Efficacy, Complications and Long-Term Outcomes of Selective Arterial Embolization of Symptomatic Giant Renal Angiomyolipoma

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Key Words
Angioembolization • Giant angiomyolipoma • Long-term outcome

Abstract
Purpose: To assess efficacy, complications and long-term outcome of selective arterial embolization (SAE) for treatment of symptomatic giant angiomyolipoma larger than 10 cm. Materials and Methods: The surgical records of 9 patients with giant angiomyolipoma managed by SAE between 1990 and 2010 were reviewed. Results: The study included 4 men and 5 women, 5 of them (55.5%) had tuberous sclerosis complex. Indication for SAE was to stop severe hematuria in all patients. Among 9 patients, early complications occurred in 55.5% including post embolization syndrome in 1 patient, recurrent hematuria necessitating repeat embolization and nephrectomy in 3 and acute renal failure in 1 patient. During a mean follow-up of 2 years, 1 patient on hemodialysis was subjected to elective nephrectomy and 5 patients (55.5%) preserved their kidneys in whom radiology showed a decrease of size of the lesions by about 1/3 of its original size and all had a stable serum creatinine level. Conclusions: SAE of giant renal angiomyolipomas can be safely done to stop active bleeding in 2/3 of cases. Additional treatment may be necessary in 1/3 of patients and preservation of kidneys is amenable in 1/2 of cases.

Introduction
Angiomyolipoma is a benign tumor composed of mature or immature fat, thick walled blood vessels and smooth muscle elements in varying proportions. There are 2 varieties of renal angiomyolipoma, one associated with tuberous sclerosis (TS or Boureville disease) and the other that appears as an isolated lesion. In the first case, renal angiomyolipomas are most often multiple, bilateral, symptomatic and without female or male predominance. In the second case, renal angiomyolipomas are single, often asymptomatic, have a female predominance and are typical of the fifth and sixth decades of life \cite{1}.

The most common presentation of angiomyolipomas is an incidental finding, however, once a size of 4 cm is reached, symptoms may develop in up to 68–80\% of patients, such as loin pain, hemorrhage, which may be life threatening, or as a palpable mass \cite{2}.

Osterling et al. \cite{3} determined that the size of angiomyolipoma and the presence of symptoms were excellent determinants for appropriate management. They recommended semiannual follow-up for small asymptomatic tumors ≤ 4 cm. Patients with large angiomyolipomas and severe symptoms should undergo immediate selective arterial embolization (SAE) or nephron sparing surgery (NSS). Recently radiofrequency and cryotherapy were introduced to the armamentarium of angiomyolipoma management \cite{4, 5}.
Semi-embolization is a valuable treatment of renal angiomyolipoma. It is a minimally invasive intervention that can control bleeding in the majority of patients. Moreover, successful super-selective embolization of the bleeding vessel preserves the function of the rest of the kidney parenchyma. Therefore, it was considered as the management of choice of symptomatic angiomyolipomas in several studies [6–9].

The management of giant angiomyolipomas is a urological challenge. Different approaches were used for management of such lesions including conservative [10], nephrectomy [11–14] and NSS [15, 16].

Reports of angioembolization in the management of giant angiomyolipoma are lacking. Few reports of embolotherapy included some patients with giant angiomyolipomas [8, 9, 17, 18] and only one study was reported including only cases of giant angiomyolipomas [19]. Our study was conducted for evaluation of the efficacy and complications of SAE of 9 patients with symptomatic giant angiomyolipomas larger than 10 cm. Also the long-term outcome of such a group of patients was evaluated.

Materials and Methods

Patients

Our institutional review board approval was given for this retrospective study. The computerized data of 13 patients who underwent SAE for giant angiomyolipoma > 10 cm from January 1990 to January 2010 at our center were retrospectively reviewed. Among the 13 patients, 4 were subjected to SAE preoperatively to avoid risk of severe hemorrhage during nephrectomy and those were not included in the analysis. All angiomyolipomas were diagnosed using computed tomography (CT) before treatment. The mean size of the angiomyolipoma was 14.3 cm (range 11–21 cm). The indication for SAE was to control severe hematuria in all 9 patients. Data collected included pre- and post-treatment lesion size, serum creatinine level, technical success, complications and long-term follow-up.

Technique of Embolization

We started with selective renal digital subtraction angiography to identify the feeding vessel of the targeted angiomyolipoma then super-selective catheterization of the feeding artery was done. Platinum micro-coils of 0.035 inch (Boston Scientific, Boston, MA, USA) were delivered through the 6F angiographic catheter (Copra II, Terumo, Osaka, Japan) for segmental arterial occlusion, while 0.018 inch helical platinum micro-coils were used through the 3F coaxial micro-catheter (Target Therapeutics, Fremont, CA, USA) for occlusion of sub-segmental peripheral arteries. Embolization with absolute alcohol and/or gelfoam was carried out after sub-selective catheterization of the branch to be occluded.

