Case Report

# Pulmonary Langerhans cell histiocytosis in a young adult with a history of vaping and smoking: A case report

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## Abstract

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare interstitial lung disease characterized by the proliferation of Langerhans cells, typically associated with smoking. It accounts for 3%-5% of adult diffuse lung diseases, although the true prevalence may be higher due to asymptomatic cases and diagnostic challenges. Recently, e-cigarette use (vaping) has emerged as a potential contributing factor in PLCH. We report the case of an 18-year-old male with a history of heavy nicotine vaping and prior light smoking who presented with pneumothorax and diffuse cystic lung lesions. Lung biopsy confirmed PLCH through CD1a and S100 positivity. Smoking cessation led to symptomatic and functional improvement, although long-term outcomes remain uncertain. This case highlights vaping as a possible risk factor for PLCH, distinct from traditional smoking, and underscores the need for further research into vaping-related pulmonary diseases. A multidisciplinary approach is essential for the diagnosis and management of PLCH.

**Keywords:** Cystic lung disease, Pneumothorax, Pulmonary Langerhans cell histiocytosis, Smoking, Vaping.

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## Introduction

Langerhans cell histiocytosis (LCH) is a rare disease characterized by the abnormal proliferation of dendritic-cell-related histiocytes, known as Langerhans cells, which destructively infiltrate tissues. The etiology of LCH remains unknown. LCH peaks in incidence during the first year of life and decreases in frequency thereafter, rarely occurring in individuals over the age of 20 [1]. From neonates to the elderly, LCH can involve any organ; however, the lungs are notably affected in both adults and children [1]. Additionally, children with extrapulmonary LCH who later develop pulmonary Langerhans cell histiocytosis (PLCH) are often smokers [2].

PLCH is part of a group of rare lung diseases and may account for about 3%-5% of all adult diffuse lung diseases [3] The actual prevalence might be higher due to asymptomatic cases, spontaneous remissions, and difficulties in identifying advanced forms [4]. PLCH is often characterized by the presence of Langerhans cells with eosinophilic cytoplasm and irregular nuclei, expressing markers such as CD1A, S100, and langerin (CD207) [5]. These cells form granulomas and contribute to the destruction of lung tissue [6].

Clinically, PLCH presents with symptoms ranging from cough and dyspnea to spontaneous pneumothorax. Diagnosis typically involves imaging studies and biopsy with microscopic examination. Treatment options vary based on disease extent and severity, including smoking cessation, corticosteroids, and, in severe cases, systemic therapies like chemotherapy. Despite treatment, PLCH can lead to significant morbidity due to progressive lung damage [2].

Given the rarity and complexity of PLCH, early recognition and appropriate management are crucial [7]. The diagnosis of PLCH can be challenging due to its nonspecific clinical presentation and radiologic findings, which often overlap with other cystic lung diseases. Histopathological confirmation via lung biopsy is frequently required to establish a definitive diagnosis [8].

Management of PLCH is complex, primarily involving smoking cessation, which can lead to disease stabilization or regression. However, in cases of progressive disease despite tobacco abstinence, treatment options are limited and may include chemotherapy agents such as cladribine or cytarabine [9].

As research continues to advance our understanding of LCH, a multidisciplinary approach remains essential to improving outcomes for affected patients.

While numerous case reports on pulmonary Langerhans cell histiocytosis (PLCH) have been documented, only one patient with a history of predominant e-cigarette use was reported [10]. Here, we add this case to contribute to the understanding of this potential association.

## Case summary

An 18-year-old man, lived in rural area of southern Thailand, with a history of heavy, everyday nicotine vaping for 4 years and prior cigarette smoking for 3 years (totaling a 7 pack-year smoking history), with no underlying disease or history of trauma, presented with a sudden onset of dyspnea. He reported progressive severity of coughing over the previous 2 months and then presented with acute dyspnea which was sent to the emergency room.

Initial physical examination showed decreased breath sounds in the right lung, and a chest radiograph revealed a large pneumothorax in the right lung and numerous tiny, irregular-shaped cysts diffusely present in both lungs. Emergency intercostal drainage of the right chest was performed. Further CT scans of the chest and abdomen were performed, revealing diffuse, symmetrical, numerous, small, irregular-shaped cysts in both lungs, with no abdominal mass detected (Figure 1). A bone scan showed increased radiotracer uptake at the right scapula and right sacroiliac joint, raising suspicion for disease involvement.

