Case Report

Tuberous sclerosis diagnosed in adult age

Alper Alp[1], Sibel Demiral Sezer[2], Mehmet Tanrisev[3]

SUMMARY

Tuberous sclerosis (Bourneville Disease, Vogt triad) is an autosomal dominant hereditary disease characterized by hamartomas. It can affect all body organs, but is most commonly seen on the skin, brain, eyes, lungs, heart and kidney. We describe the successful management of a case of forty two years old women who presented to us with complaints of nausea, vomiting, bilateral flank pain.

KEY WORDS: Tuberous sclerosis, Shagreen patch, Hamartomas, Bilateral angiomyolipomas.

Pak J Med Sci January - March 2011 Vol. 27 No. 1 208-211

How to cite this article:

Alp A, Sezer SD, Tanrisev M. Tuberous sclerosis diagnosed in adult age. Pak J Med Sci 2011;27(1):208-211

INTRODUCTION

Tuberous sclerosis is generally diagnosed during childhood by neurologic and dermatologic findings.[1] Tuberous sclerosis arises as a result of mutations in the TSC1 (9q34) and TSC2 (16p13) genes, which code for the proteins hamartin and tuberin.[2] There is an equal distribution in both genders. In children, the disease may present with autism, epilepsy, and cardiac failure whereas in adults it usually presents with kidney failure, and pulmonary and dermatologic manifestations.

CASE PRESENTATION

A 42-year-old woman presented to the local health center in March 2007 with complaints of nausea, vomiting, bilateral flank pain and urine discoloration. An abdominal ultrasonography (USG) was performed following the detection of an abdominal mass in physical examination. Both kidneys appeared to be larger than normal, hyperechogenic lesions of various sizes were observed, and an appearance consistent with hemangioma was identified in the liver. Therefore, a computed tomography (CT) scan of the whole abdomen was performed. Following identification of bilateral kidney lesions on the abdominal CT, the patient was referred to our hospital for further examination.

She was hospitalized in our internal medicine service. The patient had a history of childhood convulsion. After receiving anticonvulsant treatment for a short period of time, the medication was discontinued. There was no previous specific diagnosis. The physical examination demonstrated that the patient was conscious, cooperative and oriented. Her arterial blood pressure was 120/70 mmHg, pulse was 76/min, height was 160cm and weight was 55 kg. There were numerous adenoma sebaseum on her face (Fig-1), periungual fibromas (without trauma anamnesis) around the toenails (Fig-2), forehead plaques (Fig-3), Shagreen patches around the lumbar region, hypomelanotic macules on the back (Fig-4). In abdominal USG, a mass lesion of 190 mm on the long axis of the liver and 10 x 8 cm in diameter that was consistent with hemangioma was identified in the right posterior lobe; hyperechogenic lesions of 18 x 8 cm in diameter on the right and 18 x 15 cm on the left kidney regions were also identified, together with multiple septated cysts of 38 mm in the right ovary and 37 mm in the left ovary. Thereafter, an abdominal CT scan was performed, and heterogenous solid regions with a

1. Dr. Alper Alp,
2. Dr. Sibel Demiral Sezer,
3. Dr. Mehmet Tanrisev,
1-3: Tepecik Education and Research Hospital, Yenisehir / Izmir, Turkey.

Correspondence:

Dr. Alper Alp,
Tepecik Education and Research Hospital
Yenisehir / Izmir,
Turkey.
E-mail: alperalp20@hotmail.com

