

Diffuse Lymphangiomyomatosis with Lung and Extrapulmonary Involvement— a case report

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Lymphangiomyomatosis (LAM) is an extremely rare disease. It most commonly involves the lung; however, benign angiomyolipoma of the kidney may be present. Diffuse type LAM is even rarer. This report presents a case of lymphangiomyomatosis in bilateral lungs, kidneys, liver, retrocrural space and retroperitoneal space without stigmata of tuberous sclerosis.

Key words: Lung, Lymphangiomyomatosis

Lymphangiomyomatosis (LAM) is a very rare tumor occurring exclusively in women of reproductive age. The most common presentations are progressive exertional dyspnea, spontaneous pneumothorax, and, less frequently, chylothorax [1, 2, 3]. Histologically, it is characterized by an abnormal proliferation of atypical smooth muscle in lymphatic vessels, blood vessels and airways. LAM most commonly involves the lung; however, smooth muscle proliferation may also involve extrapulmonary sites [2, 3, 4]. High-resolution chest computed tomography (HRCT) scan is an important diagnostic tool for pulmonary LAM. It reveals numerous randomly scattered thin-walled cysts of various sizes surrounded by normal lung parenchyma and bronchovascular bundles at periphery of cyst walls.

CASE REPORT

A 35-year-old non-smoking married woman suffered from progressive exertional dyspnea and short of breath in recent years. The dyspnea gradually deteriorated, aggravated by pregnancy but did not improve after delivery. She visited local hospital and chest X-ray disclosed emphysematous change with overinflation of bilateral lung fields (Fig. 1). She was referred to our hospital for further evaluation and management. During the admission, physical examination revealed decreased breathing sound, tactile fremitus and hyper-resonant percussion of bilateral chest fields. There were no symptoms of mental retardation, seizure attack history, adenoma sebaceum, pleural effusion, chylothorax, pneumothorax, abdominal fullness or pain. High-resolution chest computed tomography (HRCT) scans was performed, and demonstrated diffuse fine thin-walled cysts randomly distributed throughout the lungs (Fig. 2). Pulmonary function tests performed on the same day showed obstructive ventilatory defect (FEV1 = 48%; FEV1/FVC: 24%; FVC: 1.99), severe obstructive lung disease was impressed. Exercise

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pulmonary function test showed severe pulmonary ventilation and perfusion (V/Q) mismatch and in pending pulmonary hypertension. Open lung biopsy revealed smooth muscle proliferation around destructed cystic alveolar spaces and along adjacent interalveolar septa, suggestive of pulmonary lymphangioliomyomatosis (LAM) (Fig. 3). The smooth muscle nature of the cell was confirmed by positive HMB45 immunostaining. The diagnosis of pulmonary LAM was then established. The abdominal computed tomography (CT) scan with and without contrast enhancement showed some hypodense attenuation lesions in right lobe of liver and multiple heterogeneously enhancing lesions with some hypodense component in bilateral kidneys, retrocrural space and retroperitoneal space (Fig. 4, 5). Analysis of CT numbers revealed negative Hounsfield unit of these mass lesions, indicating fat content. Under the conditions of characteristic pathologic findings on lung biopsy, typical cystic appearance on chest CT scan and hepatic angiomyolipoma, typical renal angiomyolipomas with abdominal lymphadenopathy, diffuse lymphangioliomyomatosis was then diagnosed. Therefore she visited OPD for regular follow up and received medroxy-progesterone medication. Because the clinical condition did not improve after medical treatment, she received left single lung transplantaion several months later. The patient was discharged uneventfully.

DISCUSSION

Lymphangioliomyomatosis (LAM) is a disorder of unknown etiology which exclusively affects reproductive women [1, 2, 4, 5]. It is a rare lung disease that was first described in the medical literature by von Stossel in 1937. The most common presentations are progressive exertional dyspnea, spontaneous pneumothorax, and, less frequently, chylothorax [2, 3]. Histologically, LAM is characterized by an abnormal proliferation of atypical smooth muscle cells, with no associated inflammatory cells in lymphatic vessels, blood vessels and airways, which can lead to air trapping, overinflation, formation of cysts, pneumothorax, chylothorax and alveolar hemorrhage. Although these cells are not considered cancerous, they act somewhat like cancer cells in that they grow uncontrollably. HMB45 is a monoclonal antibody with specific immunoreactivity for malignant melanoma and it constitute a highly specific and highly sensitive diagnostic marker for LAM [5]. It may also be useful in patients with only minor smooth muscle proliferation, in whom the diagnosis of LAM is difficult to be

