

C A S E R E P O R T

Pulmonary langerhans cell histiocytosis in a young non-smoking female — too many rituals spoil the lung

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Abstract. Pulmonary Langerhans cell histiocytosis (PLCH) is a rare idiopathic cystic interstitial granulomatous lung disease seen almost exclusively in cigarette smokers. It typically occurs between 20–40 years of age and equally distributed among both sexes. Management includes smoking cessation, avoidance of second-hand smoke, and close follow-up. Corticosteroids may be required in those with symptomatic disease with worsening lung function despite smoking cessation and progressive nodular stage of the disease. Here, we report an interesting case of biopsy proven PLCH in a young never smoker female. Detailed questioning revealed significant exposure to incense smoke, highlighting a rare presentation of non-cigarette smoke related PLCH. Avoidance of incense smoke combined with oral prednisolone (0.5mg/kg) tapered over 6 months led to complete resolution of symptoms, disappearance of nodules in high resolution computed tomography (HRCT) of the thorax, and improvement in lung function. (www.actabiomedica.it)

Key words: PLCH, female, non-cigarette smoke.

Introduction

Pulmonary Langerhans cell histiocytosis (PLCH), an isolated form of Langerhans cell histiocytosis, is an uncommon cystic interstitial granulomatous lung disease occurring in the 3rd and 4th decade of life but it can be found across a wider age spectrum and also occurs at a slightly older age in females (1). It is invariably associated with cigarette smoking and this includes current and ex-smokers, which lead to its inclusion in smoking-related interstitial lung disease along with respiratory bronchiolitis-Interstitial lung disease (RB-ILD) and desquamative interstitial pneumonia (DIP) (2). However not all smokers develop the disease with host related factors in addition to cigarette smoke are involved in the pathogenesis of the disease (3). Our case report describes a novel association of non-cigarette smoke (NCS) exposure leading to PLCH and a brief review of the literature.

Case History

A 19-year-old Caucasian female presented to the emergency room (ER) with complaints of acute onset dyspnea and right-sided pleuritic chest pain for the last 4 hours. On admission, she had tachycardia, tachypnoea, was hypotensive, and falling oxygen saturation (Spo₂- 70% on room air). Respiratory system examination revealed hyperresonant note on percussion and bronchial breath sounds (amphoric character) on auscultation in the right hemithorax. Right-sided tension pneumothorax was suspected, which was confirmed with a chest radiograph. A puncture was made with a 16-gauge needle in the right 2nd intercostal space (ICS) in mid-clavicular line as a life-saving procedure. Gush of air came out through the needle and she had partial symptomatic relief. An intercostal drain tube (ICDT) size -14Fr was placed in right 4th ICS in mid axillary line

(safety triangle). After ICDT insertion, her vitals normalized, and she was shifted to medical ward.

She had complaints of dry cough, exertional dyspnea, and constitutional symptoms such as fever and weight loss for the past 1 year. Chest radiograph done 12 months back revealed bilateral reticulonodular infiltrates (Fig.1A). she was suspected to have pulmonary tuberculosis and was initiated on empirical anti-tubercular treatment (ATT). Despite being on ATT, there was little clinical improvement. During hospital stay, she developed a simultaneous left-sided pneumothorax and was managed with tube thoracostomy (Fig.1B). Following complete resolution of pneumothoraces, chemical pleurodesis with doxycycline was done as per institutional protocol to prevent recurrence (Fig. 1C).

Cystic lung disease was suspected and a high-resolution computerized tomography (HRCT) of the thorax was done which revealed multiple nodules, cavitary nodules, architectural distortion, and

bizarre shaped cysts with predilection for the upper zone of lung and relative sparing of costophrenic sulci (Fig. 1D-E). There was no history of tobacco smoking or passive smoking. However, there was history of significant exposure to smoke. Her father is a priest in the temple and she used to take part in all rituals and prayers of the temple which involved burning incense for the past 5 years. The patient did not consent for Video assisted thoracoscopic surgery (VATS) lung biopsy. Bronchoscopy with Bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) were performed. BAL fluid analysis revealed > 5 % CD-1a cells and TBLB disclosed Langerhans cells in bronchiolar walls with immunohistochemistry staining positive for CD1a, CD68 and CD207. There was no extrapulmonary organ involvement. She was labelled as case of isolated Pulmonary Langerhans cell histiocytosis (PLCH) and was advised strict avoidance of exposure to any kind of smoke. Pulmonary function tests (PFT) disclosed a moderately severe

