

CASE REPORT

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# Atypical case of pulmonary Langerhans cell histiocytosis presenting as miliary nodules

Michelle Low, Katharine Lasley, Pranav Singh

## ABSTRACT

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare smoking-related interstitial lung disease affecting primarily young adult smokers. Diagnosis is made with typical radiographic findings of centrilobular nodules and cystic lesions on high resolution computed tomography (HRCT) confirmed with tissue biopsy. We describe a case of a 59-year-old man presenting with chronic tobacco use and cough who was found to have an atypical radiographic finding of miliary nodules on HRCT that was confirmed as PLCH on transbronchial lung biopsy.

**Keywords:** Interstitial lung disease, Miliary nodules, Pulmonary Langerhans cell histiocytosis, Smoking

### How to cite this article

Low M, Lasley K, Singh P. Atypical case of pulmonary Langerhans cell histiocytosis presenting as miliary nodules. Case Rep Int 2022;11:100106Z06ML2022.

Article ID: 100106Z06ML2022

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doi: 10.5348/100106Z06ML2022CR

## INTRODUCTION

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare interstitial lung disease of clonal dendritic cell infiltration that primarily affects young adult smokers with peak incidence at 20–40 years of age [1]. Among biopsy-confirmed interstitial lung disease, PLCH comprises 4–5% of cases, and of those >90% have a history of tobacco use [2]. Alterations in mitogen-activated protein kinase (MAPK) including BRAF deletions have been observed in majority of lesions, and in refractory disease, identifying these aberrations can help guide targeted treatment [3]. The etiology has yet to be fully understood but is thought to be initiated by an inflammatory response to cigarette smoke with nodular and eventual cystic lung destruction [4]. As such, the radiographic findings of PLCH typically include granulomatous nodules and cystic lesions in the upper and middle lobes [5]. Symptoms range from asymptomatic to respiratory failure, but most commonly include nonproductive cough, dyspnea, fatigue, weight loss, and chest pain [5]. Definitive diagnosis is established with immunohistochemistry for >5% CD1a or CD207 positive cells obtained through bronchoalveolar lavage, lung biopsy, or cystic bone lesion biopsy [1, 6]. Herein we describe an atypical presentation of bilateral miliary nodules requiring transbronchial lung biopsy to diagnose PLCH.

## CASE REPORT

A 59-year-old nicotine-dependent man with reported history of adolescent asthma and chronic obstructive pulmonary disease was referred to pulmonology clinic following a chest X-ray with incidental new findings of upper lobe interstitial nodularity suggestive of granulomatous disease. Upon presentation to pulmonology clinic his only complaints were chronic cough for 10 years duration and exertional dyspnea. Given his radiographic findings high resolution computed tomographic (HRCT) examination and vasculitis workup was ordered. Blood work was only significant for elevated erythrocyte sedimentation rate (ESR) 80 mm/h, elevated C-reactive protein (CRP) 2.3 mg/dL, and elevated eosinophils 5.3% with  $0.6 \times 10^3/\mu\text{L}$  absolute eosinophils.

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Received: 27 July 2021  
Accepted: 15 October 2021  
Published: 04 February 2022

Tuberculosis Quantiferon test, vasculitis workup, and angiotensin converting enzyme (ACE) levels were within normal limits. High resolution computed tomography examination revealed innumerable tiny bilateral pulmonary nodules consistent with miliary pattern (Figure 1). Bronchoscopy with transbronchial lung biopsy was subsequently performed and found to contain focal areas of histiocytes associated with CD1a positive cells on immunohistochemistry, confirming PLCH (Figure 2). The patient was educated on the disease progression and thus strongly advised with smoking cessation. Exertional dyspnea symptoms were controlled with long-acting bronchodilator and inhaled corticosteroid.

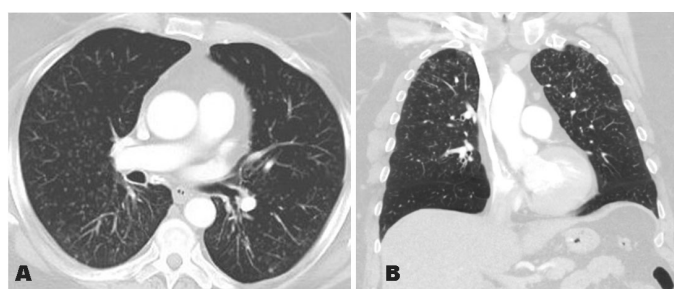


Figure 1: High resolution chest CT with contrast. (A) Parenchymal window. Notice the peripheral tree-in-bud formation and bilateral diffuse nodular (1–2 mm) distribution without coexisting cystic formation that normally exists with PLCH. (B) Coronal slice. Nodular distribution extending throughout the upper, mid, and lower lung fields.

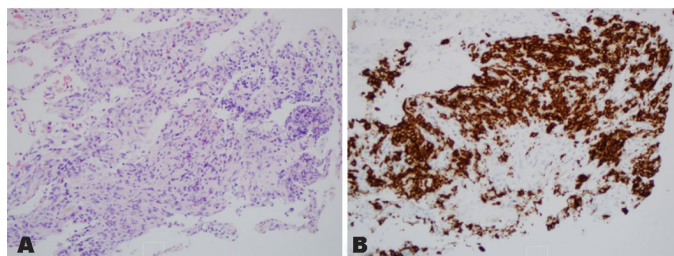


Figure 2: Left upper lobe bronchial biopsy pathology. (A) H&E stain revealing a focal area of loose histiocytes associated with increased eosinophils. This is associated with a few reactive pneumocytes and thickening of the alveolar septa in that area. (B) Immunohistochemical staining positive for CD1a confirming Langerhans cell histiocytosis.

