
Case Report

Tuberous Sclerosis With Bilateral Angiomyolipomas

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ABSTRACT

A case of a 30-year-old female with tuberous sclerosis, a genetic, rare, variably expressed disease is described in the present case report. Clinical symptoms were unexplained fever, pain in lumber areas and gross hematuria. Computed tomography scan of the abdomen revealed enlarged, heterogeneous kidneys, with low density tumors corresponding to angiomyolipomas. Computed tomography scan of the chest showed bilateral, diffuse, small thin-walled cysts in the lungs

characteristic for pulmonary lymphangiomyomatosis. CT scan of the brain revealed subependymal calcifications. These three diagnostic features are rarely exhibited in a single patient. Bilateral renal angiomyolipomas and pulmonary lymphangiomyomatosis are some presentations of tuberous sclerosis and the coexistence of both conditions may cause devastating morbidity and mortality.

INTRODUCTION

Tuberous sclerosis (TS) is an autosomal dominant disorder characterized by the formation of hamartomatous lesions in multiple organs, with a birth incidence of around one in 10,000. However, with more sensitive screening, internationally reported prevalence may be as high as one in 6,000. The disease results from mutations in one of two genes, TSC1 (encoding the protein hamartin) or TSC2 (encoding the protein tuberin), which have an important role in the regulation of cell proliferation and differentiation¹. Angiofibromas on the face, renal angiomyolipomas, and pulmonary lymphangiomyomatosis are some of the major features of this disease. Diagnosis is usually established on the basis of physical examination, radiological findings or both, and the presentation of the disease varies substantially. The classical clinical triad of popular facial nevus, seizures and mental retardation is reported in 50% of the patients². We report a case of a female patient with TS presenting with typical skin lesions on face, long standing history of seizures and bilateral angiomyolipomas.

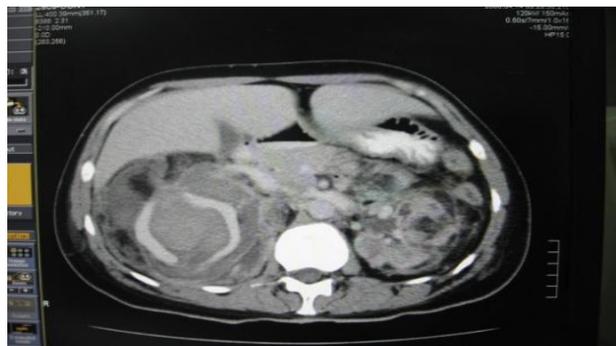
CASE REPORT

A 30-year-old woman was admitted to the hospital

with a 2-month history of un-explained fever, pain in both lumber regions and gross hematuria for 15 days. She had history of epileptic seizures, angiofibromas and skin discoloration on the regions of the face and nose since her childhood. Her parents and 3 brothers were alive and healthy. There was history of mental retardation in 1st degree relatives. On examination, the patient appeared pale, and her vital signs included a blood pressure of 140/90 mmHg, a heart rate of 90 bpm and temperature 100°F. Auscultation of the chest revealed normal vesicular breathing and normal heart sounds. Her abdomen was tense and painful to palpation, but there were no signs of peritoneal irritation. There was a palpable mass 15 x 15 cm occupying the right upper abdomen. Laboratory evaluation revealed a hemoglobin level of 10.0 g/dL, platelet count of $410 \times 10^3/\text{mm}^3$, WBC count was 10,000/ml, serum creatinine was 1.2 mg/dL, urea 68 mg/dL, sodium 140 mEq/L and potassium 4.3mEq/L. Her LFTs and coagulation profile were within normal limits. The urinalysis revealed 15-20 pus cells/HPF, field full of RBCs and proteins ++. Her abdominal ultrasonography revealed bilateral grossly enlarged kidneys with solid and cystic

areas. Her abdominal computed tomography scan demonstrated enlarged, heterogeneous kidneys, with multiple fat-density areas corresponding to renal angiomyolipomas. In this background, there was a 5x7 cm cystic area with high density tubular structure at upper pole of right kidney with multiple concentric rings (Figures-1), large aneurysm related to angiomyolipoma.

Figure-1
Plain CT scan of abdomen showing B/L enlarged kidneys with fat density areas



Plain computed tomography of the chest revealed cystic formations in the lungs, bilaterally which were consistent with lymphangioleiomyomatosis of TS (Figure-2).