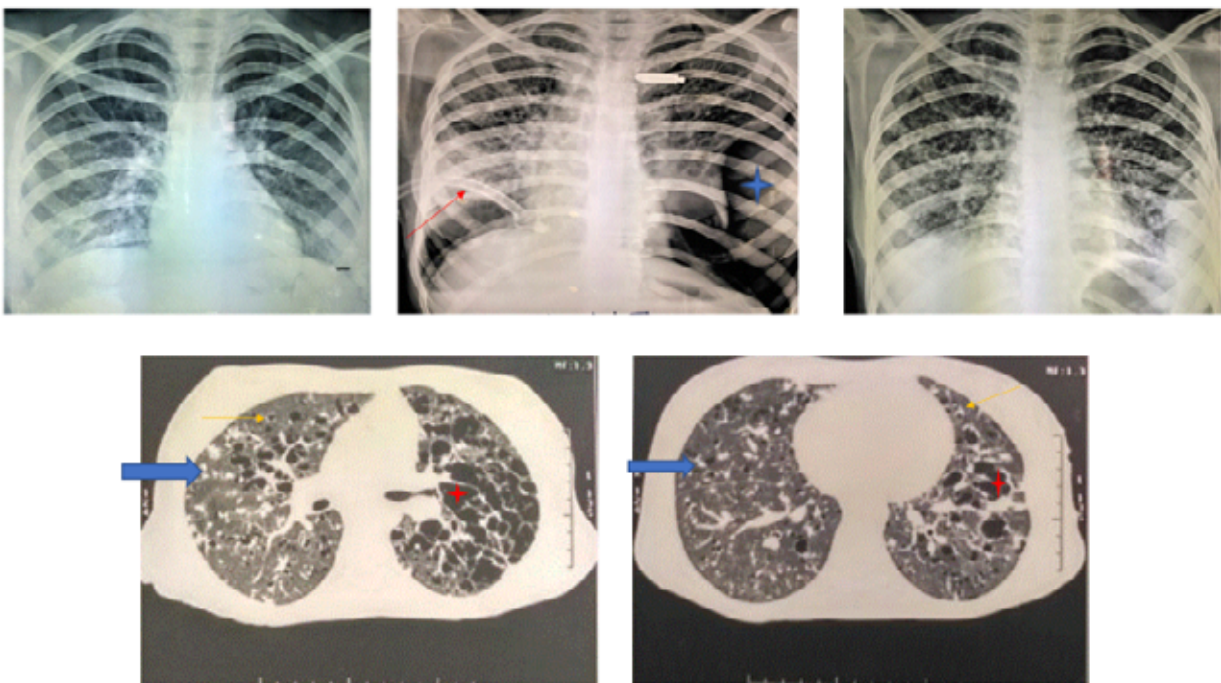


Figure 1A-E. 1(A) Chest Radiograph showing fine reticulonodular infiltrates. 1(B): Chest radiograph showing simultaneous left sided pneumothorax (blue Asterisk) and ICDT on the right side (red arrow). 1(C): Resolution of bilateral pneumothorax. 1D and 1E: High resolution computed tomography (HRCT) of the thorax lung window axial section showing nodules (blue arrows), cavitary nodules (yellow arrows) and bizarre shaped thick-walled cysts (red Asterix).

obstruction (FEV1- 55% predicted) and severe impairment in diffusion capacity of carbon monoxide (DLCO)- 39 % predicted. Despite avoidance to smoke, she was symptomatic and so she was initiated on oral corticosteroids. Her respiratory and constitutional symptoms subsided on steroid therapy. Steroids were gradually tapered and discontinued after 6 months. Follow up chest radiograph showed clearing of reticulonodular infiltrates and repeat HRCT revealed complete resolution of nodules with only the cysts persisting (Fig. 2A-C). PFT showed satisfactory improvement in lung volumes and DLCO (FEV1- 66% predicted and DLCO- 52% predicted). She was advised to avoid smoke exposure and to report in case of any respiratory symptoms.

