



GLOBAL JOURNAL OF MEDICAL RESEARCH: D
RADIOLOGY, DIAGNOSTIC AND INSTRUMENTATION
Volume 18 Issue 1 Version 1.0 Year 2018
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

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GJMR-D Classification: NLMC Code: WI 800



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Pulmonary Langerhans Cell Histiocytosis in a Male Teenager - A Case Report with Emphasis on HRCT Findings

Joana Ruivo Rodrigues ^α, Bernardete Rodrigues ^σ, Filipa Costa ^ρ & Duarte Silva ^ω

Abstract- Pulmonary Langerhans cell histiocytosis (PLCH) is a rare pulmonary disorder with characteristic imaging features. It usually affects young adults and is associated with cigarette smoking. PLCH is listed in the gamut for cystic lung disease and should be considered by the radiologist if the appropriate findings are identified. The authors report an advanced case of PLCH in a young male with a smoking load of 6 pack-year. The prognosis is variable with frequent regression, stabilization, or recurrence of disease.

I. INTRODUCTION

The lungs in Langerhans cell histiocytosis can be involved primarily or secondarily in any age group. Pulmonary Langerhans' cell histiocytosis (PLCH) is referent to the solitary lung involvement and is a rare cystic lung disease.

The focus of this article is the description of a rare case of a cystic pulmonary disease related to cigarette smoking, the PLCH. Radiographic and Computed Tomography findings of the patient are described and the most imaging features of this pathology are here highlighted.

II. CASE PRESENTATION

A 19 year-old man presented to the emergency department with a 1-month history of dyspnea after prolonged dry and non-productive coughing episodes. He had no thoracalgia or fever. At 18 years-old he had an episode of acute onset dyspnea and recurred to the emergency department in a peripheral hospital where he performed a chest radiograph with the diagnostic of spontaneous pneumothorax and any other diagnose. He did not take regular medications. He has worked in an aviary since his sixteen years and has a smoking load of 6 pack-year.

On physical examination, there were no signs of cyanosis, clubbing or lymphadenopathy. At physical examination vesicular breath sounds were present and no adventitious sounds were heard throughout both lungs.

The postero-anterior chest radiography done at arrival (Fig.1) revealed the presence of diffuse cystic changes throughout the upper and mid lung zone. A thoracic High Resolution Computed Tomography (HRCT) was suggested to further characterize these findings.

The HRCT demonstrated diffuse bilateral, bizarre shaped, coalescent and thin-walled cysts. The majority of them measured more than 1 cm in diameter and some of them were partially septated and confluent. The cysts had a predilection for the mid and upper zones and a regional sparing of the costophrenic recesses and lung bases (Fig. 2). In both lungs there were a few nodules, some of them with central cavitation and with irregular margins (Fig.3). No pneumothorax or pleural effusion were present.

Pulmonary function tests revealed mild mixed restriction and obstruction with discrete loss of diffusion capacity (DCLO=74%). Bronchoscopy revealed normal airways. A bronchoalveolar lavage (BAL) specimen was negative for microorganisms, the differential cell count revealed 68 % macrophages, 28% lymphocytes and CD4/CD8= 0,98. The Cluster of Differentiation 1a (CD1a) was positive. The α_1 -antitrypsin (A1AT) was negative, excluding the diagnosis of pan-lobular emphysema. The abdominal ultrasonography and the skeletal radiography didn't reveal any lesion.

The patient was diagnosed Pulmonary Langerhans cell histiocytosis taking into account the typical clinical history (initial episode of pneumothorax and progressive dyspnea with low DCLO); the typical imagiologic features (pulmonary bilateral diffuse bizarre cysts and nodules, sparing the costophrenic recesses and bases); and the positive immunohistochemical staining for CD1a surface antigen, specific for Langerhans cells. The cardiac thoracic surgeons team taking into account the extension of the cystic lesions and the operative risk chose not to perform the lung biopsy. Despite the patient was advised to stop smoking he continued to do it and his pulmonary function has been deteriorated considerably.

