

## Renal angiomyolipomatosis and bleeding aneurysms in a tuberous sclerosis context: selective artery embolization in a girl with end-stage renal failure

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### Abstract

Recent developments in endovascular radiological techniques and devices have rendered embolization a major therapeutic option prior to surgery in many renal vascular or neoplastic diseases. A 19-year-old female patient, with a diagnosis of tuberous sclerosis complex (TSC) in childhood, was admitted with severe anemia. Polycystic kidney disease in end-stage renal failure appeared four years before and the patient has been undergoing peritoneal dialysis. The patient's medical history also included bilateral renal angiomyolipomas (AMLs). One year earlier, a unilateral endovascular embolization was performed to repair a bleeding aneurysm at the right renal upper pole. A second bilateral ruptured renal aneurysm was diagnosed at admission. To continue with peritoneal dialysis and prevent intrarenal hemorrhage and intraperitoneal bleeding, an urgent bilateral renal AE was performed. Two months later she underwent a bilateral retroperitoneal nephrectomy. The posterior surgical approach, preserved the peritoneal surface area and adequate conditions to continue dialysis. At histology, bilateral AMLs were confirmed and a renal cell carcinoma of the right kidney was concurrently discovered.

She undergoes continuous peritoneal dialysis. Urgent selective renal AE represents a feasible treatment for bilateral AML bleeding. It is safe and feasible before performing nephrectomy in patients with end-stage renal failure.

### Introduction

Recent developments in endovascular radiological techniques and devices have rendered embolization a major therapeutic option prior to surgery in many renal vascular or neoplastic diseases.<sup>1,2</sup> Renal artery embolization (AE) to treat proximal or distal renal vessel occlusion has a low morbidity and, when used to treat selective distal occlusions has a low impact on renal function compared to surgical procedures. In adults, indications for embolization in nephrology include post-biopsy arteriovenous fistulas, renal graft intolerance, functional exclusion and polycystic kidney disease before transplantation.<sup>1,2</sup> Other conditions, such as arterial aneurysms, arteriovenous malformations and angiomyolipomas, mostly in tuberous sclerosis complex (TSC) have also been indicated.<sup>1</sup>

TSC is an autosomal dominant disorder with multisystem clinical manifestations. The brain, retina, kidneys, heart, and skin are most commonly affected.<sup>3-7</sup> Angiomyolipomas, renal cysts, and renal cell carcinoma are classical features of renal involvement in TSC.<sup>8-9</sup> Renal angiomyolipomas (AMLs) are found in 50–80% of TSC patients and are usually bilateral with a high female preponderance, suggesting a hormonal influence.<sup>8,10-12</sup> Renal AML can increase in size by more than 3 cm<sup>13-15</sup> which may lead to retro peritoneal hemorrhage and renal insufficiency. Renal cysts are found in around 20% of patients, but polycystic kidney disease, a relatively rare manifestation of TSC, is present in less than 2% cases.<sup>8,10-12</sup> We report a case of severe anemia, the result of spontaneous rupture of renal aneurysms, in a girl affected by TSC with bilateral AMLs and end-stage renal failure, who underwent bilateral artery embolization (AE) before a retro peritoneal nephrectomy in order to preserve conditions compatible with peritoneal dialysis.

### Case Report

A 19-year-old female patient was admitted to our surgical unit with severe anemia (Hb 4.1 g/dL). Impaired growth was noted (weight 39.5 kg; height 146 cm; BMI 17.6 kg/m<sup>2</sup>). She had a heart rate of 78 beats

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**Key words:** renal artery embolization, angiomyolipoma, bleeding aneurysms, tuberous sclerosis context, end-stage renal failure.

**Contributions:** GPe surgical management of the patient, drafting the article, critical revision of the article; MGV radiological management and endovascular treatment; MM, GR, SA surgical management of the patient; GPa, MMSD nephrological management of the patient; EU histological analysis, drafting the article; VC drafting the article, literature review, critical revision of the article.

