


# Chronic cough and weight loss in an adolescent marijuana smoker

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Angela Onorato M.D.<sup>1,2\*</sup>, Jana Shapiro M.D.<sup>1,2\*</sup>,  
Lindsay Griffin M.D.<sup>1,2</sup>, Monica Aldulescu M.D.<sup>1,2</sup>,  
Nicoleta C Arva M.D.<sup>1,2</sup> and Avani Shah M.D.<sup>1,2</sup> 

## Abstract

Marijuana is the most widely used illicit drug in the United States. As marijuana becomes legalized in more states and its use increases among adolescents, pediatricians must be aware of the impact of marijuana on pediatric health. Marijuana smoking as well as cigarette smoking has been associated with numerous lung diseases, including chronic bronchitis and bullous lung diseases. This case report postulates that regular marijuana smoking may be associated with pulmonary Langerhans cell histiocytosis, a severe lung disease that lacks definitive treatment and can cause respiratory failure. Given the potential risk of life-threatening lung diseases, pediatricians must screen adolescents with respiratory symptoms for marijuana use. In addition, this case underscores the need for further research and improved understanding of the relationship between marijuana smoking and lung disease.

## Keywords

Marijuana use, oncology, pulmonary Langerhans cell histiocytosis, respiratory medicine

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## Introduction

In the United States, marijuana has been the most widely used illicit drug among adolescents for decades. In 2018, 36% of 12th graders and 11% of 8th graders reported using marijuana within the last year, with 5.8% of 12th graders reporting daily use.<sup>1</sup> Given the prevalence of marijuana use, there is growing interest in identifying the impact of regular marijuana smoking on lung health. A 2018 *Chest* review article by Tashkin<sup>2</sup> summarizes 10 cross-sectional and prospective cohort studies that explore the significant association between heavy marijuana smoking and symptoms of chronic bronchitis (cough, wheeze, increased sputum, and/or dyspnea), even after controlling for concomitant tobacco use. Case reports of pneumothorax, pneumomediastinum, and bullous lung disease associated with marijuana smoking have also been published.<sup>2</sup> In addition, smoke produced from marijuana contains the same procarcinogens in similar quantities found in tobacco smoke. However, the way marijuana is smoked may affect the amount of procarcinogens deposited in the airway, making a direct comparison of the quantity of procarcinogens deposited in the airway by marijuana and tobacco smoke difficult. Regardless, the presence of procarcinogens in marijuana smoke suggests a possible link to cancer, although a clear association has not yet been established.<sup>3,4</sup>

We present a case of isolated pulmonary Langerhans cell histiocytosis (PLCH) diagnosed in a 16-year-old male with a history of heavy marijuana smoking who presented with recurrent, spontaneous bilateral pneumothoraces.

## Case report

A previously healthy 16-year-old African American male presented to his pediatrician's office for 5 months of cough. He had a productive, progressive cough which was exacerbated by activity and worse in the morning. In addition, he had an unintentional 30-pound weight loss over the previous 8 months, dropping from the 95th to the 75th percentile for weight. He had no chest pain, shortness of breath, fatigue, or activity limitation during this time. He reported smoking three blunts (marijuana rolled in a tobacco leaf

<sup>1</sup>Northwestern University Feinberg School of Medicine, Chicago, IL, USA

<sup>2</sup>Division of Pulmonary and Sleep Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

