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CLINICAL IMAGING

Pulmonary lymphangioleiomyomatosis High-resolution CT findings in 11 patients and compared with the literature

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Abstract

We retrospectively evaluated the high-resolution computed tomographic (HRCT) findings in 11 women patients with pulmonary lymphangioleiomyomatosis (LAM). Numerous, thin-walled cysts distributed diffusely throughout the lungs and ranged in size from a few millimeters to several centimeters were seen on HRCT in all patients. Other findings at HRCT included interlobular septal thickening (six patients), ground-glass opacity (one patient) and architectural distortion (one patient). Our study found that HRCT imaging findings were similar to the literatures reported, except that majority of our cases also have interstitial changes. HRCT may help establish this diagnosis when diagnosis by clinical findings is uncertain and chest radiographs showed normal or nonspecific findings.

Keywords: Lymphangioleiomyomatosis; Lung; High-resolution computed tomography

1. Introduction

Lymphangioleiomyomatosis (LAM) is a rare disease of unknown etiology affecting women only. It is characterized by abnormal proliferation of atypical smooth muscle cells in the pulmonary lymphatic vessels, blood vessels and airway, leading progressively to respiratory failure and ultimately death [1]. LAM has been reported in women more than 70 years old of age and has also been reported in a man [2]. The most common pulmonary symptoms in patients with LAM are progressive dyspnea on exertion, spontaneous pneumothorax and cough. Other common symptoms and signs include resting dyspnea, hemoptysis, chylous pleural effusion and chest pain. High-resolution computed tomography (HRCT) findings of LAM of the lung have been described [3–13]. The purpose of our study was to retrospectively evaluate the HRCT findings of pulmonary LAM in 11 patients in a 3500-bed medical center and to see if there are any imaging findings different from those reported in the literatures.

2. Materials and methods

We retrospectively reviewed medical records, chest radiographs and HRCT scans obtained in 11 patients who were diagnosed with LAM between November 1993 and December 2001 in the Chang Gung Memorial Hospital, Taiwan. All the patients have no evidence of tuberous sclerosis. All patients were women and ranged in age from 29 to 46 years (mean age: 38 years). Ten of 11 patients of LAM were biopsy proven. The diagnosis was made at biopsy by open lung biopsy in three patients, by video-assisted thoracoscopic lung biopsy in four patients and using transbronchial biopsy in three patients. An experienced pathologists analyzed all pathologic specimens. One patient did not have a tissue diagnosis of LAM and the diagnosis inferred from classic clinical features and typical findings on the HRCT. The duration of the disease, estimated from time of onset of symptoms, was available in eight patients (including first pneumothorax to the time of our evaluation),

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ranged from 1 month to 10 years (mean: 40 months). Two patients who had clinical diagnosis of asthma did not improved after therapy for more than 2 years, underwent HRCT suggested LAM and was proved by open lung biopsy. In three patients, the duration of symptoms could not be evaluated.

All patients underwent thin-section CT of the chest. The HRCT scans were obtained with a variety scanners. All HRCT scans were performed at end inspiration with patients in the supine position. Four of 11 patients had initial expiratory HRCT scans too. Thin-section CT scanning was performed with 1-mm collimation at 10-mm intervals, a high-spatial-frequency reconstruction algorithm, 1-s exposure, 140 kVp, 200 mA, without injection of contrast material. The scans were imaged with both soft-tissue (width: 400 HU, level: 30 HU) and lung (width: 1000 HU, level: − 700 HU) windows setting.

Two radiologists interpreted the chest radiographs and HRCT images together, and a consensus was reached. On chest radiographs, the presence and distribution of cysts, reticular or nodular opacities increased lung volume, pleural effusion, pneumothorax and lymph nodes enlargement were determined specifically. We defined cysts as areas of hyperlucency with walls 1 mm or more in thickness. Reticulation was defined as a network of lines without central lucencies. Lung volume was considered increased when the anterior part of the seventh rib was seen above the highest part of the right hemidiaphragm.

