A Case-Report on the Presentation of Pulmonary Langerhans Cell Histiocytosis

Justin Z.Y. Shen*, Vivek Gautam and Simin Nasr

Department of Family Medicine, The Wright Center for Graduate Medical Education, School of Osteopathic Medicine Arizona, A.T. Still University, Scranton, United States

Corresponding Author*

Justin Z.Y. Shen
The Wright Center for Graduate Medical Education,
School of Osteopathic Medicine Arizona,
A.T. Still University,
Scranton,
United States
E-mail: JustinShen@atsu.edu

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Abstract

Pulmonary Langerhans Cell Histiocytosis (PLCH) is a rare disorder of the lungs characterized by the accumulation of $CD1a^+$ cells in loosely formed granulomas in small airways. A patient with PLCH commonly presents with a smoking history with peak onset between 20 to 40 years of age. PLCH outcomes show a shorter survival rate than the general population and require lung transplantation for survival. In this report, we describe a 42-year-old Caucasian female who presents with a unique episode of bilateral spontaneous pneumothorax and shortness of breath. Pathological samples of the pulmonary biopsy showed Langerhans cells stained positive for CD1a and S100, consistent with the diagnosis for PLCH. The patient was further counseled on smoking cessation with eventual symptom improvement.

Keywords: Pulmonary langerhans cell histiocytosis • Caucasian female • Pneumothorax • Langerhans cells

Introduction

Pulmonary Langerhans Cell Histiocytosis (PLCH) is characterized by the accumulation of $CD1a^+$ cells in granulomas of the small airway leading to destruction of respiratory bronchioles and affecting individuals between the ages of 20 to 40 years old [1-3]. Patients with PLCH may present with respiratory symptoms, including nonproductive cough, dyspnea, fatigue, fever, weight loss, and pleuritic chest pain. Further, approximately 30 to 45% of patients with PLCH presented with spontaneous pneumothorax [4]. In addition, patients with PLCH in the early stages may present with nodules between 1 to 10 mm on chest radiography and eventually thick-walled or thin-walled cysts in a later stage of PLCH [5]. In this report, we will discuss the case of a middle-aged woman who spontaneously developed a pneumothorax, later discovered as secondary to Pulmonary Langerhans Cell Histiocytosis (PLCH).

Case Presentation

A 42-year-old Caucasian female with no significant past medical history but a 25-pack-year smoking history presented to her local urgent care with shortness of breath, chest pain, and cough. She was later prescribed Keflex (cephalexin) under the impression of bacterial pneumonia. However, after two weeks, the patient still presented with her initial symptoms with no improvements from her antibiotics. She was advised to go to her nearest local emergency department when she presented at her urgent care facility a second time. From the emergency department she was discovered to have a left-sided pneumothorax *via* chest radiograph and was eventually placed on nebulizer treatment (albuterol-ipratropium) along with a left-sided chest tube placement. The patient was later transferred to a higher care facility for further assessment.

Upon management at the higher care facility, the patient was later discovered to have another spontaneous pneumothorax occurring on the right side. She eventually received another chest tube on her right side. The patient underwent further surgical biopsy of the left upper lobe, left lingula wedge, and left pleura peel preserved in a formalin container. On microscopic examination, there is the presentation of cellular proliferation composed of langerhans cells admixed with eosinophils, macrophages, and lymphocytes. With immunohistochemical staining, the langerhans cell were highlighted by CD1a (Figure 1) and S100 markers (Figure 2), directing the diagnosis of pulmonary langerhans cell histiocytosis. Further inspection presented no evidence of Lymphangioleiomyomatosis (LAM) due to negative HMB45 staining. Eventually, the patient was stable enough to have the left-sided chest tube removed while the right-sided pigtail catheter remained in place for drainage of serosanguineous fluid.

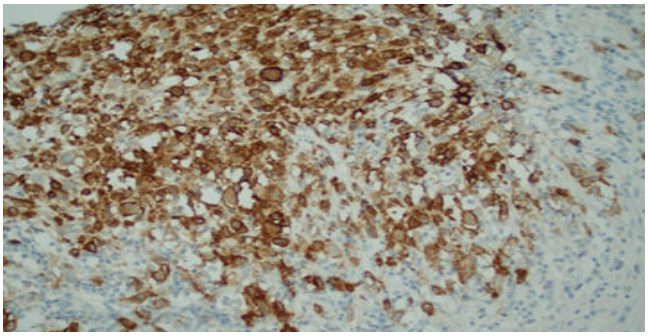

Figure 1. 20X CD1a staining.

