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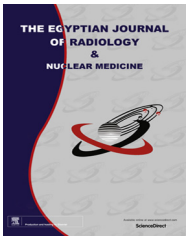

ORIGINAL ARTICLE

Role of high resolution computed tomography (HRCT) of the chest in the diagnosis of lymphangioleiomyomatosis (LAM) – A serial study of 15 patients

Youssriah Y. Sabri [a], **Iman M. Hamdy Ibrahim** [a,*], **Heba Mostafa Ahmed** [a], **Hebatallah H. Assal** [b]

[a] *Diagnostic and Intervention Radiology Department, Faculty of Medicine, Cairo University, Egypt*
[b] *Chest Department, Faculty of Medicine, Cairo University, Egypt*

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KEYWORDS

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Abstract *Aim of work:* To highlight the characteristic high resolution computed tomography (HRCT) findings in 15 patients diagnosed with lymphangioleiomyomatosis (LAM), narrowing the wide range of ILD and allowing accurate diagnosis preventing unnecessary interventional procedures.

Patients and methods: 15 female patients ranged in age from 17 to 55 years (mean age = 40.33 years). ILD was suspected based on clinical examination and chest radiographs. They were referred to do HRCT chest for further assessment. A 64 MSCT scanner was used.

Results: All patients showed bilateral multiple cysts showing upper lobar predominance in 13.3% of cases and lower lobar one in 6.7%. The size of the cysts ranged from few mms to 3 cm with variable wall thickness. Pneumothorax was reported in three patients and pulmonary hypertension in 15 cases.

Conclusion: HRCT is a valued diagnostic tool for diagnosis of LAM showing characteristic features for the disease.

1. Introduction

Lymphangioleiomyomatosis (LAM) is a rare disease of unknown etiology that affects women in their child bearing period, and it occurs in 1–5 per million women. It can arise sporadically or in association with tuberous sclerosis complex

* Corresponding author.
E-mail address: iman92@yahoo.com (I.M.H. Ibrahim).
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(TSC). It mainly affects the lungs promoting cystic destruction, but it can also affect other organs (1,2).

LAM is characterized by proliferation of the atypical smooth muscle cells in the lung. Small airway obstruction secondary to proliferation of smooth muscle cells surrounding the bronchioles leads to air trapping and parenchymal cysts formation which is associated with increased lung volume and with possibility of pneumothorax. Chylothorax may occur secondary to thickened lymphatic walls and interstitial lymphatic edema. Involvement of the pulmonary veins by proliferation of their walls' cells leads to venous distension and pulmonary venous hypertension and may lead to pulmonary hemorrhage (1).

The most common symptom in LAM is progressive dyspnea while fatigue, dry cough, chest pain, wheezing and hemoptysis are common presentations. Spontaneous pneumothorax can occur in 40–80% of the patients. Around 10–20% of patients will sooner or later develop respiratory failure within 10 years (2).

High Resolution Computerized Tomography (HRCT) is an important modality in the evaluation of interstitial lung disease including interstitial cystic lung disease. Characteristic HRCT features of LAM are diffused thin-walled cysts surrounded by normal lung without regional sparing. Pneumothorax is a frequent finding in complicated cases due to rupture of the air containing cysts (3).

The purpose of this study was to highlight the characteristic HRCT findings of LAM, thus narrowing the wide range of ILD and allowing accurate diagnosis without the need of unnecessary interventional procedures.

2. Patients and methods

2.1. Patients

The study was approved by the hospital ethical committee and informed consent was obtained assuring respect of the confidentiality of the medical records.

Fifteen female patients were enrolled in this study.

They were subjected to thorough clinical examination including history taking, general and chest examination. Chest radiographs and pulmonary function tests were performed.

Based on their initial clinical examination and chest radiographs, interstitial lung diseases were suspected and they were referred to our radiology department during the period from January 2011 to November 2015 to do HRCT for further assessment.