* Received for Publication: October 7, 2010

* Accepted: November 3, 2010

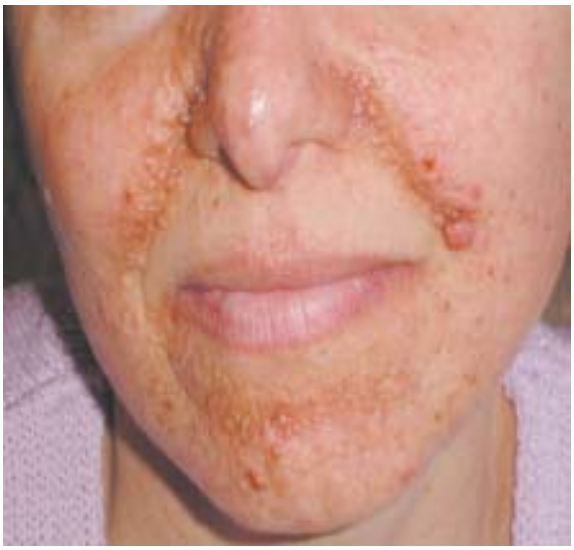

Fig-1: Facial adenoma sebaseum.

size of 18 x 7.5 x 7.5 cm in the right kidney and 18 x 15 x 10 cm in the left kidney, which were consistent with bilateral angiomyolipoma, were identified (Fig-5). The diagnosis of tuberous sclerosis was achieved following verification of calcified subependymal hamartomas in brain CT (Fig-6), tuber formations related to tuberous sclerosis in the subependymal region in cranial magnetic resonance imaging (MRI), and bilateral hamartomatous lesions during ophthalmologic consultation.

The hemogram of our patient revealed white blood count (WBC) of 2.99; hemoglobin (Hgb) of 9.2 gr/dL; hematocrit (HCT) of 28%; mean corpuscular volume (MCV) of 93 fL; MC hemoglobin concentration (MCHC) of 32.9 gr/dL; red cell distribution width (RDW) of 13%; and platelets of 232000. Complete

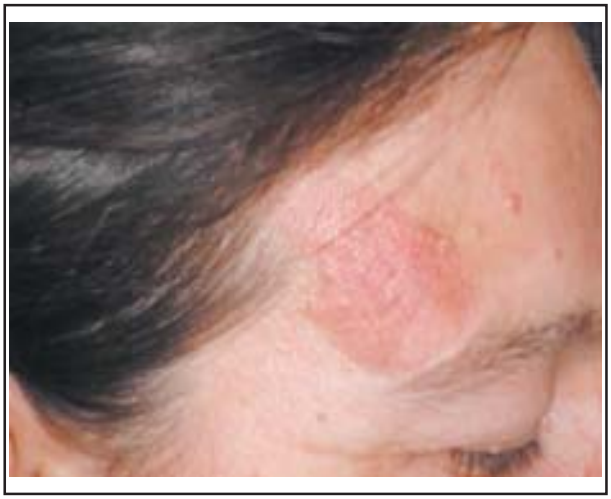

Fig-3: Forehead plaque.

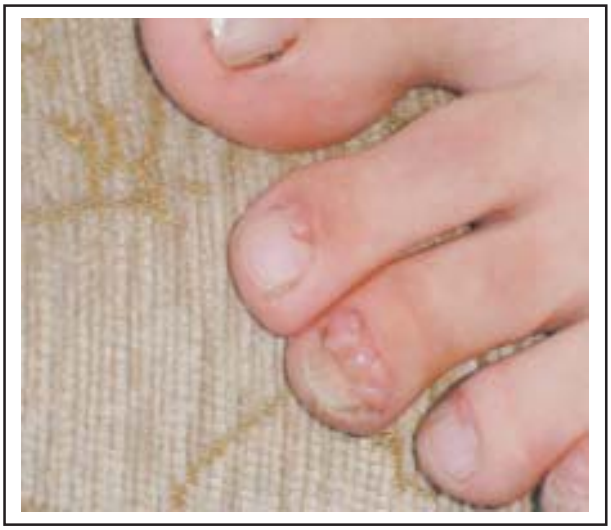

Fig-2: Periungual fibromas.

