Selective Arterial Embolization of Giant Renal Angiomyolipoma Associated with Tuberous Sclerosis Complex Using Particular and Liquid Embolic Agents

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ABSTRACT

Renal angiomyolipoma (AML) is a benign hamartomatous tumor that is sometimes associated with the tuberous sclerosis complex. We report a 23-year-old man who presented with acute abdominal pain and hematuria. Computed tomography (CT) revealed large heterogeneous right renal mass of 17×13×13-cm diameter, consistent with AML, and acute and subacute hemorrhages. Digital subtraction angiography revealed massive tumor vascularization and multiple aneurysms associated with right renal artery branches. First, polyvinyl alcohol particles were used for the selective embolization of AML. Then, N-butyl cyanoacrylate (glue) mixed with lipiodol in a 1:3 ratio was injected for the permanent embolization of AML. CT scan revealed 59% reduction in size at 5 months after embolization. This case illustrates the selective embolization of giant renal AML with the combination of particular and liquid embolic agents with a significant reduction in size during the follow-up period.

Keywords: Angiomyolipoma, renal, treatment, selective arterial embolization

Introduction

Renal angiomyolipoma (AML) is a benign hamartomatous tumor comprising variable amounts of adipose tissue, smooth muscle, and abnormal blood vessels. Approximately 20% of AMLs are associated with the tuberous sclerosis (TS) complex [1, 2]. Because AMLs are usually asymptomatic, tumors of >4-cm diameter are usually symptomatic and present with retroperitoneal and/or urinary bleeding, which can be life threatening [1, 3, 4]. The standard treatment option in symptomatic patients with AML is nephron-sparing surgery [1, 2, 5]. However, in the past two decades, selective arterial embolization (SAE) has been used as the first-line treatment option in patients presenting with acute bleeding as well as prophylactically to prevent future bleeding complications [3, 6]. This case represents a successful embolization of giant renal AML with the combination of particular and liquid embolic agents.

Case Presentation

A 23-year-old male patient was admitted to the emergency department with acute abdominal pain and hematuria. On laboratory analysis, hemoglobin (Hb; 8.1 mg/dL) and hematocrit (HTC; 36%) values were decreased. Blood pressure was stable at approximately 100/70 mmHg with a mean heart rate of 76 bpm. Patient's history revealed the diagnosis of TS with right kidney AML, which was under follow-up. Non-enhanced computed tomography (CT) scan revealed bilateral subependymal calcific nodules around the foramen of Monro and lateral ventricles consistent with TS (Figure 1). Contrast-enhanced CT scan of the upper and lower abdomen showed well-defined right renal mass of 17×13×13-cm diameter containing adipose [−40 Hounsfield units (HU)] and heterogeneous soft-tissue structures consisted with AML. Hyperdense and isodense collections within the mass and in pelvis were also observed consistent with acute and subacute hemorrhages that occurred at different times (Figure 2). Selective digital subtraction angiography (DSA) of the middle and lower branches of the right renal artery revealed multiple pseudoaneurysms and tumor vascularization (Figure 3). According to angiographic findings, we intended to embolize the AML. After placing a 5-F cobra catheter within the lower branch of the right renal artery, the first part of embolization was performed using 355- to 500-µm non-calibrated polyvinyl alcohol (PVA) particles (Contour; Boston Scientific, Marlborough, Massachusetts). Following particular embolization, *N*-butyl cyanoacrylate (NBCA) glue

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(Histoacryl, B. Braun) mixed with ethiodized oil (Lipiodol® Ultra-Fluid, Guerbet, France) in a 1:3 ratio was injected for permanent embolization. After embolization, the hypervascularization of AML and pseudoaneurysms completely disappeared with the preservation of the viable upper pole of renal parenchyma. The patient was stable and discharged without any complication. Abdomen CT scan showed modest reduction in the size of the mass [59% reduction; 10×10×12 cm) at 5 months after embolization.