2.2. Methods

The scans were performed using a sixty-four section MDCT scanner (Aquilion, Toshiba Medical Systems, Japan). HRCT scans were acquired at end inspiration with patients placed in supine position. No contrast media was administered. The detailed technical parameters of the HRCT scans are mentioned in Table 1.

2.3. Data analysis and interpretation

Following acquisition, axial cuts were sent to the workstation for post processing and reconstruction.

Table 1 HRCT technique using Toshiba Aquilion MSCT 64 channels set.

Scout	kV 120 Holding breath	mA 50
Scan type	Helical full 0.5 s	
Detector row	64	
Helical thickness	1.0 mm	
Pitch	1.484	
Speed (mm/rotation)	0.5	
Detector configuration	64 × 0.5	
Beam collimation	32.0 mm	
Interval mm	1.0	
Gantry tilt	0.0	
FOV	Depend on the patient' size	
kV	120–140	
mA	120–160	
Total exposure time	4–16 s	

Axial, sagittal and coronal reconstructed images are taken. For lung window images the windows are adjusted at WL −700 and WW 1000. Mediastinal window is also taken at WL 50 and WW 300 to evaluate mediastinal structures.

Items that were evaluated in HRCT scans are as follows:

- cysts: presence, distribution and predominant size and wall thickness,
- interlobular septal thickening and reticulations,
- presence of nodules and their sizes,
- ground-glass opacities.

Three radiologists with different years of experience interpreted the scans and a consensus was reached suggesting the typical HRCT features in LAM.

Eleven of the patients were biopsy proven to have LAM using open and transbronchial lung biopsies after doing the HRCT scans. The other four patients had no pathological diagnosis of LAM and the diagnosis was deduced from the classic clinical features and the typical HRCT findings of LAM.

Screening CT brain and CT abdomen were done in all patients. No extra pulmonary manifestations or signs of tuberous sclerosis were detected.

3. Results

Fifteen female patients ranging in age from 17 to 55 years (mean age 40.33 years) were enrolled in this study.

All patients had progressive dyspnea and dry cough. Three had chest pain.

HRCT abnormalities were noted in all included patients.

All patients showed bilateral lung cysts (n = 15, 100%). Cysts were bilateral and rather symmetrical in 14 cases (93.3%) (Fig. 1) and more evident on the left side in one case (6.7%).

The scans revealed that the cysts were equally distributed throughout the lobes of both lung fields in 12 cases (80%), with an upper lobar predilection in two cases (13.3%) (Fig. 2) and a lower lobar one in one case (6.7%).

