipiodol appearing substance demonstrating active secretion from renal paraenchyma (A), shell like calcifications seen (B), and renal stone that was found with surrounding substance (C & D). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Lipiodol® is a weak sclerosant with the ability to corrode plastic syringes, this property could lead to its entering into the collecting system.<sup>3</sup> It is likely that the Lipiodol® in the collecting system resulted in a supersaturated solution which contributes to the conditions needed for renal stone formation. The favorable supersaturated solution and microcalcifications that were seen clustered on the embolization material led us to infer that Lipiodol® acted as a nidus for the stone formation.

#### 4. Conclusion

We report a unique case of symptomatic nephrolithiasis development with erosion of embolization material two years after renal AML embolization with Lipiodol®. It appears that the Lipiodol® erosion into the renal collecting system may have acted as a nidus for stone formation. This is an important consideration for the patient, urologist, and interventional radiologist when proceeding with selective embolization for renal angiomyolipomas.

#### Consent

Informed consent obtained from patient and documented in electronic medical record.

#### Declarations of interest statement

None.

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