CT scans were assessed for the presence, distribution and predominant size of the cysts, interlobular septal thickening, thickness of the walls of the cysts, the presence of nodules and their sizes, ground-glass opacity and the presence of lines. Cysts were classified as small (< 1.0 cm in diameter), intermediate (1–2 cm in diameter) and large (< 2.0 cm in diameter). Interlobular septal thickening were identified as thickened interlobular septa. Intralobular interstitial thickening was assumed if small lines occur in the secondary lobules. Nodule was defined as a discrete, round, focal opacity of soft-tissue attenuation. Architecture distortion was considered present when interlobar fissures and hila were displaced or when bronchial or vessels were distorted. Ground-glass opacity was defined as an area of increased attenuation in which underlying vessels were visible. CT scans were also assessed for the presence or absence of the pleural effusion, pneumothorax and lymph nodes enlargement. Lymph node enlargement was defined as lymph nodes greater than 1.0 cm along its short axis or 1.5 cm in the long axis. HRCT was evaluated for the presence and severity of underlying disease in each of two equal pulmonary zones from apex to lung base. The upper zones were above the level of the carina and the lower zone below the level of carina. Zonal predominance was assesses as being upper, lower or diffuse. Upper zonal predominance was considered present when of the abnormalities were above the level of the tracheal carina and lower lung zonal predominance was considered present when most of the abnormalities were below this level.

CT findings were also correlated with the PFT. Pulmonary function tests were performed in all patients. Spirometry was performed to measure forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) as recommended by the American Thoracic Society [14]. Only seven patients had diffusion capacity of the lungs for carbon monoxide (DLCO) obtained (four patients DCLO was not available). With use of the single breath-hold technique of Burrows et al. [15], the percentage predicted value of DLCO was determined.

3. Results

Two patients had no evidence of parenchymal disease on chest radiographs. The chest radiographs were abnormal in

Table 1
Clinical and high-resolution CT findings of patients with LAM

Patients/age (years)	Duration of symptoms	CT findings											
		Cysts			Interstitial pattern				Pulmonary function tests others				
		Small	Intermediate	Large	Ground-glass	Nodules	Septa	Distortion	PE	PN	FVC (%)	FEVI (%)	DLCO (%)
1/40	10 years	0	0	−	0	0	+	0	0	0	84	63	65
2/29	?	0	0	+	0	0	0	0	+	+	76	42	29
3/31	8 years	0	0	+	0	+	0	0	0	+B	71	60	N/A
4/44	5 years	0	−	0	0	0	+	0	0	0	57	13	N/A
5/46	20 days	0	+	0	0	0	0	+	0	+	68	50	N/A
6/40		+	0	0	0	0	+	0	0	0	72	69	88
7/35	3 years	−	0	0	0	0	+	0	0	0	71	51	35
8/46	2 years	−	0	0	0	0	0	0	0	0	111	95	N/A
9/35		0	0	+	+	0	+	0	0	+	63	47	28
10/35	1 year 10 months	0	+	0	0	0	+	0	+B	0	35	22	11
11/36	10 years	0	+	0	0	0+	0	0	+	+B	71	60	54

+, found; 0, not found; N/A, not available: ground-glass, ground-glass opacity; septal, interlobular septal thickening; distortion, architectural distortion; PE, pleural effusion; PN, pneumothorax; DLCO, diffusion capacity of the lungs for carbon monoxide; FVC, functional vital capacity; FEV1, forced expiratory volume in 1 s; (%), percentage of predicted value; B, bilateral.

nine patients (82%). Chest radiographs revealed diffuse interstitial pattern with an equal distribution of changes in all lung zones in three patients, more severe in the lower lung zones in six patients. There are no patients with upper lung zones predominance. The most common finding was reticular opacity in 8 of 11 patients (73%). One patient had combined cysts and reticular pattern (9%). Lung volumes were increased in five patients and normal in six patients. Pneumothorax was seen in four patients. Pleural effusion was found in one patient (9%). Nodular opacity was not seen in any patient. No radiographic signs of mediastinal or hilar lymphadenopathy.