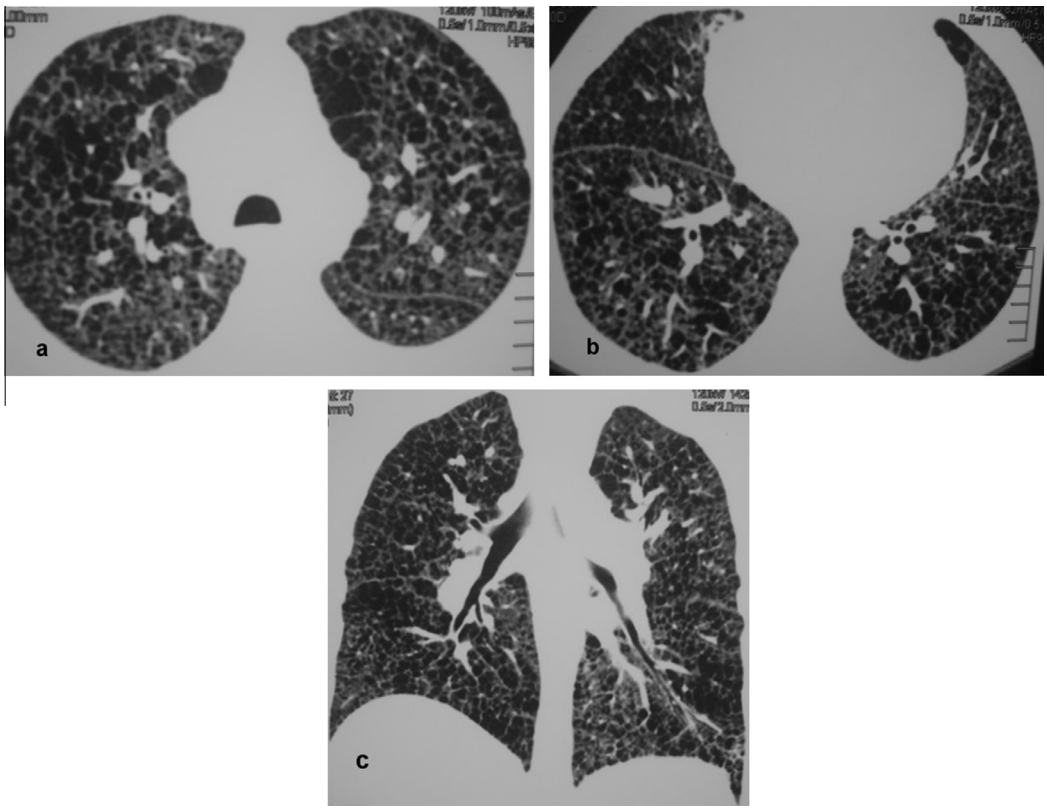

Fig. 1 (a–c): 40-year-old female patient with LAM presenting with dyspnea and dry cough. HRCT axial (a, b) and coronal (c) images show numerous bilateral air-filled cysts evenly distributed in the lung lobes with thickened fissures. All cysts are less than 1.5 cm in diameter.

Numerous cysts showing variable sizes were seen in 13 cases (86.7%) while two cases (13.3%) presented fewer cysts.

The size of the cysts was noted to be ranging from few mms to 1.5 cm in all cases (Figs. 1–3); however, in five cases (33.3%) few cysts reached a size ranging from 2.5 to 3 cm (Fig. 2).

Most of the cysts showed wall thickness ranging from being barely perceptible to nearly 1.5 mm in thickness.

All cases showed air-filled cysts. In only two cases (13.3%) few opaque cysts (fluid-filled) were noted (Fig. 3).

Pneumothorax was noted in three patients (20%) (Fig. 3).

Thickened interlobular septa and thickened fissures were seen in three cases (20%) (Fig. 2).

Pulmonary hypertension was detected in all cases (100%).

PFT in all cases showed combined restrictive and obstructive changes.

4. Discussion

LAM is a rare slowly progressive lung disease affecting almost exclusively young women in their reproductive age. It occurs sporadically or in association with tuberous sclerosis complex. LAM is characterized by smooth muscle proliferation leading to cystic remodeling of the lung parenchyma. The disease has no curative treatment till now, but the ongoing research in the genetic and molecular pathways regarding the disease's pathogenesis could lead to targeted therapy (4).

All patients in our study were females as reported in the literature; however, some researchers reported LAM in males as in studies by Henske et al., 2012 and Miyake et al. 2005 (4,5).

Combined restrictive and obstructive pulmonary function test changes were noted in all patients in our study, while a study conducted by Antn et al., 2009 that included 72 patients showed that obstructive changes occurred in 39 patients (54.2%) and restrictive changes in nine patients (12.5%) (6). Another study dated 1999 and conducted by Chu et al. found out that 26% of the patients developed restrictive pulmonary function test (7).

HRCT revealed bilateral lung cysts in 15 cases in our study (100%) showing variable size and number. Cysts were bilateral and symmetrical in 14 cases (93.3%). Similar results were shown in a study by Lim at al., 2004 that included 11 female patients, all of them showing bilateral symmetrical cystic changes, and in a study by Chu et al., 1999 that included 35 patients (7,8).