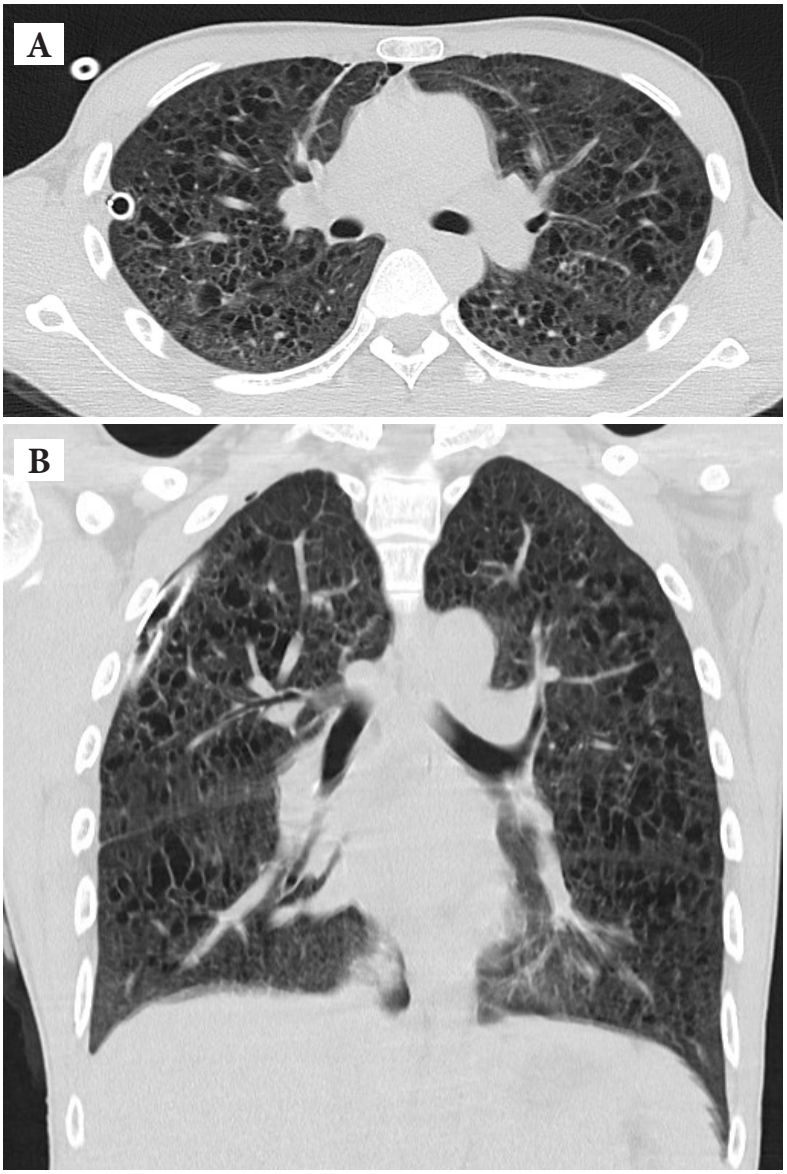
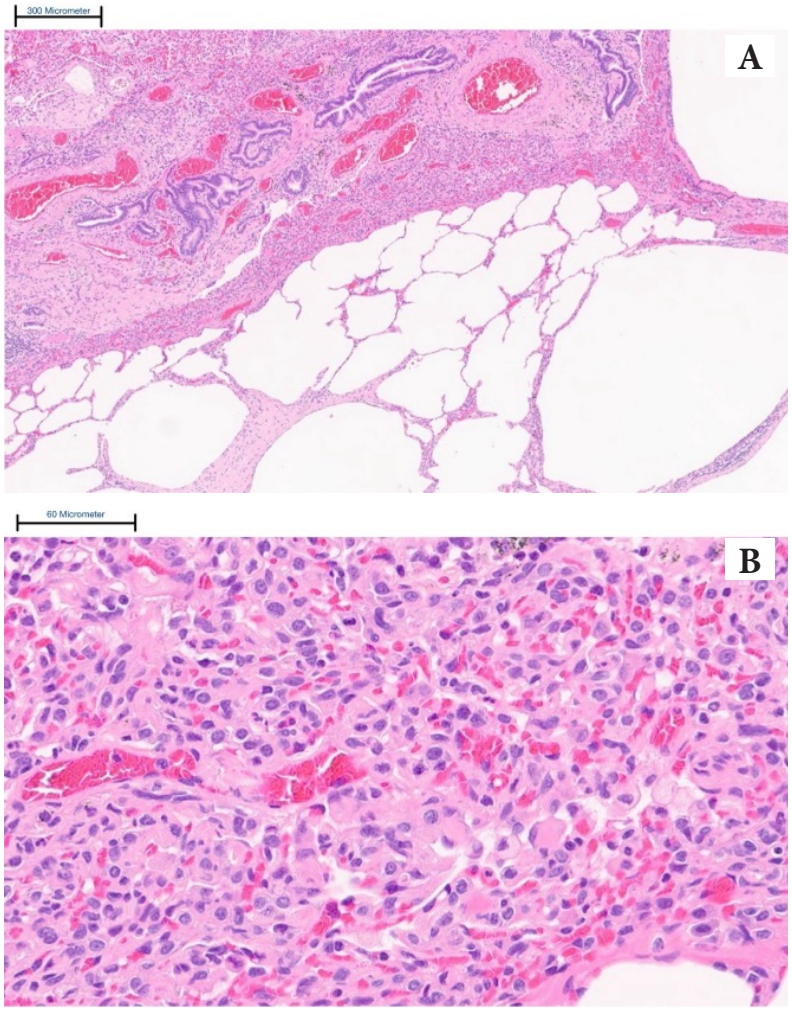



