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Huge Renal Cyst; Unusual Presentation of Tuberous Sclerosis in an Adult Patient

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Abstract: A twenty four years old unmarried female patient having complaints of abdominal distention and menstrual irregularities for 3 months, underwent ultrasound which revealed a large cyst in abdomen and pelvis which was suspected as an ovarian cyst. She presented to Radiology department of Sir Ganga Ram Hospital, Lahore for the request of CT Abdomen and pelvis with contrast. CT scan displayed a huge unilocular cyst arising from lower pole of right kidney occupying most of the abdomino-pelvic cavities. This cyst had mass effect, displacing adjacent abdominal structures to left side. Besides that, both kidneys also showed innumerable cysts and mixed attenuation small nodules which were presumed to be angiomyolipomas. Sections through lower lungs showed bilateral intra-parenchymal cysts. These features were in favor of Tuberous sclerosis complex. For confirmation, MRI Brain with contrast was performed which also revealed few subependymal lesions along bilateral lateral ventricles with multifocal white matter signal abnormalities involving internal capsules, right medial temporal and left high parietal lobes. All of these features meet the diagnostic criteria for labeling a patient with tuberous sclerosis, but in this patient the uniqueness lies in its unusual presentation as a massive renal cyst having pressure effects over surrounding structures.

Key words: Angiomylolipoma · Renal cyst · Tuberous sclerosis complex · Subependymal hamartoma

INTRODUCTION

Tuberous sclerosis (TS) is an autosomal dominant inherited neurocutaneous syndrome characterized by a variety of hamartomatous lesions in various organs. TS can affect both sexes and all ethnic groups. The estimated prevalence ranges from one in 6000 to one in 12 000 [1].

This disorder affects multiple organs i.e. skin, CNS, heart, kidneys, eyes and lungs [2]. Tuberous sclerosis was first described by Bourneville in 1880 and later on by Vogt in 1908. Mean age of diagnosis is 7.5 years and more than 81% patients are diagnosed up to 10 years of age [3]. Generally the classical triad seen in 29% of patients is mental retardation, seizures and cutaneous angiofibromas but 6% present with none of the three characteristics [1, 2]. Here we present a case report of a 24 year old female who had renal, brain and lung involvement due to Tuberous sclerosis complex having an unusually large renal cyst causing abdominal pain.

Case Report: A 24 year old unmarried female patient presented to the Radiology department of Sir Ganga Ram hospital , Lahore with the request of CT scan Abdomen and Pelvis, on 31st July 2017, having complaints of abdominal distention and menstrual irregularities for last 3 months. Her abdominal ultrasound showed a large cystic mass occupying abdomino-pelvic cavities, predominantly on right side. CT scan revealed a huge fluid density unilocular cyst occupying most of the abdomino-pelvic cavities centered on right side within lower pole of kidney, measuring 36x21x24cm, lesion had no intra-cystic enhancing or solid components. Significant mass effect was evident with marked displacement of bowel loops and mesentery contra-laterally along with elevation of liver. Residual upper pole of right kidney was identified in left iliac fossa measuring 5x3.4cm. Kidneys also contained numerous tiny cysts and mixed fat and soft tissue attenuation nodules, probably angiomyolipomas. Sections through visualized lungs displayed multiple intraparenchymal cysts bilaterally with subsegmental atelectasis in right lobe.

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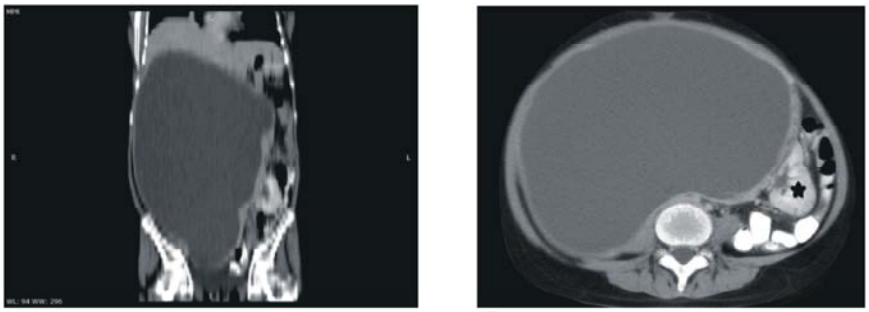
Above mentioned features were suggestive of Tuberous sclerosis and MRI Brain with contrast was performed for further confirmation. It revealed sub-ependymal lesions along bilateral lateral ventricles measuring up to 10mm in size with largest showing low T2WI signal suggesting calcification. Multifocal white matter signal abnormalities were also seen involving bilateral internal capsules, right medial temporal and left high parietal lobes. No mass effect or midline shift was obvious. No intra or extra axial mass lesion detected.