The alcohol was slowly injected by hand at a rate of approximately 0.1–0.2 ml/s, a test injection, at the same rate, was first performed to confirm the absence of reflux. The injected amounts were 2 ml of alcohol in an inter-lobar branch and a 3 ml in a segmental branch. Each injection was followed by infusion of 1 ml of saline at the same rate. Micro-coils were used alone for embolization in 2 cases and in combination with alcohol in 3 cases, alcohol was delivered alone in 1 case and gelfoam alone in 1 case and combined alcohol and gelfoam in 2 cases.

The technical success of the procedure was documented by angiography at the end of the embolization procedure. The choice of the embolic agents depended upon the availability in the department and the type of individual lesion.

Follow-Up

All post-embolization complications were recorded. The short-term effects of embolization were evaluated after 3 months with renal ultrasound or CT and estimation of serum creatinine level. Then regular follow-up with ultrasound or CT and estimation of serum creatinine level was performed every 3 months for one year, then every 6 months thereafter. Medical and radiological records were reviewed to obtain data of symptoms, tumor size and length of follow-up. If a repeat embolization or surgical intervention was used to control persisting symptoms or tumor growth this was considered a failure of the initial treatment.

Results

The patients included 4 men and 5 women, with a mean age of 32 years (range 26–55 years); 5 of the 9 (55.5%) had the TS complex. The tumor was bilateral in 6 patients (66.7%) of whom 5 had TS. When the tumor was unilateral it was more common on the right side (2/3, 66.7%) than on the left side (1/3, 33.3%). The lesions were single in 3 (33.3%) patients and multiple in the remaining 6 (66.7%).

All patients in the series presented with severe hematuria, and 1 patient with bilateral angiomyolipoma was on hemodialysis at first presentation. At initial presentation hypertension and anemia were present in 1 (11.1%) and 7 (78%) patients respectively.

In all patients the treatment was technically successful, with de-vascularization of the feeding vessels apparent on angiography (fig. 1). Early post-embolization complications were observed in 5 (55.5%) patients, including 1 patient (11.1%) with signs of post-embolic syndrome with the patients having fever, pain and nausea, and conservative management was successful in this patient. Recurrent severe hematuria occurred in 2 patients and nephrectomy was performed 2 and 3 months post embolization. In another patient hematuria recurred 10 days after SAE and repeat embolization was carried out and after 2 weeks from the second SAE the patient presented with hematuria, shock and large retroperitoneal hemorrhage and nephrectomy was carried out. So the embolization treatment resulted in cessation of he-
Fig. 1. A case of TS with bilateral giant angiomyolipomas with large right intralesional aneurysm and perianeurysmal hematoma. a Axial post contrast CT of the abdomen shows large fatty containing angiomyolipoma with a large markedly enhanced aneurysm (straight arrow) and perianeurysmal hematoma (curved arrow); b Coronal reformatted CT renal angiography with a large intra-renal aneurysm (arrow); c Sub-selective renal angiography with filling of the large aneurysm (arrow); d Post embolization angiography shows micro-coils (arrow) with no filling of the aneurysm; e Coronal post contrast reformatted CT scan at early post-embolization shows a completely occluded aneurysm with evidence of micro-coil (curved arrow) with reduction in the size of the sub-capsular hematoma (straight arrow).
maturia in 6 out of 9 patients (66.7%). One patient with bilateral angiomyolipoma, subjected to bilateral angiography and left angioembolization, developed acute renal failure and serum creatinine increased from a basal value of 1.2 up to 9.2 mg/dl. This was self-limiting and renal function returned to normal with conservative treatment in 1 month.

The mean follow-up period was 2 ± 1.9 years (range 0.5–7 years). During such a long follow-up no patients developed neo-onset hypertension. Among the 6 patients with preserved kidneys, one patient on hemodialysis was subjected to elective nephrectomy. Among the remaining 5 patients, radiological examination showed a decrease of the size of lesions in all but about 1/3 of its original size, 3 patients (60%) developed recurrent attacks of minor hematuria that were managed conservatively without the need for repeat embolization and all 5 patients had a stable serum creatinine level.

**Discussion**

Management of giant angiomyolipoma is demanding. Many such patients may have bilateral renal affection so the choice for treatment should balance between the need to prevent life-threatening bleeding and the issue to preserve as much functional renal parenchyma as possible. For this purpose a variety of methods have been proposed and the reported series of giant angiomyolipomas recommended conservative treatment [10], SAE [19] or surgical approaches [11–16].

