



PULMONARY LANGERHANS CELL HISTIOCYTOSIS IN A YOUNG ADULT SMOKER: A CASE REPORT

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ABSTRACT

Introduction

Pulmonary Langerhans Cell Histiocytosis (PLCH) remains a rare and enigmatic disorder among interstitial lung diseases, primarily targeting young adult smoker. It becomes a diagnostic challenge due to its variable clinical manifestations and radiological features.

Case Presentation

A 27-year-old male with a significant smoking history presented with progressive dyspnea and pleuritic chest pain. High-resolution computed tomography (HRCT) of the chest revealed classic findings of multiple nodules, cavitary lesions, and cysts with upper and mid-lung predominance, complicated by a spontaneous pneumothorax. A diagnosis of PLCH was made based on the clinical and radiological characteristics. The patient was treated with emergent chest tube insertion. Afterward, he also received a nine-day course of high-dose systemic corticosteroids and broad-

spectrum antibiotics. Following stabilization of his acute condition and completion of these interventions, rigorous implementation of smoking cessation counseling was performed. Follow-up at eight months revealed significant symptomatic relief and notable radiological regression of lesions on HRCT

Conclusions

This case underscores the pivotal role of HRCT in the non-invasive diagnosis of PLCH in order to determine the acute management strategies required for life-threatening complications and reaffirms smoking cessation as the most potent long-term therapeutic intervention.

Keywords

Cystic lung disease, High-resolution computed tomography, Pulmonary Langerhans Cell Histiocytosis, Smoking, Young adult smoker.

INTRODUCTION

Pulmonary Langerhans Cell Histiocytosis (PLCH) remains a significant challenge within the spectrum of diffuse cystic lung diseases. Formerly known as histiocytosis X, PLCH has been more defined as a clonal disorder of myeloid dendritic cell precursors, driven by somatic mutations that constitutively activate the MAPK signaling pathway [1, 2]. This molecular understanding has fundamentally shifted its perception from a purely reactive inflammatory disease into an "inflammatory myeloid neoplasm" [1,3]. PLCH predominantly affects young adults, typically between the ages of 20 - 40, with a slight or no gender predilection [1, 2]. The most prominent epidemiological feature is its profound association with cigarette smoking, observed in up to 90-95% of adult cases, implicating tobacco smoke as a critical etiological factor in disease initiation and progression [1-4]. Emerging evidence also suggests a potential link between electronic cigarette (vaping) use and PLCH development, broadening the scope of inhaled risk factors [5].

PLCH may present as a wide spectrum of manifestations, ranging from asymptomatic individuals with incidental radiological findings to those with respiratory failure. Symptoms include non-productive cough, exertional dyspnea, fatigue, chest pain, and weight loss [1,2]. A well-recognized and sometimes initial presentation is spontaneous pneumothorax, occurring in a few patients but with significant impact [3]. The diagnostic cornerstone of PLCH is high-resolution computed tomography (HRCT) of the chest. The characteristic HRCT signature includes a combination of small, poorly defined nodules and thin-walled, often bizarrely shaped cysts, typically with a bilaterally symmetric distribution and a striking predominance in the upper and mid-lung zones, sometimes with relative sparing of the costophrenic angles [3, 4]. These findings, when correlated with a compelling smoking history and young age, often allow for a confident clinical-radiological diagnosis, potentially avoiding the need for invasive biopsy in select cases, although histopathological confirmation demonstrating CD1a and CD207 positive Langerhans cells remains the gold standard, especially in atypical presentations [3,6,7].

The management for PLCH is multifaceted. Smoking cessation is the most important intervention and is associated with disease stabilization or regression in a significant proportion of patients [1,3,7,8]. For patients with progressive disease, significant symptoms, or multisystem involvement, pharmacological therapies may be considered. Corticosteroids are sometimes used empirically, but their efficacy is not well-established by robust clinical trials [8]. For more severe or refractory cases, chemotherapy agents such as cladribine or cytarabine are often recommended based on expert consensus [8]. The advent of targeted therapies against the MAPK pathway, such as BRAF inhibitors (e.g., vemurafenib, dabrafenib) and MEK inhibitors (e.g., trametinib), has revolutionized the treatment of refractory multisystem LCH, including cases with pulmonary involvement, particularly those harboring BRAF V600E mutations [2,6,8]. This report presents a case of PLCH in a young adult smoker, highlighting the classic clinical and radiological features, the diagnostic utility of HRCT, and the transformative impact of smoking cessation.