urine analysis demonstrated erythrocytes (++), density of 1013, and a pH of 7. Erythrocyte sedimentation rate was 17 mm/hour, iron (Fe) was 36, ferritin was 255 (5-148); vitamin B12 and folic acid values were normal, BUN was 20 mg/dl, creatinine was 0.9 mg/dL, and low-density lipoprotein (LDL) was 914 U/L. Occult blood in the stool was negative. The 12-derivation electrocardiography (ECG) showed sinus rhythm and it was in normal ranges. No pathology was identified on the chest X-ray. In the transthoracic echocardiography, 65% ejection fraction, and normal echocardiographic findings was evidenced. No specific treatment was prescribed to the patient, and she was followed-up. Without complaints during this follow-up period, the patient was invited for control exam one year later (March 2008). Abdominal USG was repeated and 3-grade of right kidney had 96 x 50 mm size, 2-grade of left kidney had 71 x 33 mm size, also a 22 mm diameter cyst in the right

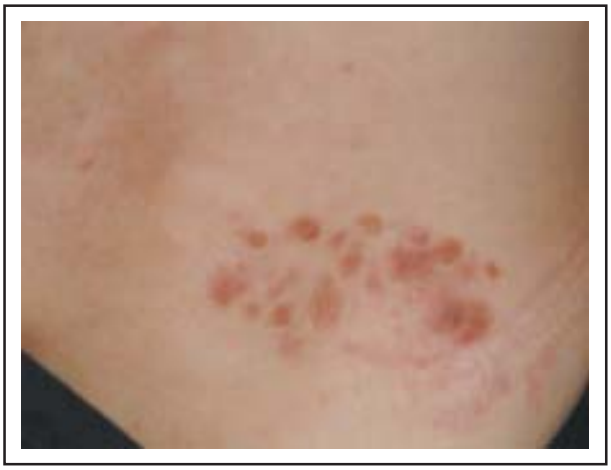

Fig-4: Shagreen patches and hypomelanotic macules.

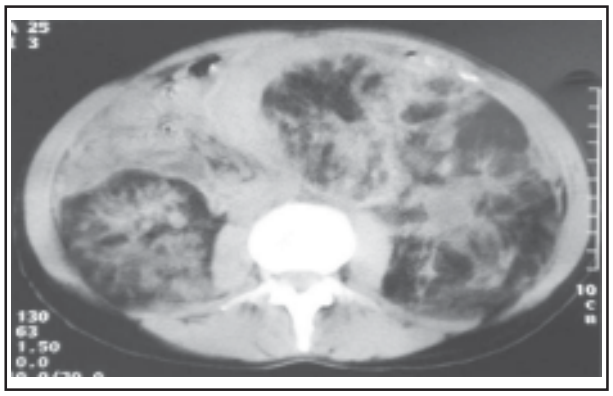

Fig-5: Bilateral renal angiomyolipomas in abdominal CT scan.

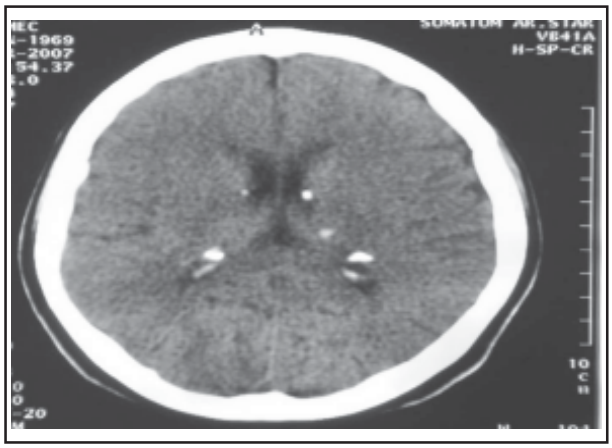

Fig-6: Calcified subependymal hamartomas in cranial CT scan.