Danforth et al. [10] presented 2 patients with TS complex and giant angiomyolipomas. The first patient initially presented with bilateral renal angiomyolipomas replacing 70% of his parenchymal volume. He was managed conservatively for 21 years and his renal function remained stable during this interval. The second patient initially presented with bilateral renal angiomyolipomas that were not amenable to NSS. After removing her non-functioning left kidney, the 24-cm angiomyolipoma in her right kidney was managed conservatively for 20 years. During which she had 44 transfusions and 11 hospitalizations before uncomplicated right nephrectomy and subsequent need for hemodialysis. They recommended this approach for those patients in whom intervention would likely compromise renal function and/or who were poor candidates for invasive or surgical intervention. An obvious drawback of such a line of treatment is that patient should have life time observation for their disease.

NSS has been used in management of angiomyolipoma. Boorjian et al. [20] reviewed 58 patients undergoing partial nephrectomy for renal angiomyolipoma, and found that renal function was preserved and no patient required retreatment during a median follow-up of 8 years. Also NSS has been reported in the management of giant angiomyolipomas [15, 16]. Although a clear advantage of a surgical procedure such as partial nephrectomy is the elimination of the need for recurrent angiography and SAE, partial nephrectomy in such huge masses may be very difficult and any surgical intervention is likely to greatly reduce renal function. Also, characteristics of TS complex associated angiomyolipomas such as large size and multiplicity have limited the role of NSS.

Since the introduction of therapeutic percutaneous trans-catheter renal artery embolization, it has been used successfully for managing a variety of benign and malig-
nent urological conditions including renal angiomyolipomas (table 1). Ramon et al. [8] described the experience of 41 patients with 48 kidneys containing angiomyolipoma treated by SAE with an average follow-up period of 4.8 years. Successful SAE was achieved in 40 patients (91%), and avoidance of surgery was achieved in 96% of the kidneys. During follow-up, 98% kidneys were preserved. In a recent study of 34 patients with angiomyolipoma treated by SAE, Chick et al. [9] reported that radiological success was achieved in 97%, with only one lesion growing by >2 cm. The combined clinical and radiological success rate was 85%, with 2 patients undergoing surgery, and 2 having repeat embolization.

To the best of our knowledge, only a single study was reported and included only patients with giant angiomyolipomas managed by SAE. This study included 16 patients who underwent SAE for 23 angiomyolipomas > 10 cm. Ten of the 16 patients (62%) had all their angiomyolipomas treated in one session, whereas 6 (38%) required multiple sessions. Patients were followed-up for a mean of 29 months. No patient had an increase in mean serum creatinine level during the follow-up period. Two of the 16 patients (12%) required repeat embolization due to angiomyolipoma re-growth (n = 1) or reperfusion (n = 1) seen on surveillance imaging. One of the 16 patients (6.2%) had an angiomyolipoma hemorrhage 59 months after embolization. They concluded that embolization of giant renal angiomyolipomas can be safely done without loss of renal function [19]. Our study included 9 patients with angiomyolipomas, among them 4 (44.4%) required nephrectomy and the remaining 5 (55.6%) patients required no further embolization but 3 of them (60%) developed repeat hematuria. All of them showed reduction of the size of the tumor and all had stable serum creatinine levels. Our results are poorer compared to the previous report [19], and it is possible that the acute presentation of our cases accounts for this higher failure rate.

Although SAE is a minimally invasive procedure in management of angiomyolipoma, it is not devoid of complications and the reported rate of any complication is approximately 10% [22]. The most commonly reported being post embolization syndrome, which is most likely due to an inflammatory response to necrotic tissue and consists of one or more of the following symptoms: fever, nausea, vomiting, and pain [2]. In our study 1 patient (11.1%) developed post embolization syndrome in the first day after embolization that resolved with oral NSAIDs and intravenous antibiotics (third generation cephalosporines). Other reported complications after SAE include abscess formation [23], pulmonary hypertension [24] and lipiduria [25]. In our study we had a significant complication in 1 patient with bilateral angiomyolipomas who developed acute renal failure immediately after bilateral angiography and left SAE. This was due to contrast nephropathy, however this was self-limiting and the patient returned to a normal serum creatinine level after 1 month of conservative treatment.

The present study had some limitations. First, it was a retrospective study and therefore sample bias might have been present. Second, we did not use a uniform embolization technique. Finally, we lost a lot of our patients to surgery and thus the long-term outcome of SAE was derived from only 5/9 patients.

Conclusion

SAE of the giant renal angiomyolipomas is effective in controlling hemorrhage in 2/3 of these patients. The short-term deleterious effects are frequent and up to 1/3 of patients with repetitive renal bleeding will eventually require a repeat SAE or nephrectomy. Long-term preservation of renal function and viable parenchyma is amenable in half of the patients. Patients with giant angiomyolipomas treated by SAE must be aware of the need for continued close disease surveillance.
References