Respiratory Medicine Case Reports 46 (2023) 101928

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case Report

Pulmonary Langerhans cell histiocytosis diagnosed using transbronchial lung cryobiopsy: A case report☆

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ARTICLE INFO

Keywords:
Bronchoscopy
Cystic lung disease
Pulmonary langerhans cell histiocytosis
Transbronchial lung biopsy
Transbronchial lung cryobiopsy

ABSTRACT

A 63-year-old Japanese woman with multiple cysts in both lungs on chest computed tomography (CT) was referred to our hospital after a thorough examination, including a transbronchial lung biopsy (TBLB), failed to provide a diagnosis. Based on the findings on chest CT and pathological examination of the bronchoalveolar lavage fluid and transbronchial lung cryobiopsy (TBLC) specimen, the patient was diagnosed with pulmonary Langerhans cell histiocytosis (PLCH). TBLC may replace TBLB as the main diagnostic technique for PLCH, although further studies are required to determine the usefulness of TBLC for the diagnosis of PLCH.

1. Introduction

Langerhans cell histiocytosis (LCH) is a rare histiocytic neoplastic disorder affecting both children and adults. It has a wide variety of clinical manifestations, including unifocal, single-system multifocal, single-system pulmonary, or multisystem disease [1]. Pulmonary LCH (PLCH) occurs as part of multisystem LCH or as an isolated disease (single-system PLCH) [2].

Transbronchial lung biopsy (TBLB) is the primary diagnostic tool used to obtain tissue samples from patients with suspected PLCH [3]. However, the diagnostic power of TBLB is relatively low [3,4]. Therefore, surgical lung biopsy (SLB) remains the gold standard owing to its high diagnostic capacity. Transbronchial lung cryobiopsy (TBLC) is drawing attention for the diagnosis of interstitial lung diseases (ILD) as it is less invasive than SLB and has a higher diagnostic power than TBLB due to the ability to obtain larger samples [5,6]. However, the usefulness of TBLC for the diagnosis of PLCH remains unknown. Here, we report a case of PLCH diagnosed using TBLC.

Abbreviations: PLCH, Pulmonary Langerhans cell histiocytosis; TBLC, transbronchial lung cryobiopsy; CT, computed tomography; TBLB, transbronchial lung biopsy; LCH, Langerhans cell histiocytosis; SLB, surgical lung biopsy; ILD, interstitial lung diseases; HRCT, high-resolution computed tomography; CI, confidence interval.

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https://doi.org/10.1016/j.rmcr.2023.101928
Received 15 August 2023; Received in revised form 12 September 2023; Accepted 7 October 2023
Available online 12 October 2023

2. Case presentation

A 63-year-old female visited her primary-care physician with complaints of cough and dyspnea upon exertion. She was referred to her previous physician, and multiple cysts were noted in both lungs on chest computed tomography (CT). The patient was referred to our hospital after a thorough examination, including TBLB, failed to provide a diagnosis. The patient had smoked 10 cigarettes/day for 40 years and had a history of breast-implant surgery, but no history of occupational exposure. Vital signs at the time of admission were clear consciousness; blood pressure, 111/71 mmHg; pulse rate, 76/min; respiratory rate, 18 breaths/min; oxygen saturation, 98% (room air); and body temperature, 36.7 °C. No superficial lymph nodes were palpable, and no abnormal sounds were heard in either lung. No other abnormalities were observed in the skin, joints, or muscles. Laboratory tests on admission revealed white blood cell count, 6,300/μL; hemoglobin concentration, 13.9 g/dL; platelet count, 22.4 × 10^3/μL; C-reactive protein concentration, 0.91 mg/dL; and Krebs von den Lungen-6 (KL-6) concentration, 641 U/mL. No antibodies specific for connective-tissue disease such as anti-SS-A/Ro60 and/or anti-SS-B/La found in Sjögren syndrome or tumor markers such as soluble interleukin-2 receptor, that are commonly associated with lymphoma, were detected.

Chest radiography (Fig. 1a) revealed granular shadows, predominantly in the upper and middle fields of both lungs. High-resolution CT (HRCT) of the chest revealed multiple cystic lesions with thick walls and nodular shadows, predominantly in the upper lobe (Fig. 1b). We considered PLCH, lymphangioleiomyomatosis, Sjögren syndrome, lymphoma, and amyloidosis as differential diagnoses based on HRCT findings. Bronchoalveolar lavage fluid from the right middle lobe (B5) revealed a total cell count of 4.0 × 10^5 cells/mL (96% macrophages, 4% lymphocytes) and 5.1% CD1a-positive cells. TBLC performed at B3 of the right lung revealed scarred fibrotic lesions around the airway (Fig. 2a). Immunostaining was positive for CD1a, S100, and BRAF (Fig. 2b). No complications, such as pneumothorax or bleeding, were observed after TBLC. Based on the chest CT findings and results of pathological examination of the bronchoalveolar lavage fluid and TBLC specimen, the patient was diagnosed with PLCH, although fibrotic interstitial pneumonia was also considered as a differential diagnosis based on the pathological findings. CT from the head to the pelvic region, confirmed the absence of abnormalities in other organs such as the bones, liver, spleen, and thyroid. The patient stopped smoking for one year; the cough decreased, and chest radiography and HRCT showed improvement in the thick-walled cysts and granular shadows (Fig. 3).

