



## Case Study

### A young man with multiple pulmonary cysts

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#### ABSTRACT

Several diseases cause cystic or cyst-like parenchymal lung abnormalities including adult pulmonary Langerhan's cell histiocytosis (PLCH), lymphangioleiomyomatosis (LAM), emphysema, end-stage interstitial lung disease, and cystic bronchiectasis. Many of these diseases can now be diagnosed with high accuracy by the use of high-resolution computerized tomography (HRCT). In fact, HRCT of chest has proved a major breakthrough in the diagnosis of these diseases. We are presenting a young man with a cystic lung disease in which, the HRCT findings were virtually diagnostic of that disease. The clinical and HRCT findings of this disease along with its differential diagnosis are discussed in this paper.

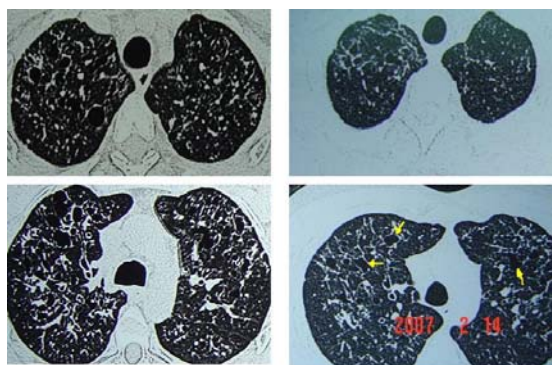
#### CASE HISTORY

A 24 year old, Indian man was referred to chest clinic because of worsening cough and exertional breathlessness despite a six-month treatment with anti-tuberculous medications. Six months prior to this referral, he was admitted to hospital for investigation of cough and exertional breathlessness of six months duration. At that time, he was found to have miliary shadows on chest radiograph (**Figure 1**). During that admission, extensive work-up failed to prove miliary tuberculosis. Three samples of sputum for Acid-fast bacilli (AFB) smear and culture were negative, tuberculin test was negative, and transbronchial lung biopsy revealed unremarkable lung parenchyma, with no granuloma or malignancy detected in the biopsy specimen. Bronchoalveolar lavage for AFB smear and culture was also negative and cytology showed 80% macrophages, 12% neutrophils, lymphocytes 5%, and eosinophils 3%. Due to the high prevalence of tuberculosis in Qatar, empirical treatment for miliary tuberculosis was started and he was discharged home to be followed up in tuberculosis clinic. Despite six months of anti-tuberculous medications, his symptoms persisted. He continued to have dry cough and breathlessness on mild exertion. He had no history of hemoptysis, fever, skin rash or joint pain. He was a heavy smoker; he smoked 20 cigarettes per day for 10 years prior to his presentation and worked as a mechanic. He never kept birds or pets at home

and did not travel during the previous year. Physical examination done in chest clinic revealed a young man with frequent coughing but not tachypneic or cyanosed, and there were no signs of pulmonary hypertension or clubbing. His chest examination revealed normal breath sounds bilaterally with no crackles or ronchi. Oxygen saturation by pulse oxymeter was 96%. His blood count, blood urea nitrogen and serum electrolytes were normal. Pulmonary function testing revealed FEV1 76% of predicted, FVC 73% of predicted, and FEV1/FVC 87%, with DLCO 70% of predicted. High resolution computerized scan (HRCT) of chest was done (**Figure 2**).



**Figure 1:** Chest radiograph of the patient showing diffuse reticular and tiny miliary shadows



**Figure 2:** HRCT of the chest showing variable-sized cysts, with irregular, thin, and thick walls distributed predominantly in the upper lobes (arrows). Micronodular infiltrates are also seen.

**QUESTIONS**

**Question 1:** What are the findings on HRCT of the chest? What is the diagnosis?

**Question 2:** Is lung biopsy mandatory for diagnosis in this patient?

**Question 3:** If lung biopsy is done, which stain is usually used?

**Question 4:** What will you advise this patient?

**ANSWERS**

**Answer to question 1:** The HRCT of the chest shows multiple thin and thick wall cystic changes that are predominant in the upper lobes along with micronodular opacities that are diffusely scattered all over the lungs. Being a young smoker with the predominant involvement of the upper lobes by the cystic changes and the presence of associated micronodular infiltrates, are almost diagnostic of adult pulmonary Langerhan's histiocytosis.

