Clinical Case Report

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Successful management of isolated pulmonary Langerhans cell histiocytosis in a 50-year-old man with early diagnosis using transbronchial cryobiopsy

A case report

Yan-mei Feng, PhD[a], Yi-shi Li, PhD[a], You-lun Li, PhD[a], Pu Wang, PhD[a,*], Rui Guo, PhD[b,*]

Abstract

Rationale: Isolated pulmonary Langerhans cell histiocytosis (PLCH) is rare in adults. The gold standard diagnosis requires surgical lung biopsy. However, few cases have been diagnosed with transbronchial cryobiopsy (TBCB) sampling in the early stages of the disease, particularly in China.

Presenting concerns: A 50-year-old man was referred for dry cough and exertional dyspnea of more than 1 week. High-resolution computed tomography (HRCT) of the chest revealed symmetric nodules and cyst lesions with upper lobe infiltrate. Further history taking indicated that he had smoked 20 cigarettes per day for more than 30 years. Therefore, PLCH was highly suspected. However, he refused surgical lung biopsy, and TBCB was attempted to complete diagnosis.

Diagnosis: Emission computed tomography excluded the possibility of extrapulmonary involvements, and pathological findings supported the diagnosis of isolated PLCH.

Interventions: Smoking cessation and prednisone treatment were used for patient management.

Outcomes: The symptoms receded with significant improvement of chest HRCT during 2-months of follow-up.

Lessons: Early diagnosis contributes to the prognosis of isolated PLCH in adults, and TBCB may be an alternative to conventional surgical lung biopsy for pathological diagnosis of PLCH.

Abbreviations: BAL = broncho-alveolar lavage fluid, CT = computed tomography, HRCT = high-resolution CT, LCH = Langerhans cell histiocytosis, PLCH = pulmonary Langerhans cell histiocytosis, TBCB = transbronchial cryobiopsy.

Keywords: early diagnosis, isolated pulmonary Langerhans cell histiocytosis, prognosis, transbronchial cryobiopsy

1. Introduction

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare disorder, caused by the abnormal proliferation and infiltration of the lung by Langerhans cells.[1] Langerhans cell histiocytosis (LCH) predominantly affects children, although it does rarely occur in adults.[2] Epidemiological data show that Caucasians are more likely to be affected by PLCH, although there are uncommon cases in African and Asian populations.[3,4]

The treatment and prognosis of PLCH depend largely on the stage of the disease and whether other organs are involved. Early diagnosis can improve clinical outcomes. High-resolution computed tomography (HRCT) is an important tool for early screening of suspected PLCH, but histological results are still the gold criteria for definitive diagnosis.

In China, trans-bronchoscopy and surgical lung biopsy are recommended to obtain tissue samples from most patients with suspected PLCH.[5] However, the relatively low diagnostic power of trans-bronchoscopy lung biopsy limits the further application of this technique.[6] Although surgical lung biopsy remains the gold standard method for its greater diagnostic capacity, it may also yield to sampling error. In addition, taking such factors as its purely diagnostic function, the risks attendant on anesthesia, and the invasiveness of the procedure into consideration, many

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[a] Department of Respiratory and Critical Care Medicine, [b] Department of Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China.

[*] Correspondence: Pu Wang, Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China; (e-mail: miss_miao@163.com), Rui Guo, Department of Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China (e-mail: guo-rui5@163.com).

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patients with suspected PLCH are reluctant to choose this method.

Transbronchial cryobiopsy (TBCB) is a less invasive technique that has recently been introduced as a promising and safer alternative to surgical lung biopsy in the diagnostic approach to interstitial lung diseases.[7–9] However, there has been limited experience with this technique in the diagnostic field of PLCH.

We report a case from an Asian adult population in which a suspected chest HRCT indicated possible PLCH. Instead of surgical lung biopsy, TBCB was subsequently used to obtain tissue samples, and histological findings confirmed PLCH. Because the diagnosis occurred in the disease's early stages, the patient received timely treatment and recovered over the course of the 2 months of follow-up.

2. Case report

A 50-year-old man complained of dry cough and exertional dyspnea of more than 1 week and was admitted to our hospital for further evaluation. He denied fever, night sweats, and weight loss. There was no history of hemoptysis, leg swelling, or recent contact with tuberculosis patients or irritant gas. Physical examination showed asymmetric breath sounds without rales and wheezing. Radiological examinations were arranged. Chest x-ray disclosed no signs of pneumothorax, and further HRCT showed bilateral and symmetric infiltration of micro-nodules and small-sized cyst lesions, predominantly involving the upper lung fields (Fig. 1A). On the other hand, laboratory tests, including routine peripheral blood cell tests, tumor screening, tests for connective tissue diseases, and cultures for pathogenic microorganisms from sputum and bronchoalveolar lavage fluid (BAL) were normal.

