Journal of the Postgraduate Institute of Medicine 2023; 10(1): E208 1-6

https://doi.org/10.4038/jpgim.8357

Case Report

A rare case of pulmonary Langerhans cell histiocytosis in an older non-smoker

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Key words: **PLCH, non-smoker, rubber fumes, corticosteroids, HRCT**

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Received: 12 Oct 2021, accepted revised version : 04 Apr 2023, Published: 30 Jun 2023

Competing Interests: Authors have declared that no competing interests exist

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Introduction

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare granulomatous interstitial lung disease of unknown aetiology which typically occurs between 30 to 40 years of age [1]. The relative frequency of the disease among men and women is controversial, where some studies report an equal incidence, and some show a slight female preponderance [2]. The principal epidemiological factor associated with PLCH is smoking (90-100%) which includes current smokers, ex-smokers and passive smokers [3]. No occupational or geographic risk factors for PLCH have been identified so far [2]. Here, we report a rare case of PLCH in a non-smoker who was an employer at a rubber factory for the past 25 years with significant exposure to industrial fumes.

Case presentation

A 52-year-old male managed for chronic obstructive airway disease (COPD) with long-acting muscarinic antagonists and long acting beta agonist inhalers with good control of disease for the past 4 years, on regular clinic follow up, presented with dry cough and progressive shortness of breath [modified research medical council dyspnoea scale (mMRC) Grade 4] for one week. He denied any wheezing, diurnal variation of symptoms or constitutional symptoms. He did not complaint of polyuria, polydipsia, bone pain, fractures, skin rashes or enlarged lymph nodes. There was no family history of connective tissue diseases or malignancies. He denied any history of active or passive smoking but had been employed at a rubber factory for the past 25 years with significant exposure to industrial fumes.

In 2017, he had presented to the local hospital with dry cough and shortness of breath for a period of one month (mMRC Grade 1). Chest X- ray (CXR-PA) performed at the time revealed features of emphysema and high-resolution computed tomography (HRCT) of

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the chest showed evidence of emphysema with early bronchiectasis. He was started on combined inhalers and was managed as for COPD. One year into treatment, in 2018, the patient had developed sudden onset, right sided, pleuritic-type chest pain and shortness of breath (mMRC Grade 4) and was managed as for a right-sided spontaneous pneumothorax with intercostal drainage, without further complications.

During the current admission, the patient was dyspnoeic at rest with a respiratory rate of 36 breaths per minute. He was thin built with a body mass index of 18 kg/m^2. He was not cyanosed nor clubbed. There were no skin rashes, palpable lymph nodes or bilateral pitting ankle oedema. His oxygen saturation on air was 88% with hyper-resonant percussion note in all lung fields. On auscultation, he had diffuse course crepitations with vesicular breathing. His pulse rate was 90 beats per minute and regular and his blood pressure was 110/80 mmHg. Heart sounds were normal without features of cor pulmonale. The rest of the systems examination was normal.

An arterial blood gas analysis was performed which showed evidence of type 1 respiratory failure. He was given controlled supplemental oxygen and, in the meantime, further investigations were arranged. His full blood count revealed evidence of neutrophil leucocytosis (white cell count 12x10^3 u/L, neutrophil percentage 80%) with a C reactive protein level of 58 mg/dl and erythrocyte sedimentation rate of 45mm/1st hour. Serum electrolytes, serum creatinine and liver functions were normal. Sputum bacterial and tuberculosis cultures were negative. CXR-PA (Figure 1) revealed a bilateral reticular nodular pattern which involved mainly the bilateral upper zones of the lung.