CASE REPORT

A 27-year-old male presented with a three-month history of progressively worsening dyspnea, initially on moderate exertion and subsequently limiting his daily activities. He also reported a sharp, right-sided pleuritic chest pain. He denied any associated fever, chills, night sweats, hemoptysis, or significant unintentional weight loss. His past medical history was notable for a recent episode of cutaneous Herpes Zoster, for which he had completed a course of oral immunosuppressive therapy. He had no known drug allergies. A significant risk factor was his extensive smoking history: he had been smoking approximately 20 cigarettes daily for the past ten years, amounting to a 10-pack-year history. He denied any use of electronic cigarettes or other inhaled substances. There was no family history of interstitial lung disease, tuberculosis, or other genetic disorders.

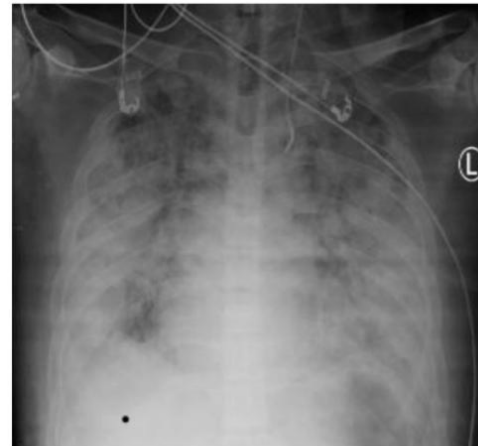
On physical examination, the vital signs were within normal limits. General examination revealed no digital clubbing, peripheral cyanosis, or palpable lymphadenopathy. Auscultation of the chest revealed bilateral vesicular breath sounds with fine, late inspiratory crackles, predominantly

audible over the upper lung zones posteriorly. No wheezes or rhonchi were detected. Cardiovascular and abdominal examinations were unremarkable.

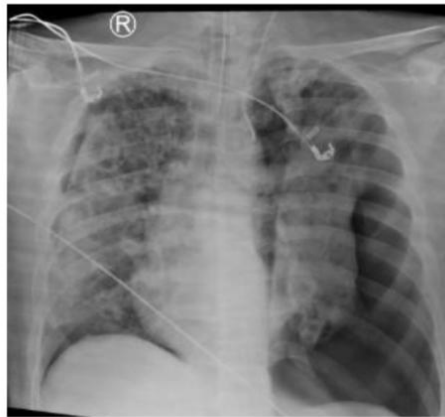
Initial investigations included a posteroanterior and lateral chest radiograph. The chest X-ray demonstrated bilateral reticular opacities, suggestive of an interstitial lung process, along with areas suggestive of early fibrotic changes, particularly in the upper lung zones. A small right-sided pleural effusion was also noted. Lung volumes appeared relatively preserved. (Figure 1)



A



B



C



D

Figure 1 (A to C) Initial X-ray examination of the patient (D) Thorax X-ray 8 months following treatment

Given these findings and the patient's symptoms, a high-resolution computed tomography (HRCT) scan of the thorax was performed without intravenous contrast to provide a more detailed assessment of the lung parenchyma. The HRCT scan revealed multiple, variably sized pulmonary cysts distributed throughout both lungs, with a clear predominance in the upper lobes and a peripheral distribution. These cysts exhibited both thin-walled and partially thickened walls; the largest cyst measured approximately 3.8 cm in its greatest dimension. Areas of subpleural consolidation and subpleural nodular opacities were also observed. The overall HRCT pattern, characterized by the combination of nodules, cavitary lesions, and cysts with an upper lobe and peripheral predominance, was highly characteristic of Pulmonary Langerhans Cell Histiocytosis. The imaging also confirmed the presence of a small right-sided pleural effusion. Notably, the costophrenic angles were relatively spared, a classic feature of PLCH. (Figure 2)