**Answer to question 2:** The HRCT appearance is almost diagnostic. Although lung biopsy may be used to confirm the radiological diagnosis, it is not mandatory with such typical clinical and radiological presentation.

**Answer to question 3:** Immunohistochemical staining with monoclonal antibodies directed against the membrane antigen CD1a is used to stain the Langerhan's cells. Positive staining for intracellular S100 protein, although widely used in the past to identify Langerhan's cells, is not specific to these cells and can also be observed in other cell type.

**Answer to question 4:** Smoking cessation is mandatory due to the strong association between PLCH and smoking that suggests a causal role of smoking in this disease.

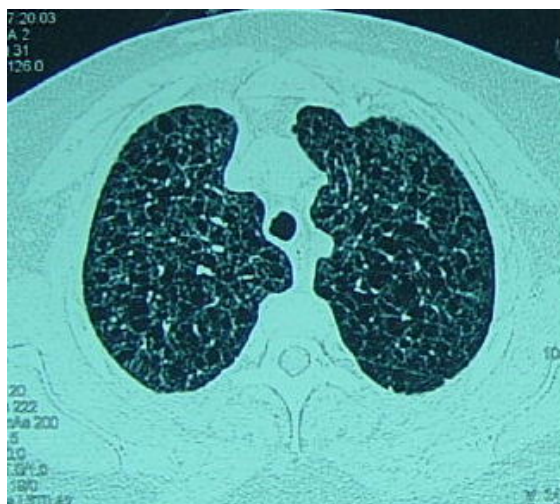
**Table 1:** Characteristic CT appearance of major cystic lung diseases

	<b>PLCH</b> (Figure 2)	<b>Lymphangiomyomatosis</b> (Figure 3)	<b>Centrilobular emphysema</b> (Figure 4)	<b>Bronchiectasis</b> (Figure 5)
<b>Cyst size</b>	Variable	Variable	Variable with centrilobular arteriole in the center of the cyst	Variable
<b>Cyst wall thickness</b>	Both thick and thin	Thin	Invisible	Thick with signet ring appearance
<b>Cyst shape</b>	Variable, irregular, confluence of adjacent cysts	Usually rounded	Polygonal, may be variable	Variable
<b>Cyst distribution</b>	Predominantly upper lobes, sparing of costophrenic angles	Diffusely and uniformly distributed all over the lungs	Mainly upper but can be anywhere	Variable
<b>Micronodules</b>	Present	Usually absent	Absent	Usually absent
<b>Clinically</b>	Almost always in smokers (usually young)	Almost all are females of childbearing age	Usually smokers	Sputum production

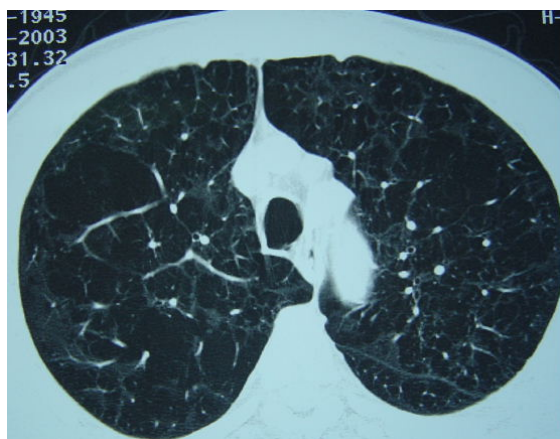
**DISCUSSION**

Pulmonary Langerhan's cell histiocytosis (PLCH) in adults is a rare disorder of unknown etiology that occurs almost exclusively in smokers [1]. There is usually a considerable

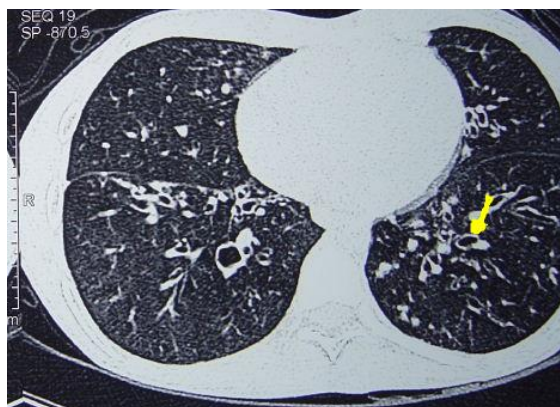
time delay before the diagnosis is made. The average interval between the onset of clinical symptoms and diagnosis is about six months [2]. The etiology of PLCH remains obscure, but the strong association (90-100%) with