Further history-taking revealed that the patient was a heavy smoker and smoked 20 cigarettes per day for more than 30 years. Therefore, PLCH was highly suspected. However, the patient refused surgical lung biopsy. Therefore, TBCB was tried for tissue collection. He was deeply sedated and intubated with a rigid tracheoscope. A flexible bronchoscope was inserted through the rigid tube into the selected bronchus. Then, a 1.9 mm flexible cryoprobe was placed in the bronchoscope and reached the target tissue. The probe tip was cooled for approximately 4 to 7 seconds, and then the probe, with frozen lung tissue attached, was retracted with the bronchoscope. During this procedure, minor bleeding occurred; however, due to the continuous application of suction and ice saline washing, there was no active bleeding. Six tissue samples from the right upper lobe were obtained, with an average dimension of 3 to 4 mm. Hematoxylin and eosin staining showed nodular interstitial peribronchiolar lesions infiltrating the wall of the distal bronchioles and alveoli. Higher-magnification images revealed that some atypical cells with round or fusiform nuclei and eosinophillic cytoplasm that could be Langerhans cells were intermingled in tissues, along with 2 eosinophils (Fig. 2A and B). Immunohistochemical examinations showed that proliferating cells were positive for S100 and CD1a. The tissue cells and epithelial cells were positive for PGM-1 and CKpan, respectively (Fig. 2C and D). In addition, emission computed tomography excluded the possibility of extrapulmonary LCH involvement. Therefore, it could be concluded that this patient had isolated PLCH. Thus, smoking cessation and prednisone treatment at a dose of 1 mg/kg body weight were initiated for therapy.

Over the course of the 2-month follow-up, the patient experienced complete resolution of symptoms. HRCT of the chest showed that the lesions of micronodules and cysts in the bilateral lungs decreased significantly after strict smoking cessation and prednisone treatment (Fig. 1B). Finally, the patient was discharged with a dosage reduction of prednisone to 0.75 mg/kg/d, and arrangements were made for subsequent follow-up.

This study adhered to the tenets of the Declaration of Helsinki, and the ethics committee of the First Affiliated Hospital of Chongqing Medical University approved the study (20188501). Written informed consent was obtained from the patient for the publication of this report and related images.

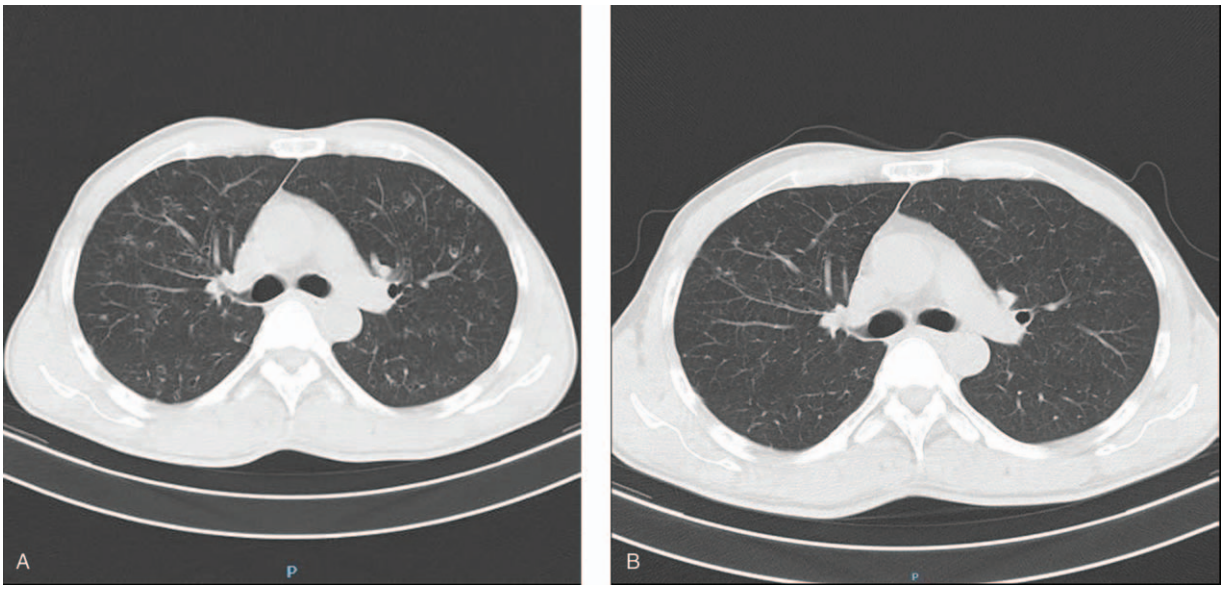

Figure 1. High-resolution computed tomography of the chest showed bilateral multiple micro-nodules and small-sized cyst lesions that were mainly located in the upper lobe (A); however, at the 2-month follow-up, most lesions had resolved (B).