## DISCUSSION

Pulmonary Langerhans cell histiocytosis has been classically characterized by lesions that are bilateral, symmetric, and have upper lobe predominant nodules and cysts sparing the lung bases. Though the concurrence of centrilobular nodules and cysts sparing the lower lung fields is a diagnostic feature of PLCH, radiographic findings can vary depending on the stage of disease [7, 8]. Early stages of PLCH are characterized by bronchiolocentric nodules generally 1–10 mm in size and can be cavitating. As the disease progresses cysts

predominate and can transform from thick-walled (>2 mm) to thin-walled (<2 mm), eventually resulting in end-stage fibrocystic patterns remaining in the upper- and middle-lung fields [4, 8]. This spectrum of nodular and cystic changes along the course of disease makes PLCH difficult to diagnose on radiographic findings alone as it can mimic other pathologies including hematogenous spread of metastatic disease, primary malignancy, and miliary tuberculosis [6, 8].

This rare case of PLCH presenting as diffuse miliary nodules without co-existing cystic lesions demonstrates the importance of considering uncommon diagnoses in the face of unique lesions characteristic of other disease processes [8]. As evidenced in this case, it can be challenging to diagnose PLCH with non-characteristic lesions without a high index of suspicion, as it was only following extensive workup ruling out other etiologies that PLCH was confirmed on transbronchial lung biopsy.

Smoking cessation remains the most critical component of PLCH management but can include immunosuppressive and chemotherapies, though such treatment is not proven to reduce long-term mortality or improve lung function [9, 10]. Extrapulmonary manifestations of LCH include skeletal involvement as bone lytic lesions, dermatologic lesions, and central nervous system involvement most commonly diabetes insipidus. Overall prognosis is favorable as early smoking cessation can result in regression of the interstitial changes in early manifestations of PLCH [11]. However, complications can include initial manifestations of pneumothorax in approximately 15% of patients to pulmonary hypertension in >75% of symptomatic patients in advanced stages [2, 10, 12–14]. Publishing reports suggest a median survival of 10–12 years following the disease diagnosis.

## CONCLUSION

Diagnosis of PLCH includes lung biopsy and radiographic findings on HRCT of centrilobular nodules and cystic lesions in various stages typically in the upper and middle lobes. Practicing physicians should be aware that a miliary distribution can be an atypical radiographic presentation of PLCH. PLCH as a result should be part of the differential diagnosis in a patient who tests negative for tuberculosis with miliary radiographic findings, and further investigation, including a biopsy of the lesion, should be pursued.

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## Author Contributions

Michelle Low – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation

of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Katharine Lasley – Conception of the work, Design of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Pranav Singh – Conception of the work, Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

## Guarantor of Submission

The corresponding author is the guarantor of submission.

## Source of Support

None.

## Consent Statement

Written informed consent was obtained from the patient for publication of this article.

## Conflict of Interest

Authors declare no conflict of interest.

## Data Availability

All relevant data are within the paper and its Supporting Information files.

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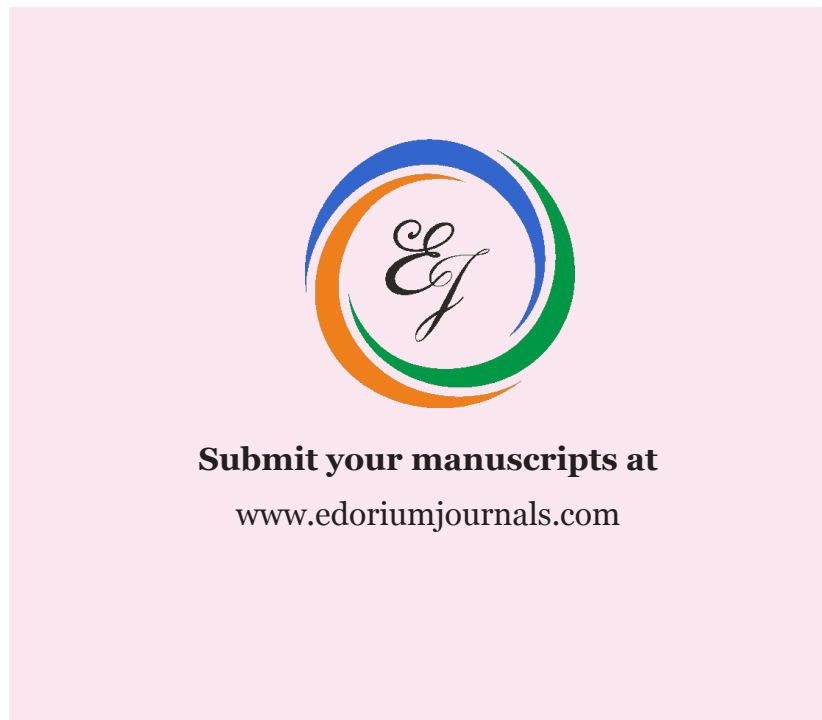
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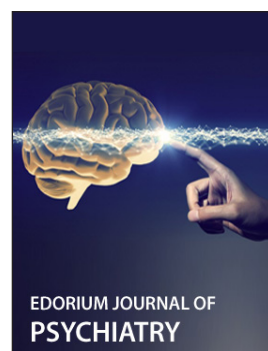
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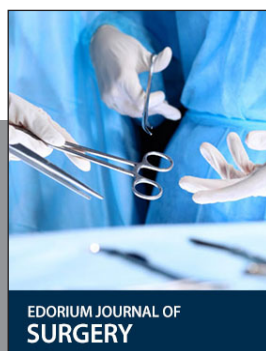
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