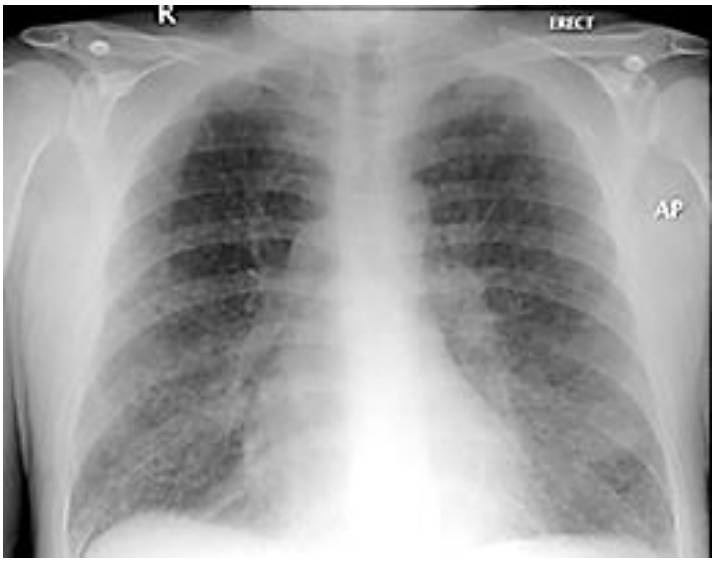

Figure 1: Chest X-ray PA showing bilateral symmetrical reticular nodular shadows

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HRCT chest (Figure 2) showed multiple nodular and cystic spaces of varying sizes which were bizarre shaped, mainly involving the upper and middle lobes with sparing of extreme lung bases.

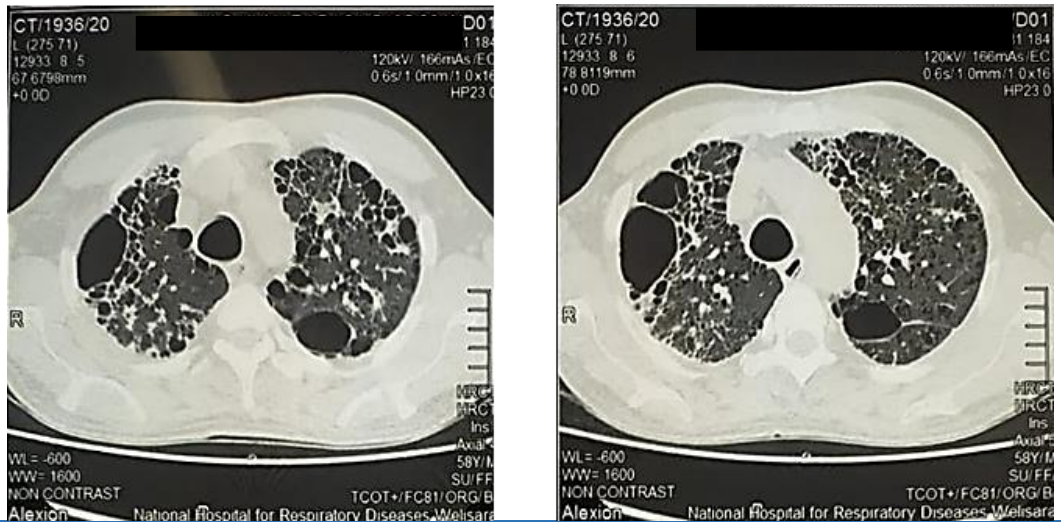

Figure 2: High resolution computed tomography of the thorax lung window axial section showing nodules and bizarre shaped thick walled cysts.

There was increased lung volumes with intervening lung showing evidence of centrilobular emphysema. The HRCT findings were highly suggestive of PLCH. His pulmonary function tests disclosed a surprisingly normal forced expiratory volume in the first second (FEV1) of 96% predicted, forced vital capacity (FVC) of 80% predicted and FEV1/FVC of 90% predicted but he had severe impairment in diffusion capacity of carbon monoxide (DLCO) of 17% predicted. (N.B. that the patient did not have the printed report and these values were copied from his clinic book) His skeletal survey was negative and there was no evidence of other system involvement. He refused bronchoscopy and lung biopsy but with the characteristic HRCT findings and the given history we were able to come to a diagnosis of LCH with isolated pulmonary involvement. Following the diagnosis, the patient was advised to avoid exposure to occupational fumes but despite such avoidance patient developed a disease flare three months later. He was started on oral prednisolone 1mg/kg/day and on-demand home oxygen therapy was arranged. Four months into therapy, the patient is not oxygen dependent and is on a tapering dose of prednisolone with overall improvement of quality of life.