III. DISCUSSION

Langerhans cell histiocytosis is the most common primary histiocytic disease that affects the

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lung. The infiltration of specialized dendritic cells (Langerhans cells) can cause a single disease site (PLCH) or can involve multiple organs [1].

The Langerhans cells were described for the first time by Paul Langerhans in 1868, based on clinical observations [2]. These cells are usually within the airway mucosa and lung parenchyma and they increase in number with exposure to cigarette smoke. Smoking releases multiple chemokines, proteases, and enzymatic reactions, which produce damaging free radicals that destroy lung architecture leading to airway fibrosis [3]. The Langerhans cells can be identified by immunohistochemical staining for CD1a surface antigen or by the presence on electron microscopy of Birbeck granules [4]. The bronchiolar, interstitial, alveolar and vascular compartments of the lung are affected in PLCH. The varying degrees of interstitial inflammation, alveolar macrophage infiltration, and proliferative vasculopathy of both arteries and veins are caused by inflammatory bronchiolitis with loosely formed nodules of dendritic cells that are collected around small airways. Pathologic inspection shows nodules being replaced by advanced bullous and cystic lesions, often in association with hyperinflation and late-stage fibrosis with honeycombing [5].

PLCH can appear in all ethnic groups and can involve patients of all age groups, being most often diagnosed in patients between the ages of 20 and 40 years and being rare in children[5]. Women and men are equally affected[6]. The precise prevalence and incidence of LCH are unknown, however in a study which describe more than 500 patients with lung diseases and surgical lung biopsy the PLCH was diagnosed in 3.4% of the cases [7]. About 90% of patients have a smoking history; however the role of smoking in disease pathogenesis is incompletely understood [5].

Patients are asymptomatic in 25% of the cases when diagnosed of PLCH. In 2/3 the patients present with nonspecific symptoms like non-productive cough or dyspnea, and usually these symptoms have insidious onset and patients may attribute them to smoking. The disease can present for the first time with spontaneous pneumothorax in 10–20% of cases [6]. Pneumothorax tends to recur and may be bilateral. A minority of patients can have fever, weight loss and malaise [8].

On chest auscultation adventitious sounds are rarely present even in the presence of extensive radiological abnormalities. When advanced disease is present pulmonary hypertension and *cor pulmonale* can be seen [8].

The pulmonary function tests can show different patterns: obstructive, restrictive, or mixed. The carbon monoxide diffusing capacity (DCLO) is decreased in up to 90% of patients [9].

The radiographic appearance of PLCH is variable depending on the stage of disease, ranging

from small peribronchiolar nodular opacities to multiple irregularly-shaped cysts. Distribution of the lesions is the key for the differentiation of PLCH from other cystic lung diseases [10,11]. Differential diagnosis depends on whether nodular or cystic change is the dominant feature. In the early phase, when nodules are the dominant feature, it should be considered granulomatous diseases, metastases and miliary tuberculosis. In later phase, when cysts are prominent, it should be considered: lymphangiomyomatosis (LAM) (woman with diffuse distributed, regular shaped and sized cysts); cystic bronchiectasis; centrilobular emphysema; *Pneumocystis jiroveci* pneumonia; idiopathic pulmonary fibrosis (basal and subpleural distribution and reduced lung volumes); lymphocytic interstitial pneumonitis (LIP) [8-10].

The chest radiographic appearance usually is abnormal with bilateral and symmetrical, predominantly upper and mid-lung zone, nodules up to 1 cm in size, with irregular borders, usually sparing costophrenic angles and lung bases [8,10]. In the early stages of disease bilateral nodular and reticulonodular changes can be present. In the late stages, prominent cystic are dominant and nodules may regress[12]. In PLCH the lung volumes are preserved or increased [8,10]. Pneumothorax and pulmonary arterial hypertension are complications of PLCH[10].