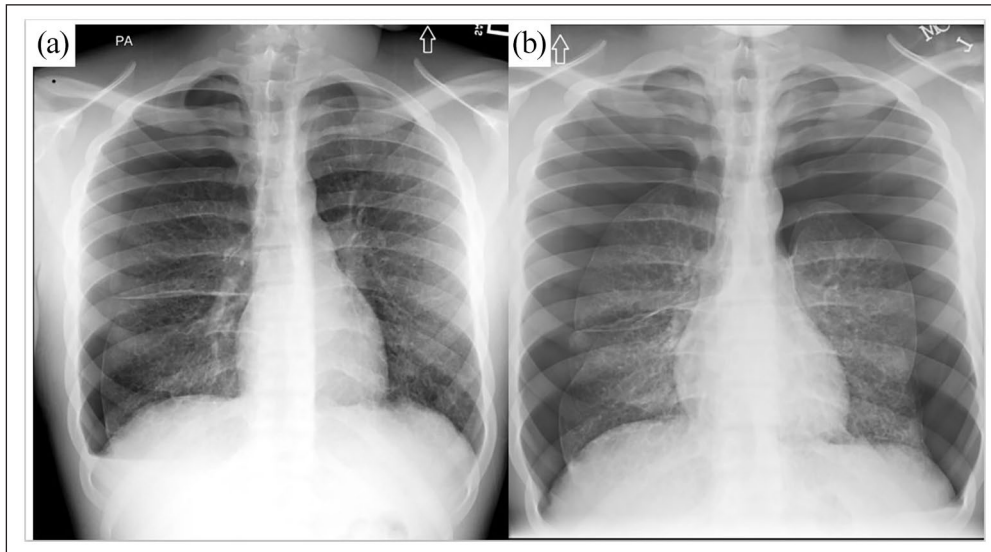
\*Contributed equally as co-first authors.

### Corresponding Author:

Avani Shah, Division of Pulmonary and Sleep Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 E. Chicago Avenue, Box 43, Chicago, IL 60611, USA.

Email: avshah@luriechildrens.org





**Figure 1.** (a) Chest radiograph showing large right pneumothorax. (b) Chest radiograph showing recurrent large right pneumothorax and new left pneumothorax 1 week later.

exterior of a hollowed out cigar) per day for 3 years and one cigarillo two to three times per week for several months. He reported no other drug use, including smoking or vaping of any other products. His physical exam was only significant for asymmetric breath sounds. Chest radiographs showed a right pneumothorax (Figure 1(a)), which prompted hospital admission. His pneumothorax resolved with chest tube placement, and he was discharged 3 days later. Four days after discharge, he developed acute onset of chest pain and shortness of breath without any associated history of trauma. Chest radiograph showed bilateral pneumothoraces (Figure 1(b)), for which he was admitted and had bilateral chest tubes placed. Further evaluation is noted in Table 1.

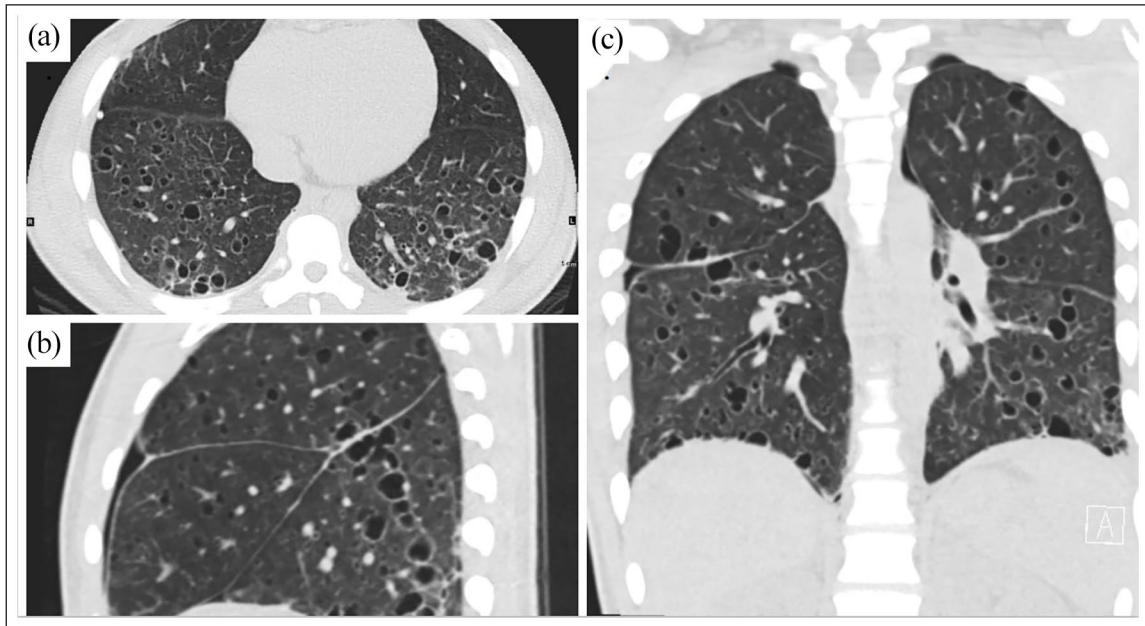
Computed tomography (CT) of the chest was performed for recurrent pneumothorax, which showed innumerable thin-walled cysts throughout the lung parenchyma bilaterally, distributed primarily in subpleural areas and lower lobes (Figure 2). These findings prompted further workup including video-assisted thoracoscopic surgery (VATS) with right apical lung biopsy. Macroscopic examination of the wedge biopsy demonstrated subpleural cystic spaces. Histologic examination of the lung parenchyma (Figure 3) showed collections of large cells that were positive for CD1a immunohistochemical stain (Figure 3(d)). CD207 testing was not available at our institution. However, given the clinical picture with the radiologic findings, PLCH was the most plausible diagnosis. Further testing for the most common manifestations of multisystem Langerhans cell histiocytosis (LCH) was performed. This workup included a skeletal survey with plain radiographs to evaluate for bone involvement, screening for diabetes insipidus with a basic metabolic panel and urine electrolytes, as well as BRAF (V600E) mutation testing of the lung tissue. These tests did not show evidence of multisystem involvement by LCH, so a diagnosis of isolated PLCH was made.