**Figure 1.** *(A) Axial CT shows bilateral diffuse ground glass opacities and multiple bizarre-shaped lung cysts, proven pulmonary Langerhans cell histiocytosis. The percutaneous chest drainage tube in right hemithorax is also seen. (B) Coronal non-contrast CT shows bilateral diffuse ground glass opacities and multiple bizarre-shaped lung cysts predominantly in mid and upper lung zones with relatively spared costophrenic angles, proven pulmonary Langerhans cell histiocytosis. The percutaneous chest drainage tube in right hemithorax is also seen.*

The specimen received for pathologic evaluation was a wedge biopsy specimen from the right middle lobe. Gross examination revealed multiple cystic spaces in the lung parenchyma. Microscopic examination revealed scattered aggregates of Langerhans cells with surrounding cystic changes (Figure 2A). The Langerhans cells are large and have convoluted nuclei, abundant eosinophilic cytoplasm, and an indistinct border (Figure 2B). The aggregates are admixed with eosinophils and lymphocytes. The remaining lung parenchyma revealed chronic inflammation and interstitial fibrosis. The pleura is unremarkable. Immunohistochemical stains are positive for S100 (Figure 2C) and CD1a (Figure 2D). The histologic and immunohistochemistry profiles support the diagnosis of Langerhans cell histiocytosis.



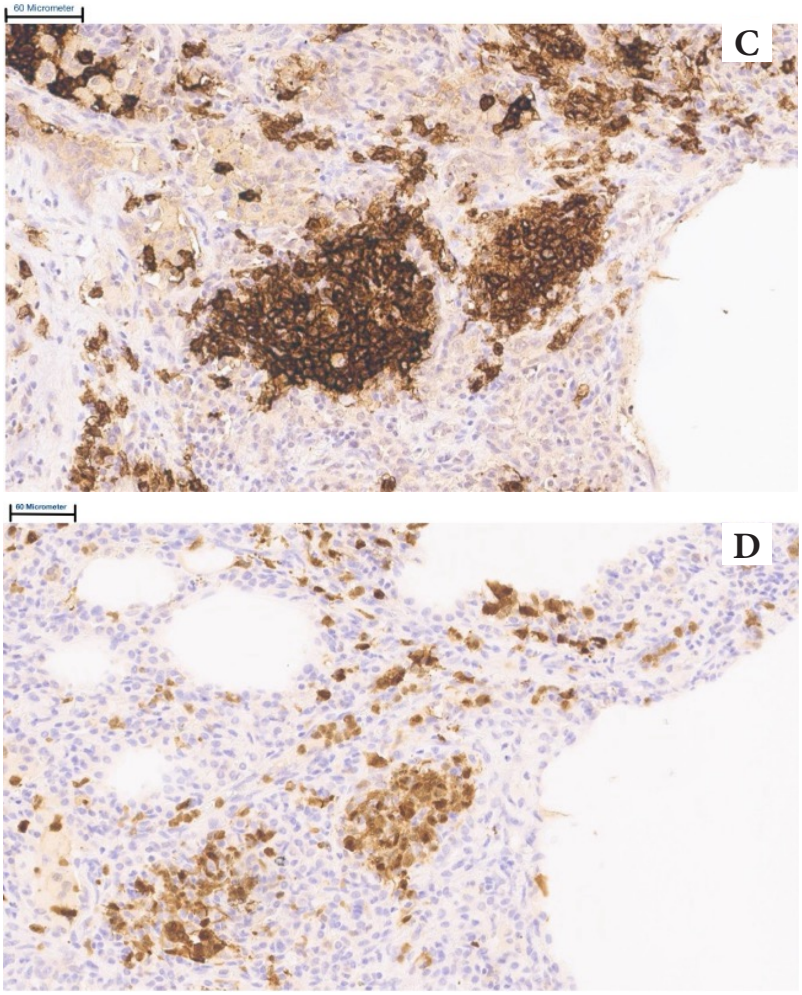



**Figure 2.** *Microscopic examination, (A) H&E section (100x) showing aggregates of Langerhans cells with cystic changes, (B) H&E section (400x) showing large Langerhans cells with convoluted nuclei and abundant eosinophilic cytoplasm, (C) S100 immunostaining showing cytoplasmic and nuclear positivity in Langerhans cells (400x), and (D) CD1a immunostaining showing membranous positivity in Langerhans cells (400x).*

After smoking cessation for 2 months, the symptoms of cough and phlegm improved markedly, and lung function tests also demonstrated improvement; however, there was no follow-up CT.