Lobar distribution of the cysts in our study showed equal distribution in all lung lobes in 12 cases (80%), upper lobar predominance in 2 cases (13.3%) and lower lobe in one case (9%). According to Lim, 2004, equal lobar distribution was noted in nine patients (82%) and upper and lower lobar distribution in one case each (9%) (8). Another study by Theiling et al., 2015, the distribution of the cystic lesions was significantly more pronounced in the apical and intermediate lung zones compared to the lung bases (9). Koyama et al., 2003,

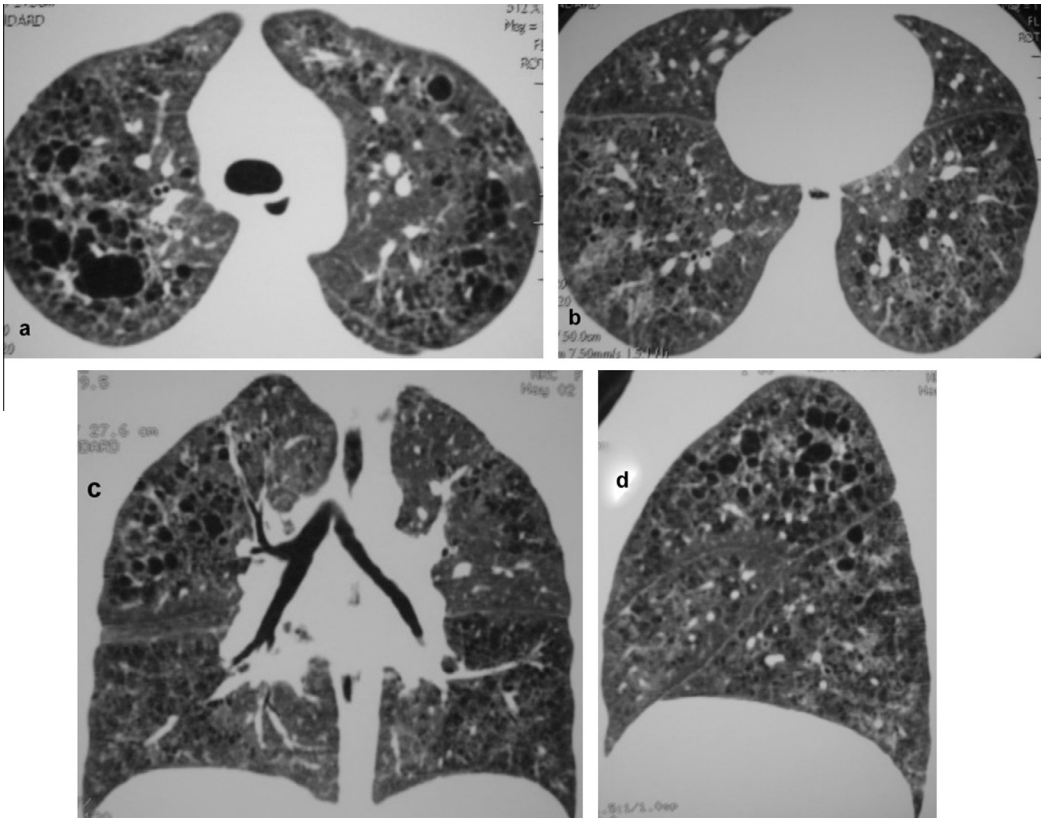

Fig. 2 (a–d): 35-year-old female patient with LAM presenting with dyspnea and dry cough. HRCT in axial (a, b), coronal (c) and sagittal (d) reconstructed images showing bilateral numerous air-filled cysts, predominantly upper lobar (a, c, d) together with thickened interlobular septa and fissures. Most cysts are less than 1.5 cm in diameter; however, a right upper lobar cyst (a) is seen measuring about 2 cm.