**Figure 3:** HRCT in a woman with lymphangioleiomyomatosis showing diffuse, rounded, and thin walled cysts.



**Figure 4:** HRCT in a patient with emphysema showing multiple polygonal translucencies, with almost invisible walls.



**Figure 5:** HRCT in a patient with cystic bronchiectasis showing dilatation of the bronchioles with thickening of their walls. Signet ring appearance is seen (arrow)

cigarette smoking suggests a role for tobacco smoke in the pathogenesis of this disease. The details regarding how tobacco smoke triggers the formation of PLCH lesions remains imprecise. An immune response to a component of tobacco smoke has been

suggested [1]. Although PLCH occurs predominantly in smokers, it is unclear why only a small percentage of smokers have this problem, suggesting that other unknown factors are in play. Furthermore, the development of PLCH following Hodgkin's disease or its treatment has also been reported previously. This may raise the question of common etiologic factors between smoking and Hodgkin's disease or immunosuppression [3]. PLCH predominantly affects young adults, with a frequency peak at 20-40 years of age. Accurate epidemiological data for PLCH are not available and the exact incidence of the disease is unknown [1]. Although there does not appear to be gender predominance, female patients with PLCH tend to present later in life. The most common symptoms are dry cough and exertional breathlessness. Pneumothorax may develop in about 10-20% of cases. Hemoptysis is uncommon and should not be attributed to PLCH until other causes (particularly lung cancer in these smoking patients) have been ruled out [1,2,4,5]. HRCT of the chest has revolutionized the diagnostic approach of PLCH. The CT scan findings of typical cystic changes that predominantly affect the upper lobes, along with micronodular infiltration in an adult smoker are virtually diagnostic of this disorder [6,7,8]. Many reports have confirmed the high diagnostic reliability of HRCT in PLCH.[6,7,8] Less inter-observer variability has been reported with radiographic diagnosis of PLCH as compared to other lung diseases [7]. **Table 1** describes the distinguishing clinical and CT scan appearance of the major cystic lung diseases. Open lung biopsy may not be required when the CT scan appearance is typical for PLCH, particularly in young adults with a history of heavy smoking. Lung biopsy may be needed in selected cases when the CT scan shows isolated micronodular changes [6]. The lung pathology typically reveals the presence of Langerhan's cells, which can be confirmed by immunohistochemical staining with monoclonal antibodies directed against the membrane antigen CD1a. Positive staining for the intracellular S100 protein, although widely used to identify Langerhan's cells, is not specific to these cells and can be observed in neuroendocrine cells and some macrophages [1]. Pulmonary function testing (PFT) is abnormal in the majority of patients with PLCH. DLCO is reduced in more than 75% of patients. Pure restrictive, obstructive, or mixed pattern can be observed [9]. The course of adult PLCH is variable and unpredictable, ranging from a symptomatic course to progressive disease that leads to respiratory

failure and death over periods of months [9]. Although smoking cessation is considered a mandatory step in the treatment of patients with this disorder, nevertheless, no randomized double-blind studies have been published regarding treatment of this disorder. The long-term effectiveness of smoking cessation on the natural history of PLCH remains controversial, and only few case reports documenting partial or complete improvement of the disease following smoking cessation have been published in literature [10,11,12]. Glucocorticoid therapy attenuates the constitutional symptoms and is advocated on empirical grounds in the treatment of recent-onset symptomatic nodular PLCH. It should be highlighted, however, that there are no evidence-based data for the use of this treatment in PLCH [1]. Our patient had a significant clinical and radiological improvement that occurred in temporal association with smoking cessation, which may add evidence to the effectiveness of smoking cessation as a treatment modality for PLCH. However, the long-term efficacy of this type of therapy needs to be elucidated in future. PLCH should be a diagnostic consideration in young smoking patient with cystic lung disease.

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