



A Rare Presentation of Tuberous Sclerosis Complex: Infected Renal Angiomyolipoma and Recurrent Abscess Formation

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Abstract

Tuberous Sclerosis Complex (TSC) is an autosomal dominant genetic disease commonly associated with the formation of tumors involving multiple organ systems, often in the form of skin changes and neurological deficits. Cerebral involvement, however, strongly impacts the quality of life as it can be presented with one or more of the following consequences as seizures, developmental delay, intellectual disability, and autism. Renal involvement is generally less commonly seen, in the form of benign renal Angiomyolipomas (AML). Complications of infection and abscess formation from AMLs are rare, and recurrence of such events is even more so, as management calls for the aid of specialists from multiple fields. This case report describes a pediatric TSC patient, who presented with recurrent renal AML infections and abscesses, to heighten awareness of such rare yet dire events.

Introduction

Tuberous Sclerosis Complex (TSC) was first described in 1862 by German neurologist Friedrich Daniel von Recklinghausen and later characterized and classified in 1880 by French neurologist Désiré-Magloire Bourneville. It is an autosomal dominant genetic disorder with incomplete penetrance that affects approximately 1.5 million people worldwide. This disorder is commonly associated with the formation of hamartomas (benign tumors) that involve numerous different organs, mainly brain, eyes, heart, kidneys, skin and lungs. It is primarily classified as a neurocutaneous disorder due to classically observed calcified nodules accompanied with characteristic glial cell tumors in the brain.

We report a 7-year-old female patient with a known diagnosis of multisystem TSC, involving the brain, liver, heart, and kidneys. The patient was brought with fatigue and fever on presentation. She was noted with multiple small bilateral renal AMLs, as well as apparent abscess formation in her right kidney. She was subsequently treated with closed drainage and intravenous antibiotics, followed by maintenance with oral antibiotics with complete resolution of the AML-associated abscess. Twenty

months later, the patient presented similarly again, noted with another infected AML with small abscess formation in the right kidney. Given its size, the abscess resolved with IV and oral antibiotics without drainage. This case is unique because of the rare complication of infected AML and recurrent abscess formation in a pediatric TSC patient.

Case Report

The patient is a 7-year-old girl born uneventfully by normal spontaneous vaginal delivery. She was noted with normal development until 7 months when she presented with her first seizure episode. She was soon diagnosed with tuberous sclerosis, autistic spectrum disorder, and global developmental delay; she currently attends a center for special education. The patient lives with her parents and siblings, none noted with a similar presentation. She also underwent vagal nerve stimulation at 6 years of age and currently takes anti-convulsant treatment regularly for seizure management. The patient underwent baseline renal ultrasound in the outpatient department; this revealed multiple bilateral hyper-echogenic lesions of various sizes, suggestive of AMLs with overall apparent stability (Figure 1).

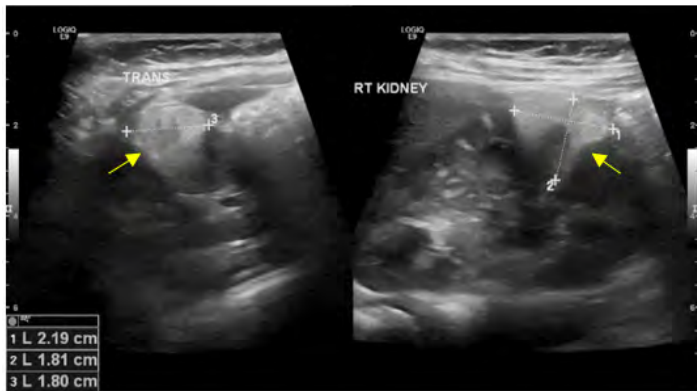


Figure 1: Renal ultrasound revealed normal sized kidneys with preserved corticomedullary differentiation. There are multiple bilateral, variable sized hyper-echogenic lesions suggestive of AMLs. The largest one on the right side measured as 2.1 x 1.8 cm (arrows) and the largest on the left side as 0.5 x 0.6 cm (not shown).

