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Pulmonary Tuberous Sclerosis

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ABSTRACT

Pulmonary involvement in tuberous sclerosis is very rare and seems to be associated with a more benign course. We present a 21-year-old woman with bilateral angiomyolipoma. She developed spontaneous pneumothorax which was successfully managed by tube thoracostomy. No recurrence of pneumothorax has been observed up to the present (4 years follow-up). ***(Tanaffos 2009; 8(2): 64-68)***

Key words: *Tuberous Sclerosis, Pneumothorax, Thoracostomy*

INTRODUCTION

Tuberous sclerosis (TS) is a rare autosomal dominant disorder recognized mainly for its dermatological and neurological manifestations. Its approximate incidence is about 1 in 500,000 live births (1). Lesions of the kidney, lung, bone, heart, liver, ovary, spleen, adrenal, thyroid and pancreas have been described. The renal lesions most commonly associated with TS are angiomyolipoma and epithelial cyst, which are often multiple and bilateral, and may occur singly or in combination (2,3). The prevalence of renal angiolipoma in cases with TS is estimated to be 40 to 80% (3,4).

Estimates of the fraction of patients with tuberous sclerosis who have lung disease vary widely from <1 to over 50 percent (5-7). There is a marked female predominance when pulmonary involvement is present (8). Most affected individuals present with dyspnea. In some, the onset is heralded by a spontaneous pneumothorax, which eventually occurs in approximately one-third of patients (9,10). Hemoptysis and chest pain are important symptoms as well and chylothorax is a rare complication (11,12).

We report a young woman with angiomyolipoma, TS and dermatologic manifestations who presented with spontaneous hydropneumothorax as the first sign of pulmonary involvement that was managed by tube thoracostomy.

CASE SUMMARY

A 21-year-old non-smoking female presented

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with a 2-week history of shortness of breath and left-sided chest pain. She had a history of seizures, facial angiofibroma, shagreen patches on the trunk, and hypopigmented patches on the abdomen, trunk and right foot since childhood. Her family history was negative for seizures. She had never used oral contraception but had been using medications for seizures.

Her temperature was 37.6 ^{o}C, pulse rate was 115/min., and respiration rate was 28/min. Her blood pressure was 110/70 mmHg.

Physical examination was notable for decreased breath sounds over the left hemithorax. *Laboratory findings*: white blood cell count was 11,700 per cubic millimeter, with 76% neutrophils and 24% mononuclear cells. The levels of hemoglobin, blood urea nitrogen, creatinine and electrolytes were normal, as were the hematocrit, platelet count and blood sugar.

A sample of arterial blood drawn while the patient was breathing room air revealed that the partial pressure of oxygen was 55 mmHg. Chest-x-ray showed a 100% left pneumothorax with a mild hydrothorax at the same side (Fig. 1).

Tube thoracostomy was performed and the left lung was completely re-expanded. Computed Tomography scanning of the abdomen disclosed a mass with a predominantly fatty density, 6.5 by 4.7 cm, in the lower pole of the right kidney, and a similar mass, 2.4 by 2.8 cm in the lower pole of the left kidney.

The size and volumes of the two kidneys were larger than normal (Fig. 2). Brain CT-scan obtained without the intravenous administration of contrast material, showed focal calcifications in the right cerebellum and paraventricular area (Fig. 3). Echocardiography of the heart was reported normal.