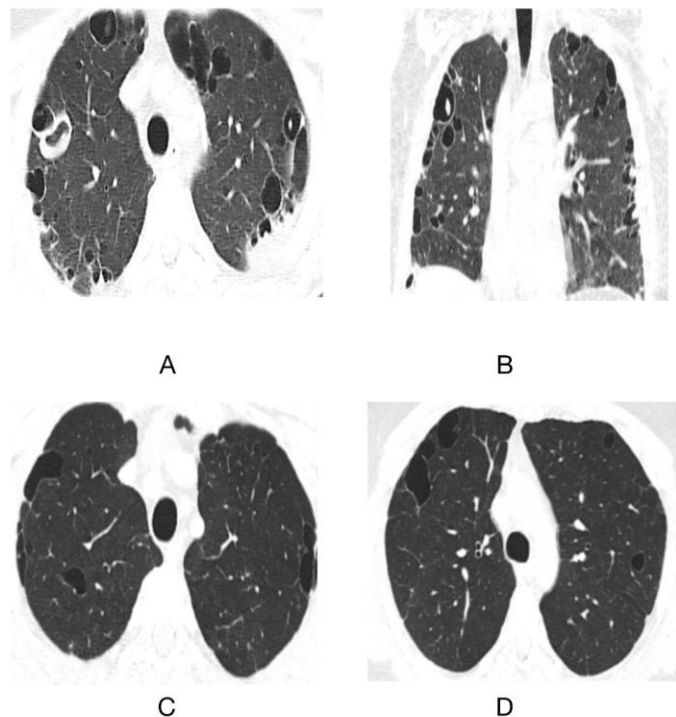


Figure 2 (A and B) Initial HRCT presentation of the Patient (C and D) Follow-up HRCT post treatment

During the course of his initial evaluation, the patient developed an acute onset of severe dyspnea and right-sided chest pain. A repeat chest X-ray at that time revealed a large left-sided tension pneumothorax (Figure 1C). This was managed emergently with the insertion of a chest tube connected to a water-seal drainage (WSD) system, leading to successful re-expansion of the lung and symptomatic relief. In conjunction with the management of his pneumothorax, the patient was initiated on a nine-day course of high-dose systemic corticosteroids protocol and broad-spectrum intravenous empiric antibiotics. The rationale for the high-dose steroids was to reduce perilesional inflammation potentially contributing to air leak and pleural irritation, also addressing any possible concurrent inflammatory component of his underlying PLCH. Antibiotics were administered due to a suspected infectious component that could not be entirely ruled out initially.

Based on the young age, significant smoking history, classic HRCT findings, and the complication of spontaneous pneumothorax, a clinical diagnosis of PLCH was made. The HRCT findings were deemed sufficient to support the diagnosis, and a multidisciplinary team consensus was reached to prioritize smoking cessation and close clinical and radiological follow-up, with the understanding that lung biopsy would be considered if the clinical course was atypical or if there was no response to initial management. Following stabilization from his acute pneumothorax and completion of the course of steroids and antibiotics, the patient received intensive counseling regarding the critical importance of smoking cessation. He was enrolled in a comprehensive smoking cessation program, which included behavioral counseling and pharmacological support with nicotine replacement therapy. No specific long-term pharmacological therapy for PLCH (such as chemotherapy) was initiated at this stage, given the decision to prioritize smoking cessation and monitor the response.

The patient was closely followed up in the outpatient clinic. He reported successful abstinence from smoking. At his eight-month follow-up, he was significantly improved symptomatically, with resolution of his dyspnea and chest pain. A repeat HRCT scan performed at

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this time showed a remarkable relative improvement in the appearance of the upper and middle lung fields (Figure 2C and 2D). There was a noticeable decrease in the number and size of the nodular lesions, and many of the cystic lesions appeared less prominent, with some resolution of the subpleural consolidation. Residual cystic changes and minimal fibrotic strands were still present, consistent with the expected sequelae of PLCH following smoking cessation. The patient was advised to continue abstaining from smoking and was scheduled for regular clinical and radiological follow-up to monitor his progress.

