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Tuberous Sclerosis Presenting With Acute Kidney Failure, Pyelonephritis, and Polycystic Kidney Disease

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Tuberous sclerosis complex (TSC) is a multisystemic inherited autosomal dominant disease characterized by the development of hamartomas in the brain and kidneys. In about 2% of patients, polycystic kidney disease is present, which may result in different stages of renal insufficiency. Acute kidney failure has not been reported in infants with TSC. We report a female infant with TSC who was admitted to hospital with pyelonephritis, acute kidney injury, and polycystic kidney disease.

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Case Report

INTRODUCTION

Tuberous sclerosis complex (TSC) is a multisystemic autosomal dominant disease characterized by the development of hamartomas in the brain and kidneys.[1,2] Tuberous sclerosis complex and autosomal dominant polycystic kidney disease (ADPKD) are both inherited autosomal dominant disorders.[3] There is a considerable variation in the clinical presentation of TSC, and various organ systems may be affected. These include most likely the central nervous system, kidneys (cysts, angiomyolipoma, and rarely, renal cell carcinomas), skin, cardiovascular system, and eyes.[4,5] Renal cystic disease predominantly appears as a single cyst, but in about 2% of patients, it appears as polycystic kidney disease, which may result in different stages of renal insufficiency.[6] The frequency and type of renal lesions positively correlate with the age of the patients, and the age of onset of cysts is about 9 years.[7] However, they may be present as early as during the first year or months of life or even at birth.[8,9] From the radiologic point of view, cystic diseases observed in TSC resemble those in ADPKD.[10] Renal cysts may also be microcystic, so they are sometime undetectable by different kinds of imaging studies.[11] To our knowledge, there is no case report of acute kidney injury in infantile TSC patients. We report a case of acute kidney injury accompanying TSC and ADPKD, which was resolved with appropriate management and antibiotic therapy for pyelonephritis.

CASE REPORT

A 7-month-old girl was referred to our hospital with acute pyelonephritis and high serum creatinine level. The presenting symptoms were fever, anorexia, vomiting, and malodorous urine. She had been born to nonconsanguineous parents and there was no maternal complication during pregnancy. At the time of admission, her examination was unremarkable except for tachycardia (pulse rate,120 per minute), high temperature, and mild dehydration. Her growth indexes were as follows: body weight, 7100 g; height, 68 cm; and head circumference, 42 cm. Laboratory studies including complete blood count, blood culture, and liver function test were normal. On admission, plasma creatinine level was elevated (0.9 mg/dL) and glomerular filtration rate was 36 mL/min/1.73m^2 based upon Schwartz formula. Urinalysis revealed leukocyturia and bacteriuria, and urine culture showed more than 100 000 colony forming units

of *Escherichia coli*. Patient's laboratory tests are demonstrated in the Table.

Due to renal insufficiency, the patient underwent a further detailed clinical assessment. Ultrasonographic examination indicated bilateral enlarged kidneys (right kidney, 97 cm and left kidney, 95 cm) with multiple cystic lesions (maximum size, 31× 40 mm; Figure 1). No apparent abnormalities were observed in the abdominal and pelvic ultrasonographies. Echocardiographic and respiratory studies were also normal. Renal ultrasonographic evaluation of parents showed no pathologic findings. A dimercaptosuccinic acid renal scintigraphy demonstrated globally reduced function of both kidneys with bilateral cortical defects (Figure 2). On further physical examination, 7 previously undetected small hypopigmented skin areas (3 mm to 4 mm) were found on the chest, abdomen, and thighs (Figure 3). Ophtalmologic examination revealed no abnormality. The brain computed tomography scan showed periventricular subependymal nodules and a small calcified focus in the right periventricular region (Figure 4).

Hospital and Postdischarge Laboratory Results

Parameter	On Admission	After Discharge
Blood urea nitrogen, mg/dL	14	8
Serum creatinine, mg/dL	0.90	0.37
Blood urea nitrogen-creatinine ratio	40	25
Serum sodium, mEq/L	144	138
Serum potassium, mEq/L	5.7	4.5
Serum bicarbonate, mEq/L	16	22
Serum calcium, mg/dL	8.5	9.0
Serum phosphorus, mg/dL	7.0	5.2
Serum uric acid, mg/dL	6.5	4.2
Urine sodium, mEq/L	55	46
Urine specific gravity	1010	1020

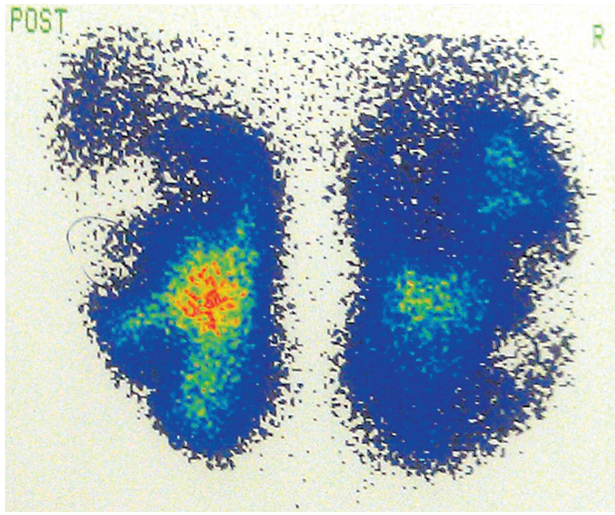

Figure 2. Dimercaptosuccinic acid renal scintigraphy scan shows globally reduced function of both kidneys with bilateral cortical defects.

