Case report

Initial presentation of Pulmonary Langerhans cell histiocytosis as recurrent spontaneous pneumothoraces

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ABSTRACT

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare cystic lung disease. The natural history is often unpredictable making it difficult to diagnose. We report a 63-year-old male with dyspnoea, chronic cough and recurrent respiratory tract infections, who developed progressive multifocal cystic lesions on pulmonary nodule surveillance over 4 years. He was a heavy smoker with a history of multiple spontaneous pneumothoraces in his teens. Extensive investigations culminated in a thoracoscopic wedge resection, which identified histiocytic nodules staining positive for CD1a and thus confirming the diagnosis of PLCH. It is now apparent that PLCH was the likely cause of his pneumothoraces.

1. Introduction

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare cystic lung disease. It involves the clonal proliferation of myeloid dendritic cells which share phenotypic similarities with cutaneous Langerhans cells.

It is a unique form of Langerhans cell histiocytosis and remains difficult to diagnose due to its widely heterogeneous clinical presentations and typically insidious natural history. Patients with symptomatic PLCH may present with a non-productive cough, dyspnoea, chest pain, constitutional symptoms and rarely haemoptysis [1–6]. The chest pain experienced is often pleuritic and it is frequently associated with spontaneous pneumothoraces. Recurrent pneumothoraces can occur in up to 10% of patients with PLCH [7].

The epidemiological data on PLCH is sparse. However, it is known that PLCH occurs almost exclusively in cigarette smokers and accounts for approximately 3–5% of interstitial lung diseases [3,7–9]. No other epidemiological factors, such as geographical or occupational predispositions, have been identified [7].

The complex relationship between PLCH, smoking and pneumothoraces is explored in this case report.

2. Case report

2.1. Case presentation

A 59-year-old male presented to our hospital with unintentional weight loss, fatigue and night sweats. He was a heavy smoker, with a 60 pack-years history and a background of multiple bilateral spontaneous pneumothoraces. He had recurrent episodes of pneumothorax in his late teenage years and subsequently underwent definitive management with surgical pleurodesis in 1974. He had no significant family history of malignancy or respiratory diseases. He was an office worker, who did not have risk factors for interstitial lung disease including asbestos, toxic gas, mould and bird exposures.

His initial CT thorax, abdomen and pelvis identified multiple bilateral indeterminate lung parenchymal nodules. He was scheduled for pulmonary nodule surveillance on referral to the respiratory department and was advised to stop smoking.

He experienced minimal respiratory symptoms and continued to smoke cigarettes for the next 4 years, after which time he began to develop a chronic cough, progressive dyspnoea and recurrent lower respiratory tract infections.

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2.2. Investigations

He was further investigated at the age of 63 to establish the cause for his deterioration over this period of pulmonary nodule surveillance.

A CXR at this time showed a bilateral reticulomacronodular infiltration with associated cysts throughout all zones (Fig. 1). A CT Thorax revealed progression with extensive multifocal cystic lesions and nodules throughout all lobes (Fig. 2a–c). His pulmonary function tests suggested an obstructive pattern with no bronchodilator response; FEV1 66%, FVC 106%, FEV1/FVC 0.62, TLCO 77% (102% when adjusted for alveolar volumes). Transbronchial biopsies showed normal lung parenchyma with no specific abnormalities. The bronchoalveolar lavage (BAL) was also negative on routine cultures and ZN stain with a benign cytology.

He was further investigated with a thorascopic wedge resection which revealed histiocytic nodules that positively stained for CD1a with abundant pigmented alveolar macrophages and scattered inconspicuous eosinophils (Fig. 3a–d). These features were consistent with a diagnosis of PLCH.

2.3. Outcome and follow-up

He was eventually diagnosed with PLCH after extensive investigations. He had no evidence of extrapulmonary disease which is typical for PLCH. He has since ceased smoking and his most recent CT Thorax suggests interval reduction in the number of cavitating lesions. It is now apparent that PLCH was the likely cause of his pneumothoraces.