ovary, and a 46 mm diameter cyst in the left ovary were observed. In abdominal MRI, mass lesions consistent with large angiomyolipomas in both renal regions, with the larger one located on the left side, were observed. They occupied the entire retroperitoneal space and covered the normal renal parenchymal structure (Fig-7). An enlargement of the left kidney's collecting system was also observed. Tuberous sclerosis found in the splenic pulp, with a diameter of up to 1cm, was considered to have findings associated with parenchymal involvement or infiltration of the spleen. Thick capsulated and septated cystic mass lesions, with diameters of 3 cm in the right adnexal region and 5 cm in the left adnexal region were observed. Biochemical analysis revealed BUN: 29 mg/dL, creatinine: 0.7 mg/dL, sodium: 144 mmol/L, potassium: 4.7 mmol/L, thyroid-stimulating hormone (TSH): 0.81, and hemogram revealed red blood cell (RBC): 3.7, Hb: 12.5 mg/dL, and Hct: 35%. Creatinine clearance was approximately 100 ml/min. Results of the neurological examination were normal.

Accompanied with all these findings diagnosis of tuberous sclerosis in the adult age, presentation with urinary system symptoms, absence of mental retardation, and normal creatinine clearance as well as symptom absence despite imaging scans consistent with renal failure, make this case interesting enough to be submitted as a case presentation.

DISCUSSION

Tuberous sclerosis is an autosomal dominant disease characterized by the development of benign neoplasia (hamartomas) on the skin and internal organs.[3] It is seen in one per 10.000 live births.[4] These hamartomas can be formed from mature adipocytes,

Table-I: Diagnostic Criteria for Tuberous Sclerosis**

Major Findings	*Minor Findings*
* Facial angiofibromas or forehead plaque	* Multiple randomly distributed pits in dental enamel
* Non-traumatic ungual or periungual fibromas	* Hamartomatous rectal polyps.
* Hypomelanotic macules (3 or more)	* Bone cysts
* Shagreen patches (connective tissue nevus)	* Gingival fibromas
* Multiple retinal nodules hamartomas	* Non-renal hamartomas
* Cortical tuber	* Multiple renal cysts
* Subependymal nodules	* Cerebral white matter migration lines
* Subependymal giant cell astrocytoma	* Retinal achromatic patches
* Cardiac rhabdomyoma	* Confetti-like skin lesions
* Renal angiomyolipoma ·	* Lymphangioleiomyomatosis

* Lymphangioleiomyomatosis

** Definite Diagnosis: Presence of either 2 major or 1 major+2 minor criteria.
Most Likely Diagnosis: Presence of 1 major+1 minor criteria .
Less Likely Diagnosis: Presence of either 1 major or 2 minor criteria independently.[6]

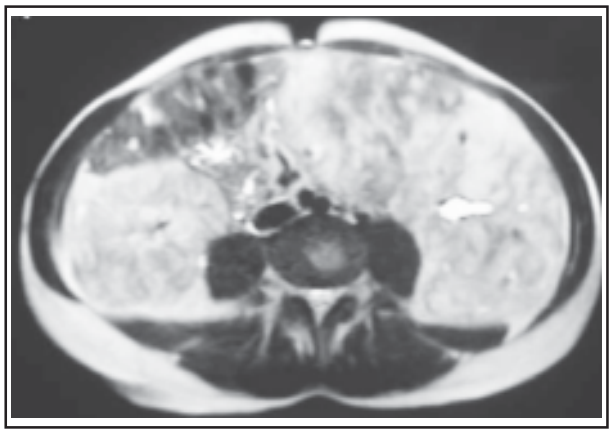

Fig-7: Lesions consistent with bilateral renal angiomyolipoma in abdominal MRI.

smooth muscle cells and blood vessels. Half of the cases have a family history, whereas spontaneous mutation or incomplete penetrance is responsible for the other half.[5] There is an equal distribution in both genders.