High-resolution CT is the most sensitive imaging technic to show the spectrum of imaging features of PLCH, and these findings reflect the macroscopic appearance of the disease [10]. Brauner et al postulated the following sequence of abnormalities seen on CT scans: nodules, cavitory nodules, thick-walled cysts, thin-walled cysts, and confluent cysts [11]. The nodules are more pronounced early in the disease, may range in number from a few to innumerable, measuring typically 1-5 mm in diameter, with centrilobular distribution and irregular margins. They may cavitate and become cysts, which are more pronounced later in the disease. Cysts are surrounded by normal lung, measuring up to 2 cm and in late stage are thin-walled. The confluence of 2 or more cysts results in bizarre shapes cysts[10,11].

The inspection on bronchoscopy typically reveals normal airways, but bronchoalveolar lavage (BAL) specimens are usually cellular. The majority of the cells are alveolar macrophages, consistent with the fact that most patients are smokers. BAL cellular composition may demonstrate an increase in CD1a-positive cells, with 5% or greater considered highly supportive of the diagnosis [8].

Surgical biopsy is the main approach for the definitive diagnosis of PLCH, however it is an invasive procedure. Lung biopsy can generally be avoided when the HRCT findings are characteristic and concordant with the clinical history[8, 13]. CT findings of cysts and nodules in the middle and upper lung zones with

sparing of the lung bases are considered virtually diagnostic of PLCH[10].

About 50% of patients have clinical and radiographic stability, while up to 25% will demonstrate spontaneous regression[9]. Smoking cessation alone for most patients result in symptom stabilization [8,9]. Despite limited evidence of benefit corticosteroids are frequently used in the management of PLCH [8]. Lung transplantation is an option for patients with rapid deterioration of pulmonary function, although smoking cessation needs to be demonstrated to consider this option, as pulmonary LCH can recur if the patient continues to smoke. Pulmonary hypertension or respiratory failure are the main causes of mortality related with PLCH [9].

In conclusion, PLCH is a rare interstitial lung disease of unknown cause that primarily affects young adult cigarette smokers who typically present with cough, dyspnea, and mildly decreased diffusing capacity. High-resolution CT findings may be diagnostic of PLCH in the appropriate clinical setting, as shown in our case.

Conflict of interest

The authors wish to confirm that there are no known conflicts of interest associated with this publication and there has been no financial support for this work that could have influenced its outcome.

