Simultaneous rupture of two renal artery aneurysms in a patient with tuberous sclerosis complex

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ABSTRACT

Tuberous sclerosis complex (TSC) is an autosomal dominant multisystem neurocutaneous genetic condition. It is characterized by TSC-associated neuropsychiatric disorders, epilepsy, tumors, and angiomyolipoma in multiple organs, such as the skin, lungs, and kidneys. TSC is also associated with the development of aneurysms of the medium and large arteries, including the renal arteries. This condition will usually be diagnosed early in life, and active surveillance is required of tumor and aneurysm growth to prevent life-threatening events. We have presented the case of a 41-year-old patient with TSC that had not been previously diagnosed. The patient had presented with retroperitoneal hematoma secondary to the rupture of two left renal artery branch aneurysms that had likely developed within the angiomyolipoma. (J Vasc Surg Cases and Innovative Techniques 2021;7:364-7.)

Keywords: Autosomal dominant; Coil embolization; Postembolization syndrome; Renal artery aneurysm; Tuberous sclerosis

Tuberous sclerosis complex (TSC), also known as epiloia or Pringle-Bourneville phacomatosis, is an autosomal dominant inheritance, neurocutaneous genetic condition with various clinical manifestations. It is characterized by hamartomas, which can affect multiple organs, including the skin, heart, lungs, kidneys, and central nervous system.[1] In 1905, Campbell and Vogt established a triad to characterize TSC: neuropsychiatric disorders, epilepsy, and sebaceous adenomas or angiofibromas.[2] TSC is caused by two pathogenic variants in tuberous sclerosis proteins 1 (TSC1) and 2 (TSC2). TSC1 on chromosome 9 produces hamartin, and TSC2 appears on chromosome 16 and encodes protein tuberin. Most cases of TSC occur sporadically owing to spontaneous pathogenic variants in either chromosome; however, it occurs more frequently with TSC2.

The renal manifestations of TSC include renal cysts, chronic kidney disease, renal cancer, and tumors known as angiomyolipomas (AMLs), which are extremely common and observed in ≤80% of cases involving the kidneys. AMLs have abundant blood vessels with elastin-poor structures that are thought to cause aneurysm formation within the tumor that can grow rapidly, leading to rupture.[3] However, aneurysms can develop in TSC in the medium and large arteries, including the aorta, independent of the presence of an AML.[3] The current guidelines have recommended treatment of the AML when it is symptomatic or has reached 4 cm in size and the treatment of an aneurysm when it is symptomatic or ruptured or, if asymptomatic, when it has reached 2 cm in size. Angiographic arterial embolization is the preferred and recommended treatment for both, with surgical intervention recommended only if embolization is unsuccessful.[4] These lesions cause marked morbidity and mortality owing to progressive enlargement, leading to kidney dysfunction and complicated hemorrhage if they rupture. The lesions can be treated by either open surgical intervention or angiographic arterial embolization.[5]

CASE REPORT

A 41-year-old man with a medical history of epilepsy and no surgical history was transferred to our institution because of bleeding of a left parenchymal renal aneurysm. Computed tomography (CT) of the abdomen and pelvis performed at an outside hospital showed evidence of a completely abnormal appearance of the left kidney with multiple angiolipomas involving the entire perirenal space measuring 22 cm, with associated multiple small aneurysms and a large fusiform aneurysm measuring 9 × 4 cm without evidence of active contrast extravasation. The right kidney also showed evidence of extensive angiolipomas. CT at his presentation to our hospital 48 hours later demonstrated a 15-cm left retroperitoneal hematoma with active bleeding (Fig 1). Additional CT findings included bilateral lower lung small cystic spaces compatible with lymphangioleiomyomatosis, small pericardial effusions, splenomegaly, and a liver cyst. Previous evaluations included magnetic resonance imaging (MRI) of the brain because of a history of

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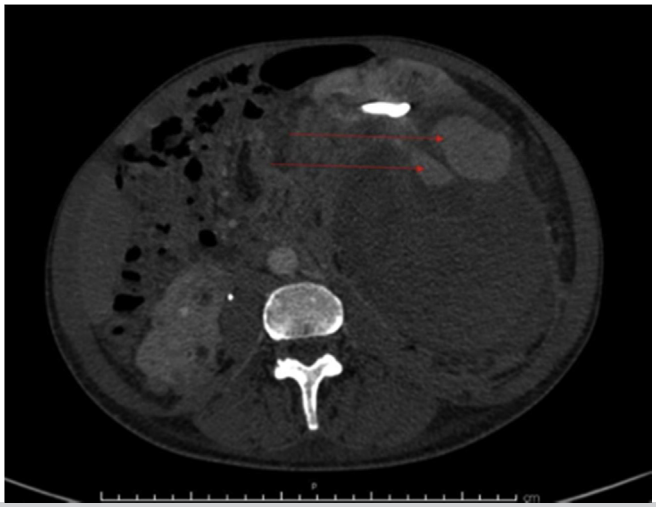

Fig 1. Abdominal computed tomography scan showing areas of contrast extravasation (*red arrows*).

seizures with findings of cortical and subependymal tubers, no giant cell astrocytoma, and a 2-cm cystic lesion on the left anterior mandibular subcutaneous tissue.