**Table 1.** Test results.

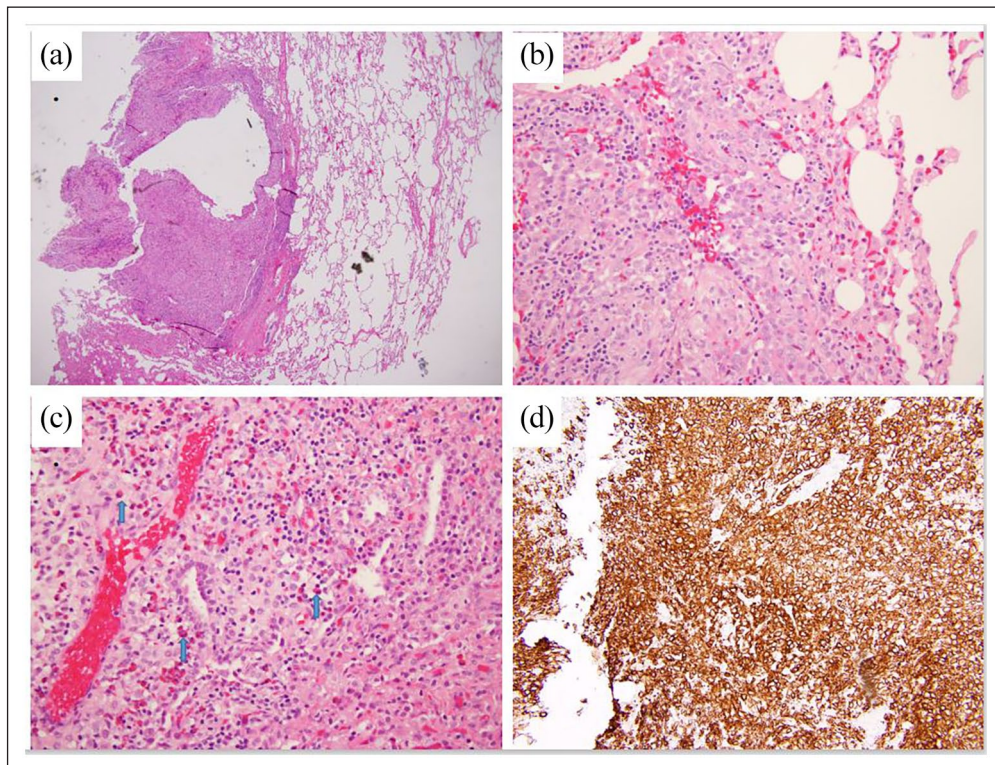
Test	Result
WBC	5.6 thou/ $\mu$ L
Hemoglobin	13.3 g/dL
Hematocrit	38.3%
Platelets	303 thou/ $\mu$ L
Sodium	138 mEq/L
Potassium	4.3 mEq/L
Chloride	102 mEq/L
Bicarbonate	26.1 mEq/L
Blood urea nitrogen	9 mg/dL
Creatinine	0.6 mg/dL
Glucose	91 mg/dL
C-reactive protein	0.8 mg/dL
Calcium	9.4 mg/dL
Protein	7 g/dL
Albumin	3.9 g/dL
Total bilirubin	0.5 mg/Dl
Alkaline phosphatase	94 IU/L
Alanine aminotransferase	39 IU/L
Aspartate aminotransferase	29 IU/L
Spirometry (FEV1, FVC, FEV1/FVC ratio)	107% predicted, 116% predicted, 80
DLCO	91% predicted