Based upon these findings, fulfilling the diagnostic criteria (Table 1), patient was labeled as a case of Tuberous sclerosis.



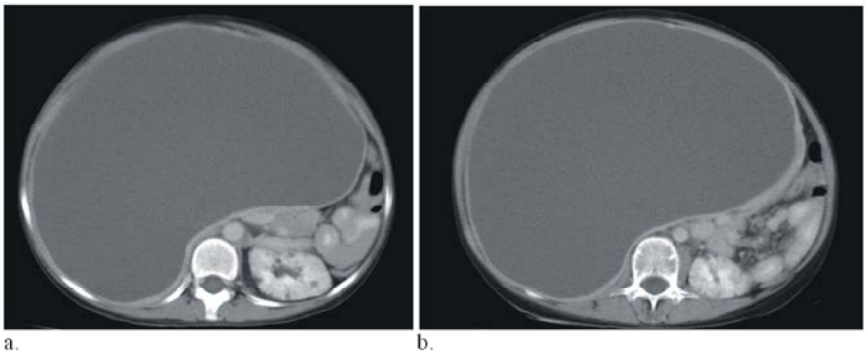
1. A 1B.

Image 1: Coronal (A) and axial (B) Contrast enhanced CT scan displays huge cyst replacing lower half of right kidney, displacing residual upper half to left iliac fossa (Dark star).

Table 1: Diagnostic Criteria for tuberous sclerosis [4]

Major features	Minor Features
1. Hypomelanotic macules (more or three, at least 5mm diameter)	1. Confetti skin lesions
2. Angiofibromas (more or three) or fibrous cephalic plaque	2. Dental enamel pits (more or three)
3. Ungual Fibromas (more or two)	3. Intraoral fibromas (more or two)
4. Shagreen Patch	4. Retinal achromic patch
5. Multiple retinal hamartomas	5. Multiple renal cysts
6. Cortical dysplasia	6. Non renal hamartomas
7. Subependymal Nodules	
8. Subependymal giant cell astrocytoma	
9. Cardiac rhabdomyoma	
10. Lymphangioleiomyomatosis	
11. Angiomyolipomas (more or two)	

Definite diagnosis: Two major features or one major feature with ≥2 minor features
Possible diagnosis: Either one major feature or ≥2 minor features



a. b.

Image 2, a & b: CECT abdomen parenchymal phase reveals mixed hypo and hyper dense renal parenchymal lesions in left kidney, indicative of angiomyolipomas. Similar lesion are also present in residual right kidney (Not shown here)

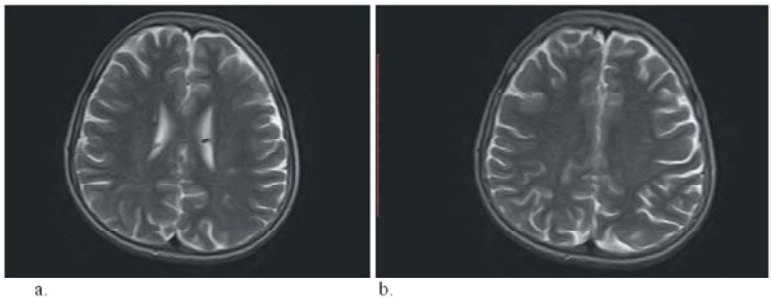


Image 3 a, & b: T2weighted images through brain demonstrate subependymal soft tissue and low intensity probably calcified lesions bilaterally besides cortical and subcortical white matter T2 bright lesions suggestive of hamartomas

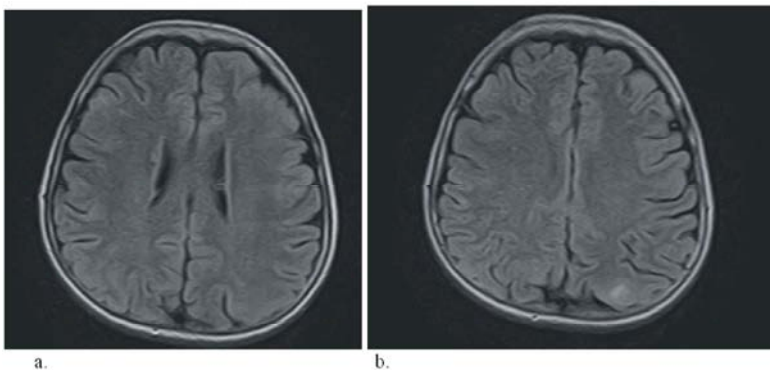


Image 4a & b: Axial FLAIR images display similar subependymal and white matter lesions as are visible in image 3