DISCUSSION

Pulmonary Langerhans Cell Histiocytosis (PLCH) remains an enigmatic entity in interstitial lung disorders. In our case, the demographic profile and significant smoking history immediately place PLCH high on the differential diagnosis for his respiratory symptoms. The association of PLCH with cigarette smoking in adults is quite apparent, affecting 90-95% of all patients [1,2]. Components of cigarette smoke are thought to act as chemoattractants for Langerhans cell precursors, inducing the release of pro-inflammatory cytokines, and creating a local pulmonary environment conducive to the survival and proliferation of pathogenic LC clones harboring MAPK pathway mutations [1,2,5]. The recent identification of PLCH in individuals with a history of heavy vaping, as reported by Hirunpat et al. (2025), suggests that other inhaled substances may also carry risk, warranting further investigation [8].

The clinical presentation in this case aligns with the common symptomatic spectrum of PLCH, which includes non-productive cough (46.2%), exertional dyspnea (53.8%), and chest pain (11.5%) [3]. The development of a spontaneous tension pneumothorax is a life-threatening complication of PLCH, occurring in up to 10-30% of patients at presentation and up to 45% during their disease course [2]. This complication arises from rupture of subpleural cystic lesions into the pleural space and requires prompt intervention, as seen in this patient.

High-resolution computed tomography (HRCT) was the defining factor in diagnosing PLCH in this patient. The HRCT findings of multiple heterogenous small nodules, cavitory nodules, and

thin-walled (as well as partially thick-walled) cysts, as well as bilateral and symmetric distribution with upper and mid-lung zone predominance and relative sparing of the costophrenic angles, are considered highly characteristic for PLCH [3, 4]. A recent retrospective cohort study emphasized that HRCT can lead to a correct diagnosis in 84% to 90% of cases without biopsy [3]. Chang et al. (2025) further detailed the HRCT responses to therapy, highlighting its utility in both diagnosis and monitoring of the disease [4]. The presence of subpleural consolidation and nodular opacities, as seen in this case, can also be part of the active inflammatory phase of the disease. While HRCT is often diagnostic in the appropriate clinical setting, histopathological confirmation demonstrating CD1a-positive and CD207-positive Langerhans cells remains the gold standard [1].

The long-term management of PLCH is fundamentally anchored in smoking cessation. This intervention is repeatedly emphasized as the single most effective strategy for halting disease progression and can lead to significant clinical and radiological improvement, as dramatically illustrated in this patient [2, 3]. The profound impact of smoking cessation in this case, leading to symptomatic resolution and marked radiological improvement within eight months, serves as a powerful testament to its efficacy. For patients who continue to smoke, the disease often progresses, leading to respiratory failure, pulmonary hypertension, or recurrent pneumothoraces. The role of pharmacological therapies in PLCH is less clearly defined due to the disease's rarity and the lack of large, randomized controlled trials. As mentioned, corticosteroids are sometimes used empirically in patients with progressive disease or significant symptoms, but their efficacy remains unproven, and they are associated with potential side effects, especially with long-term use [8]. For patients with severe, progressive, or multisystem LCH, cytotoxic chemotherapy agents such as cladribine or cytarabine are often recommended based on expert consensus and smaller studies [8].

The prognosis of PLCH is variable. While many patients achieve stability or improvement with smoking cessation, a significant minority (estimated at 25-30%) may experience disease progression leading to respiratory failure, pulmonary hypertension, or recurrent pneumothoraces [2]. Factors associated with a poorer prognosis include continued smoking, extensive cystic changes on HRCT at presentation, severely reduced DLCO, and the development of pulmonary hypertension, which can occur in more than 10% of patients and is not always directly correlated

with the severity of parenchymal disease [2, 5]. Long-term follow-up is essential for all PLCH patients, even those who initially improve, as late relapses or the development of complications can occur. The Histiocyte Society blueprint for LCH research emphasizes the need for a deeper understanding of the cell-of-origin and the biological dynamics of the disease over its natural history to improve clinical decision-making and patient outcomes [7].

CONCLUSION

This case report illustrates the pivotal role of high-resolution computed tomography (HRCT) in identifying the pathognomonic radiological features of PLCH, often allowing for a confident clinical diagnosis and prompt treatment, addressing the immediate life-threatening complication and potential inflammatory components of the disease.

DECLARATIONS

Consent

Written informed consent for the publication of the data was obtained from the patients

Data availability

No data associated with this article

Underlying data

All data underlying the results are available as part of the article and no additional source data are required

Competing interests

None to be disclosed

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