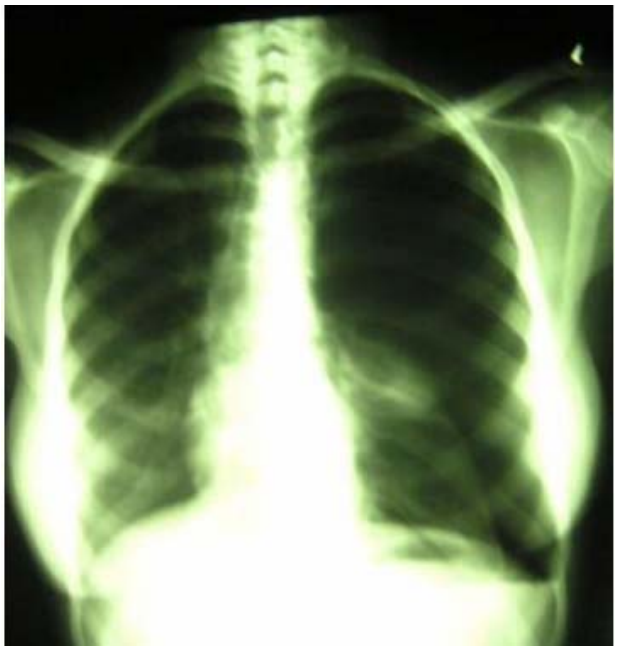

Figure 1. The posteroanterior chest radiograph reveals a large collection of air gas in the left hemithorax. The heart and mediastinum are shifted towards the left side of hemithorax. Blunting of the left costophrenic angle is shown.

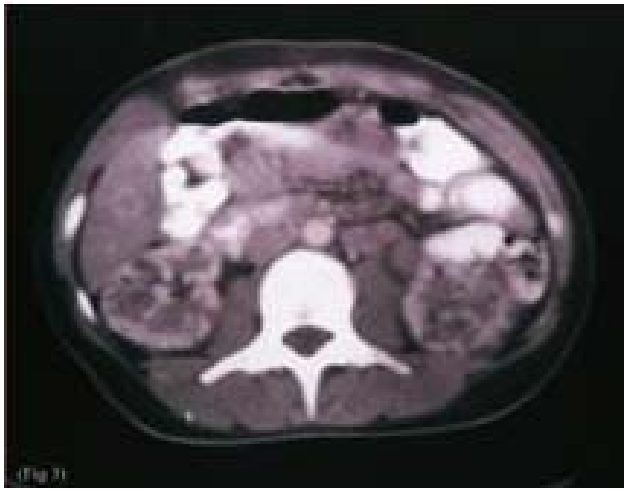

Figure 2. CT-scan of the abdomen, demonstrating a mass, 6.5 by 4.7 cm in the lower pole of the right kidney, and another mass 2.4 by 2.8 cm in the lower pole of the left kidney. The density of the masses is predominantly fatty.

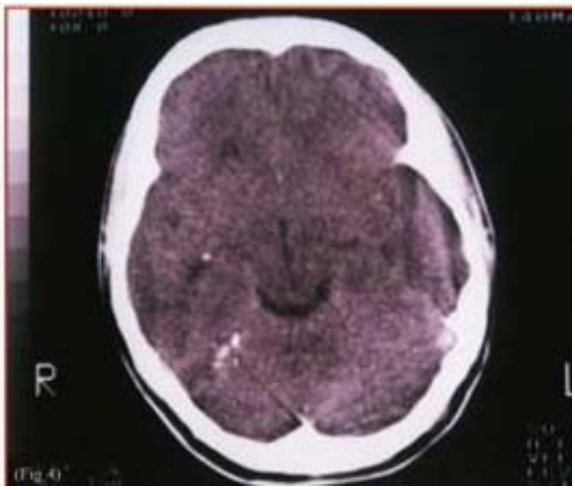

Figure 3. CT-scan of the brain, revealing calcifications in the right cerebellum and paraventricular area.

DISCUSSION

The pulmonary manifestations of tuberous sclerosis are indistinguishable from those of lymphangioleiomyomatosis (LAM) (9).

The clinical, radiographic and pathological findings are similar to pulmonary lymphangioleiomyomatosis and pulmonary tuberous sclerosis. However, these diseases can be distinguished by features such as seizures or skin lesions, which are usual in TS and always absent in LAM (13).