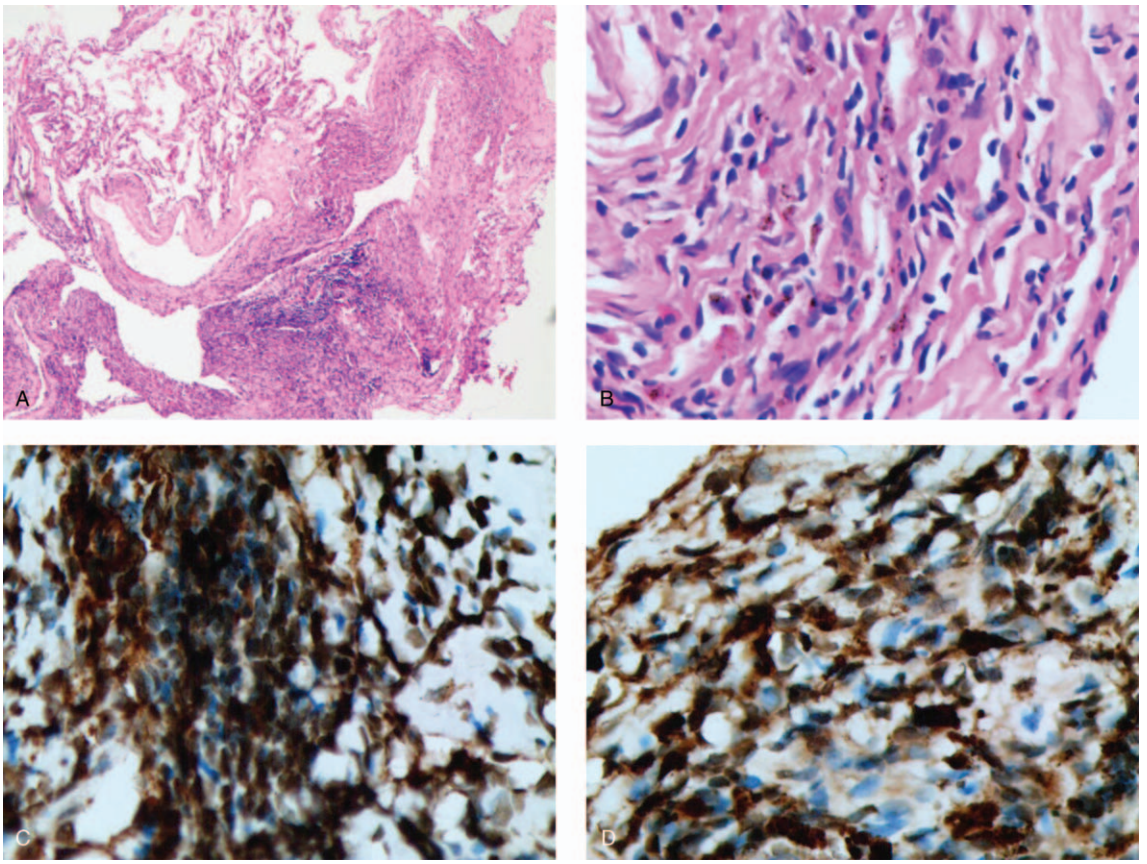

Figure 2. Pathology slides of the transbronchial specimen with hematoxylin eosin staining (×10) showed a nodular interstitial peribronchiolar lesion expanding into the surrounding alveolar septa and alveoli (A). A high-powered microscope (×100) showed some atypical cells with round or fusiform nuclei and eosinophilic cytoplasm suspected to be Langerhans cells and 2 eosinophils could also be seen (B). Immunohistochemical examinations showed that proliferating cells were positive for S100 and CD1a (C and D).

