Paediatrica Indonesiana

VOLUME 53 January • 2013 NUMBER 1

Case Report

Renal manifestations in tuberous sclerosis patients: two case reports

Oke Rina Ramayani, Rosmayanti, Rafita Ramayati, Rusdidjas

Tuberous sclerosis (TS) is a neuro-cutaneous disorder, characterized by mental retardation, epilepsy, and facial angiofibromas. The incidence has been estimated to be 1 case per 6000 live births. Although rare, this disorder is a cause of mental retardation with severe epilepsy.[1] Scientists have found manifestations of this disorder not only in brain and skin, but also in the eyes, heart, lungs, and kidneys, so it has been renamed tuberous sclerosis complex (TSC).[2]

The kidney is the organ most frequently involved in TS, with angiomyolipomas (AMLs), renal cysts, nephrocalcinosis, cancer, hypertension, and impaired renal function.[3] Renal cysts and AMLs may rupture and increase the risk of bleeding, leading to the need for operative procedures. Also, renal failure or hypovolemic shock due to bleeding AMLs may lead to death. Overall, renal failure is the second most frequent cause of death in TSC patients, after status epilepticus and/or bronchopneumonia.[4] Because of the rare incidence of TS, as well as the various renal manifestations observed, we describe two TS cases with renal manifestations.

Two patients with TS came to H. Adam Malik Hospital in Medan. The patients were aged 12 years (in the first time she came to H. Adam Malik Hospital) and 7 years. Both patients

Table 1. Characteristics of the two cases

Characteristics	Case 1	Case 2
Age, years	14	7
Sex	Female	Male
Skin	Adenoma sebaceum	Normal (no sign of adenoma sebaceum)
Epilepsy age of onset, years	2	3
Renal involvement	AMLs	Decreased renal size
eGFR, mL/min/1.73m^2	140	187
Outcome	Alive until now (as 14 yo)	Alive until now (as 7 yo)

eGFR: estimated glomerular filtration rate

From the Department of Child Health, University of North Sumatera Medical School/ H. Adam Malik Hospital, Medan, Indonesia.

Reprint requests to: Oke Rina Ramayani, Division of Nephrology, Department of Child Health, University of North Sumatera Medical School, H. Adam Malik Hospital, Jl. Bunga Lau No.17 Medan 20136, Indonesia. Tel.+62-61-8361721, +62-61-8365663, Fax. +62-618-361721. E-mail: *oke_rina@yahoo.com*

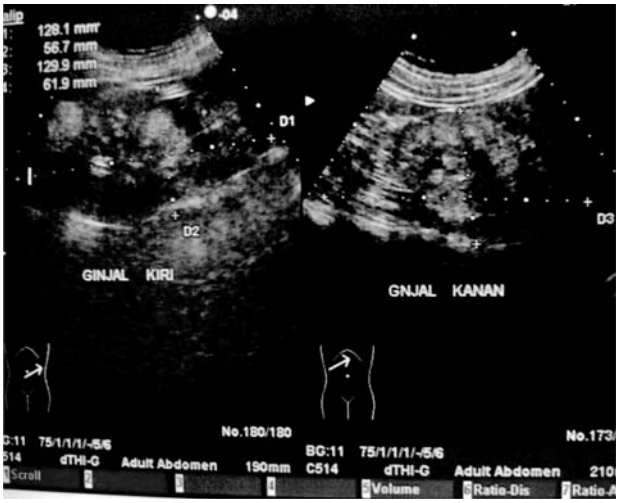

Figure 1. Renal ultrasound in Case 1. Multiple hyperechoic lesions in both kidneys suggesting AMLs. Left and right kidney sizes were 12 x 5.6 and 12 x 6.2 cm, respectively.

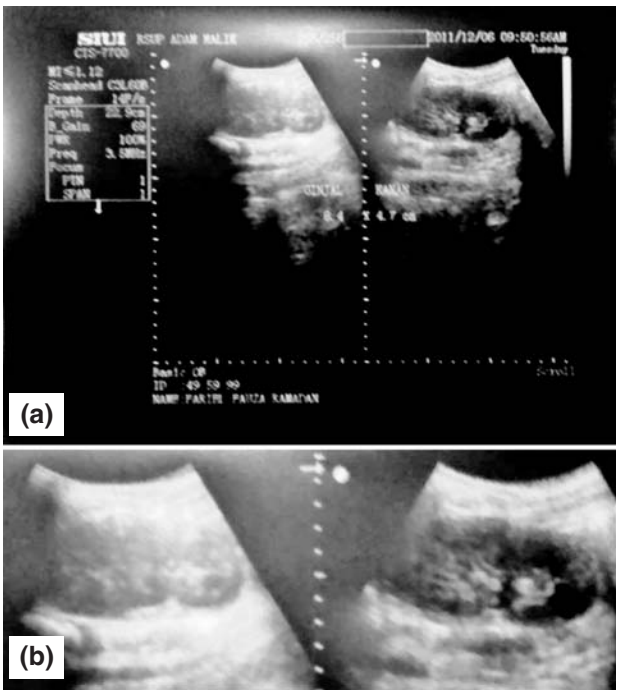

Figure 2. Renal ultrasound in Case 2. (a) Parenchyma was normal. Echo structure of cortex and medulla did not differentiated well. Left and right kidney sizes were 7.5 x 5.2 cm and 8.4 x 4.7 cm, respectively. (b) Magnified renal ultrasound

survived. Characteristics of the patients are shown in **Table 1**.