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FIGURES

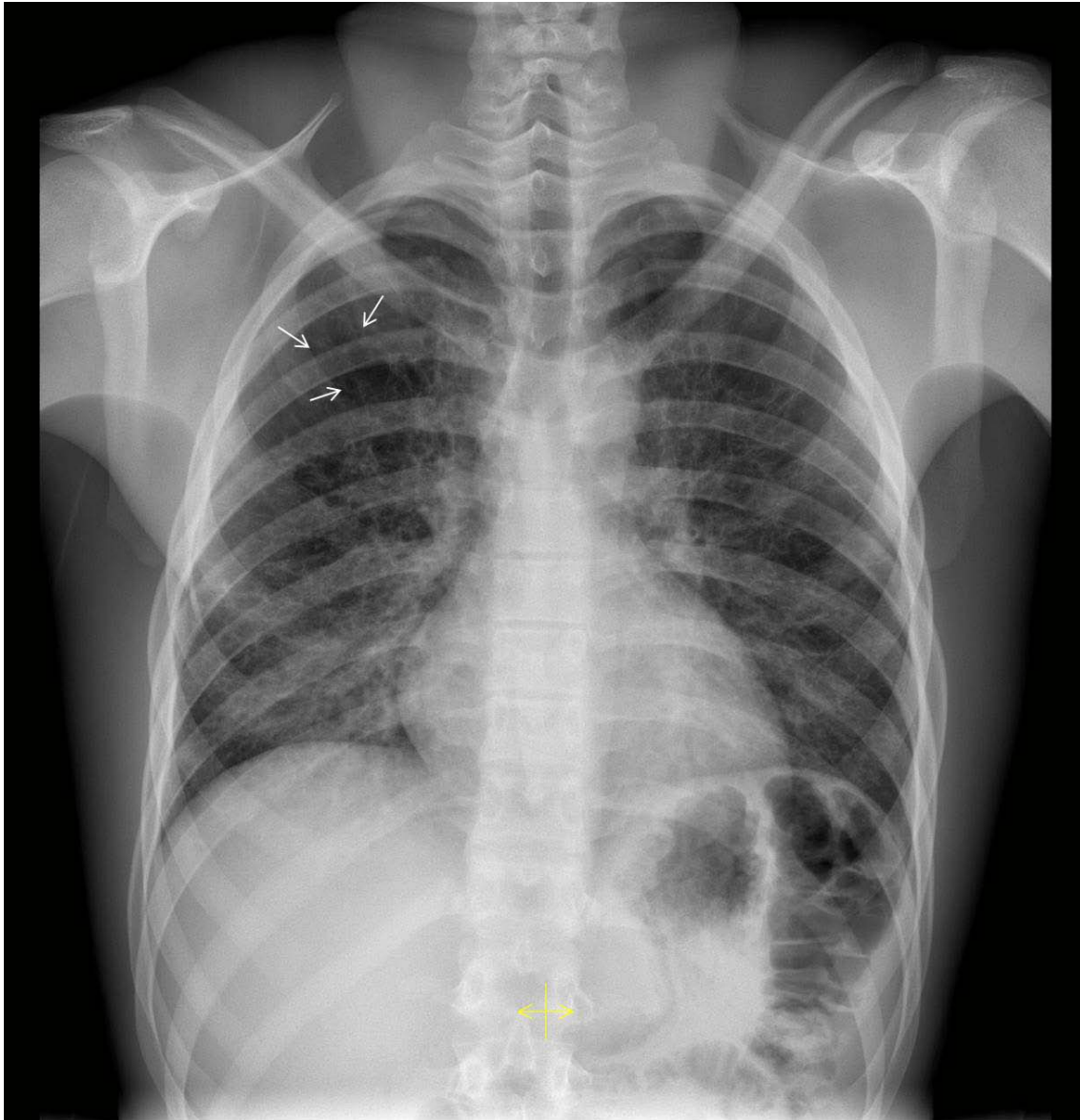


Figure 1: Chest radiography with postero-anterior incidence demonstrating cystic structures distributed diffusely in the upper and mid lung and more prominent on the right upper lung (arrows).