3. Discussion

LCH is a rare disease, characterized by the monoclonal proliferation and infiltration of multiple organs by Langerhans cells, including bone, skin, liver, and lung.[1] Retrospective studies have shown that about 24% of this population present with isolated lung involvement or as part of a multiorgan disease. Although most patients with isolated PLCH have good prognosis, in a subgroup, respiratory impairment progressively develops, and they die due to respiratory failure or complications such as pneumothorax, pulmonary arterial hypertension, or another condition. This phenomenon may be closely related to different factors, including the status of basic lung function at diagnosis, the involvement of other organs, and the timing of intervention. This supports the possible impact of early diagnosis on prognosis.

However, in clinical practice, it is not easy to make a definitive diagnosis of this condition. One reason for this is that the clinical manifestations of isolated PLCH are not typical or even asymptomatic. HRCT of the chest provides useful information for initial diagnosis. The classic findings of imaging are nodular and cystic changes, and the clinical course of the disease can be classified according to the frequency of cystic changes.[10] The imaging findings reported in this case are consistent with the features of PLCH, and they indicated an early stage of the disease.

However, differential diagnoses are necessary to exclude pathogenic infection, cancer, and connective tissue disease.[11] In this case, after we had excluded the above factors and taken long-term tobacco use into consideration, PLCH was highly suspected. Under these conditions, histopathologic information is essential to provide a definitive diagnosis. Previous studies[10,12] have used bronchoscopy or BAL to seek evidence of Langerhans cells, but their diagnostic power is limited. Additionally, transbronchial lung biopsy is not currently recommended for the histological diagnosis of idiopathic interstitial pneumonias.[13] Although surgical lung biopsy remains the gold standard in final diagnosis, taking the risk/benefit ratio into account, the inherent invasively nature of a biopsy, and possible complications, many patients with PLCH do not undergo a surgical lung biopsy in clinical practice. In this case, the patient also refused the surgical method.

Therefore, TBCB was selected as an alternative to tissue collection. Although this technique was initially used as a diagnostic tool for lung cancer,[14] interest is rapidly growing in the application of TBCB in the diagnostic field of interstitial lung diseases.[15,16] Multiple studies have shown that TBCB can avoid the crush artifact that occurs in standard transbronchial forceps biopsies and also provide larger specimens.[17] In addition, the median time of hospitalization and the procedure-related mortality is lower compared to surgical lung biopsy.[18] However, only limited information is available on the diagnostic

power of TBCB for PLCH, particularly in China.[5] In this case, the tissue size obtained using TBCB was larger than previously reported conventional transbronchial biopsies, thus providing sufficient information for histological analyses and contributing largely to the successful diagnosis of PLCH using TBCB. The biopsy findings for this patient indicated the accumulation of suspected Langerhans cells positive for S100 and CD1a, which confirmed the final diagnosis. Although minor bleeding occurred in this case, this complication is generally manageable and the incidence is comparable between TBCB and transbronchial lung biopsy.[19]

Smoking cessation is the cornerstone of treatment. In the early stages of the disease, most patients have good prognosis if they do not have exposure to tobacco. However, if respiratory impairment occurs, corticosteroids may be attempted, although there is no definitive clinical evidence for the benefits of this approach.[20] Despite all of these treatments, some patients may also develop respiratory failure. In this scenario, lung transplantation is the last resort.[2] Thus, again, we emphasize the importance of early diagnosis of PLCH.

4. Conclusions

Histopathological examination remains the gold standard for the diagnosis of PLCH. TBCB is a promising strategy and may become an alternative to surgical lung biopsy. Large-scale studies are necessary to investigate the relative feasibility, diagnostic power, and safety between these 2 methods. Long-term follow-up will help determine the contribution of early diagnosis to the prognosis of isolated PLCH.

Author contributions

Conceptualization: Yan-mei Feng, Pu Wang.
Data curation: Yan-mei Feng, Yi-shi Li, You-lun Li, Pu Wang, Rui Guo.
Formal analysis: Yan-mei Feng, Rui Guo.
Funding acquisition: Yan-mei Feng, Rui Guo.
Investigation: Yan-mei Feng, Yi-shi Li, You-lun Li, Pu Wang.
Methodology: Yan-mei Feng, Yi-shi Li, You-lun Li, Pu Wang.
Project administration: Yan-mei Feng, Yi-shi Li, You-lun Li, Pu Wang.
Resources: Yan-mei Feng, You-lun Li, Pu Wang.
Software: Yan-mei Feng, Rui Guo.
Supervision: Yan-mei Feng, Pu Wang, Rui Guo.
Validation: Yan-mei Feng, Pu Wang.
Visualization: Yan-mei Feng, Rui Guo.
Writing – original draft: Yan-mei Feng, Rui Guo.
Writing – review & editing: Yan-mei Feng, Pu Wang, Rui Guo.

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