3. Discussion

Pulmonary Langerhans cell histiocytosis is a challenging disease to diagnose and manage. A review of the diagnostic approach and management of this case is discussed below.

3.1. Diagnostic approach

Chest Radiography - The symmetrical reticulomacronodular infiltration and normal lung volumes on the CXR are commonly seen in PLCH [3]. The associated cysts often suggest advanced disease. PLCH also generally affects the middle and upper zones with sparing of the costophrenic angles, however, in our case there was complete lung involvement [3,7,10].
Computed Tomography - The nodulocystic pattern on the CT Thorax is typical of PLCH. The predominant finding of innumerable cystic lesions throughout all lobes again indicates advanced disease [3]. This is further emphasized by the presence of scattered thin walled cysts. A review of our patient’s previous imaging demonstrated stepwise disease progression from nodules to cavitated nodules to thick walled cysts and more recently thin walled cysts [7,11]. The cysts seen were mostly focal and varied in size, which can be expected in cases of advanced PLCH [7].

Pulmonary Function Tests - PFTs are variable in PLCH and do not always correlate with the extent of disease seen on imaging [7]. However, the reduced diffusion capacity in this case would be consistent with the parenchymal destruction in PLCH. This is observed in 70–90% of PLCH cases [6,12,13]. The obstructive pattern is also commonly noted, especially in advanced disease [7].

Bronchoscopy, Bronchoalveolar Lavage and Transbronchial Biopsy - BAL and transbronchial biopsies are usually non-diagnostic in PLCH and it is therefore not surprising that these did not reveal the diagnosis in this case [14]. BAL is typically non-specific and commonly reports increased cell counts which are mostly due to alveolar macrophages [7,22], which reflects cigarette smoke exposure. The focal distribution of the lesions in PLCH is the most likely cause for the low diagnostic yield from transbronchial biopsies. Recent studies report a diagnosis from transbronchial biopsy only occurs in 15–50% of cases [14–16].

Surgical Biopsy and Histopathology - A surgical lung biopsy, usually video-assisted thoracoscopy, is required for a definitive diagnosis in patients with non-diagnostic imaging, BAL and TBLB. In this case, the thorascopic wedge resection provided a larger lung tissue sample to define the underlying histological pattern. The specimens obtained showed small airway destruction and the histiocytes stained positive for CD1a, which is characteristic of PLCH. CD1 antigen (CD1a) is uniquely expressed in Langerhans-like dendritic cells and it is not observed in other cells of histiocytic origin [17]. S100 protein staining is less specific [15].

3.2. Further management and prognosis

The 5 year survival estimate for PLCH is mostly reported as >75% [5,12,18]. Smoking cessation is the first line treatment for PLCH. It is an effective monotherapy and approximately 60% of patients will improve without further interventions [19]. In our case, an interval reduction in the number of cavitating lesions was noted on a follow up CT Thorax.

Systemic glucocorticoid therapy can be used for patients with progressive symptoms despite smoking cessation but there is limited evidence for its efficacy [20–22].

Chemotherapeutic agents, such as Cladribine and Cytarabine, have been used in patients who are unsuitable or do not respond to glucocorticoids [3,23–25]. These again have a limited role and their
immunosuppressive properties result in a significant risk of opportunistic infections [3]. A clinical trial on the efficacy and tolerance of Cladribine in the treatment of PLCH is currently ongoing [3].

Therapies targeting mitogen activated protein kinase (MAPK) pathway mutations have been utilised, particularly in those with BRAFT mutations, but recurrence of PLCH has been reported on completion of therapy and their role remains unclear [26–28].

Finally, lung transplant has been used in patients with advanced disease but recurrence of PLCH in the allograft has been reported [19, 29].

Declaration of competing interest

The authors of this article certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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