## Discussion

Over 90% of PLCH patients are current or former smokers, with an average smoking history of 27 pack-years [11]. In contrast, our patient had a relatively low smoking exposure of 7 pack-years over 3 years prior to transitioning to vaping. However, the patient's history of prolonged and unspecified vaping raises the possibility of its contribution to the development of PLCH.

From our search, there is only one case report on nicotine vaping-associated PLCH [10] that also described a patient with a prior history of cigarette smoking who engaged in heavy, daily nicotine vaping. However, that patient also used marijuana regularly, both in edible and combustible forms. In contrast, our case involves a patient with a history limited to cigarette smoking and nicotine vaping, which may provide a clearer association between vaping and the development of PLCH.

In Vaping Product Use-Associated Lung Injury (EVALI), common CT findings include ground-glass opacities (GGO), consolidation, and patterns of organizing pneumonia (OP), which can be diffuse or lower-lobe predominant, often sparing subpleural or lobular regions. However, multiple parenchymal cysts are atypical but possible and may overlap with PLCH findings. In this case, the lung findings showed diffuse GGO without consolidation or an OP pattern, which, although not definitive, makes PLCH the more likely diagnosis [7].

While the strong association between smoking and PLCH has been known for some time, the mechanism remains unclear. Previous studies propose that smoking leads to the accumulation of CD1a+ cells in the lungs. Granulocyte-macrophage colony-stimulating factor (GM-CSF), produced by normal bronchiolar epithelium, plays an important role in the proliferation and differentiation of Langerhans cells [12].

Other smoking-related factors contributing to airway diseases include the production of the connective tissue growth factor (CTGF), transforming growth factor-beta (TGF-β1), the platelet-derived growth factor (PDGF)-A and -B, and

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CCL20 in the airway walls [13]. Osteopontin, a glycoprotein with chemokine activity, induces the chemotactic recruitment of macrophages, monocytes, and dendritic cells, including Langerhans cells [14].

E-cigarettes, or vaping, were invented in 2003 by a Chinese pharmacist and became widely used by 2011, with over 7 million users globally [15]. In 2019, the Centers for Disease Control and Prevention (CDC) announced an "Outbreak of Lung Injury Associated with the Use of E-Cigarette or Vaping Products" [16]. The CDC reported 805 patients with lung injuries linked to e-cigarette or vaping products. Among these, 69% were male, with a median age of 23 years. Of the 63% of patients who used substances in e-cigarettes or vaping products in the 30 days preceding the symptom onset, 76.9% reported using Tetrahydrocannabinol (THC)-containing products, and 56.8% reported using nicotine-containing products.

Nicotine, a substance found in all tobacco products since its introduction in 1492, has been studied extensively. The smoking history of PLCH patients, averaging 27 pack-years, implies a total nicotine exposure of approximately 270 milligrams, assuming an average cigarette contains 10-12 mg of nicotine [17]. E-cigarettes, with varying concentrations of nicotine ranging from 0-24 mg/ml in cartridges to up to 100 mg/ml in refill fluids, may provide substantial nicotine exposure [18]. Our patient, although unaware of the exact nicotine concentration in the e-cigarettes used, reported heavy daily vaping, raising concerns about its potential role in stimulating Langerhans cell-related pathogenesis.

In addition to nicotine, other smoking-related substances, vitamin E acetate, found in THC-containing e-cigarettes or vaping products, has also been associated with lung injury. Inhalation of this compound interferes with the normal lung function, though its role in PLCH remains unclear [19]. Notably, while lung injuries related to vaping typically manifest within 30 days of exposure, PLCH patients often have a much longer history of tobacco use, with a median duration of approximately 20 years.

## Conclusion

In summary, while e-cigarette use has grown globally, especially among adolescents, its association with pulmonary diseases remains an area of active research. The spectrum of clinical and pathological diagnoses related to vaping continues to expand. In this case report, the patient was definitively diagnosed with PLCH, but the mechanism remains unclear. Future studies on the correlation between PLCH, other cystic lung diseases, and e-cigarette use would be of significant interest.

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