DISCUSSION

TS has been considered to be caused by mutations of two genes known as TSC1 and TSC2. Linkage analysis in multigenerational families and positional cloning were used to map these genes [4, 5]. The TSC1 gene consists of 23 exons and is transcribed into an 8.6-kb messenger RNA. It is located on the long arm of chromosome 9 (9q34) and encodes a 130-kDa protein called hamartin. The TSC2 gene consists of 41 exons and is distributed over 44 kbp of genomic DNA. It is situated on the short arm of chromosome 16 (16p13) and encodes a 200-kDa protein called tuberin. The location of the TSC2 gene is contiguous with the PKD1 gene, which can explain why multiple renal cysts are sometimes found in patients with TS [6]. TSC1 and TSC2 are tumor suppressor genes whose function is to help regulate cell growth and differentiation. If they are altered by mutation, disturbed control of cell growth results in formation of tumors throughout the body. A variety of mutations can occur in TS patients. The frequency of mutations in TSC2 is higher than in TSC1. There is some evidence from case series that mutations in TSC2 tend to result in more severe disease [7].

The proteins hamartin and tuberin interact with high affinity and coexist as a complex in cells in a variety of organs, including the kidneys, brain, lungs and pancreas [8]. Normally, direct phosphorylation or inactivation of tuberin regulates the Ras homologue expressed in brain (Rheb), which is a specific GTPase downstream of tuberin. If the functions of tuberin are altered, Rheb-GTP is excessively generated, resulting in enhanced stimulation of the mammalian target of rapamycin (mTOR), which plays an important role in the control of cell growth and proliferation. Although the precise role of hamartin is not clearly known, it also has an influence on mTOR activation [8].

Renal disease is a major cause of mortality in TSC. Lifelong surveillance and early intervention is warranted. SUDEP is also an important cause of mortality. Patients with learning disabilities are at significantly greater risk of early mortality and this implies the need for greater vigilance for TSC-related complications in this group. Female patients are vulnerable to pulmonary and renal disease. Pancreatic lesions are a rare but potentially treatable cause of mortality [9].

Skin manifestations are hypopigemnted macules, facial angiofibromas (80-90%) Shagreen patches (80%)

and ungual fibromas (15-50%). CNS involvement is seen in 90-95% of cases, most patients (75-80%) presenting with myoclonic seizures in first two years of life. Lesions include subependymal nodules, cortical tubers, subependymal giant cell astrocytoma (SEGA) and white matter lesions. Cortical tubers and subependymal nodules are more prevalent almost in 95-100% of patients. MRI is much more sensitive than CT in detection of CNS involvement. Cardiac manifestations include formation of rhabdomyoma (Benign skeletal muscle tumor). In 75% of patients it occurs before age of 1 year and can occur in fetal life as well. However many show regression of tumor spontaneously before age of 4 years. Pulmonary manifestations include lymphangio-leiomyomatosis and multifocal micronodular pneumocyte hyperplasia. It occurs in 1-2.3% of patients with tuberous sclerosis particularly in females (26-39%). Renal involvement is seen in the form of angiomyolipomas (AML), renal cysts and development of renal cell carcinoma (RCC). AML is more common (55-75%) than renal cysts. It is benign tumor of kidney composed of abnormal vessels, immature smooth muscles and fat cells. With the help of CT, it is very easy to diagnose AML because of detection of fat within tumor [10, 11].

Tuberous sclerosis has a wide spectrum of radiological manifestations ranging from CNS involvement, renal AML and cardiac rhabdomyoma. Identification of various imaging features is essential to suspect and initiate prompt search for involvement of other organ systems, even if clinical signs are not obvious.

CONCLUSION

The reported case is unique in this way that most of the patients with Tuberous sclerosis present in infancy and childhood up to 10 years of age with symptoms of mental retardation, seizures and facial angiofibromas, but in our case, presenting symptom was abdominal distention at the age of twenty four with no history of seizures or mental retardation.

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