After supportive therapy for fever and dehydration and antibiotic therapy for pyelonephritis (ceftriaxone, 75 mg/kg/d for 7 days), clinical symptoms improved, laboratory abnormalities resolved, and laboratory tests showed normalization of urinalysis, urine culture, and glomerular filtration rate.

DISCUSSION

Renal involvement may have great impacts on the course of TSC because of the risk of morbidities and mortalities secondary to acute or chronic kidney failure. It seems that renal complications may be a leading cause of death in patients with TSC.[12] Renal

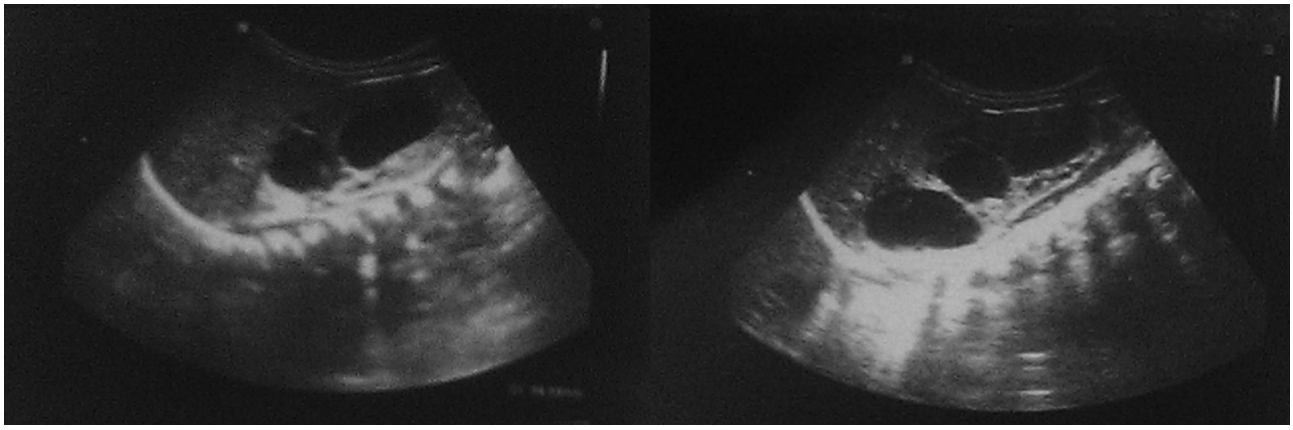

Figure 1. Ultrsonographic features of the kidneys showing multiple cystic lesions.

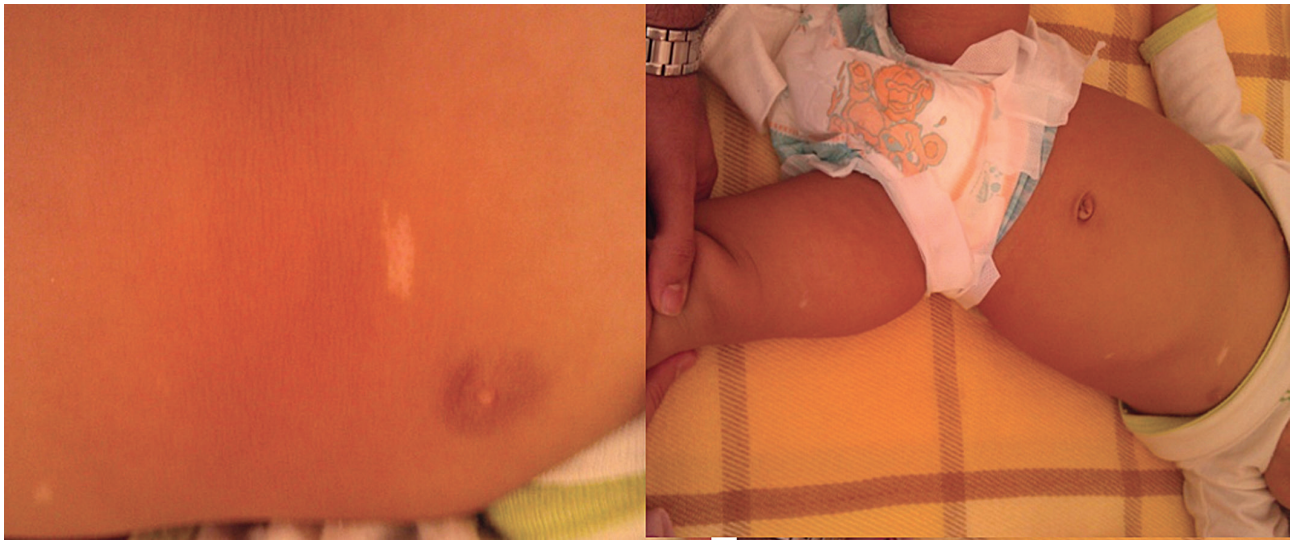

Figure 3. Hypopigmented macules on the chest, abdomen, and thigh.