3. Discussion

We presented a case in which PLCH was diagnosed using TBLC but not TBLB, suggesting that TBLC may be more useful for the diagnosis of PLCH.

Single-system PLCH is thought to be a distinct entity that is almost exclusively observed in active or former smokers. The diagnosis of single-system PLCH is typically made based on characteristic chest HRCT imaging or histopathological findings after SLB or TBLB [7]. HRCT is an important tool for early screening of suspected PLCH, but histological findings remain the gold standard for a definitive diagnosis. TBLB is the primary diagnostic tool for obtaining tissue samples from patients with suspected PLCH [3]. However, the diagnostic yield of TBLB ranges from 17% to 50% [3,4,8]. In contrast, in patients with other types of cystic lung disease, such as lymphangioleiomyomatosis, the diagnostic yield of TBLB is higher, ranging from 57% to 86% [3,9–11]. Several reasons have been cited to explain why TBLB may be not helpful for the diagnosis of PLCH. These include sampling error because the disease can be focal and patchy in distribution, fewer active nodules in advanced disease, and small size of the biopsy sample. PLCH tends to be located more distally, around the respiratory and terminal bronchioles, potentially making bronchoscopic access to the diseased acinar tissue difficult. Langerhans cells can be crushed during TBLB and typical pathological findings of PLCH may be difficult to appreciate [4].

In recent years, TBLC has been explored as a less-invasive alternative to SLB. With this technique, larger samples without crush

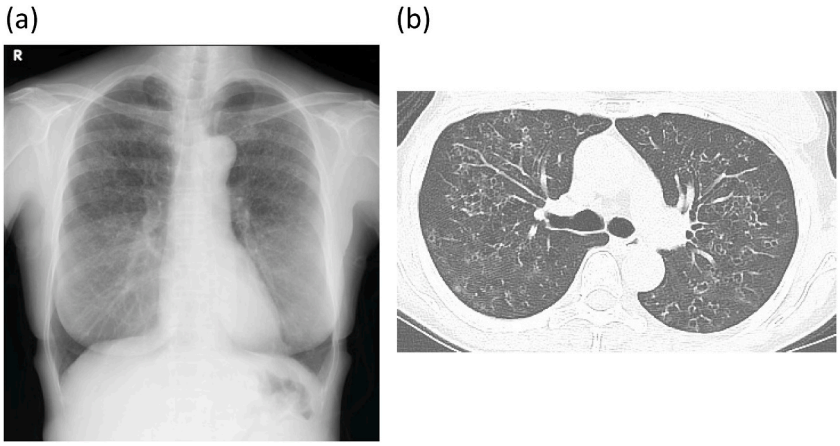

Fig. 1. Radiological findings on admission. (a) Chest radiograph shows granular shadows predominantly in the upper and middle fields of both lungs. (b) Chest high-resolution computed tomography shows multiple cystic lesions with thick walls and nodular shadows predominantly in the upper lobe. Some cystic lesions are irregular in shape.