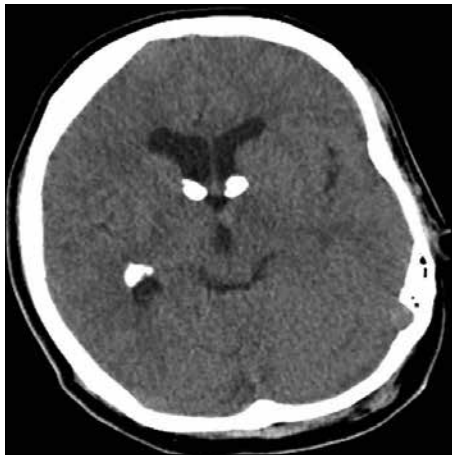

Figure 1. Axial non-contrast CT scan revealed bilateral subependymal calcific nodules around the foramen of Monro and lateral ventricles

Discussion

Renal AML is an uncommon benign tumor, and approximately 20% cases are associated with the TS complex [1-4]. Because it is benign in nature, asymptomatic cases can be managed by active surveillance [1, 2]. Approximately 60% of patients with large AMLs present with a combination of acute bleeding, flank pain, hematuria, and palpable mass. Tumors over 4 cm often experience hemorrhage and internal tumaro growth. The main indications for treatment are abdominal pain, internal tumor growth, retroperitoneal hemorrhage, and gross hematuria [2, 3, 7].

AML can be easily diagnosed by ultrasound (US), CT, and MRI findings. On US, AMLs almost always appear as a hyperechoic mass due to the fat component of the tumor, an area of negative attenuation value (<−20 HU), and high signal intensity on T1-weighted on CT MR images. However, not all AMLs demonstrate these classic imaging findings; RCC also appears hyperechoic on US in approximately one third of the cases [1-3, 8]. Histopathological examinations should be performed in case of suspicious lesions [2]. In our patient, CT revealed a low-attenuation renal mass compatible with fat (−40 HU), which was consistent with AML.

The treatment options for renal AML include SAE, nephron-sparing surgery, radiofrequency and cryoablation of the tumor, and nephrectomy [1-3]. Symptomatic patients with AMLs over 4 cm require surgical intervention. Selective nephron-sparing surgery is the gold standard if radiological diagnosis is certain. However, radical nephrectomy should be the procedure of choice if malignancy is suspected [1, 3, 7]. Surgery allows the complete resection of the tumor and pathologic confirmation. Surgery can

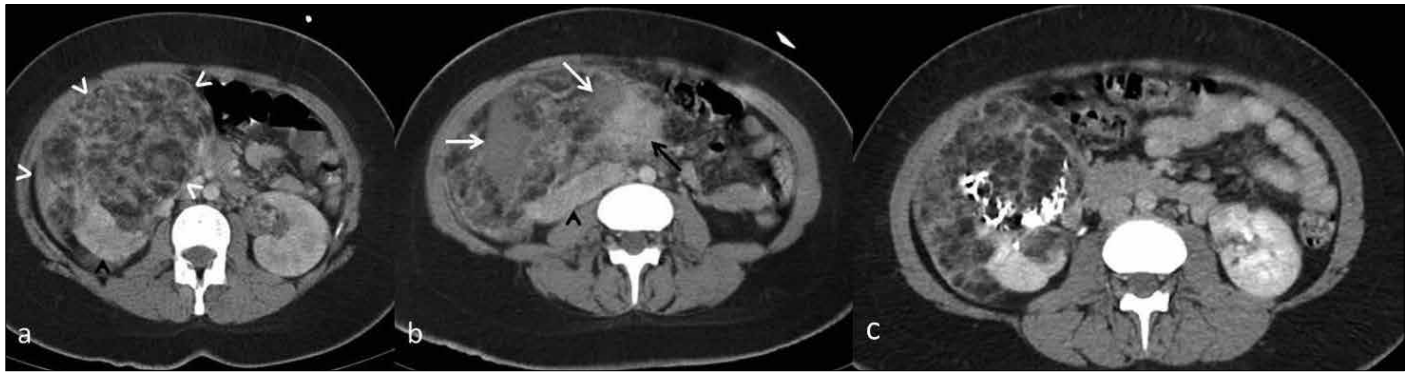

Figure 2 a-c. Axial contrast-enhanced CT images show huge angiomyolipoma (white arrowheads) with large fatty components (a), hyperdense acute (white arrows) and isodense former (black arrow) hemorrhagic areas and the right kidney parenchyma (black arrowheads) displaced inferior and medial by mass (b), and significant reduction (59%) in size of mass 5 months after embolization (c)