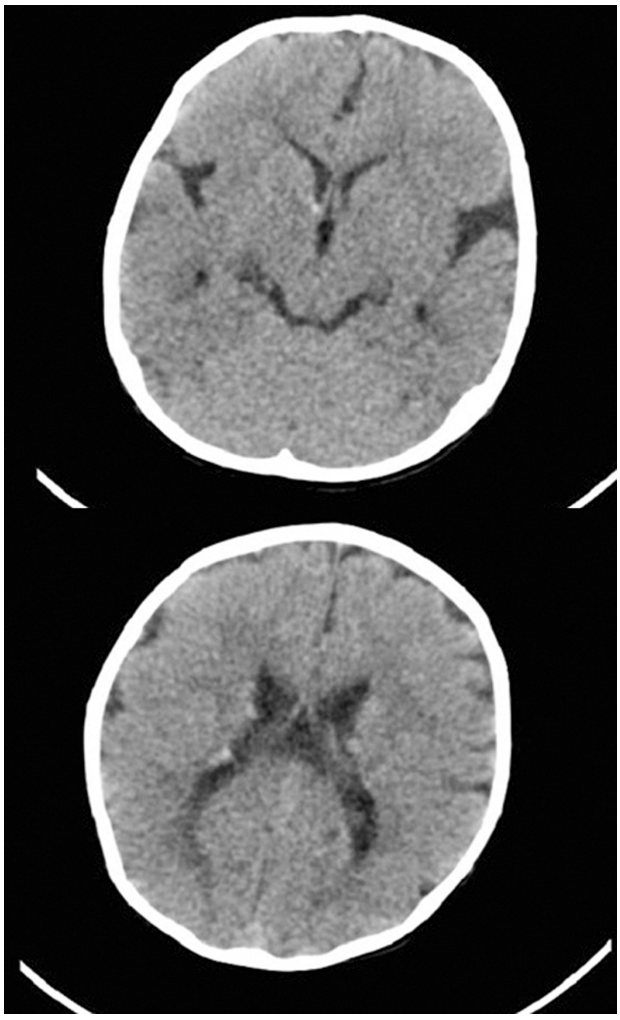

Figure 4. Brain computed tomography scans showing periventricular subependymal nodules and a small calcified focus in the right periventricular region.

involvement is the second most common cause of mortality after nervous system abnormalities, but in adult patients, renal complications are the most common cause of death.[13,14] The frequency of renal lesions positively correlated with age. As a matter of fact, the age of onset for cysts appearance is usually at 9 years and for chronic kidney disease is 7.2 years. However, these problems may be present as early as the first year of life or even at birth.[15-17]

Most frequently there are single cysts, but presentation as polycystic kidney disease during early childhood has also been reported.[18-21] According to many studies there are infantile or neonatal cases with early manifestations of both TSC and ADPKD.[22-26] Clarke and colleagues reported that although end-stage renal failure is rarely encountered in TSC patients, it does contribute to significant morbidity and mortality.[27] Acute kidney injury may occur due to anticonvulsant therapy, use of nonsteroidal anti-inflammatory medications, rhabdomyolysis, and hypoxic renal injury, which is induced by prolonged seizures.[28] In one reported case this complication occurred due to acute bleeding into a cyst and renal capsule.[29] There is no case report of acute kidney injury in infantile TSC patients. In our opinion, the patient had acute on chronic kidney failure. Because of the multiple cysts in the kidneys, the patient was at least in chronic kidney disease stage 1 and an infection episode decreased kidney function temporarily to chronic kidney disease stage 3. In our patient, the acute kidney injury was resolved

with proper hydration and antibiotic therapy. Although there were clinical signs of dehydration in the patient's physical examination, the blood urea nitrogen-creatinine ratio was 15 and the urine specific gravity at presentation was 1010 and random urine sodium concentration was 55 mEq/L. In the course of treatment the glomerular filtration rate reached 90 mL/min/1.73 m^2 and the serum creatinine reached 0.37 mg/dL. Because of diffuse cystic disease and a background of chronic interstitial, the urine and biochemical indices such as the ratio of blood urea nitrogen to creatinine, urinary sodium concentration, and serum specific gravity are not trustable for detection of acute kidney injury, but prompt response to antibiotic therapy is in favor of acute kidney injury due to pyelonephritis. Since the urine output did not decrease before admission and during the hospital care, we think the acute kidney injury was rather due to urinary tract infection than dehydration or pre renal azotemia. The interesting points in this patient were: (1) there was no history of cerebral disease or seizure and the patient was referred with only a chief complaint of fever and anorexia and mal odor urine; (2) multiple hypopigmented skin lesions of this patient had not been adequately detected in recent hospital course and before; and (3) the presence of acute kidney injury without significant symptoms and signs of dehydration and prompt recovery of acute kidney injury after antibiotic therapy.

CONFLICT OF INTEREST

None declared.

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