Figure-2
Plain CT scan of chest showing bilateral multiple cyst formations in the lungs (arrows), lymphangioleiomyomatosis



Her plain CT scan of brain revealed multiple calcified areas in sub-ependymal areas and regions of falx, again suggestive of tuberous sclerosis (Figure-3).

Figure-3
Plain CT brain showing calcified areas in falx and sub-ependymal areas



DISCUSSION

The benign, non-invasive lesions of tuberous sclerosis can appear in any organ like the brain, heart, skin, eyes, kidneys, lung, and liver. Therefore, TS has a wide clinical spectrum. The diagnosis of definitive TS is based on specific clinical features and requires the presence of two major criteria, or one major and two minor³. Some of the major clinical features include pulmonary lymphangio-leiomyomatosis, renal angio-myolipomata, Shagreen patches, peri-ungual fibromas, cardiac rhabdomyomas and facial angiofibroma. The most frequent cause of death in patients with TS is renal complication. Multifocal, bilateral angiomyolipomas are found in about 70-90% of adult patients, and the prevalence increases with age, being less frequent in children. These lesions are more often prevalent in women, suggesting a hormonal component to the tumor growth⁴. The angiomyolipomas are composed of varying amounts of mature adipose tissue, smooth muscle and abnormal blood vessels. The demonstration of fat in the tumorous lesions with negative attenuation in CT scan is pathognomonic of angiomyolipoma. Thin-section unenhanced CT is essential to visualize the fat content of angiomyolipoma⁵. Progressive enlargement of tumors and hemorrhage into the lesion can result in flank pain, a palpable tender mass and gross or microscopic hematuria

and interfere with renal function. Tumors larger than 4 cm in diameter have a greater risk of spontaneous or traumatic rupture resulting in hemorrhagic complications, which is the most common cause of death in patients with TS. Some patients with TS carry a contiguous germline deletion that affects both the **TSC2** gene and the adjacent gene, polycystic kidney disease type 1 (**PKD1**), resulting in a polycystic kidney phenotype that leads to early renal insufficiency. In our patient, the family history indicates that she inherited a germline mutation in the **TSC2** gene. Renal cell carcinoma can occur in approximately 2-3% of adults with TS⁶. Pulmonary LAM is a rare progressive disease that predominantly affects women of childbearing age. Estrogen is thought to play a role in disease progression since it does not present prior to menarche and only rarely after menopause, and is exceptionally rare in men. LAM probably affects 1-3% of patients with tuberous sclerosis. Although some articles report the occurrence of LAM in 1 to 3% of the patients with TS, it seems that this incidence is much higher. Recent article report an incidence ranging from 26 to 34%. It is characterized by alveolar smooth-muscle proliferation leading to air trapping, pulmonary hemorrhage and lymphatic extravasation, and cystic destruction of the normal lung parenchyma. Some of the manifestations are shortness of breath, coughing, chest pain, pneumothorax, chylous pleural effusions, hemoptysis, and eventually respiratory failure, but asymptomatic cases may occur. Pulmonary function tests can show an obstructive or restrictive pattern. Classical CT findings (diffuse, homogeneous, small thin-walled cysts) and compatible clinical history can be highly suggestive of LAM. It is extremely difficult to treat and the long-term prognosis is poor with the average duration of survival from the time of diagnosis near to 10 years. Treatment consists of supportive management. Hormonal therapy has been tried but without consistent success. Sirolimus (rapamycin) is being explored as another potential treatment, but additional trials will be needed to assess efficacy and potential side effects.

Cortical/subcortical tubers are a common radiographic manifestation of tuberous sclerosis. The typical appearance of a tuber on computed tomography (CT) is that of a hypodense.

lesion in a cortical/ subcortical location with or without focal gyral expansion. They may show calcification on CT in as many as 50% of cases and may also enhance⁷. The present case was a rare patient exhibiting a number of major diagnostic criteria including bilateral renal angio-myolipomas, sub-ependymal and cortical tubers, pulmonary LAM (lymphangio-leiomyomatosis), facial fibromas and Shagreen patches. She had mental retardation and seizures since childhood. The renal involvement became evident at the age of 30 years when she presented with hematuria. Luckily, the pulmonary involvement was not that advanced. She requires annual pulmonary-function testing which may be useful to monitor lung function and provide a measure of disease progression. Monitoring of renal lesions, by ultrasonography, CT, or magnetic resonance, is an essential issue in the management of TS.

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