WBC: white blood cell; FEV1: forced expiratory volume in 1 s;  
FVC: forced vital capacity; DLCO: diffusion capacity.

Once the diagnosis of isolated PLCH was established, the patient was managed in the ambulatory setting with smoking cessation only. He reported that he completely stopped smoking marijuana and tobacco products upon follow-up. Repeat chest CT at 4, 6, and 12 months after initial presentation revealed gradual improvement of the cystic lesions though

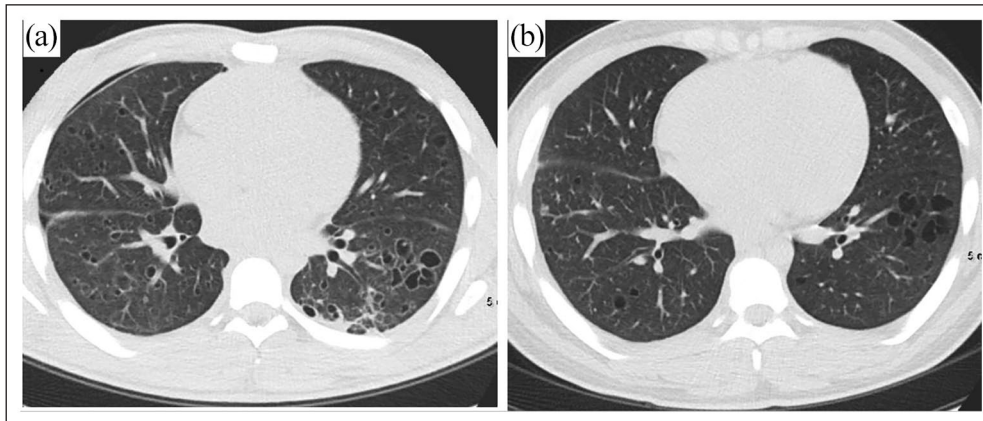


**Figure 2.** (a) Axial, (b) sagittal, and (c) coronal images from non-contrast chest computed tomography showing innumerable thin-walled cysts throughout the lung parenchyma bilaterally, in a subpleural and lower lobes predominant distribution. No discrete lung nodules seen.



**Figure 3.** Histologic examination of lung parenchymal cells. (a) Subpleural and parenchymal collections of large cells, mostly located around cystic spaces (hematoxylin and eosin). (b) Cells containing abundant eosinophilic cytoplasm, irregular convoluted nuclei, and grooves (hematoxylin and eosin). (c) Multinucleated giant cells, numerous eosinophils (arrows), and fewer lymphocytes (hematoxylin and eosin). (d) The large lesional cells were positive for CD1a immunohistochemical stain





**Figure 4.** (a) CT at initial presentation. (b) Follow-up CT 4 months later showing resolution of pneumothorax, decrease in number of thin-walled cysts, and scattered small pulmonary nodules. CT: computed tomography.

several were still present. (Figure 4). One year later, he reported no symptoms, had good exercise tolerance, and his weight increased back to the 95th percentile. In addition, pulmonary function testing showed a normal forced expiratory volume in 1 s (FEV1), normal forced vital capacity (FVC), normal FEV1/FVC ratio, and normal diffusion capacity (DLCO). The patient continues to be followed closely for monitoring of symptoms and periodic chest imaging.