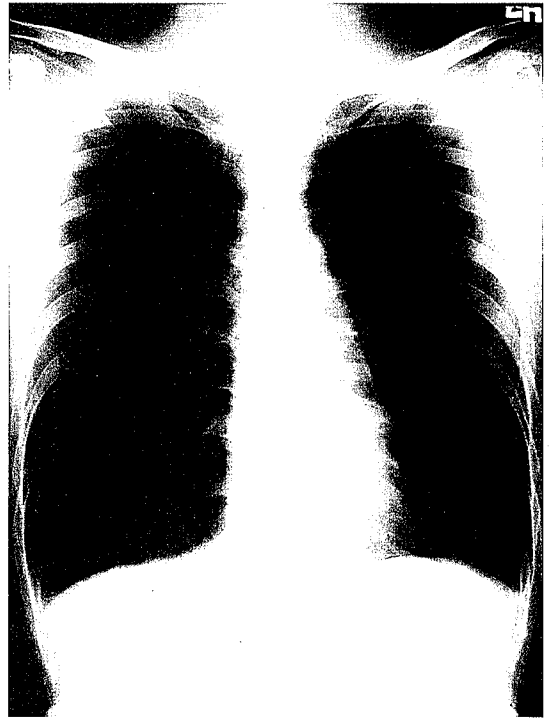


Figure 1. Chest radiograph shows emphysematous change of both lung fields and lung volume is increased.



Figure 2. High-resolution CT scan demonstrates diffuse fined thin-walled cysts, which are randomly distributed throughout the lungs.

confirmed by conventional histologic examination [5].

Smooth muscle proliferation may also involve extrapulmonary sites. The most common forms of extrapulmonary LAM include renal angiomyolipoma (20~54% of cases), enlarged abdominal lymph nodes (39%), and lymphangiomyoma (16~20%) [2, 3, 4]. Less commonly, ascites (10%) and hepatic angiomyolipoma (4%) may be present [2, 3, 4]. A few cases of LAM with renal angiomyolipoma, multiple abdominal

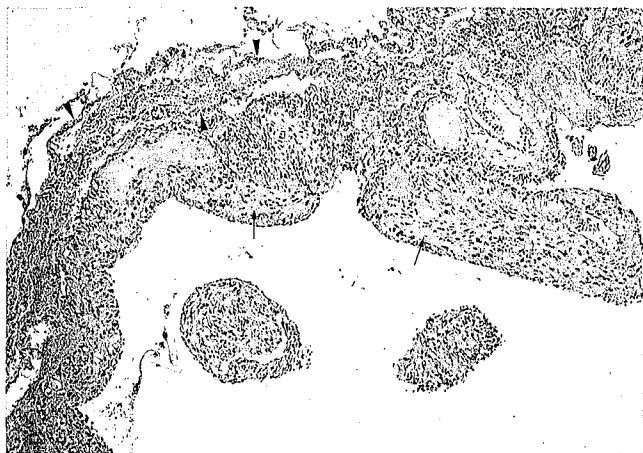


Figure 3. Open lung biopsy reveals smooth muscle proliferation (→) around cystic destruction of several alveolar spaces and along adjacent interalveolar septa (▶), suggestive of pulmonary lymphangioliomyomatosis (LAM). (H&E, x40)



Figure 5. Precontrast and postcontrast CT scans reveal some heterogeneous enhancing mass lesions in bilateral kidneys and retroperitoneal space. Analysis of CT numbers revealed negative attenuation within these lesions, a finding diagnostic of renal angiomyolipomatosis (→) and retroperitoneal lymphadenopathy (▶).



Figure 4. Precontrast CT scans of the abdomen show two extremely low density lesions at liver parenchyma and some low-attenuation lesions in retrocrural space. Analysis of CT numbers revealed negative attenuation within these lesions, a finding diagnostic of hepatic angiomyolipoma and retrocrural lymphadenopathy.

lymphadenopathy or with hepatic angiomyolipoma have been reported [1, 2, 4]; however, in this article we report LAM of bilateral lungs, kidneys, liver, retrocrural space and retroperitoneal space in one patient.

The low density lesion within right lobe of liver parenchyma appeared to be like pure lipoma of liver, but hepatic lipoma is exceedingly rare and the LAM has been proven in this patient. Therefore, the hepatic angiomyolipoma associated with LAM is more favorable (Fig. 4). Angiomyolipomatosis of kidneys was impressed by demonstration of intratumoral fat with negative attenuation values in CT within these mass lesions (Fig. 5). There are many lym-

phadenopathy with some hypodense component, which analysis of CT number revealed negative attenuation in retrocrural space and retroperitoneal space (fig. 5). However, no definite lymphangiomyoma or ascites is noted in this patient. The low attenuation areas within the enlarged lymph nodes represented chylous lymph collection, and enlarged lymph nodes could measured up to 4 cm in diameter [1]. Lymphangioliomyoma may be thick- or thin-walled, vary in size and low attenuation retroperitoneal mass, which occurs in 16~20% of patients with LAM [1, 4].