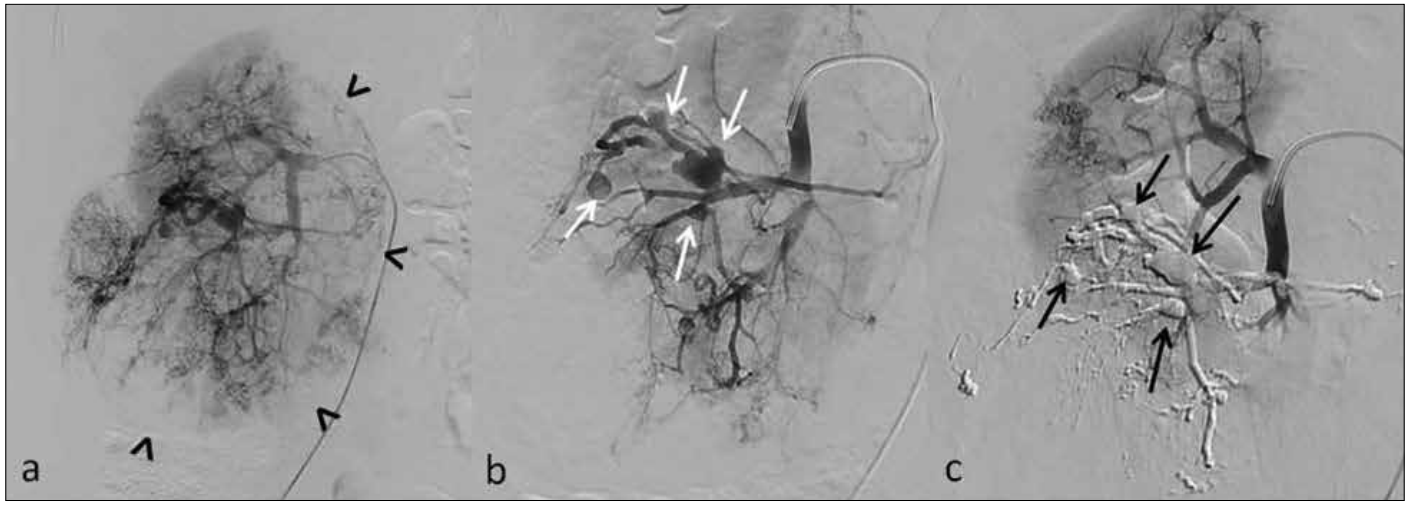

Figure 3 a-c. Pre-embolization (a, b) arterial phase DSA images show huge mass lesion (arrowheads) of the right kidney supplying multiple renal segmentary arteries and multiple aneurysms (white arrows) originating from the feeding arterial branches of the mass. Post-embolization image (c) revealed the complete disappearance of tumor vascularization and aneurysms (black arrows)

be quite difficult in cases with a complex vascular anatomy, hilar location, or multiplicity of lesions [8].

SAE has been used as the first-line management option for AML because >50% of tumors over 4 cm present with hemorrhage and one third of the patients with acute hemorrhage exhibit shock [3, 6].

Blood vessels within AMLs are abnormal and have no internal elastic lamina and form aneurysms and rupture [7]. Therefore, the selective embolization of AML is aimed at occluding these abnormal vessels and the optimal sparing of the normal renal parenchyma to maintain the maximal renal function [2, 3, 6]. Another aim of the embolization of AML is to decrease the tumor size. Because AMLs comprise varying amounts of adipose, smooth muscle, and vascular tissue, the effects of embolization are variable. Because the adipose tissue is hypovascular, it is resistant to embolization; therefore, some adipose tissues may not be adequately affected by embolization. In contrast to adipose tissues, the angiomyogenic components of AML respond to embolization to a greater extent; therefore, decrease in tumor size is more prominent in these components [6, 9]. In our patient, embolization was decided because of angiographic findings indicating abnormal tumor vascularization and aneurysms related to tumor vessels. An additional indication for embolization was the presence of acute and subacute hemorrhage within the tumor and pelvis.

Some researchers have advocated prophylactic embolization because embolization has proven to be a safe and effective procedure in experienced patients, and prophylactic embolization could be used in hypervascular AML to prevent acute hemorrhagic conditions [6].

Numerous agents can be used for the embolization of AML including particles, coils, vascular plugs, absolute ethanol, and glue. Several types of agents are available, including non-calibrated PVA particles (Contour; Boston Scientific, Marlborough, Massachusetts), acrylic polymer microspheres impregnated with gelatin (Embosphere Microspheres, Biosphere Medical, Rockland, MA) and calibrated PVA microspheres (Beadblock, Terumo, Leuven, Belgium), liquid embolic agents including NBCA (Histoacryl, B. Braun) mixed with ethiodized oil (Lipiodol® Ultra-Fluid, Guerbet, France), and Onyx® 18 (Covidien, Mansfield, MA, USA). Several microciols are also available, including Micrus (Micrus Corporation/Codman), Microvention, (Terumo), Axium (eV3), Target (Boston Scientific/Stryker), Penumbra coils 400 (Penumbra), and Barricade koiller (Balt) [3, 6, 10].

