Pulmonary Lymphangiomyomatosis (LAM) Developing Chylothorax

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Abstract

We describe a case of pulmonary lymphangiomyomatosis (LAM) with chylothorax that developed in a 46-year-old Japanese woman. This patient exhibited clinical symptoms of dyspnea and chest X-ray showed right pleural effusion. Thoracocentesis demonstrated chylous effusion. Chest computed tomography (CT) scan revealed multiple cystic lesions. Subsequent thoracoscopy revealed the chylorrhea from swelled vessels on the diaphragm. The clinical diagnosis, based on histological examinations with biopsy specimens obtained by thoracoscopy, was pulmonary LAM. Although the hormone therapy was not effective, chylous effusion was improved by the pleurodesis. Pulmonary LAM developing chylothorax is rare in Japan.

Key words: lymphangioleiomyomatosis, chylos effusion, thoracoscopy, hormone therapy, pleurodesis

Introduction

Pulmonary lymphangiomyomatosis (LAM) is a comparatively rare disease of women of reproductive age characterized by hyperplasia of atypical smooth muscle of the lung, pleura, mediastinum, thoracic duct, and retroperitoneum (1). The pulmonary manifestations are a combination of interstitial and destructive lung disease with proliferation of smooth muscle cells along lymphatics, small airways, and blood vessels and in the alveolar interstitium, interstitial fibrosis, and focal destruction of the alveolar walls (1, 2). The clinical features include dyspnea, chylous effusion, hemoptysis and spontaneous pneumothorax (3). Although several cases of pulmonary LAM have been reported, a standardized treatment has yet to be established. Herein we report the rare case of a woman diagnosed with pulmonary LAM developing chylothorax and treated with hormonal manipulation and pleurodesis.

Case Report

The patient was a 46-year-old Japanese woman, 144 cm tall and weighing 44.0 kg. She was admitted to our hospital complaining of a non-productive cough and progressive dyspnea of several days duration on April 8, 1998. She had had a medical history of abdominal mass extraction thought to be LAM 5 years earlier, however, the details were unclear. At that time, her chest roentgenogram was normal and she had not been diagnosed with pulmonary LAM. She was menstruant. She had not been diagnosed as having tuberous sclerosis. A family history of a neurocutaneous syndrome could not be elicited.

A physiological examination revealed percussion dullness over the lower right chest. The patient’s body temperature was 36.5°C, blood pressure was 120/76 mmHg, and radial pulse rate was 72/min and regular. She had neither anemia nor jaundice. A neurological examination revealed no abnormal findings. She was not noted as having adenaoma sebaecum and she was not mentally retarded.

Laboratory findings included a red blood cell count of 403x10^4/μl, a white blood cell count of 4,700/μl, and a platelet count of 35.0x10^5/μl. The hemoglobin concentration was 12.5 g/dl. The liver function and renal function tests were both within normal ranges. Total protein was 5.8 g/dl (normal, 6.3–7.8 g/dl), and serum albumin was 3.2 g/dl (normal, 4.1–5.1 g/dl). Some tumor markers, such as carcinoembryonic antigen, and carbohydrate antigen 19-9, were negative but carbohydrate antigen 125 was 273 U/ml (normal <35 U/ml). The C reactive protein concentration was 0.1 mg/dl, and the erythrocyte sedimentation rate was 9 mm/h. Serological tests for hepatitis B and C viruses were negative.

A chest radiograph on admission showed a right pleural effusion (Fig. 1). And chest computed tomography (CT) scan demonstrated diffuse multiple cystic lesions surrounded by thin walls in the bilateral lung fields (Fig. 2). An examination by
abdominal CT revealed iso-density masses in the retroperitoneum (Fig. 3). Arterial blood gas analysis revealed PaO$_2$ of 63.3 mmHg, PaCO$_2$ of 38.2 mmHg and pH of 7.41. Subsequent thoracentesis showed chylos effusion (Fig. 4) and no malignant cells. These imaging examinations and the chylothorax suggested that the pulmonary cystic lesions were LAM. The clinical diagnoses, based on these examinations, were chylothorax due to pulmonary LAM and retroperitoneal LAM.

The patient underwent a thoracoscopy because of the continuation of dyspnea and progress of pleural effusion after admission. During thoracoscopy, the chylorrhea from a swollen vessel on the diaphragm was observed (Fig. 5). A thoracoscopic lung biopsy was performed and histological examination of the biopsy specimens obtained from the cystic lesions in right S$^6$ revealed a marked smooth-muscle proliferation in the distribution of lymphatics and perivascular areas (Fig. 6). The histological diagnosis was compatible with pulmonary LAM. On the basis of this diagnosis we started the administration of leuprorelin acetate at 1.88 mg/week and progesterone at 100 mg/week since May 15 1998, and repeated every week, for four courses until June 17 1998. However, the cystic lesions in the lung fields and chylous effusion remained stable after the hormone therapy. Afterward, pleurodesis was performed on July 16, 1998 and as a result of this treatment the patient’s dyspnea was resolved and the pleural effusion was improved. She has been under close periodic observation, and there is no evidence of pleural effusion at the time of 19 months after pleurodesis.