Discussion

PLCH is an uncommon, cystic granulomatous interstitial lung disease where no precise epidemiological data are available regarding its prevalence. However, ~~but~~ in a study done on open lung biopsy for diffuse infiltrative lung disease, PLCH was found in less than 5% of such patients [4]. LCH can also affect the bone, reticuloendothelial system, nervous system, skin and other organs [5] hence pulmonary involvement can be a part of a multi-system LCH or can present in isolation. Although an association between smoking and pulmonary LCH in patients with multi-system LCH is unclear, in patients with isolated PLCH there is more than 90% association with current or past smoking [6]. Although

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cigarette smoke related PLCH has been described in the literature, PLCH associated with non-cigarette smoke is extremely rare with only four such case reports so far (Table 1).

Table 1: Case reports of non-cigarette smoke exposure related PLCH and their outcomes

Author	Article type	year	Non-cigarette smoke exposure	Management	Outcome
Dubravka et al [7]	Case report	2003	Not specified	Corticosteroids and Methotrexate	Responded
Michelle et al [5]	Case report	2008	2-chlorodeoxyadenosine	Systemic chemotherapy	Responded
Fernandes et al [8]	Case report	2015	Biomass smoke	Supportive care	Death
Benhur et al [1]	Case report	2021	Incense smoke	Supportive care and corticosteroids	Responded
Current case	Case report	2021	Rubber fumes	Supportive care and corticosteroids	Responded

There are various modalities of presentation in PLCH. The most common symptoms are dry cough and dyspnoea. In up to one third of patients, constitutional symptoms such as fever, weight loss and anorexia can be seen. In 25% of cases, disease can be asymptomatic and detected via a routine chest radiograph [2]. Spontaneous pneumothorax leads to the diagnosis in 10-20% of patients [8]. Our patient gave a history of dry cough with exertional shortness of breath, together with a history of spontaneous pneumothorax which was in favour of PLCH.

Bronchoscopy may be macroscopically normal or show nonspecific changes in PLCH. HRCT is mandatory in all patients with suspected PLCH and shows a classic picture of nodules, cavitating nodules and bizarre shaped, thick and thin-walled cysts. These changes mainly affect the upper and middle lung fields, sparing the lower lung fields. In severe disease, even the lower lung fields can be affected. Definitive diagnosis of PLCH requires a lung biopsy. However, imaging of the lung using HRCT has reduced the need for lung biopsy when combinations of nodular and cavitatory lesions are present in an appropriate clinical context. Our patients HRCT pattern was diagnostic of PLCH and it obviated the need for lung biopsy [1,2,8,9].

Since PLCH is a rare disease entity, there are no available randomized clinical trials on the treatment of this disease. Treatment of adults with PLCH is, therefore, challenging. An important intervention strategy in managing adults with smoking related PLCH is smoking cessation [10]. Optimal therapy for progressive PLCH has not been determined. Though oral prednisolone is prescribed at a starting dose of 0.5-1 mg/kg/day, tapered over 6-12 months, there are no evidence-based data for the use of steroids in PLCH in either smokers or non-smokers. Since our patient did not improve with avoidance of

occupational exposure to rubber fumes, we started him on a tapering regime of corticosteroids with significant improvement in his symptoms and quality of life.

For patients who are not candidates for or do not respond to glucocorticoids, a trial of cladribine or cytarabine, with appropriate prophylaxis against opportunistic infection is suggested [11]. The natural history of PLCH is variable, with some patients experiencing spontaneous remission of symptoms and others progressing to end-stage fibrotic lung disease. Most reports show a 5 year survival of more than 75% [1] but in some instances rapid deterioration is seen in 10-20% of patients despite immunosuppressive therapy [3].

Conclusion

Our case confirms that smoking is not mandatory for the development of PLCH, as our patient did not have either primary or second hand tobacco exposure. Rubber fume exposure should be considered as a probable risk factor.

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