Various degrees of mental deficiency, mild learning difficulties up to severe mental retardation can be detected. Neurologic events (subependymal giant cell astrocytoma and resultant conditions like hydrocephaly, epilepsy, status epilepticus) are the most common causes of mortality and morbidity. These are followed by renal complications (retroperitoneal massive hemorrhage, end stage renal failure) and cardiac events. Cardiac and neurological complications are most commonly encountered during childhood. Pulmonary involvement and renal failure are most common in adults. Pulmonary involvement is seen in 1% of the cases and is a sign of poor prognosis. It is mostly encountered in women.[7] Lung involvement may present with a clinical picture of lymphangioleiomyomatosis and pneumothorax.[1] Multifocal micronodular pneumocyte hyperplasia is rarely encountered. Renal involvement may occur in four forms: angiomyolipomas (at a rate of 60-80%), isolated renal cysts (20-30%), autosomal-dominant polycystic kidney disease (2%), and renal cell carcinoma and oncocytomas (<1%). The characteristics of angiomyolipomas, which are encountered in 1/300 of the normal population, specific for tuberous sclerosis are bilateralism and multicentricity.[8] In patients with especially large renal angiomyolipomas one should be mindful of spontaneous rupture and massive hemorrhage.[9] This condition is most frequently encountered in female patients. The findings demonstrate diversity in terms of skin lesions. Facial angiofibromas (adenoma sebaseum) are distributed on the nose and cheeks. Ungual and periungual fibromas and hypomelanotic macules may be observed. These macules arise as a result of melanin pigment deficiency, and can be detected by Wood's lamp. They should be at least three in number. Forehead plaques and Shagreen patches are the other skin symptoms.[10] Eye involvement may be in the form of retinal (astrocytic hamartomas) and non-retinal (coloboma and papillary edema-secondary to hydrocephaly) lesions. Nodular tumors and fibromas of the soft palate and tongue may be found in 11% of the cases. Their existence at the posterior pharynx location may lead to airway obstruction. Rhabdomyomas may be visualized by cardiac MRI and by echocardiography. These formations may lead to cardiac failure, arrhythmias, and ventricular hypokinesia. Hamartomas, which may occur in the gastrointestinal system, can sometimes cause hemorrhage and positive occult blood in the stool, thereby leading to anemia.

REFERENCES

1. Caldemeyer KS, Mirowski GW. Tuberous sclerosis. Part I. Clinical and central nervous system findings. J Am Acad Dermatol 2001;45:448-449.
2. O'Connor SE, Kwiatkowski DJ, Roberts PS, Wollmann RL, Huttenlocher PR. A family with seizures and minor features of tuberous sclerosis complex with novel TSC2 mutation. Neurology 2003;61:409–12.
3. Arbiser JL, Brat D, Hunter S, D'Armiento J, Henske EP, Arbiser ZK, et al. Tuberous sclerosis-associated lesions of the kidneys, brain and skin are angiogenic neoplasms. J Am Acad Dermatol 2002;46:376–380.
4. Osborne JP, Fryer A, Webb D. Epidemiology of tuberous sclerosis. Ann N Y Acad Sci 1991;615:125-127.
5. Rosai J. Urinary tract. In: Rosai and Ackerman's Surgical Pathology 2004;9(1): 1266-1270.
6. Roach ES, Gomez MR, Northrup H. Tuberous sclerosis complex consensus conference: revised clinical diagnostic criteria. J Chield Neurol 1998;13:624-628.
7. Rudolph RI. Pulmonary manifestations of tuberous sclerosis. Cutis 1981;27(1):82-84.
8. Stillwell TJ, Gomez MR, Kelalis PP. Renal lesions in tuberous sclerosis. J Urol 1987;138:477-481.
9. De Pauw RA, Boelaert JR, Haenebalcke CW, Matthys EG, Schurgers MS, De Viriese AS. Renal angiomyolipoma in association with pulmonary lymphangioleiomyomatosis. Am J Kid Dis 2003;41:877-883.
10. Kandt RS. Tuberous sclerosis and neurofibromatosis type 1 the two common neurocutaneous disorder. Neurol Clinic 2003;21:983–1004.