Discussion

PLCH, also known as eosinophilic granuloma of the lung is a rare idiopathic sporadic cystic interstitial lung disease characterized by granulomatous

infiltration and destruction of the distal bronchiole walls by CD1a+ Langerhans cells (1). It accounts for 3–5% of adult diffuse parenchymal lung diseases (DPLD) and is almost exclusively seen in smokers (90-100%) (4,5). It primarily affects young adults and initially thought to be common in men, but has been found equally in women due to increased smoking rates and second-hand smoke exposure (6,7). Although cigarette (tobacco) smoking and second-hand smoke related PLCH have been described in the literature, their association with non-cigarette smoke (NCS) is extremely rare, limited to a single case report to date (8) (table1). Multisystem LCH can involve the lung irrespective of the smoking status (9). The clinical presentation of PLCH is varied and can manifest as chronic symptomatic PLCH with respiratory and constitutional symptoms, or as spontaneous pneumothorax occurring at any time during the course of the disease and may be bilateral and/or recurrent, and finally asymptomatic with abnormal radiology seen in 10-25% of cases (1).



Figure 2A-C. 2A: Chest radiograph shows clearing of reticulonodular infiltrates in comparison with previous chest radiograph. 2B: HRCT thorax axial section shows complete resolution of nodules in comparison with previous HRCT thorax. 2C: HRCT thorax Coronal section showing upper and mid-zone predominant cysts.

Table 1. Non-Cigarette smoke related PLCH and their outcomes

Author	Article type	year	Non-cigarette smoke exposure	Management	Outcome
Fernandez et al ⁸	Case report	2015	Biomass smoke	Supportive treatment	In-hospital Death
Present case	Case report	2020	Incense smoke	Supportive treatment and Corticosteroids	Responded

HRCT of the thorax is mandatory for every suspected case of PLCH and findings depend on the stage of the disease. In the early florid stage, nodular lesions predominate. The nodules are stellate or peripherally irregular and vary in number and diameter (1–10 mm). In advanced stage Irregular, bi-lobed, cloverleaf, branched or bizarre cysts and fibrotic changes are seen (3,10). The finding of more than 5 % CD-1a and CD-207 positive cells on BAL strongly supports the diagnosis of PLCH (10). Although surgical lung biopsy is gold standard for establishing the diagnosis, if clinical and radiologic findings are typical then biopsy might not be required (11). The risk of a surgical lung biopsy should be balanced with the need for a definitive diagnosis. (1). PFT in PLCH can be either normal, obstructive, restrictive, and/or a mixed pattern and usually depends on the stage of the disease and extent of cystic involvement in HRCT. The most common abnormalities noted include fall in DLCO and obstruction with air trapping (12).

Smoking cessation and avoidance of smoke exposure are essential and are the only required intervention in majority of the cases (13). Systemic treatment is considered for symptomatic patients despite smoking cessation and those with impaired lung function. Studies have shown beneficial effects of corticosteroids in symptomatic and progressive nodular PLCH, prednisolone at a starting dose of 0.5–1 mg/kg/day tapered over 6–12 months (14,15). However, their efficacy in stabilization or remission of disease remains uncertain. Cladribine, a purine nucleoside analogue is used as a second-line agent in refractory disease. It has shown to induce remission and improve lung function (16). Lung transplantation may be required in advanced fibrotic disease. The natural history of the disease is variable yet favourable with an estimated 5-year survival more than 75% and only one-fourth progressing to respiratory failure and pulmonary hypertension (5).

Conclusion

Our case highlights a rare intriguing association of incense smoke (non-cigarette smoke) in the pathogenesis of PLCH. Avoidance of exposure to all kinds of smoke is advised and usually leads to resolution

of disease. A trial of corticosteroids may be considered in persistent symptomatic progressive disease before switching to second line therapy. Close follow up is required to prevent deterioration.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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