Ped Urol Case Rep 2015;2(1):1-6 DOI: 10.14534/PUCR.201518285

PUCR
Ped Urol Case Rep

PEDIATRIC UROLOGY CASE REPORTS

ISSN: 2148–2969

Journal homepage: http://www.pediatricurologycasereports.com

Tuberous sclerosis with bilateral renal cell carcinoma in a child: A case report

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Abstract Tuberous sclerosis complex (TCS) is an autosomal dominant disease which comes under a group of diseases known as neurocutaneous syndrome. Incidence of TCS is around 1 in 6000. The clinical triad of papular facial nevus, seizures and mental retardation is found in less than 50% of the patients. Renal lesions in TCS commonly consist of simple renal cyst and angiomyolipomas. Renal cell carcinoma though rarely associated with tuberous sclerosis may be its significant manifestations. We report a case of TCS with bilateral renal cell carcinoma in a 12 year old child with classical radiological and clinical signs.

Key words Tuberous sclerosis complex; renal cell carcinoma; children; tuberin; hamartin.

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Accepted for publication: 2 December 2014

INTRODUCTION

Tuberous sclerosis complex (TSC), also known as epiloia or Bourneville–Pringle disease, is a neurocutaneous syndrome characterized by abnormalities of both the integumentary system and the central nervous system [1,2]. TSC is a heterogeneous disease with a wide clinical spectrum varying from severe mental retardation and incapacitating seizures to normal intelligence and a lack of seizures, often within the same family [3]. The disease affects nearly every organ system, other than skin and brain, including the

Cite this article as: Choudhuri S, Mishra J, Singh GP, Hota D. Tuberous sclerosis with bilateral renal cell carcinoma in a child: A case report. Ped Urol Case Rep 2015;2(1):1-6.

heart, kidneys, eyes, lungs, and bones [4–6]. The kidney is affected in approximately 80% to 85% of the patients with TSC [7,8]. The renal events in TSC include angiomyolipoma, simple and complex cysts, and renal epithelial neoplasms, including renal cell carcinoma (RCC) [9]. However, RCC that is associated with TSC is rarely found in children [10,11]. Here, we report the case of a 12-year-old male with TSC in whom the bilateral RCC was diagnosed at a young age.

CASE REPORT

A 12-year-old boy presented with bilateral flank pain with a history of seizures. A clinical examination of the patient revealed an adenoma sebaceum on the face (Fig. 1).

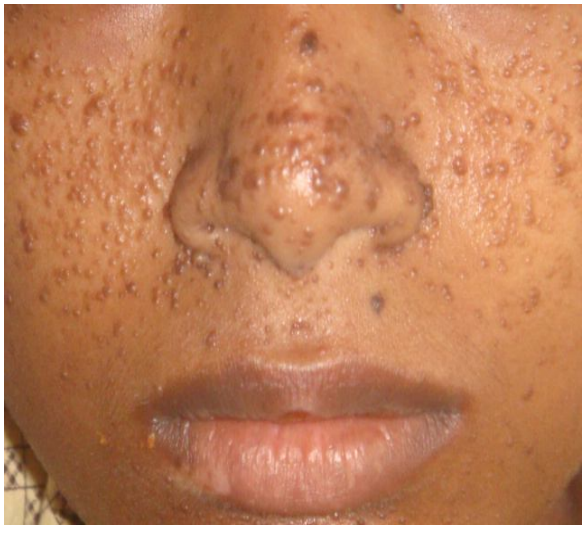

Fig.1. Adenoma sebaceum on the face.

He was mentally retarded. An ultrasonography of the abdomen showed the presence of a mixed echogenic mass with cystic, solid components and areas of fat density arising from the upper pole of both kidneys. An abdominal computed tomography (CT) showed a large heterodense lesion with an inhomogeneous enhancement arising from the upper pole of both kidneys (Fig. 2). A non-contrast brain CT revealed subependymal calcified nodules (Fig. 3). We did a left radical nephrectomy with a right nephron, sparing surgery separately on two occasions. The patient recovered uneventfully with a baseline creatinine of 1.2mg/dl. The pathology of the bilateral kidney showed RCC.

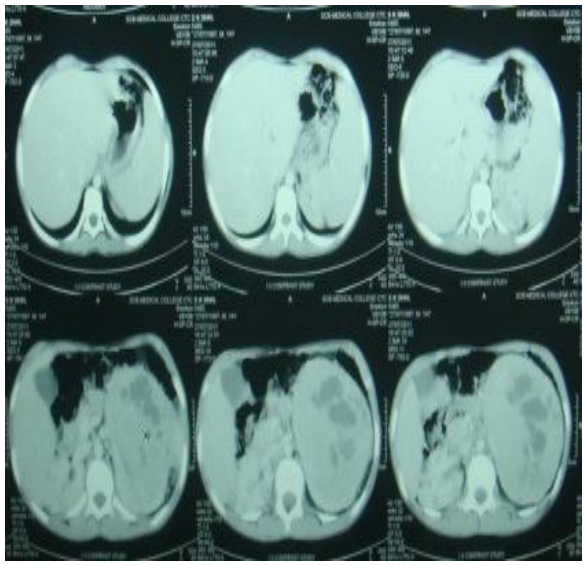

Fig. 2. Abdominal CT shows heterodense lesion involving bilateral kidney.

