

Rare Presentation of Angiomyolipoma and Renal Cell Carcinoma in a Young Male Child with Tuberous Sclerosis - A Case Report and Review of Literature

Sibi Chakravarthi¹, Hariharasudhan Sekar², Ramesh Babu³, Sandhya Sundaram⁴

¹Resident, Department of Urology, Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India,

²Associate Professor, Department of Urology, Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu India,

³Professor, Department of Urology & Renal Transplantation, Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India, ⁴Professor and Head, Department of Pathology, Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India

Abstract

Tuberous sclerosis complex commonly involves renal angiomyolipoma (AML). We report synchronous primary renal neoplasm's in an 8-year-old male tuberous sclerosis patient. He presented with hematuria and was found to have a lesion of mixed attenuation in the interpolar region of left kidney on computed tomography. Left radical nephrectomy revealed a 4.4 cm × 4 cm × 3.2 cm circumscribed gray to yellow, soft to firm lesion with solid and cystic areas. Careful examination also revealed a 0.5 cm × 0.2 cm × 0.2 cm gray-white lesion in upper pole. On microscopy, the larger lesion was reported as Fuhrman Grade 2 - pT1b pNxcM0 clear cell variant of renal cell carcinoma (RCC) and smaller lesion as AML. By immunohistochemistry, RCC was CD10 positive, and HMB 45 negative whereas AML was positive for HMB 45 and negative for CD10.

Key words: Angiomyolipoma, Child, Nephrectomy, Renal cell carcinoma, Tuberous sclerosis

INTRODUCTION

Tuberous sclerosis is an autosomal dominant disorder involving multiple organ systems with mutations in tuberous sclerosis complex 1 (TSC1) or TSC2 occupying chromosome 9q34 and chromosome 16p13, respectively. TSC1 codes for hamartin and TSC2 for tuberin, the complex of which functions as tumor suppressor gene through mTOR inhibition.¹ The simultaneous occurrence of angiomyolipoma (AML) with renal cell carcinoma (RCC) is uncommon, especially in a young male child. Clear cell variant of RCC is the most common renal cell neoplasm. The earlier classification of AML as hamartomatous lesion has been changed to neoplasm in the recent years. Studies

found that cysts, renal epithelial neoplasm, especially RCC and AML were most commonly associated with tuberous sclerosis.²

CASE REPORT

An 8-year-old male tuberous sclerosis patient presented with hematuria. Ultrasonography kidneys, ureters, and bladder revealed multiple cortical cysts in the right kidney with a space occupying lesion involving the middle segment of left kidney. Computed tomography scan showed a mass lesion of mixed attenuation with focal hypoattenuation in the interpolar region of left kidney (Figure 1). Left radical nephrectomy revealed a 4.4 cm × 4 cm × 3.2 cm well circumscribed grayish-yellow soft to firm lesion with solid and cystic areas. Careful examination also revealed a small 0.5 cm × 0.2 cm × 0.2 cm grayish-white solid firm lesion 2 cm away from primary lesion in the upper pole with a nearby cortical cyst (Figure 2). The larger lesion was reported as Fuhrman Grade 2 - pT1b pNx cM0 clear cell RCC and smaller lesion as AML (Figure 2). RCC was CD10,

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Corresponding Author: Dr. Ramesh Babu, Department of Urology & Renal Transplantation, Sri Ramachandra Medical College, Chennai - 600 116, Tamil Nadu, India. Phone: +91-9840359062. E-mail: drrameshbabu1@gmail.com

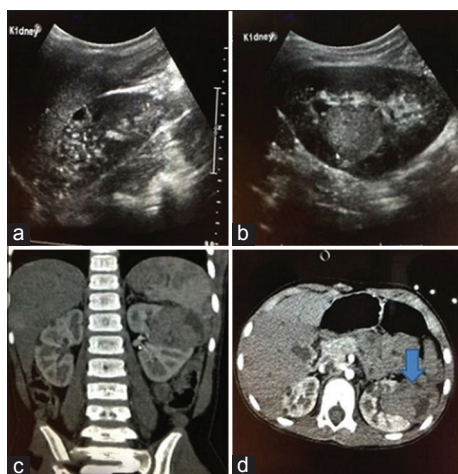


Figure 1: Ultrasonography (USG) and computed tomography (CT) showing an interpolar mass in left kidney. (a) USG – Right kidney. (b) USG – Left kidney. (c) CT – Coronal view. (d) CT – Axial view