The HRCT findings and pulmonary function tests data in 11 patients are shown in Table 1. HRCT scans showed abnormalities in all patients. All patients had thickening of interstitial structures. One patient had areas of ground-glass opacity (9%). Interlobular septal thickening was observed in six patients (55%; Fig. 1). Nodules were not observed in our patients. Architectural distortion was found in one patient (9%). Cystic lesions were seen in all patients (100%; Fig. 2). The majority of cysts had walls ranging from faintly perceptible to approximately 2 mm thick. Cystic changes were equally distributed in nine patients. Cystic lesions were more severe in the upper lung zones in one patient and a slight basilar predominance was observed in one patient. The size of the cystic lesions was up to 1 cm in three patients, 1–2 cm in four patients (Fig. 3) and more than 2 cm in four patients. The largest cyst of about 15 cm in diameter was seen in one patient. Pneumothorax was seen four patients (36%; two bilateral and two unilateral). Pleural effusions were present in three patients (27%; two right-sided and one bilateral). There was no pericardial effusion. Lymph node enlargement was found on the CT scans in only one patient and the size was about 1.5 cm in the shorter axis (9%). The enlarged lymph node was present in the right paratracheal space of the mediastinum. There is no evidence of air trapping on expiratory HRCT in four patients in whom expiratory HRCT scans were available.

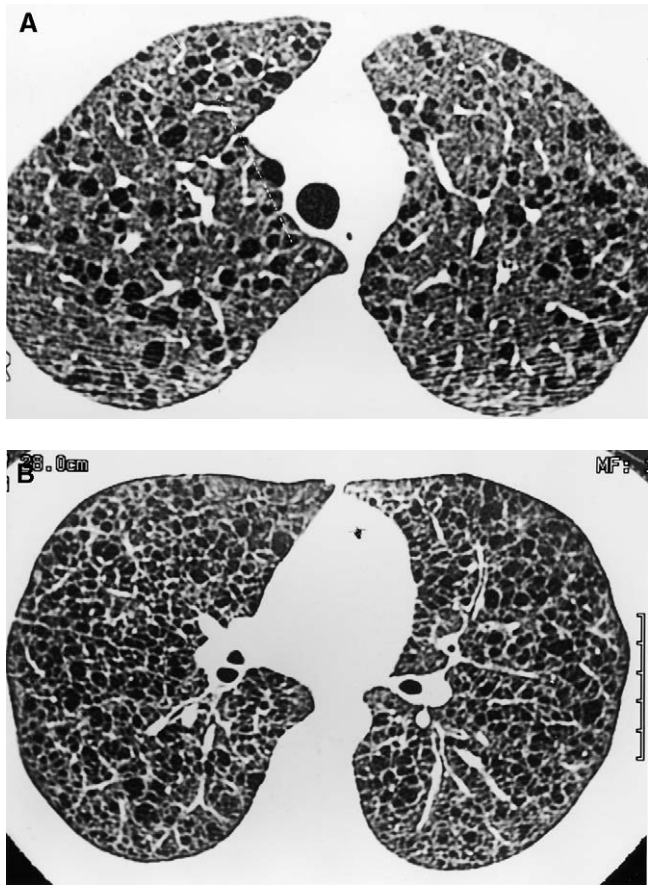

Fig. 2. HRCT of the chest of two patients with LAM. Top (A): a 40-year-old woman with milder involvement of the lungs with thin-walled cysts surrounded by normal lung parenchyma. Bottom (B): a 35-year-old woman with severe involvement of the lungs with small, thin-walled cysts (< 1 cm in diameter) in both lungs.