Case 1 was a 12-year-old (at the first time she came to H. Adam Malik Hospital) Indonesian girl with a history of seizures and mental retardation, admitted to H. Adam Malik Hospital. She was diagnosed with TS at the age of 6 years and was routinely examined in the Nephrology Division. Body weight and height were 52 kg and 151 cm, respectively. Blood pressure was within normal limits. Routine urinalysis and eGFR were within normal limits. She had taken anti-epileptic medication for the previous 10 years. Her renal ultrasound results are shown in **Figure 1**.

Case 2 was a 7-year-old Indonesian boy with a history of seizures and mental retardation, at H. Adam Malik Hospital. He had been previously diagnosed with TS and received routine examinations at the Nephrology Division. Body weight and height were 20 kg and 109 cm, respectively. Blood pressure was within normal limits. Routine urinalysis showed mild proteinuria, and eGFR was within normal limits. He had taken anti-epileptic medications for the previous 4 years. His renal ultrasound results are shown in **Figure 2**.

Discussion

The prevalence of TS in H. Adam Malik Hospital was approximately 3 cases per 41,000 outpatients in the pediatric clinic for 5 years. Two cases are described here, while the third patient was lost to follow up from the Nephrology Division.

Commonly observed renal manifestations in TSC are angiomiolipoma and renal cysts. Less than 5% of these renal manifestations transform into malignancies, such as renal cell carcinoma.[2,5] The prevalence of renal angiomiolipoma in the general population was reported to be 0.02-0.29%, mainly in adults.[6] However, in the TS population, AML prevalence was reported to be as high as 70-80%. In children, the average age at diagnosis of renal abnormalities is between 7.2 and 9.2 years for AMLs.[7] One of our cases suggests a later onset of around 12 years. However, this condition may be due to lack of knowledge about TS given its low prevalence.

Angiomyolipoma are more likely to grow than remain stable. In contrast, simple renal cysts may appear and disappear with time.[8] Complicated AMLs are usually treated by partial nephrectomy or embolisation to spare the renal tissue. Indications for total nephrectomy are limited and include uncontrolled hypertension, local tissue invasion, tumor in a renal vein or very strong evidence of malignancy.[6] In Case 1, we found no renal cysts and did not perform any surgery because of her small-sized lesions.

In Case 2, we found no cysts or masses by USG. Rakowski *et al*. found multiple, small AMLs by routine ultrasound in a 20-year-old patient who had had a normal ultrasound at the age of 18 years.[5] This example demonstrates the importance of follow-up renal imaging examinations for TSC patients throughout adulthood, even if scans are normal. Therefore, we suggest a yearly renal USG examination for our patients.

Renal failure has been described in patients with cysts more often than in those with AMLs.[9,10] In our cases, neither patient showed any evidence of renal failure, but we plan to do long-term follow-up for these patients. Periodic renal surveillance is indicated in children with TS to identify those with growing lesions or impaired renal function.[10]

In conclusion, although renal manifestations are common in TS patients, severe outcomes are rare. Therefore, TS patients need long-term follow-up to limit complications.

References

1. Leung AKC, Robson WLM. Tuberous sclerosis complex: a review. J Pediatr Health Care. 2007;21:108-14.
2. Roach ES, Sparagana SP. Diagnosis of tuberous sclerosis complex. J Child Neurol. 2004;19:643-9.
3. Schillinger F, Montagnac R. Chronic renal failure and its treatment in tuberous sclerosis. Nephrol Dial Transplant. 1996;11:481-5.
4. Au KS, Williams AT, Gambello MJ, Northtrup H. Molecular genetic basis of tuberous sclerosis complex: from bench to bedside. J Child Neurol. 2004;19:699-709.
5. Rakowski SK, Winterkorn EB, Paul E, Steele DJ, Halpern EF, Thiele EA. Renal manifestations of tuberous sclerosis complex: incidence, prognosis, and predictive factors. Kidney Int. 2006;70:1777-82.
6. Bissler JJ, Kingswood JC. Renal angiomyolipomata. Kidney Int. 2004;66:924-34.
7. Casper KA, Donnelly LF, Chen B. Tuberous sclerosis complex: renal imaging findings. Radiology. 2002;225:451-6.
8. Zimmerhackl LB, Rehm M, Kaufmehl K, Kurlemann G, Brandis M. Renal involvement in tuberous sclerosis complex: a retrospective survey. Pediatr Nephrol. 1994;8:451-7.
9. Narla LD, Slovis TL, Watts FB, Nigro M. The renal lesions of tuberosclerosis (cysts and angiomyolipomia) screening with sonography and computerized tomography. Pediatr Radiol. 1988;18:205-9.
10. Brodkiewickz A, Marciniak H, Szychot E, Walecka A, Peregud-Pogorzelski J. Angiomyolipomas, renal manifestation of tuberous sclerosis complex in 17 year old boy a case report. Ann Acad Med Stetin. 2008;54:160-5.