The patient was in her usual state of health until three weeks before presenting to the pediatric emergency department. She was reported with a decrease in her usual activity and appetite, without nausea or vomiting. She suffered from on-and-off high-grade fever with associated rigors and a 2 kg weight loss. Otherwise, review of other systems was unremarkable; she had no history of recent travel nor contact with sick individuals or animals.

The patient sought medical advice, and completed multiple initial courses of antibiotics with no improvement of her symptoms. Upon presenting to the emergency department, she was vitally stable. On physical examination, the patient was noted with normal growth parameters, with a weight of 24.5 kg (75th percentile) and height of 118 cm (50th- 75th percentile).

She looked well in appearance with no distress or dehydration. Assessment of the head, eyes, ears, nose, throat, and neck was unremarkable. Chest assessment revealed adequate bilateral air entry with vesicular breathing. Her cardiovascular examination was unremarkable, and her abdomen was soft with no organomegaly on palpation. Central nervous system examination, apart from higher mental function deficits, was grossly intact; musculoskeletal examination was unremarkable. Skin examination revealed left cervical and subclavicular well-healed surgical scars

with no erythema, swelling, or tenderness. Two hypopigmented macules (ash-leaf spots) were noted, one on her abdomen and the other on her back. The patient was admitted to the pediatric ward with suspicion of fever of unknown origin for further investigation and management. The laboratory findings and imaging studies are summarized as follows:

Electrolyte Panel	Renal Function Tests	Liver Function Tests
Na ⁺ : 148 mEq/L	BUN:5.3mg/dl	Total bilirubin: 2.1 μmol/L
K ⁺ : 4.2 mEq/L	Cre:32 μmol/L	ALT: 15 U/L
Cl ⁻ : 104 mEq/L		AST: 27 U/L
Ca ²⁺ : 2.24 mmol/L		ALP: 149 U/L
PO ₄ ³⁻ : 1.53 mmol/L		Total Protein:65g/L
Complete Blood Count	Inflammatory Markers	
Hct: 29.1%	ESR: 70 mm/hr	Serum Complement
WBC: 9270 cells/mL	CRP: 143.6 mg/L	C3: 2.21 mm/hr
Platelets: 289,000 cells/mL	Rf: 9.12 IU/mL	C4: 0.34 mm/hr
	ANA: negative	
Microbial Panel	Virus Panel	
Bacterial cultures	PCR DNA	Neuro virus panel: negative
(Throat, blood, urine): negative	(EBV, CMV): negative	
Brucella serum IgG/M: negative	PCR RNA	
Q Fever Serum IgG/M: < 1:16	(Influenza A/B, RSV): negative	
PPD/QFT-G: negative		

Table 1: The laboratory findings and imaging studies.

Renal ultrasound revealed interval progression in the size of previously noted right kidney AMLs(Figure 2). Contrast-enhanced CT scan of the abdomen revealed a well-defined homogenous fluid-attenuated lesion consistent with an abscess(Figure 3).

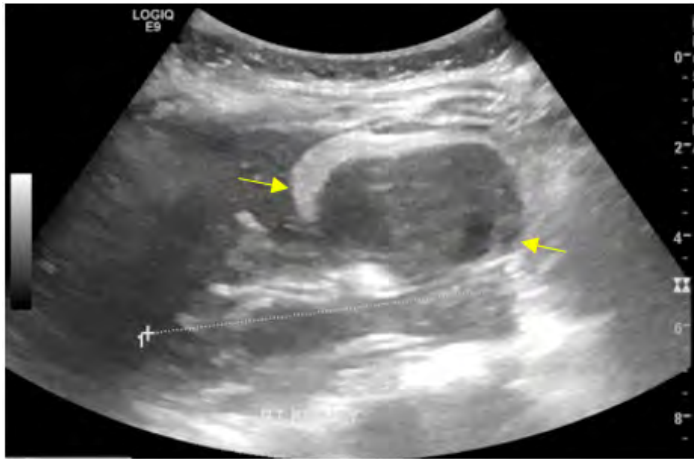


Figure 2: Interval progression in the size of previously seen right kidney mid-to-lower pole AML (arrows), now measured at 4.8 x 3 cm (compared to prior size of 2.1 x 1.8 cm), currently becoming heterogeneously predominant hypoechoic content with no internal vascularity on color Doppler.