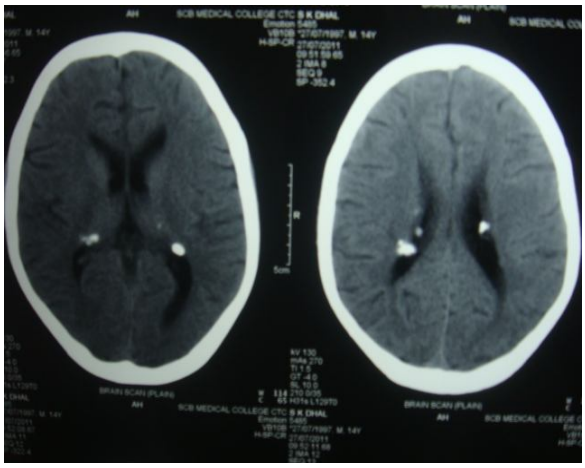

Fig. 3. Noncontrast brain CT shows multiple calcified subependymal nodules.

DISCUSSION

TSC is an autosomal dominant multi-system disorder characterized by the development of non-malignant tumors (hamartomas) in various organs. The estimated birth incidence is 1 in 6000, and ~1 million people worldwide are affected [12]. The renal involvement has a critical importance on the consequences of TSC because of the deadly progression of chronic kidney disease. Additionally, the most frequent cause of death in patients with TSC involves the central nervous system or the pulmonary system. The renal lesions are the second cause of death. Only recently, the renal complications have been considered as the leading cause of death in patients with TSC [13]. Rakowski et al. [14] reported that the percentages of the renal manifestations observed in the patients with TSC are angiomyolipomas at 85.4%, cysts at 44.8%, and RCC at 4.2%. The renal carcinomas in patients with TSC occur at an average age of 28 years [15], which is 25 years younger than the average age of renal carcinoma in the general population. There are many reports indicating renal carcinoma in children with TSC [15,16]. It may even occur in infancy [17]. Studies have suggested that 80% of the children with TSC have renal lesions by the age of 10.5 years old. The renal tumors may be single, multiple, or bilateral [16,18]. The patients with RCC may present with symptoms, such as an abdominal mass, abdominal pain, hematuria, and hypertension [19]. RCC can be difficult to distinguish radiologically from the angiomyolipomas that lack a lipomatous component. In this case, the study of immunoreactivity with the monoclonal antibodies may be useful. Human melanoma black 45 is characteristic for TSC-associated angiomyolipomas and lymphangioleiomyomatosis. Cytokeratin antibodies are typical for RCC [9,20].

There are currently no specific approaches for the treatment of TSC patients with small renal lesions. These small lesions in the majority of the patients are found to represent benign angiomyolipomas. An improved diagnostic imaging of angiomyolipomas may lead to less

unnecessary surgical interventions [21]. Conservative renal surgery is chosen to spare as many nephrons as possible, and a partial nephrectomy is recommended [16]. We did a left radical nephrectomy with a right nephron, sparing surgery separately in two occasions. The patient recovered uneventfully with a baseline creatinine of 1.2mg/dl.

The exact prognosis of TSC-associated RCC, relative to RCC in the general population, is unknown. The overall prognosis of TSC is poor, and about 75% of the cases die of complications of the renal system by age 20 [22]. In the largest published study of 49 pediatric patients with RCC, Selle et al. [11] observed considerable differences in the adult RCC in the stage distribution and outcome, probably caused by the differences in the biology of the tumors and the patients. With the follow-up ranging from 2 to 10 years, Washecka and Hanna [15] found that 12 of the 16 TSC patients with RCC reported in the literature were alive without disease. However, a subsequent review of the adult TSC patients described a much more aggressive clinical course with 4 of the 6 RCC patients dying of the disease [9]. A distant metastasis is rarely found [16].

Our case presented with classic signs of TSC. However, there is a rare combination associated with the TSC due to the involvement of a bilateral RCC in a 12-year-old boy. Additionally, the bilateral renal involvement in patients with TSC has a critical importance because of the fatal development of chronic kidney disease. The serial screening tests in the children with TSC is essential for the early diagnosis of RCC. Sparing surgery as much as possible in these patients is important.

Acknowledgements

The author(s) declare that they have no competing interests and financial support.

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