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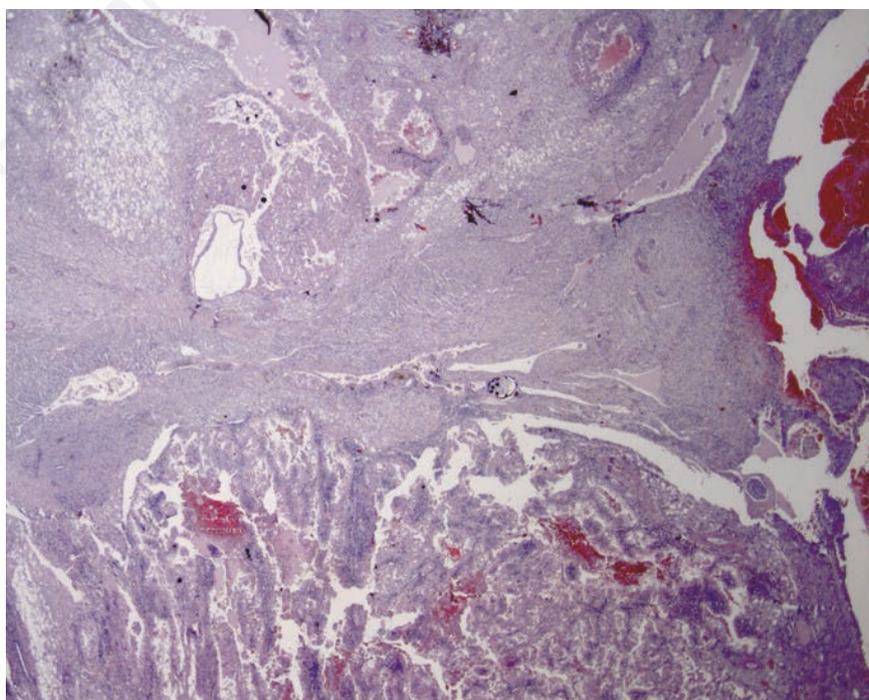
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per minute, blood pressure of 226/136 mmHg, respiration rate of 16 breaths per minute and arterial oxygen saturation of 96%. Blood analysis showed a serum creatinine level of 10.97 mg/dl (nv 0.5-1.1) and urea 109 mg/dL (nv 16-46) mmol/L. The patient also presented with bilateral AMLs, hypertension and seizure disorder. Her relatives reported difficulty in managing her home medications (antihypertensive and antiepileptic drugs) due to her intellectual disability. The patient had been diagnosed with TSC in childhood; there was a paternal family history of TSC. Polycystic kidney disease (PKD) in end-stage renal failure appeared four years prior and the patient has been undergoing peritoneal dialysis since the diagnosis. At the age of 18 years, she underwent a prior unilateral endovascular embolization to treat renal aneurysms and the procedure successfully stopped a bleeding

aneurism at the upper pole of the right kidney. Based on the patient's medical history, clinical and biochemical findings, a ruptured renal artery aneurysm was diagnosed. An urgent renal AE was considered the treatment of choice to limit hemorrhage and the risk of damage to the peritoneal dialysis catheter. The multidisciplinary team, including pediatric surgeons, interventional radiologists, pediatric nephrologists and psychologists agreed upon the choice to perform a bilateral renal AE in this complex patient. Prior to the intervention, and after being informed on the nature of the intervention, the patient and the patient's parents gave their written consent to undergo endovascular treatment. Under general anesthesia, ultrasound-guided right femoral common artery access was gained using a Terumo 6 FR 11 cm catheter. A diagnostic plain angiography scan revealed a double right renal artery. The major artery was easily catheterized with a 6 FR C2 Mac Boston-Scientific 6 F (65 cm) catheter. Through this catheter, a AMplatzer Plug-2 10 mm was released achieving artery occlusion (about 1 cm from the ostium, Figure 1A). A Sim1 Boston-Scientific 5 fr was positioned in the lower right renal artery and several Terumo Azur coils were released (Figure 1B). Upon completion of the intervention, angiography confirmed the complete embolization of the vessels (Figure 1C). The same procedure was used for the left renal embolization using a Cobra C2 catheter and Terumo 4x10 mm Azur coils (Figure 1D). With the final angiography, bilateral renal arterial thrombosis was confirmed (about 1 cm from the ostium, Figure 1D). The first cm of the renal artery was preserved to facilitate clamping during the future nephrectomy. After the procedure, the patient was transferred to the pediatric intensive care unit of our institution for observation and subsequently to the pediatric nephrology unit. Vital signs were monitored; her postoperative course was uneventful. Two months later, the patient underwent a bilateral lumbotomy and bilateral extraperitoneal nephrectomy to protect the peritoneal surface area and dialysis adequacy. Grossly, both kidneys were enlarged (left 14.5x7x6 cm; right 15x5x5.5 cm); macroscopically the tissue was almost entirely replaced by cysts alternating with solid grey and brown areas, on a background of soft and yellowish tissue with calcific deposits. Histologically, solid areas on the yellowish background were revealed to be angiomyolipoma, which extended to the adipose tissue, perirenal and the renal pelvis. Partially solid aspects (epithelioid angiomyolipoma) and partially cystic aspects (cysts with cubic or hobnail



**Figure 1. Bilateral renal artery embolization (AE).** A: amplatzer-2 Plug 8 mm transcatheter release in the juxta-ostial tract of the right renal artery; B: selective catheterization of the lower right renal artery; C: selective embolization of the lower right renal artery; D: selective left renal AE embolization and its lobar branches by transcatheter release of metal spirals.



**Figure 2. Histological aspect of the right kidney (Hematoxylin-eosin, original magnification X125): renal cell carcinoma at the bottom; solid portion of the angiomyolipoma at the top, its cystic portion on the right.**

epithelium) were observed. In the right kidney, other solid greyish areas were observed (maximum diameter 15 mm); these were classified as renal cell carcinomas (RCC), with acinar, papillary and alveolar growth patterns and cribriform aspects, Furhrman grade III (Figure 2).