**Discussion**

Pulmonary LAM is a rare devastating interstitial lung disease of unknown origin characterized by an abnormal proliferation of smooth muscle around the airway, vessels and lymphatic ducts (1, 2, 4). It occurs exclusively in women of child-bearing age (5). Patients with LAM occasionally can have extrapulmonary abnormalities including mediastinal and retroperitoneal LAM, chyrous ascites, and renal involvement with angiomyolipoma (5). Symptoms of pulmonary LAM include: dyspnea on exertion, chest pain and hemoptysis. A large number of patients will develop pneumothorax (6). Urban et al (7)
Figure 3. Image obtained by abdominal CT. Abdominal CT scan demonstrating iso-density masses in the retroperitoneum (white arrows).

Figure 4. Pleural effusion obtained by thoracentesis revealing white fluid and diagnosed as chylothorax.

described that pneumothorax, frequently recurrent, occurred in 7 of his 8 patients with LAM. Based on this consideration, we speculate that the diagnosis of female patients with pneumothorax propounds considerable problems of rupture of the cystic wall related to pulmonary LAM. Proliferation of the smooth muscle element can result in obstruction of bronchioles, producing pockets of air, bullae, and pneumothorax. The obstruction of venules may produce hemoptysis, pulmonary hemorrhage, and hemosiderosis. If chylous effusion is present, the diagnosis is clear since the effusion has been emphasized as being strongly suggestive of the presence of lymphatic obstruction.

Recently, with the development of various imaging modalities, it has become possible to diagnose pulmonary LAM. Pulmonary LAM has been described in the radiographic and pathologic literature (1, 8). The most common abnormality on chest roentgenogram is reported to be bilateral reticulonodular infil-

Figure 5. Thoracoscopy shows the chyloorrhea from swollen vessels on the diaphragm (black arrow).

Figure 6. The histology of the pulmonary cystic lesions. Microscopic findings showing marked smooth muscle proliferation in the distribution of lymphatics and perivascular areas (Azan stain, ×50).
trates (6). Other radiographic features include cysts of bullae, effusion, pneumothorax, and evidence of hyperinflation (5, 6). Chest CT scans may be useful for providing evidence of bullous formation (9). Characteristics of CT findings in patients with LAM include multiple well-defined cystic air spaces surrounded by uniformly thin walls, distributed diffusely throughout both lungs (5, 10). The differential diagnosis for LAM includes emphysema and Langerhans cell granulomatosis. Although a correlation of radiographic findings with clinical information is often suggestive, a pathologic examination of a lung tissue specimen is required for confirmation of the diagnosis of LAM. Pulmonary LAM generally consists of marked smooth-muscle proliferation, regarded as a hamartomatous process, in the distribution of the lymphatics and in the peribronchial and perivascular areas. Transbronchial biopsy via fiberoptic bronchoscopy has been used to make the diagnosis (11, 12). However, if pulmonary LAM is suspected clinically and the transbronchial biopsy is nondiagnostic, open-lung biopsy or thorascopic lung biopsy should be performed (6). In the present case, the diagnosis of LAM was established by thorascopic lung biopsy and thorascopy was useful for the observation of chylorhea. The iso-density masses in the retroperitoneum detected by abdominal CT and the abdominal mass extracted previously might have been LAM.

Kitaichi et al (10) reported the clinical and pathologic features of 46 patients with pulmonary LAM from Japan (39 patients), Korea (5 patients) and Taiwan (2 patients). They described that the patients were all females, mean age at onset was 32.0±8.9 year (range 20 to 63 year), and major symptoms at the time of onset were dyspnea (57%) and cough (33%). It is not possible to estimate the prevalence of chylorhea. Taylor et al (6) reported 32 cases of pulmonary LAM, 9 of which (28%) revealed chylorhea during the course. According to Kitaichi et al (10), only 3 of 41 patients (7%) experienced chylorhea. Cases of pulmonary LAM developing chylorax are rare in Japan.

Pulmonary LAM needs early treatment because of its progresive nature. Antiestrogen drugs such as progesterone or estrogen-receptor competitive antagonists such as tamoxifen citrate, LH-RH derivatives such as leuprorelin acetate, and estrogen-receptor competitive antagonists such as tamoxifen have been used to make the diagnosis (11, 12). However, if pulmonary LAM is suspected clinically and the transbronchial biopsy is nondiagnostic, open-lung biopsy or thorascopic lung biopsy should be performed (6). In the present case, the diagnosis of LAM was established by thorascopic lung biopsy and thorascopy was useful for the observation of chylorhea. The iso-density masses in the retroperitoneum detected by abdominal CT and the abdominal mass extracted previously might have been LAM.

References