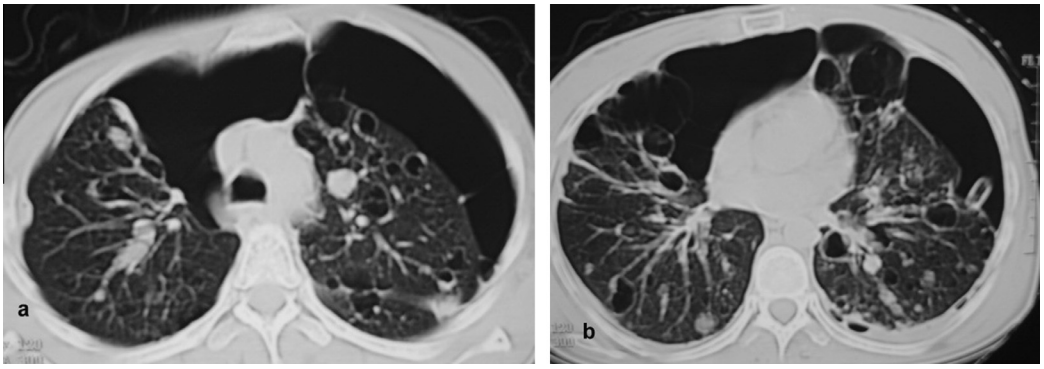

Fig. 3 a and b: 25-year-old female patient with LAM presenting recently with chest pain, progressive dyspnea and dry cough. HRCT axial images showing bilateral air-filled, opaque (fluid-filled) cysts and partially loculated pneumothorax on both sides. An intercostal tube is noted on the left side.

noted random distribution in 23 patients (64%) in their study, upper zone predominance in 11 patients (31%) and lower zone predominance in only 2 patients (6%) (10).

Regarding the size of the cysts, the range in our scans was from few mms to approximately 1.5 cm apart from few ones seen reaching a range of 2.5–3 cm in five cases (33.3%). Cysts larger in size occur in severe forms of the disease were due to coalescence of small cysts. Larger sizes were seen in few cases in other studies as that by Lim et al., where the size of the cysts reached 1 cm in 27% of their patients, 1–2 cm in 36% of the patients and more than 2 cm in 36% of the patients, while in 9% of the cases larger cysts reaching 15 cm were seen (8). Also another study by Koyama et al., 2003 reported that small (less than 1 cm) cysts were seen in 100% of the cases, medium sized cysts (1–2 cm) in 72% and larger than 2 cm in 42% of their cases (10).

Wall thickness of the cysts in our cases was imperceptibly thin (few mms). This was consistent with Lim et al., 2004 while

Koyama et al. 2003 in their study involving 36 patients stated that all their patients had wall thickness of their cysts less than 1 mm while in only 12 patients (33%) it was imperceptible and in 2 patients (6%) more than 1 mm (8,10).

Pneumothorax is one of the main pulmonary complications in LAM. It was seen in 20% of our patients which is less than what was reported in the study by Lim et al., 2004, where pneumothorax was found in 36% of the patient (four patients) (8), while Chu et al., 1999 reported it in 69% of the patients (7).

In our study, HRCT showed thickened interlobar septa and fissures in three patients (20%) with almost similar result obtained from Koyama al, 2003, who reported fissural thickening in 9 out of 36 patients (25%) (10), while in the study done by Lim et al., 2004, the percentage was much higher, around (55%) (six patients out of 11) (8).

One of the major associations of LAM is pulmonary hypertension; all of our patients developed it, which is consistent with another study that suggested pulmonary hypertension in all the subjects (11).

LAM presents very distinctive findings at HRCT; however, emphysema and Langerhans cell histiocytosis (LCH) are two main diseases that should be put into consideration in the differential diagnosis of LAM.

Emphysema presented as focal areas of low attenuation with no visible walls and with a non-uniform lung involvement. This is contradicting with the cystic lesions of LAM which are more uniformly distributed and having well defined walls and less variability regarding their size.

LCH can be differentiated from LAM by its characteristic nodules in which some of them show central cavitation presenting as cysts with irregular shape and by upper zonal preference sparring the costophrenic angles (12).

The small number of cases limited our study; however, LAM is a rare disease.

5. Conclusion

LAM is a rare disease affecting females in their reproductive age. It has a non-specific interstitial pattern in chest radiographs and characteristic HRCT findings making it possible to count on HRCT as a valued diagnostic tool, thus avoiding unnecessary interventional procedures.

Conflict of interest

The authors have nothing to declare.

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