The patient was discharged on the fourth day of hospitalization in stable clinical condition. Her clinical condition and laboratory tests were stable at 12 months follow-up. The patient undergoes continuous peritoneal dialysis.

## Discussion

Renal AMLs are found in <0.3% of the general population and account for about 3% of all kidney tumors.<sup>16</sup> The majority of AMLs occur sporadically (80-90%) while the remaining cases are associated with TSC.<sup>13-17</sup> Renal AMLs are composed of varying amounts of abnormal blood vessels, smooth muscle and adipose tissue. 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.<sup>17</sup> The main morbidity associated with AML is spontaneous life-threatening hemorrhage, which can be retroperitoneal or present with visible hematuria. Encroachment into the normal renal tissue, leading to renal failure may occur; but in most patients, as in our case, renal failure was due to PKD or loss of normal renal tissue due to multiple interventions to treat hemorrhage.<sup>9</sup>

Diagnosis and follow-up of TSC-associated renal AMLs are mainly based on imaging studies. These renal tumors are classically identified by the characteristic presence of fat observed with computed tomography (CT), magnetic resonance imaging or ultrasonography.<sup>17-18</sup>

Even though currently the optimal treatment for renal AML is debated, management recommendations are based on tumor size and symptoms, and treatment goals focus on preventing acute events, the preservation of the renal parenchyma and maintenance of long-term kidney function.<sup>10</sup> According to Krueger *et al* 2013, selective AE may be considered the first line therapy for AML presenting with acute hemorrhage<sup>14</sup> and nephrectomy should be avoided,<sup>14</sup> except in selected cases.<sup>22,24-26</sup> Recently, new immunosuppressive strategies, such as mTOR inhibitors<sup>15,19-24</sup> have been proposed for asymptomatic growing AML. This strategy should reduce the size of the AML and the risk of rupture

and bleeding, also in patients with end stage renal failure.<sup>19</sup>

Selective AE is the most commonly employed nephron sparing intervention for AML. Due to the availability of microcatheters and the superior image quality of diagnostic equipment, selective AE has gained popularity in both elective and emergency settings.<sup>1,15</sup> Technical success has been defined as tumor vascular occlusion characterized by cessation of flow in the target vessels and lack of tumor staining.<sup>13</sup> It is a technically feasible and minimally invasive procedure for controlling severe hemorrhage, improving clinical symptoms and preventing tumor progression in patients with renal AMLs.<sup>13,17,26-27</sup> We confirmed the feasibility of this approach also under urgent conditions and when renal failure was present. The risk of AML rupture is not exclusively associated with the lesion size; however, to limit the risk of retroperitoneal haemorrhage, prophylactic immunosuppressive interventions are recommended for AML with a diameter of >3 cm.<sup>19-24</sup> However, the efficacy and tolerability of everolimus in hemodialysis patients, with end-stage renal disease, remains controversial because the condition is thought to alter drug pharmacokinetics.<sup>28-33</sup> Thus, we chose not to utilize this treatment in our patient.

Nephrectomy is now usually reserved for tumors in which embolization would be difficult, if the AML vascular anatomy is complex, if embolization fails, or if malignancy is suspected.<sup>27,34-36</sup> It offers complete removal of the tumor and allows for histological evaluation. It is also associated with a lower recurrence of disease when compared to embolization, and does not increase the frequency of complications.<sup>36</sup>

In our patient, end stage renal failure was present. This prompted consideration of a nephrectomy, which was subsequently performed in order to limit the increase in renal volume. Nephrectomy was performed via lumbotomy with an extraperitoneal approach to protect the integrity of the peritoneum as well as avoid infection of the subcutaneous tunnel and the catheter exit site. The patient and her family have tolerated well the peritoneal dialysis procedure. However, it should be underscored that this procedure must be maintained for long periods; but in subjects with an intellectual disability, such as in our patient, kidney transplantation is not excluded when there is an adequate social support network.<sup>37</sup>

In this case, with the detailed histopathologic examination following the nephrectomy, a RCC of the right kidney was

also discovered. We recommend nephrectomy in TSC, especially in young patients, immediately after the dialysis procedure and before performing transplantation, to avoid frequent invasive check-ups of the native kidneys and the risks of malignant tumor development.

A multidisciplinary approach including pediatric surgeons, pediatric nephrologists and interventional radiologists should be pursued for all patients undergoing renal embolization. Pre-interventional planning and careful monitoring for complications are recommended to optimize clinical outcomes.

## Conclusions

We showed that urgent selective renal AE represents a feasible treatment for bilateral AML bleeding. Renal AE in patients with end-stage renal failure is safe and feasible before performing nephrectomy. Early identification of AML and periodic surveillance in patients with TSC is necessary after the initial diagnosis to ensure optimal care and prevention of future complications and tumor degeneration.<sup>14</sup> A multidisciplinary team provides comprehensive care and follow up in patients with renal failure and has perspectives for renal transplantation.

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