The patient's history was significant for a cognitive and learning disability. The physical examination findings were remarkable for face angiofibroma involving the bilateral cheeks, nose, and forehead, small shagreen patches, and ungual fibromas. However, TSC had never been diagnosed, and he had no family history of similar symptoms. The patient required hemorrhage from a ruptured renal aneurysm to be properly diagnosed, despite the patient having so many consistent clinical features. Although no genetic testing results were available, the patient had had five major and two minor features (Table), which confirmed the clinical diagnosis of TSC.[6]

The patient was taken to a vascular hybrid room for endovascular intervention. An aortogram with a selective left renal arteriogram were performed via right femoral artery cannulation with a renal guiding 5F sheath. The left renal artery arteriogram showed aneurysms and active contrast extravasation (Fig 2). Coils were used to embolize four of the aneurysms, two of which had ruptured. Each aneurysm was individually cannulated, and the feeding artery was embolized using four Complex Helical (18 7 × 10 mm), two Complex Helical (18.6 × 6 mm), four 2D Helical (35.6 × 2.6 mm), and four 2D Helical (5 × 2.4 mm) coils (Boston Scientific, Marlborough, Mass). The completion arteriogram of the left renal artery after the embolization procedure is shown in Fig 3.

During the postoperative period, the patient experienced fever and leukocytosis. Appropriate evaluations were performed, including complete blood count, chest radiography, and blood and urine cultures to exclude an infectious process. Postcoiling syndrome was diagnosed and was treated with conservative measures as previously reported. No further postoperative imaging studies were performed for follow-up. After 48 hours without fever, the patient was discharged home with a creatinine of 0.68 mg/dL. The institutional review board approval number was 1911025607.

Table. Major and minor features diagnostic of tuberous sclerosis complex

Feature
Major
Facial angiofibromas
Ungual or periungual fibroma
Hypomelanotic macules
Shagreen patches
Subependymal nodule
Subependymal giant cell astrocytoma
Multiple retinal nodular hamartomas
Cardiac rhabdomyoma
Lymphangiomyomatosis
Renal angiomyolipoma
Minor
Dental enamel pits
Rectal polyps
Bone cysts
Gingival fibroma
Nonrenal hamartomas
Retinal achromic patch
Confetti skin lesions
Renal cysts
Cerebral cortical dysplasia

DISCUSSION

TSC is an autosomal dominant disorder characterized by neurocutaneous manifestations such as hamartomas in multiple organs.[1] AML is the most common renal lesion, reported in 75% to 85% of patients with TSC presenting with renal manifestations and 49% to 60% overall in patients with TSC.[5] The prevalence and size of the tumors increase with age, with larger sizes seen more frequently in women owing to a hormonal effect. AMLs belong to a family of tumors now known as "PEComas," which arise from clonal proliferation of epithelioid cell-distributed blood vessels. They are composed of adipocytes, abnormal vasculature, and smooth muscle cells.[6] Renal AMLs are associated with the development of pulmonary lymphangioleiomyomatosis lesions in patients with TSC. However, pulmonary lymphangioleiomyomatosis has been seen almost exclusively in women and was not seen in our male patient. Although a significant association has been reported between renal and pulmonary involvement in female patients, the relationship between the two pathologies is not well understood.[5]

The renal symptoms in these patients are not usually related to renal disease. The findings will be noted on surveillance imaging once TSC has been diagnosed or after presentation with a mass effect, hematuria, and/or retroperitoneal hemorrhage. Furthermore, the risk of

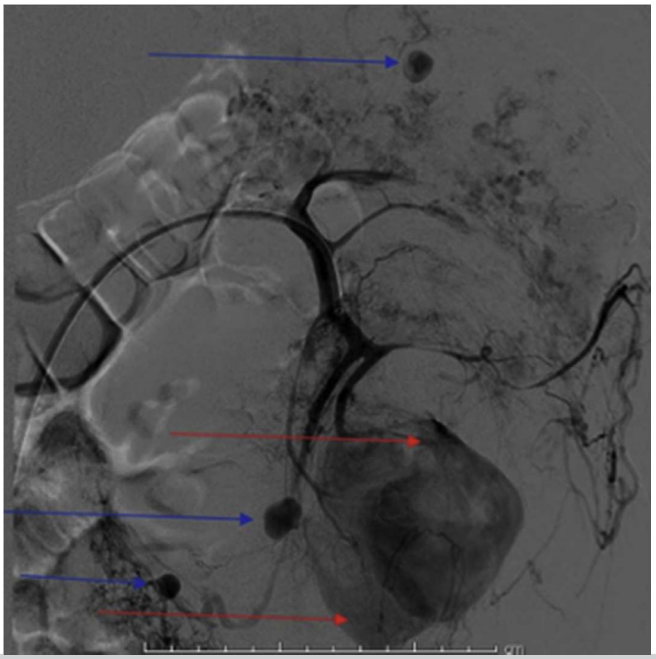

Fig 2. Selective renal artery arteriogram showing a renal artery aneurysm (*blue arrows*) and two areas of extravasation (*red arrows*).