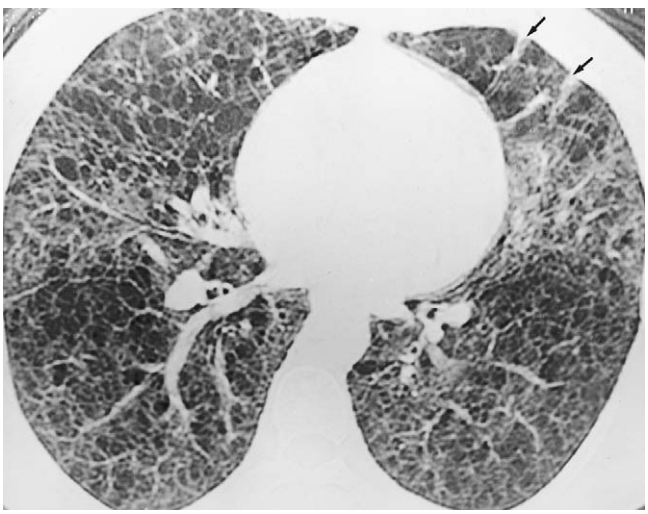

Fig. 1. HRCT image of a 44-year-old woman with LAM at the left upper lobe shows interlobular septal thickening (arrows).

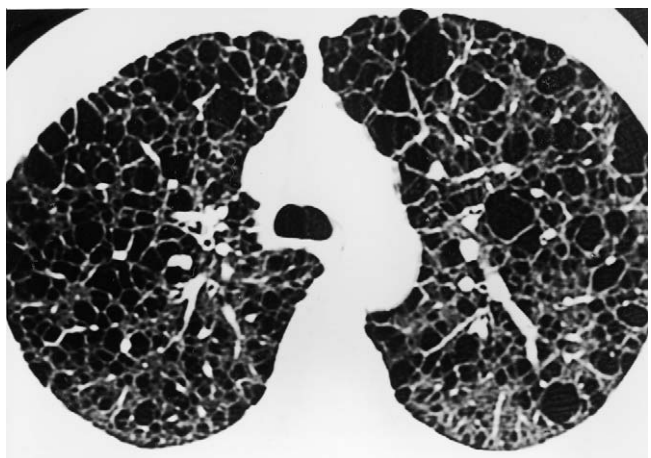

Fig. 3. HRCT image of a 36-year-old woman at upper lung zones shows numerous, thin-walled cysts of intermediate sizes about 1–2 cm in diameter.

In most patients, pulmonary function testing showed an obstructive pattern with decreased FEV1. Patients with large and intermediate cysts had more severe decreased DLCO. One patient had normal pulmonary function tests (Case 8). The FVC was below 80%, predicated in 9 of 11 patients. Most patients with severe obstruction showed large and intermediate cysts.

4. Discussion

HRCT has become a well-established tool for the evaluation of diffuse lung disease because of more reliable depiction of lung morphology, and therefore correlation between cross-sectional imaging findings and gross pathology is better. LAM is a rare disease of unknown etiology that affects women of reproductive age. It is characterized by proliferation of atypical smooth muscle cells in the lung. Proliferation of smooth muscle cells around the bronchiole results in small airway obstruction responsible for air trapping and the development of parenchymal cysts, pneumothorax and increased lung volume. Involvement of lymphatic vessels results in thickening of the walls of the lymphatics and interstitial lymphatic edema, and may lead to chylothorax. Proliferation of cells in the walls of the pulmonary veins may cause venous obstruction, resulting in venous distension, pulmonary venous hypertension and pulmonary hemorrhage.

Although 9 of 11 patients in this study showed abnormality on chest radiographs, the radiographic findings are nonspecific. In the present study, two patients had cystic lesions seen on CT scans, but chest radiographs were normal. Chu et al. [16] reported that chest radiographs were normal in 9 of 35 patients with LAM. Avilo et al. [13] reported that 36 (92%) of 39 patients in their study had lung cysts on CT scans that were not apparent on chest radiographs. In previous studies on chest radiograph findings, LAM typically appears as diffuse interstitial disease, which may have a basilar preponderance, and the lung volumes were normal or increased [3,5,6,9,10]. The reported common radiographic abnormalities of parenchymal changes consist of reticular, reticulonodular, military and multiple cysts like spaces resembling honeycombing [6,10,12,17]. In our study, reticular opacity and increased lung volume were the most common abnormality on the chest radiographs of our patients, similar to previous reports. The reticular pattern on chest radiographs may be due to summation effect of individual cyst walls [11,13]. In six of our patients, the interstitial changes were more severe in lower lung zones on chest radiographs, but could not be confirmed by CT. One may suggest that a summation effect of cyst walls leads to a basal pseudopredominance on the radiographs.