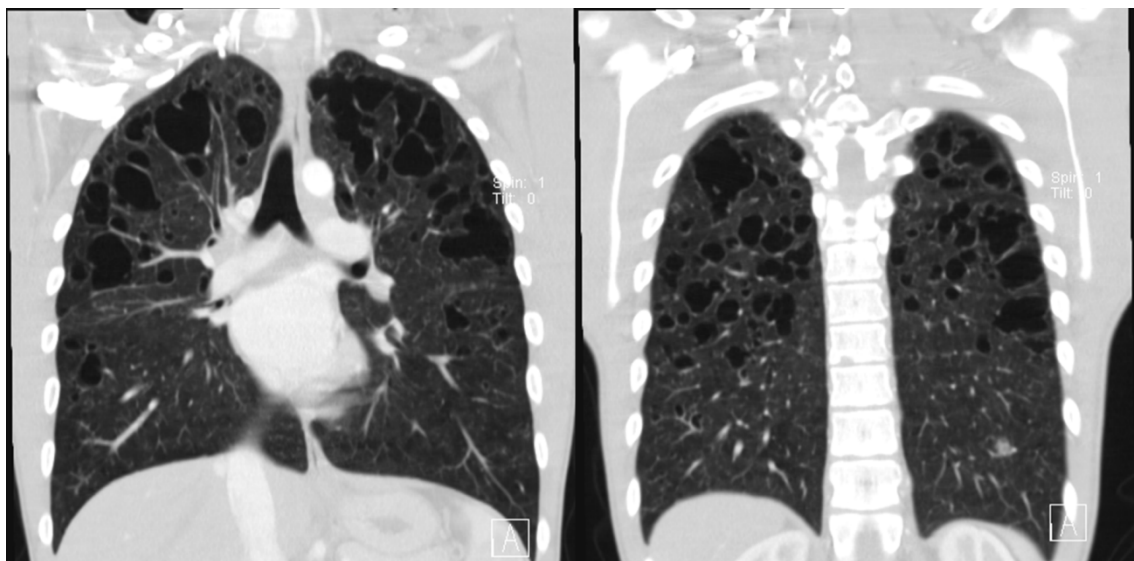


Figure 2: Coronal high-resolution CT images (lung window) showing diffuse lung cysts predominantly thin-walled, with bizarre shapes and various sizes, packed throughout the middle and upper lungs. There is relative sparing of the lung bases and costophrenic angles. Few nodules are also present.

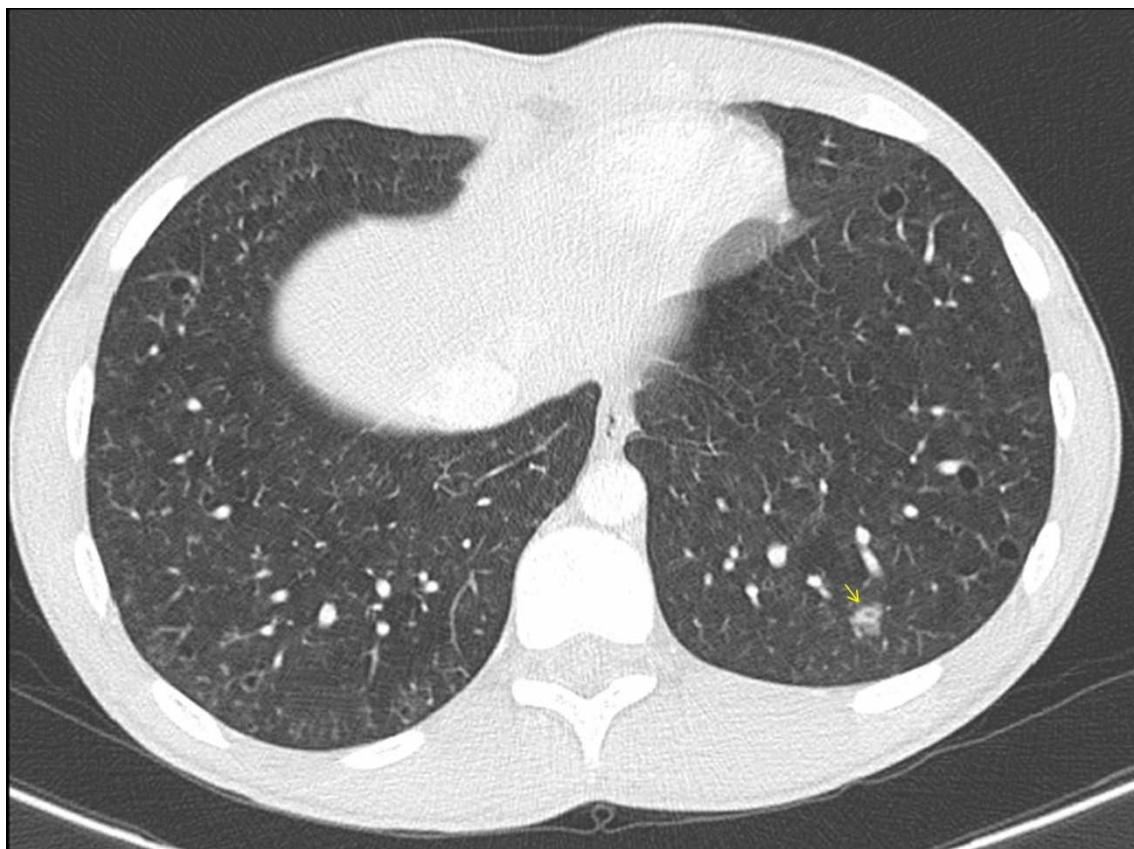


Figure 3: Axial high-resolution CT image (lung window) showing a solid peripheral nodule (arrow) with 13 mm, in the left lung base with irregular margins and central cavitation. The surrounding lung parenchyma appears normal.