The Identification of a Girl with Tuberous Sclerosis and an Unexpected Large Sized Renal Angiomyolipoma: A Case Report and Literature Review Study

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Abstract

Background: The TSC1 mutated gene, hamartin, and the TSC2 gene, tuberin, cause tuberous sclerosis, the autosomal dominant tumor syndrome. The angiomyolipoma of the kidney is a benign tumor that often happens along with tuberous sclerosis. Large renal angiomyolipoma’s associated with tuberous sclerosis are in danger of fatal hemorrhage. This study reported a case with an unexpected large size of renal angiomyolipoma’s associated with tuberous sclerosis.

Case Presentation: We report a girl aged 5 years and 9 months old with tuberous sclerosis who referred to nephrology clinic due to abdominal pain. Physical examination revealed a large mass in the right flank. Kidney ultrasound reported a large mass with approximate size of 90 mm × 60 mm in the right kidney, and abdominal CT scan also showed a non-hemogenic solid mass in the right kidney with size of 91 mm × 68 mm × 67 mm, was highly suspected for Wilms’ tumor. Since the large size of lesion and subsequent suspension for malignant tumor, partial nephrectomy was performed and through kidney biopsy an unexpected angiomyolipoma was diagnosed.

Conclusion: Considering extended studies in various populations with tuberous sclerosis and renal angiomyolipoma, this case is challenging and intriguing since she was the youngest one among patients with necessity of nephrectomy due to the large size of lesion and radiologic findings suggestive of Wilms’ tumor.

Keywords: Tuberous sclerosis; Renal angiomyolipoma; Children; Nephrectomy

Introduction

Tuberous Sclerosis (TS) is an uncommon neurocutaneous and genetic disease, arises from inactivating mutations of either TSC1 (chromosome locus 9q34.3) or TSC2 (16p13.3) genes which encode hamartin and tuberin, respectively. These proteins serve as tumor suppressors by forming complexes that controls proliferation of cells [1]. Benign tumors in patients with TS are identified in various organs including retina, lungs, heart, brain, skin and kidney [1,2]. In affected infants, cardiac rhabdomyomas, hamartomas, epilepsy and skin lesions are the most common symptoms [2,3]. The most frequent manifestations in kidneys are unilateral or bilateral renal angiomyolipoma’s, which occur in a majority of patients (34% to 80%) [4,5]. Renal angiomyolipoma’s usually appear later in life, and can associate with fatal bleeding, and hypovolemic shock [2,4,6,7].

Although renal angiomyolipoma’s usually consist of adipocytes, irregular vasculature, and smooth muscle cells, the proportions of each parts of tumor can differ in patients [8]. Renal angiomyolipoma’s with a size more than 40 mm can result in vascular aneurysm and fatal hemorrhage. Vascularity of the lesion can rise with growth of the size [4,7]. Complications are usually treated with angiographic embolization or surgical removal such as radical nephrectomy [9]. This study reported a case with an unexpected large size of renal angiomyolipoma’s (90 mm × 60 mm) associated with Tuberous Sclerosis. It was so interesting that despite large size of tumor, there were no evidences of bleeding, and kidney ultrasound and abdominal CT scan findings were representative of Wilms’ tumor.
Case Presentation

The patient was an Iranian girl aged 5 years and 9 months old and referred to nephrology clinic due to abdominal pain and a huge right flank mass. At the age of 9 months, following recurrent seizures accompanied by skin lesions the diagnosis of TS was made for this patient. Her weight was 15 kg (Z score: -2) and systolic blood pressure at first visit was 100 mmHg with no detectable diastolic blood pressure. Pulse rates were normal and there were no evidences of internal hemorrhage.

Although she was old enough (age >5 years), she had fecal and urinary incontinence and because of intellectual disability she was unable to speak. Physical examination determined different Café au lait macules and angiofibroma’s lesions on the face, limbs, trunk and borders of the fingers, and Shagreen patch in the region of lumbar vertebrates. She had a history of repetitive hand surgeries for removal of fingers lesions which restricted her movements. Physical examination of abdomen revealed a huge mobile mass in the right flank without tenderness.

Imaging test

Kidney ultrasound findings reported a large mass with a size of 90 mm × 60 mm in the right kidney, very closely resembled a Wilms’ tumor. Abdominal CT scan with intravenous contrast injection defined a non-hemogenic solid mass in the right kidney with a size of 91 mm × 68 mm × 67 mm, highly suspected to Wilms’ tumor. Additionally, various non-hemogenic lesions in middle line, spleen and the left kidney which are undifferentiated from normal parenchyma. No abdominal lymphadenopathy.

Discussion

Tuberous Sclerosis (TS) is an autosomal dominant disease, most commonly caused by TSC1 or TSC2 genes mutation and identified by benign hamartomas in about 34% to 80% of TS patients with renal angiomyolipoma [10]. It is a rare genetic multisystem disorder, presented by benign tumors which can develop in any organ system. Its prevalence in live-birth is 1 in 5,800 births and prevalence of 1 in 12,500 had been reported in total population [11]. Renal angiomyolipoma’s are benign vascular, smooth muscle tumors and are typically asymptomatic but may induce flank or abdominal pain, hematuria, abdominal mass or distension, fever, nausea, vomiting, or progressive loss of kidney function. Death due to retroperitoneal hemorrhage (Wunderlich syndrome) have been reported in cases with renal angiomyolipoma’s [12].

Growth of angiomyolipoma associated with TSC is faster than those associated with sporadic angiomyolipoma [13]. Angiomyolipoma’s with a diameter >3.5 cm have the significant risk for severe hemorrhage and selective embolization should be considered as first treatment [14]. Renal angiomyolipoma lesions are classified as small (<4 cm), medium (4 cm to 8 cm) or large (>8 cm) based on the single largest lesion in each kidney. The severity of complications is mostly related to the sizes of lesions. The mean size of 85 mm (35 mm to 200 mm) and 78 mm (45 mm to 180 mm) renal angiomyolipoma’s (sporadic or associated with TSC) referred to selective embolization, have been reported in two studies [15,16] and the individual risk of bleeding appears moderate, even in TS patients (around 6%) [5].

It has been reported that tumors sized >6 cm are at higher risk of bleeding [17], while another study showed that tumors with size of <8 cm tend to be asymptomatic [18]. Similar to our case, a recent study reported asymptomatic giant renal angiomyolipoma’s (290 mm × 215 mm × 120 mm) in a patient [19].

In a recently extended study among patients with TS, 1070 of 2065 enrolled cases (51.8%) had a history of renal angiomyolipoma. Among patients aged <18 years, 34.3% had angiomyolipoma with the
size of >3 cm. Totally 498 cases with renal angiomyolipoma (46.5%) needed to treatment, including 11/134 (8.2%) patients who were at age of 5 to 9 years (likely the age range of our case). Nephrectomy was a rare modality used for treatment in cases <18 years (5/498 cases; 1%), while in those aged >18 years, 57/572 patients (9.95%) underwent nephrectomy. The youngest age for nephrectomy was >9 years [20].

**Conclusion**

Our case is interesting since presents a girl with TS and large renal angiomyolipoma which mimicking the Wilms’ tumor findings in the imaging studies (renal ultrasound and abdominal CT scan). Despite large size of tumor there was no sign of bleeding. Patient underwent nephrectomy because of the large sized lesion and suspicion to malignant tumor. Nephrectomy rarely needed in children with TS who were at age of <18 years (1%). Considering an extended study in a large population with TS and renal angiomyolipoma, our case had been the youngest one with indispensable nephrectomy.

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**References**