## Discussion

Isolated PLCH is thought to be caused by a reactive proliferation of Langerhans histiocytic cells, which leads to peribronchiolar inflammation and destruction, causing diffuse multicystic interstitial lung disease.<sup>5,6</sup> Isolated PLCH, which is a form of single-system LCH, affects the lungs without systemic involvement,<sup>7</sup> as opposed to the multisystem LCH more commonly seen in pediatrics. PLCH affects young adults, with average age at diagnosis ranging from 20 to 40 years.<sup>6,8</sup> PLCH typically presents with cough, dyspnea, or chest pain.<sup>5,9</sup> Bullous lung disease and pneumothorax are seen as an initial presentation of PLCH in 15%–30% of cases.<sup>10–13</sup> PLCH has been highly associated with tobacco smoking, with greater than 90% of patients reporting heavy tobacco use in many studies.<sup>5,6,9</sup> While the pathogenesis is not entirely understood, smoking cessation is the most common recommendation for PLCH treatment. Some patients have complete resolution of pulmonary lesions after smoking cessation, but some others may progress to more serious complications such as severe pulmonary hypertension, respiratory failure, and involvement of other organs.<sup>14</sup> These patients require other treatments, such as steroids and chemotherapeutic agents, and some may eventually need lung transplantation.<sup>6</sup>

While PLCH is most commonly seen in adults, there are rare case reports of isolated PLCH in adolescents and even children. Some cases of PLCH in adolescents have been associated with tobacco smoking;<sup>15,16</sup> however, other reported

cases are in patients without tobacco exposure.<sup>17–19</sup> One previous case report documents PLCH in an adolescent who smoked both marijuana and tobacco.<sup>20</sup> The patient described in our case also smoked both marijuana and tobacco; however, his use of the former was far more extensive. The presented case of isolated PLCH suggests that PLCH may also be related to excessive marijuana smoking.

Marijuana smoking has been associated with numerous pulmonary diseases, including bullous lung diseases, pneumothorax, pneumomediastinum, chronic bronchitis, and possibly lower respiratory infections.<sup>2,21</sup> The causal relationship for these diseases has not been established. Bronchial biopsies obtained from heavy marijuana smokers have shown immunohistopathologic changes similar to those seen in tobacco smokers. These changes include squamous metaplasia, cellular disorganization, and increased levels of oncogene protein products,<sup>2</sup> all of which are thought to be precancerous. However, there is currently not sufficient evidence to suggest that regular marijuana smoking, when adjusted for concomitant tobacco use, is a significant risk factor for lung cancer or other lung disease such as PLCH.

Given these known associations between marijuana smoking and various forms of lung injury, especially bullous lung diseases and pneumothorax, as well as the established connection between cigarette smoking and isolated PLCH, it is reasonable to propose heavy marijuana smoking is a potential cause of PLCH. Access to marijuana continues to increase as states continue to legalize or decriminalize the substance. This increased access may benefit patients suffering from chronic conditions such as glaucoma, chronic pain, multiple sclerosis, epilepsy, chemotherapy-related nausea, and AIDS-associated anorexia.<sup>22</sup> However, legalization also presents the potential for further increase in marijuana smoking among adolescent patients. The medical community must put forth a strong effort to research and understand marijuana's short- and long-term negative effects on health, as well as the safest methods for administration.

## Conclusion

In summary, isolated PLCH is a rare, severe lung disease that lacks definitive treatment and can cause respiratory failure. PLCH is usually seen in adult tobacco smokers, but this case report is evidence that isolated PLCH can also be seen in the adolescent and young adult population. We argue that PLCH may be associated not only with tobacco use, but also with heavy marijuana smoking given that tobacco and marijuana contain similar chemical components, and marijuana has a known potential to cause lung diseases with features similar to those seen in PLCH. Marijuana is currently widely used by adolescents, and as marijuana is legalized in more states, accessibility to teens will likely continue to increase. As such, the association between marijuana smoking and adolescent lung disease should be a priority for future investigation. Furthermore, general pediatricians must be aware of the potential health risks of regular marijuana use in their adolescent patients. Pediatricians should inquire about marijuana use and consider its contributing role when evaluating adolescent patients with respiratory symptoms or pulmonary disease.

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## Declaration of conflicting interests

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## Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

## Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

## Table of contents summary

Screening for marijuana use is essential in assessing adolescents with respiratory symptoms given associations between marijuana and severe lung disease.

## ORCID iD

Avani Shah  <https://orcid.org/0000-0001-6682-5695>

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