Pulmonary Lymphangiomyomatosis Associated with Renal and Hepatic Angiomyolipoma Mass in a Patient with Tuberous Sclerosis Complex

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To the Editor: Tuberous sclerosis complex (TSC), a rare autosomal dominant and variable penetrance, affects about 10 in every 100,000 people.⁻¹ In general, it is described as a clinical triad of adenomas, mental disorders, and seizures. However, due to incomplete penetrance, symptoms may be involved in isolated organs, which may manifest as mild incomplete diseases or involve multiple organs. Pulmonary lymphangiomyomatosis (LAM) associated with both renal and hepatic angiomyolipomas (AMLs) in a TSC patient is very rare. To the best of our knowledge, only one case has been reported by Çifçi et al.⁻² Here, we present such a case with clinical and pathological analysis.

A 30-year-old married woman was referred to Taizhou Hospital with one-week history of chest discomfort, cough, breathlessness, and dyspnea on exertion after catching a cold. She had no history of asthma; and she had a history of renal AML and received right nephroureterectomy in 2002 (the tumor was composed of smooth muscle, fat, thick-walled blood vessels, and cut surfaces showed focal necrosis [Figure 1a]. The cells showed a positive reaction for HMB-45 antigen [Figure 1b]. Before she came to Taizhou Hospital, X-rays taken to the local hospital showed a 90% right pneumothorax. Her symptoms subsided after she was placed on needle aspiration and anti-inflammatory therapy. However, pneumothorax recurred and X-ray again showed 90% pneumothorax. Chest computed tomography (CT) performed in Taizhou Hospital revealed a 95% pneumothorax and a honeycomb pattern throughout the lung parenchyma bilaterally [Figure 1c]. On examination, the patient had stable vital signs. Biopsy of the right lung showed the proliferation of smooth muscle cells, arranged in bundles, beams, and papillae was distributed in a branch network composed of endothelial cells [Figure 1c]. The cells were plump or epithelioid with abundant eosinophilic cytoplasm, and they were positive to both alpha-smooth muscle actin and HMB-45 antigen. A diagnosis of pulmonary LAM was made. During surgery, a large number of 0.3–3.0 cm bullae distributed diffusely on the surfaces of both lungs were found, and the cauterization of bullae and pleurodesis was performed. However, 6 days later, pneumothorax again recurred. X-ray demonstrated a 50–60% left pneumothorax and a 10% right pneumothorax. Further, chest and abdomen CT scan showed hepatic AML in the left lobe of the liver, and the change in resection of the right kidney, and multiple left renal AML, and bilateral pulmonary LAMs, and right pleural effusion [Figure 1f and 1g]. Closed chest drainage was initiated on the left, which controlled her symptoms, and she was discharged with the diagnosis of TSC, based on the TSC diagnostic criteria update: recommendations of the 2012 International TSC Consensus Conference.⁻³

Pulmonary LAMs associated with both renal and hepatic AMLs are very rare in TSC patients. Records of the progress of the disease are helpful in identifying such an unclear complex. This young woman, who was of reproductive age, was first diagnosed with right renal AMLs in 2002. To the best of our knowledge, AMLs are benign tumors and most occur in the kidneys although they occasionally involve the liver. Based on the mixture of smooth muscle cells, thick-walled blood vessels, and fat cells, the pathological diagnosis is not difficult. However, this patient also developed left renal and hepatic AMLs later. Although the presence of a neoplasm in the liver similar to one in the kidneys is usually considered evidence of metastasis, it has been accepted that this pattern in AML is indicative of a multicentric benign tumor. Recent studies of renal or hepatic AMLs showed myoid and vascular components to be monoclonal and adipose tissue components polyclonal, which meant the tumor had proliferative activity.⁻⁴⁻⁵ Multiple AMLs appear to be individual clones, not liver metastases. However, the real challenge for her is pulmonary LAMs. Pulmonary LAMs are found mainly in young women with the typical pathological features, specifically immature surface smooth muscle cells, known as LAM cells. The excessive growth of these cells compresses the airway, which can lead to airflow obstruction, air retention, alveolar rupture, and cystic changes, resulting in the formation of the

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Pulmonary vein occlusion causes pulmonary hemorrhage, which causes chylothorax and chylous ascites. The LAMs cells are positive for HMB45 immunostaining, which may be identified from other types of smooth muscle cells. The presence of multiple cysts distributed diffusely throughout the lungs is also a distinguishing feature. These lesions produce characteristic clinical, radiologic, and pathologic findings, have poor prognosis, and pose a threat to the patient’s life.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

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