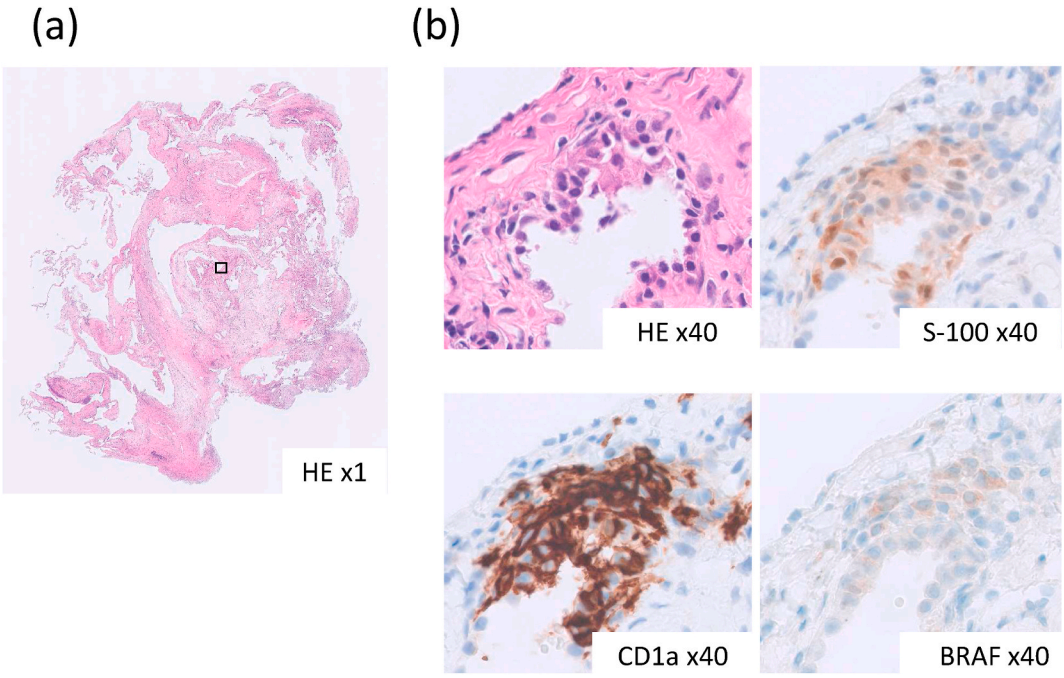

Fig. 2. Pathological findings of the lung specimen obtained using transbronchial lung cryobiopsy. (a) Hematoxylin and eosin staining shows scarred fibrotic lesions around the airway, and histiocyte-like cell clusters are seen in some areas. (b) Immunostaining is positive for CD1a, S100, and BRAF in the histiocyte-like cell clusters.

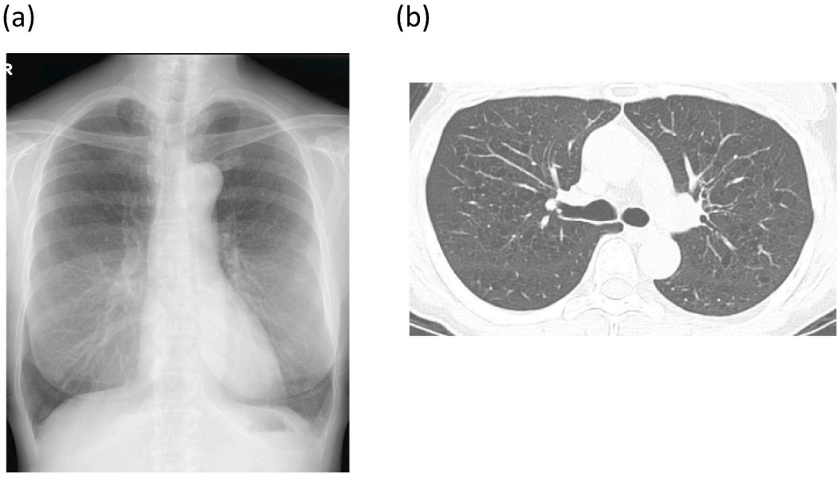

Fig. 3. Radiological findings after stopping smoking for one year. (a) Chest radiograph shows indistinct granular shadows predominantly in the upper and middle fields of both lungs. (b) Chest high-resolution computed tomography shows improvement in the thick-walled cysts and granular shadows.

artifacts can be obtained compared with the standard TBLB, although complications such as bleeding and pneumothorax may occur [12]. Two studies that compared the usefulness of TBLB and TBLC for ILD diagnosis in the same population reported diagnostic yields of 34% (95% confidence interval [CI], 19–49%) and 74% (95% CI, 60–88%) [13] and 54% (95% CI, 35–71%) and 77% (95% CI, 63–88%), respectively [14]. These studies suggest that TBLC is more useful than TBLB for ILD diagnosis. Furthermore, TBLC is regarded as an acceptable alternative to SLB for histopathological diagnosis in patients with ILD of an undetermined type in medical centers with experience in performing and interpreting TBLC [15]. To the best of our knowledge, no study has evaluated the diagnostic yield of TBLC for PLCH. However, few cases in which PLCH has been diagnosed using TBLC have been reported [8,16,17]. Furthermore, in a study of 699 cases, in which TBLC was performed to diagnose diffuse lung diseases, seven out of eight cases of PLCH (88%) were diagnosed using TBLC and one case was diagnosed using SLB after TBLC failed to provide a diagnosis [18]. However, in this case, a comprehensive view of the lesions, comparable to that obtained using SLB, was not obtained using TBLC. The smaller tissue size obtained via TBLC compared with that obtained via SLB might be a limitation for the diagnosis of PLCH diagnosis.

Our patient had slightly elevated levels of KL-6, which is a marker of interstitial pneumonia; however, HRCT showed no lesions

suggestive of interstitial pneumonia. Serum KL-6 concentrations are significantly higher in patients with PLCH than in healthy controls [19]. Thus, elevated KL-6 levels in the present case may reflect the underlying pathophysiology of PLCH.

4. Conclusion

Although the usefulness of TBLC for the diagnosis of PLCH remains unknown, the findings in this case suggest that TBLC may be more useful than TBLB for the diagnosis of PLCH. Further studies are required to clarify the usefulness of TBLC for the diagnosis of PLCH.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

All authors met the International Committee of Medical Journal Editors authorship criteria. MK wrote the manuscript. All authors contributed to the editing of the manuscript and approved the final version of the manuscript.

Declaration of competing interest

No conflict.

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