Thus far, no study has demonstrated the superiority of an embolic agent over another with regard to treating actively hemorrhaging AMLs, preventing hemorrhage, and treating symptoms [2]. Particular agents, such as PVA or embosphere, are the most commonly used in the embolization of AML. Particular embolization was commonly performed with a combination of 350- to 500-mm PVA particles to occlude the distal vascular bed followed by coils to block the arterial inflow and prevent the retrograde filling of the aneurysm and abnormal tumor vessels reference [7]. Coils should be avoided because they only provide proximal vessel occlusion, which may form collaterals around or at the distal level of occlusion, further making embolization difficult or impossible [3-6].

Another liquid embolic agent is the NBCA which is a product that polymerizes upon contact with an ionic medium and particularly when in contact with blood. The peripheral dissolution and speed of polymerization depend on the degree of dilution in an oily contrast agent lipiodol [11]. In experienced hands, glue provides a very fast and effective distal embolization with a high dilution of lipiodol (glue:lipiodol ratio, 1:3–1:6). Glue is a very effective embolic agent for the management of acute hemorrhages, aneurysms, arteriovenous malformations, and fistulas [5, 12]. In the present case, initially non-calibrated 355- to 500-mm PVA particles were used to occlude the distal vascular bed. Following PVA, we used NBCA mixed with lipiodol in 1:3 ratios. Because PVA has the risk of recanalization within 7 d, using PVA particles alone in SAE may cause re-bleeding. Therefore, we consider that the combined use of liquid embolic agent with PVA particles in embolization significantly reduces the risk of re-bleeding because the NBCA permanently occludes the tumor vascularity and aneurysms.

No studies have described the use of glue alone or in combination with other embolic agents. Because glue is a permanent embolic agent, its use in embolization needs a high level of experience. Accidental embolization or reflux of glue into non-targeted arteries may result in catastrophic complications [5].

Ethanol is a liquid embolic agent that provides permanent occlusion at the arteriolar and capillary level distal to the level of collateral inflow and causes tumor tissue necrosis. The major risk with the use of ethanol is non-target embolization resulting from the reflux out of tumor-feeding vessels, which can result in devastating consequences [6, 11].

Complications of SAE include pain, post-embolization syndrome, vascular injury, hematuria, renal infarction with abscess formation, renal failure, infections, accidental embolization, and intraprocedural rupture. Post-embolization syndrome occurs as a result of renal tissue necrosis and is characterized by nausea, vomiting, fever, abdominal pain, and leukocytosis. The syndrome has been reported to occur in up to 80% of cases and is conservatively treated [2, 11]. In our case, no complication was encountered during embolization and postoperatively.

Ramon et al. [3] in their study evaluated 41 patients (48 kidneys) with AML who were treated by SAE using a mixture of 96% ethanol and PVA particles with a minor complication rate of 11%. The mean tumor size was 10.3 cm. Retroperitoneal hemorrhage did not occur during the follow-up. The freedom from surgery at 5-year follow-up was 94% for SAE [3]. Bardin et al. [5] have recently reported 23 symptomatic patients with AML treated by SAE using various embolization agents including particles, coils, and liquid agents; six of these patients were treated because of acute retroperitoneal hemorrhage and the remaining 17 patients were treated prophylactically. Major complications occurred in three patients (renal abscess in two and femoral psodoaneurysms in one) and minor complications in 14 patients as a post-embolization syndrome. The mean AML size reduction was 26.2% after mean 20.5 months of follow-up. Lee et al. [12] also have recently showed that the mean AML size reduction was between 33% and 43% within and after 6 months follow-up, respectively. In the present case, mean 59% tumor size reduction was observed within 5 months follow-up.

In conclusion, renal AML is a benign hamartomatous tumor. AMLs >4 cm in diameter are usually symptomatic and present with retroperitoneal hemorrhage, which can be life threatening. Our case represents the successful embolization of giant renal AML with the combination of particular and liquid embolic agents with 59% tumor size reduction in 5 months follow-up.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Farabi Hospital School of Medicine.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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