The appearances of LAM on HRCT have been described in the literatures [3,5–13,17]. The most characteristic finding of the disease was multiple thin-walled cysts uniformly distributed in both lungs. The size of the cysts varied from few millimeters to several centimeters and the cysts walls were barely perceptible to 2 mm in thickness. According to one study, the largest cyst was 20 cm in diameter. In our study, the HRCT findings were similar to literatures reported. Multiple cystic lesions were distributed diffusely throughout the lungs in majority of our patients. The walls of the cystic spaces are very thin and ranged from imperceptible to about few millimeters in this thickness. The size of cystic lesions ranged from few millimeters to 15 cm in diameter. In the present study, rather uniform small cysts not larger than 2 cm were observed in seven patients and larger cysts up to 15 cm were observed in four patients. Larger cysts that were seen suggested to be formed by coalescence of smaller cysts. The size of the cystic lesions tends to be larger in severe disease, as reported in the literatures [10,13]. In our study, majority of patients with severe airflow obstruction showed large and intermediate cysts, as those reported in published literatures [12,13]. The presence of interstitial changes in LAM is controversial. In the present study, interstitial changes were detected in most of our patients. In our study, six patients showed thickening of interlobular septa and this finding was also reported in previous studies [5,6,12]. The interlobular septa thickening may be due to involvement of lymphatic vessels by the disease process. Several studies report that cystic airspaces are bounded by normal lung parenchyma [7–12,16] and most reticular patterns on chest radiograph were corresponded to a cross-sectional appearance of innumerable, contiguous small cysts [11].

Air trapping was not seen in our study. Air trapping, a very rare finding in LAM, has been reported in two patients [12,18]. Kircher et al. [12] reported this finding might be due to later stages of the disease examined by CT. Areas of ground-glass opacity were seen in only one patient in our study. This finding presumably represents areas of pulmonary hemorrhage [10]. Lymphadenopathy was seen in 1 of the 11 patients in our study. Kircher et al. [12] reported that enlarged lymph node was seen in 1 of the 11 patients in their series and Sherrier et al. [6] reported that lymphadenopathy was seen in 4 of the 7 patients with complete CT scans. Microscopically, the involved lymph node also showed proliferating smooth muscle cells.

Despite the very characteristic features of LAM at HRCT, the major diseases to be considered in the differentiated diagnosis are emphysema and Langerhan's cell histiocytosis (LCH). Emphysema appeared as focal areas of decreased density that lacked a visible wall and lung involvement is less uniform. The cystic spaces in LAM, compared with those in emphysema, tend to be more uniform, better defined and less variable in size. In addition, identification of residual core lobular structures in the centers of the cystic spaces, characteristic of emphysema, is also helpful in differentiating these two diseases. LCH may be distinguished from LAM on CT by the presence of nodules and cavitary nodules by more irregular shape of the cysts, and by upper lung zones involvement, with spares of the costo-

phrenic angles [19]. Recently, Keyzer et al. [20] reported a case of LAM that mimicked LCH and they suggest that LAM may be variable at an early stage of the disease.

Our study has several limitations. First, the number of patients that was evaluated in this retrospective study was small. LAM is a rare disease; therefore, the number of patients should be small. Second, our estimation of the extent of parenchymal abnormalities and size of the cysts on HRCT was visual. This semiquantitative method may not have reflected the exact extent of disease.

In conclusion, HRCT is a valuable diagnostic tool for work-up of LAM and the typical appearance of LAM is multiple thin-walled cysts uniformly distributed throughout the lungs. The HRCT findings of LAM in our study were not different from reported literatures, except that majority of cases have interstitial changes. Although LAM is s rare disease, it should be suggested in women in their reproductive age with characteristic high-resolution CT features when nonspecific interstitial pattern was depicted on chest radiograph.

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