TS affects males and females equally; whereas, LAM occurs only in females. Pulmonary involvement, which is frequent in LAM, almost always occurs in premenopausal women with TS, and thus this condition seems to depend on hormonal influences. In a review of the literature published in 1972, 28 well-documented cases were identified, 27 in women ranging in age from 21 to 50 years (14). Clinical manifestations of pulmonary involvement are also similar to those of LAM. Respiratory symptoms are usually first noticed between 20 and 45 years of age (15). In a series of 9 patients, pneumothorax complicated the course of disease in four (15).

Another study screened 23 asymptomatic women with TS for pulmonary involvement using thoracic CT-scan. The overall prevalence of abnormal findings on CT-scan was 52 percent. Nodular changes were noted in 10 patients (43%). Characteristic cystic changes were present in 9 patients (39%). All nine had angiomyolipomas (6).

Lung function studies reveal hypoxemia, obstructive and restrictive patterns of ventilation and decreased DLCO.

In many cases, the symptoms deteriorate during the menstruation period or in the course of a pregnancy (16,17). Pulmonary involvement in tuberous sclerosis carries a poor prognosis, with progressive disease being common. Death occurs secondary to respiratory insufficiency, often within five years of the onset of symptoms.

Pulmonary TS affects women almost exclusively, who rarely suffer from mental retardation and who usually have a better life expectancy than patients with TS (18). On the other hand, there are some striking similarities between patients with pulmonary TS and LAM: affected patients are women in the childbearing age, in which pneumothorax often occurs (18). The pathologic characteristics of TS and LAM are virtually identical in most cases (19).

In LAM, chylothorax is a frequent complication (17,19); whereas, angiomyolipoma often occurs in pulmonary TS (20). Similar to LAM, pneumothorax is common, being reported in up to 50% of patients who have TS and pulmonary involvement (15).

The most common manifestations of kidney involvement in TS are renal hamartoma (angiomyolipoma) and cysts, occurring in 50 to 80% of cases (3,4). Although most patients remain asymptomatic, as in this case, symptoms may occur with increasing size, rupture of hemorrhage, replacement of normal renal parenchyma or impingement on juxtaposed structures.

The exact incidence of renal cysts is unknown

because they are often asymptomatic (2). These cysts have been implicated as the cause of renal insufficiency, chronic renal failure and hyperreninemic hypertension, which have been reported to be the earliest signs of TS in young children (21). The diagnosis of TS should be considered when bilateral renal angiomyolipomas are characteristic appearance of mixed fat and soft tissue attenuation on CT-scan. Extrathoracic manifestations of TS are seen in virtually all patients and most commonly include seizures, renal angiomyolipoma, cerebral calcification, skin lesions, and retinal hamartoma (15).

Pulmonary lesions have demonstrated some response to hormonal manipulation. Hormone-modulating treatment in TS can be started with androgen (22), then with oophorectomy (17), followed by antiestrogen therapy with tamoxifen (23), or medroxyprogesterone (25,26), or both (25).

Available therapies have to be regarded as experimental, due to the lack of control studies.

However, hormonal treatments seem to be most appropriate in the context of previous hormonal dependence of the disease, demonstration of steroid receptors in involved lung parenchyma (16,23,25) and clinical exacerbation with discontinuation of steroid therapy in some patients (25).

At this time, the most successful therapy for pulmonary TS or LAM is lung transplantation in end-stage disease. The benefits of hormonal manipulations are documented only by means of pulmonary function or blood gas data and not by chest CT data or survival rate. Hormonal treatments have no effect on cystic changes and honeycombing, based on some reports on hormonal treatment for lymphangioleiomyomatosis in patients with TS (24,27).

Tamoxifen treatment succeeded in one patient, progesterone treatment failed in another, and treatment with both medications failed in two (24).

In this patient, pneumothorax resolved with chest tube. It has been four years since the treatment and the pulmonary and renal function of the patient have been stable.

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