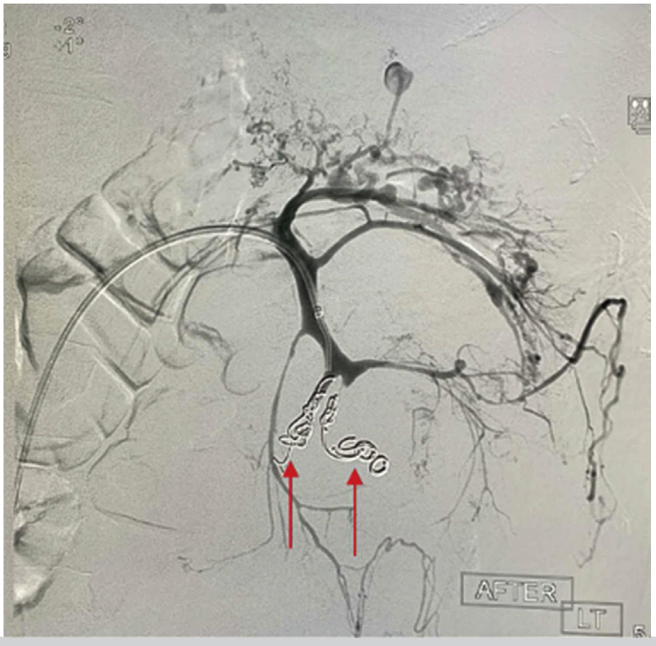

Fig 3. Left renal artery arteriogram after embolization (*red arrows*).

significant hemorrhage correlates with the size of the tumor itself, the degree of vascularity, and the size of the aneurysms within the AML. A tumor size >3 cm or aneurysmal size >5 mm have been associated with an increased risk of bleeding. Tumors >4 cm are more likely to grow and to develop micro- or macroaneurysms.[7,8]

The primary reasons to intervene with renal AMLs are to alleviate symptoms of pain, mass effect, renal disease, and/or to prevent hemorrhage. Most patients with TSC will be diagnosed early in life, with renal MRI performed to determine the baseline renal status. In contrast, our 41-year-old patient had had an initial presentation with a 22-cm AML with an associated 9-cm fusiform ruptured aneurysm and evidence of the clinical features of TSC not previously diagnosed. Active surveillance with MRI every 1 to 3 years has been recommended for small, stable, asymptomatic aneurysms and AMLs. The creatinine, glomerular filtration rate, and blood pressure should also be measured annually. Inhibition of mTOR (mammalian target of rapamycin) has been used in some clinical trials to reduce the tumor size and avoid complications in patients with AML.[9] The current guidelines have recommended treatment of the AML when it is symptomatic or has reached 4 cm in size and treatment of aneurysms when symptomatic or ruptured and, if asymptomatic, when the size has reached 2 cm. Angiographic arterial embolization has been the preferred and recommended treatment for both, with surgical intervention recommended only if embolization has been unsuccessful. The indications for repair include symptomatic lesions, women in childbearing age, masses >4 cm, and aneurysm >2 cm. However, no data are available to indicate the need for surgery according to the growth rate. The use of open surgical procedures depends on location of the lesion, and the options simple aneurysmorrhaphy and partial or total nephrectomy.[10]

The endovascular techniques include selective embolization, which will significantly decrease the risk of hemorrhage and morbidity of open surgical approaches and preserves nephrogenic function.[11,12] Diagnostic renal arteriography of our patient revealed a large AML with four aneurysms, two of which had ruptured. All four aneurysms were successfully cannulated and individually embolized. Embolization obliterates the blood supply to the AML reducing the growth of both AMLs and aneurysms and stops active bleeding. However, patients can develop postembolization syndrome,[13] which consists of a low-grade fever, abdominal pain, and increased C-reactive protein levels. It will usually resolve within 1 week without treatment.[14] Despite this limitation, embolization continues to be the safe and preferred therapy for acute hemorrhage and the most successful kidney-sparing procedure in the presence of acute life-threatening hemorrhage.[11]

CONCLUSIONS

Renal artery aneurysm rupture is a fatal complication related to TSC. Because of the known complications such as those presented in our case report, we suggest that a combination of imaging modalities such as abdominal ultrasound and/or computed tomography

should be performed for all patients with TSC once it has been diagnosed. Aneurysms that are ≥2 cm should be treated to decrease the risk and complications of rupture. Selective embolization of renal artery aneurysms is a safe and efficacious technique to stop acute hemorrhage resulting from ruptured renal aneurysms.

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