The chest radiographic findings in LAM are variable [6]. In early stage, the chylous pleural effusion may dominate, or proliferation interstitial muscle bundles may produce a micronodular or military pattern [6]. Chylous pleural effusion may be unilateral or bilateral. The CT attenuation of chylous pleural effusion is usually indistinguishable from that of other protein rich effusion. LAM induced chylothorax usually recur and in large amount [1]. Septal lines due to the lymphatic obstruction appear, producing a coarse reticular pattern [6, 7]. In more advanced disease, the chest radiograph shows hyperinflation, small cysts areas that may be superimposed on a coarse reticular pattern, and sometimes a pneumothorax [6]. In addition, dilatation of the thoracic duct could be identified in 26% patients with LAM. The clinical features and the presentation of chest radiograph are often nonspecific [8], so the high-resolution chest CT (HRCT) scan is an important diagnostic tool for pulmonary LAM. The HRCT of LAM patient reveals numerous randomly scattered thin-walled cysts of various sizes surrounded by normal lung

parenchyma.

Because LAM occurs almost in women of child-bearing age and exacerbations are suspected to be related to pregnancy, exogenous estrogens, and contraceptive pills, it has been suggested that hormonal factors play an important role in the development of LAM [8]. Hormonal therapy, if beneficial, should be started as soon as possible, before irreversible major lung destruction occurs [3]. A recent paper reports that tuberous sclerosis gene mutations are a cause of lymphangioliomyomatosis [1, 9]. The mutations are found in the angiomyolipoma cells and LAM cells from four women with LAM [1]. The mutations are not present in normal lung, kidney or blood cells, indicating that these women with LAM do not have the inherited disease, tuberous sclerosis [1].

Other interstitial lung diseases, such as Histiocytosis X, tuberous sclerosis, idiopathic pulmonary fibrosis, acinar emphysema and bronchiectasis should be differentiated from LAM. Histiocytosis X of lung is more frequent in young men, and predominant of cysts and nodules in the upper lung fields with sparing of costophrenic angles. Pulmonary LAM and tuberous sclerosis differ in terms of their clinical setting. LAM usually occurs in female in whom there is no mental deficiency and no clinical evidence of central nervous system damage [7]. The autosomal dominant transmission of tuberous sclerosis shows of neurologic or cutaneous manifestations such as seizure, mental retardation, adenoma sebaceum, or cephalic calcifications [3, 7]. Idiopathic pulmonary fibrosis can be differentiated from LAM by the small irregular thick-walled cysts and may distribute more peripherally. In acinar emphysema, the bronchovascular bundles are usually in central position of cyst. HRCT scan is clearly a sensitive modality for the diagnosis of early pulmonary LAM, even when chest X-ray is inconclusive. It may be indicated in spontaneous pneumothorax or renal angiomyolipoma in women of childbearing age [1, 2, 3, 5].

Early reports of LAM revealed most patients died within 10 years. In present study, Kaplan-Meier plot showed survival probabilities of 91% after 5 years, 79% after 10 years, and 71% after 15 years of disease duration [3]. In a recent worldwide retrospective study of 34 cases of lung transplantation for pulmonary LAM, the survival rate was 69% at 1 year and 58% at 2 years [3]. There are particular complications in patients with LAM, such as excessive bleeding from pleural adhesions during surgery, pneumothorax of the native lung, chylothorax and hemorrhage, therefore the survival rate of post lung transplantation patients was lower than LAM patients without transplantation

surgery. Although disease-related complications are frequent and recurrence is possible but rare, we consider that lung transplantation is indicated in patients with end-stage LAM [1, 3, 4, 8].

In conclusion, LAM is a rare serious progressive disease that predominantly affects women of child-bearing age and leads to chronic respiratory insufficiency [1, 3]. The radiologist is often the first to suggest the diagnosis of LAM because the thoracic high-resolution CT findings are very characteristic [1, 3]. Abdominal CT scan or ultrasound examination may be indicated in women of childbearing age presenting with multiple thin-walled cysts on chest HRCT scan [3, 10].

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瀰漫性淋巴血管平滑肌增生症：病例報告

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瀰漫性淋巴血管平滑肌增生症是一種罕見的疾病，大部分發生在生育年齡的婦女，最常影響的器官是肺臟。肺臟以外的地方，例如：腎臟的血管肌肉脂肪瘤也有人報導，而瀰漫性淋巴血管平滑肌增生症則更是少見。本文報告一例在兩側肺臟、腎臟、肝臟、橫隔膜後及後腹腔的瀰漫性淋巴血管平滑肌增生症。

關鍵詞：肺臟；淋巴血管平滑肌增生症