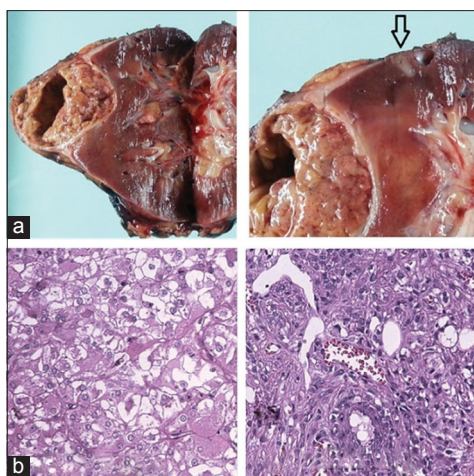


Figure 2: (a) Gross showing large solid mass lesion and small multiple yellowish lesion. (b) Large lesion showing features of clear cell renal cell carcinoma and small lesions showing features of angiomyolipoma

CA IX positive and negative for HMB 45 whereas AML was HMB 45 positive and CD10, CA IX negative (Figure 3).

DISCUSSION

Tuberous sclerosis has a incidence rate of 1 in 6000¹ 80% of TS patients develop renal lesions of which AML is the most common followed by cysts and RCC.^{1,3,4} AML develops very early in the patients with tuberous sclerosis. In addition to these identifiable macroscopic diseases, renal tissue that is radiologically normal can also have microscopic AML.⁵ Clear cell variant of RCC was found to be the most common epithelial renal neoplasm in tuberous sclerosis patients.⁶ When compared to sporadic RCCs, those associated with tuberous sclerosis tend to be

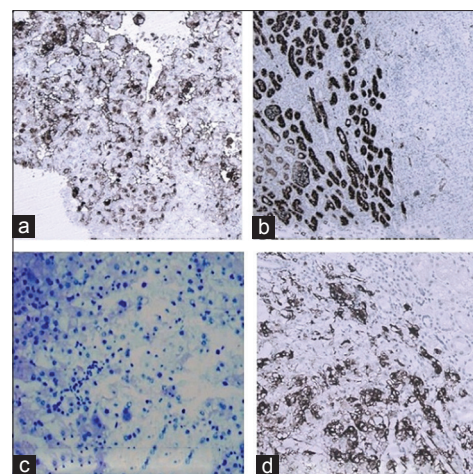


Figure 3: Immunohistochemistry - clear cell renal cell carcinoma (RCC) positive for RCC (a) RCC CD10 (x100), (b) RCC HMB 45 (x100), and angiomyolipoma (AML) positive for HMB 45 (c) AML CD10 (x100), (d) AML HMB 45 (x100)

multiple, affecting younger age with increased female: male ratio. Renal lesions are now the second most common cause of death following central nervous system lesions. Jun *et al.* reported three primary renal neoplasms in a 62-year-old male which were two RCC (chromophobe and clear cell variants) and one epithelioid AML.⁷ According to Jimenez *et al.* who evaluated 11 cases of tuberous sclerosis with AML and renal lesions, clear cell RCC was present in six cases with increased female: male ratio. Clear cell RCCs were HMB 45 negative and AML were HMB 45 positive.⁶ Guo *et al.* studied RCC in 18 tuberous sclerosis patients and found that RCCs are often multiple with female preponderance, younger age at diagnosis, and AML association in 17 patients.⁸ Even though multiple synchronous renal tumors have been reported in non-tuberous sclerosis patient,⁹ Bjornsson *et al.* found that tuberous sclerosis associated RCC occurs much earlier than sporadic RCC and was associated with TSC tumor suppressor gene.² In 2009, Khallouk *et al.* reported a 35-year-old tuberous sclerosis patient with AML and RCC in both the kidneys stressing the importance of radical surgery when malignancy is highly suspected.⁴ Regular follow-up of the other kidney is essential to monitor the occurrence of AML or RCC. AMLs are known for their bilaterality and spontaneous bleeding tendencies which require careful follow-up as therapy by embolisation may prevent nephrectomy or chronic kidney disease which is known to occur in tuberous sclerosis patients.¹⁰

Points to Ponder

- Concurrent presence of AML and RCC is a very rare occurrence in a young male child with tuberous sclerosis
- A meticulous and systematic examination of the kidney tissue is mandatory to rule out multiple lesions

- Immunohistochemistry proves useful in delineating these varied lesions.

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