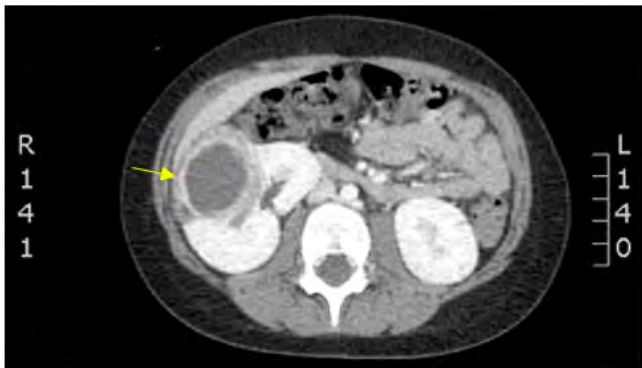


Figure 3: Contrast-enhanced CT scan of the abdomen: lesion noted with well-defined homogenous fluid attenuation with peripheral thick wall enhancement (arrow), seen in the mid-to-lower pole of right kidney surrounded by fat stranding consistent with the abscess. There are numerous fat-attenuated lesions, variable in size, involving both kidney cortices, consistent with noted AMLs.

The patient was started on IV piperacillin- tazobactam, and she showed some clinical improvement. Following the radiological findings which confirmed right kidney abscess, a multidisciplinary meeting that included the interventional radiologist, infectious disease consultant, pediatric surgeon, primary physician, and the patient's parents was held. The decision of percutaneous drainage was made by the team with the family's approval. Her condition improved dramatically after abscess drainage, and her fever subsided with notable decrease in CRP and ESR. In addition, her appetite and usual level of activity returned to her prior state of health. Drained fluid culture revealed no growth. IV piperacillin-

tazobactam treatment continued for three weeks. Upon complete resolution of symptoms, the patient was discharged with oral antibiotic amoxicilline-clavulanate for planned outpatient follow-up in two weeks. However, two days post-discharge, she returned to the emergency department with fever and decrease activity. The patient was then re-admitted to the pediatric ward for sepsis work-up, and IV piperacillin- tazobactam was resumed. Notable lab values were increased CRP (233 mg/L) and ESR (50 mm/hr); other lab values were within normal limits.

Renal ultrasound revealed fluid collection in the right kidney; the interventional radiologist was consulted for guided drainage. The draining tube was kept for one week, and the patient showed improvement with drops in inflammatory markers and no fever. Repeat ultrasound revealed remarkable decrease in size of fluid collection in the right kidney; further microbial workup, including gram stain and bacterial, fungal, and acid-fast species culture of draining tube and fluid samples, were negative. After discharge on oral cefdinir, the patient continued regular follow-up in the Infectious Disease (ID) clinic and completed two weeks treatment of oral antibiotics. Inflammatory markers and renal ultrasound on follow-up were satisfactory, and her condition remained well. Twenty months later, she presented again with fever and fatigue. Physical examination was unremarkable. However, notable lab values were high inflammatory markers with negative blood and urine cultures. Repeated renal CT scan revealed small fluid collection at the upper pole of the right kidney suggestive of a small abscess (Figure 4).

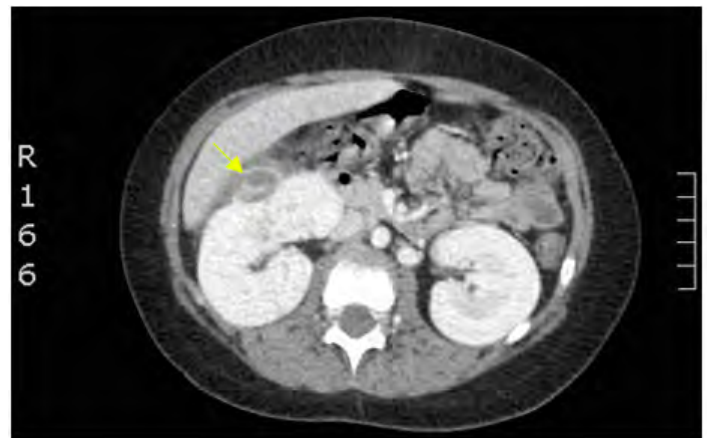


Figure 4: Follow up renal CT scan: thick-walled fluid collection (arrow) noted within the mid-to-lower pole of the right renal AML. Compared to prior presentation, latest fluid collection was notably smaller.