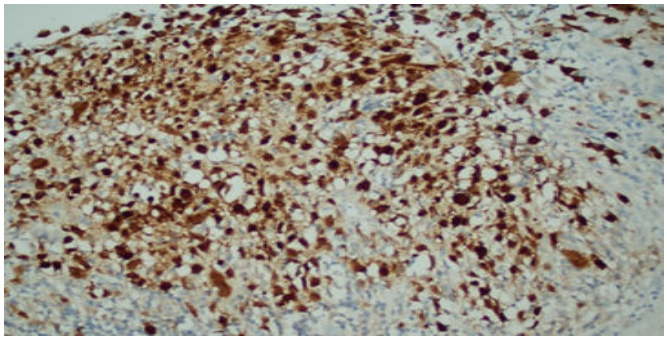

Figure 2. 20X S100 staining.

Upon diagnosis and stabilization, the patient was discharged on supplemental oxygen, albuterol-ipratropium, and guaifenesin for symptomatic management of dyspnea and cough. She was further provided nicotine patches with the aim of smoking cessation to

prevent the further progression of her PLCH diagnosis. After discharge, the patient had her right-sided pigtail catheter removed from the outpatient surgical center. During follow-up in the outpatient center, the patient has stopped smoking and slowly weaning off oxygen supplementation with significant improvement from her initial symptoms.

Discussion

PLCH commonly presents with nonproductive cough, dyspnea, fatigue, fever, weight loss, and pleuritic chest pain. In one case-series study including 7 individuals, it was found that all had presentations of shortness of breath, and four of the 7 had a productive cough. One individual was found to have rales upon auscultation [6]. The initial presentation of shortness of breath and rales on physical examination may explain why our patient initially may have been suspected of a pulmonary infection which led to her being treated with cephalexin from the beginning. Further, it has been reported that pneumothorax complication was seen in 16 of 102 patients with confirmed PLCH [7]. However, what made the presentation of pneumothorax in our case interesting is the occurrence of bilateral pneumothorax, which has been shown to be rare and fatal [8].

The current prevalence of langerhans cell histiocytosis (non-pulmonary) is 1-2/1,000,000. However, the prevalence of pulmonary langerhans cell histiocytosis is unknown due to asymptomatic presentation. In Japan, it has been reported that PLCH prevalence is 0.07/100,000 in women and 0.27/100,000 in men [9].

Pulmonary biopsy, whether from surgical or bronchoscopy, is required to make a definitive diagnosis for PLCH. Diagnosing PLCH requires immunohistochemical staining with monoclonal antibodies against CD1a or with electron microscopy with a presentation of birbeck granules. In the case of our patient, her PLCH diagnosis was confirmed by surgical pulmonary biopsy with positive immunohistochemical staining for CD1a along with S100.

Smoking causes langerhans cell to accumulate in the lungs, eventually leading to PLCH [10]. Therefore, it is important to encourage smoking cessation as a part of therapy management for PLCH. Further treatment should include prednisone 0.5-1.0 mg/kg daily for progressive PLCH disease, although the efficacy remains unclear. In patients with PLCH and reactive airway disease, a trial of inhaled corticosteroids along with long-acting β_2 agonists may provide some benefit [11]. However, in the case of our patient, she was treated with albuterol-ipratropium, a short-acting β_2 agonist and short-acting muscarinic antagonist, which has provided symptomatic relief. Aside from smoking cessation and steroid use in the management of PLCH, cladribine, a purine analog that reduces DNA synthesis *via* inhibition of DNA polymerase has been shown to improve dyspnea in 4 of 5 patients with PLCH [12]. Arguments have been made regarding PLCH as rather neoplastic; especially due to BRAFV600E mutation noted in langerhans cell histiocytosis. This has led to the use of BRAF inhibitors as a tactic for the stabilization of PLCH. Specifically, a study showed 14 individuals with LCH with BRAFV600E mutation treated with vemurafenib resulted in 6 of 14 treatment responses [13].

Conclusion

In this case report, our patient presented with the initial impression of bacterial pneumonia. She was subsequently started on antibiotics, however, her symptoms have worsened. Eventually on workup she was found to have bilateral pneumothorax. On further pathologic biopsy, our patient was diagnosed with pulmonary langerhans cells histiocytosis based on positive CD1a and S100 immunohistochemical staining.

The initial clinical features of PLCH may include cough, dyspnea, and fever which can be mistaken as possible pneumonia from initial impression; as in the case for our patient. This shows how PLCH can initially be mistaken as pneumonia. PLCH, today, still remains rare in its prevalence and diagnosis is rather made based on incidental findings from images or the presentations of spontanoues pneumothorax which require further investigation with pulmonary biopsy. This case shows the importance of having a broader differential when presented with symptoms of pneumonia and how; although rare, PLCH should still be considered a part of differential diagnosis when presented with pneumonia.

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