Tuberous Sclerosis and Polycystic Kidney Disease: A Rare Association

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Abstract
Tuberous sclerosis complex (TSC) and autosomal dominant polycystic kidney disease (ADPKD) are two different genetic diseases. Although these two diseases are associated very rarely, the association is well recognized. This occurs due to a large deletion involving both PKD-1 and TSC-2 genes on chromosome 16. This is also known as TSC-2/PKD-1 contiguous gene syndrome.

We report a 26-year-old female patient with TSC who presented with severe metabolic acidosis due to renal failure. She had palpable enlarged kidneys bilaterally. CT scan of abdomen revealed bilateral enlarged lobulated kidneys studded with multiple cysts which was consistent with the diagnosis of ADPKD.

Introduction
Tuberous sclerosis complex is an autosomal dominant disorder manifested in children and adults characterized by hamartomatous growth in various organs and typical neurological features.¹ Prevalence of tuberous sclerosis is up to 1 in 6000 in different population.² This occurs due to damages in two suppressor genes namely TSC1 and TSC2 located on chromosome 9 (9q34) and chromosome 16 (16p13.3), respectively.³ Neurological manifestations include epilepsy, mental retardation and autism. Major dermatological features are facial angiofibromas (adenoma sebaceum), periungual fibromas, shagreen patches and hypopigmented macules.⁴⁵ Among other systems, involvement of kidney, lung and heart are not uncommon. Here we report a case of tuberous sclerosis that had a rarely associated renal disease.

Case Report
A 26-year-old unmarried female was admitted in the Medical ward with breathlessness for two days. She did not have any history of fever, cough, expectoration, chest pain or palpitation. She was a known case of seizure disorder since early childhood and she also had difficulty in learning at school. She was diagnosed as tuberous sclerosis four years ago on the basis of epilepsy, facial angiofibromas (Figure 1), hypomelanotic macules, cortical tubers and multiple subependymal nodular lesions in MRI of brain (Figure 2). Since last two years she was on a stable dose of two anti-epileptic drugs (valproate sodium and topiramate). She did not have any convulsion in last 6 months before this admission.

She was dyspneic at rest and looked pale. Her respiratory rate was 48/min. Pulse rate and blood pressure were 120/min and 130/80mmHg, respectively. Auscultation of respiratory system revealed normal vesicular breath sound bilaterally. Cardiac auscultation was also within normal limits. Oxygen saturation in pulse oxymeter was 95% in room air. Arterial blood gas analysis showed PO₂ 98 mmHg, PCO₂ 10 mmHg, pH 7.16, HCO₃ 7.1 mmol/L with a base deficit of 24.6 mmol/L and anion gap of 23.4 mmol/L. Routine hemogram revealed anemia with normal leucocyte and platelet counts. Blood biochemistry revealed serum creatinine 4.3 mg/dL with normal electrolytes. Her estimated GFR (MDRD) was 11.6 ml/min/1.73m².

A thorough clinical examination revealed bilateral palpable enlarged kidneys, which was later confirmed by ultrasound and CT scan of abdomen. CT scan of abdomen (without contrast) revealed bilateral enlarged lobulated kidneys studded with multiple cysts with cortical thinning (Figure 3).

There was neither any family history of tuberous sclerosis nor any kind of kidney disease in family. Genetic analysis was not done as patient’s parents did not give consent for the same.

The patient was treated with intravenous sodium bicarbonate,
blood transfusion and hemodialysis. She is presently on maintenance hemodialysis and her antiepileptics were continued in adjusted dosage.

**Final Diagnosis:** Tuberous sclerosis with polycystic kidney disease of adult type (sporadic) with chronic renal failure.

**Discussion**

Renal involvement is not uncommon in tuberous sclerosis (TS) and includes angiomyolipomas (85.4%), cystic disease of kidney (44.8%) and rarely renal cell carcinoma (4.2%). Renal failure in TS is rare (1% of patients) though this is the second most common cause of mortality after the central nervous system causes. Both angiomyolipomas and cysts are more common and numerous when TSC-2 locus is affected rather than TSC-1.6

A little over thirty cases of tuberous sclerosis associated with polycystic kidney disease have been reported worldwide.6 Cystic disease in tuberous sclerosis is of two types – (1) simple renal cysts and (2) adult polycystic kidney disease/autosomal dominant polycystic kidney disease (ADPKD). Adult polycystic kidney disease is a different genetic disorder from TS, occurs due to mutation of PKD-1 gene in chromosome 16 (85%) and PKD-2 gene in chromosome 4 (15%). About 90% of APKD cases are autosomal dominant and the rest are due to spontaneous mutation of either of these two genes.9 Renal cysts in ADPKD gradually increase in number and size, ultimately causing renal failure. Molecular analysis has shown both TSC2 and PKD1 genes lie immediately adjacent to one another on chromosome 16. ADPKD may occur with TS when there is a large deletion involving PKD-1 and TSC-2 genes. This is known as TSC-2/PKD-1 contiguous gene syndrome. This syndrome is known to occur in 2% of TS patients.10 Sampson et al showed constitutional deletion of both TSC-2 and PKD-1 was associated with severe renal cystic disease which was radiologically and morphologically similar with ADPKD.3

A baseline renal ultrasound (USG) before 5 years of age and repeat USG every 2–3 years, has been recommended to detect renal manifestations of TS early. If angiomyolipomas or cysts are observed, yearly USG follow-ups are needed.6 This patient fulfilled criteria for tuberous sclerosis.4 Enlarged kidneys studded with cysts in imaging and her age of presentation of renal failure were consistent with adult type polycystic kidney disease/ADPKD, though there was no family history of polycystic kidney disease. Because of the rarity of this syndrome we report this case. Also this case emphasizes the importance of USG screening of kidneys in patients with TS to avoid late complications of chronic kidney disease.

**References**