The patient responded well to IV piperacillin-tazobactam treatment for two weeks and was subsequently discharged home in generally well condition on oral amoxicillin-clavulanate. She continued regular follow-up at the ID clinic. Follow-up renal

ultrasonography revealed marked reduction in the size of the collection in the right kidney (Figure 5).

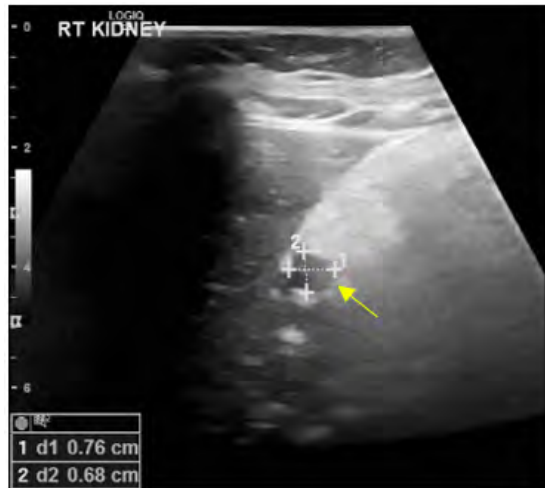


Figure 5: The previously seen cystic fluid collection (arrow) within AMLs of the right renal lower pole showed interval regression in size, measuring 0.7 x 0.6 cm (compared to prior measures at 4.8 x 3 cm).

Discussion

TSC disorder roots from the characteristic tuber-like cerebral nodules, calcifying overtime and hence becoming sclerotic. This is an autosomal dominant genetic disease with incomplete penetrance that affects approximately 1.5 billion people worldwide, with a birth incidence of 1 in 6000 [1]. Among all races, ethnicities, and genders, at least two children born each day is anticipated to develop TSC. Two major gene loci have been identified: TSC1 on chromosome 9q34 (TSC1, MIM no. 191100), which encodes hamartin, and TSC2 on chromosome 16p13.3 (TSC2, MIM no. 191902), which encodes tuberlin. These gene products are assumed to function as tumor suppressors by establishing a protein complex that regulates cellular growth, differentiation, and proliferation [2]. Therefore, mutational loss of heterozygosity appears to drive towards tumor development, causing otherwise benign tumors (hamartomas) to form in such vital organs as the brain, kidneys, heart, eyes, lungs and skin [3].

Renal Angiomyolipomas (AMLs) are usually benign tumors derived from perivascular epithelioid cells. They contain abnormal smooth muscle cells, blood vessels, and adipose tissue in variable proportions. Renal AMLs are relatively uncommon in the general population (1-2%). However, among the TSC patient population, 50-75% of cases develop renal AMLs, often as incidentally reported renal masses. Larger masses are most commonly notable for risk of hemorrhage complications [4-6]. In TSC, AMLs tend to arise bilaterally, at younger ages in both genders. AMLs are the most common renal lesions associated with TSC, far outnumbering

cystic lesions and Renal Cell Carcinoma (RCC). As the incidence and size of renal masses both increase with age, AMLs become a significant cause of morbidity and mortality among adults with TSC [7].

Complications from AMLs are rare but often severe, depending on the size and content of the mass. One study described 10 cases from 63 patients with renal AMLs in which CT imaging revealed the following complications: compression of pyelocalyceal system (3 cases), intratumoral bleeding (2 cases), rupture of subcapsular/perirenal/pararenal hematoma (4 cases), and extensive intrarenal/parapelvic hematoma and cystic degeneration (1 case) [1]. Although renal abscess formation is well recognized after endovascular intervention for embolization of AML, review of literature on renal AMLs, however, revealed no cases reported with similar complications of spontaneous recurrent infections and abscess formation [8].

Conclusions

This chronology of rare incidents, reported in a case of a 7-year-old girl with TSC, seizures, and developmental delay, indicates the need for greater awareness of AML-associated infectious complications and recurrences. Additionally, the limited literary sources focused on such complications, to our current knowledge, warrants further research into their presentation, investigation, management, and follow-up.

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