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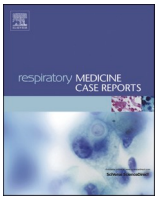

Case Report

Case of pulmonary Langerhans cell histiocytosis presenting as ground-glass opacity in the lower lung

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ABSTRACT

Nodules and cysts with upper lobe predominance on chest computed tomography (CT) are highly suggestive of pulmonary Langerhans cell histiocytosis (PLCH). Herein, we describe a case of PLCH that presented with the unusual CT findings of subpleural ground-glass opacity (GGO) and traction bronchiectasis mostly in both lower lungs. No nodules or cysts were observed in the upper or middle lung areas. Video-assisted thoracoscopic biopsies were performed at the right lower lobe. Biopsy specimens showed findings consistent with those of scarred PLCH. To the best of our knowledge, this is the first case of PLCH presenting as GGO in the lower lungs.

1. Introduction

Nodules and cysts with upper lobe predominance on chest computed tomography (CT) are highly suggestive of pulmonary Langerhans cell histiocytosis (PLCH) and may obviate the need for biopsy. Reticular opacities are findings indicating more advanced disease. Herein, we describe a case of PLCH diagnosed by biopsy at the ground-glass opacity (GGO) area in the lower lung.

2. Case presentation

A 56-year-old man presented to our hospital with a recent paroxysmal cough on July 29, 2022. The patient had a medical history of diabetes mellitus and a smoking history of 36 pack-years. He was a construction worker for 20 years.

His vital signs were stable. Laboratory tests revealed no remarkable findings. Pulmonary function test (PFT) showed mildly restrictive insufficiency with a forced vital capacity (FVC) of 74 % (3.70 L) of the predicted normal value and forced expiratory volume in 1 s/FVC of 85 %. The diffusion capacity for carbon monoxide (DLCO) was 61 % (16.0 mL/min/mmHg). In the 6-min walking test (6MWT), the patient walked for 600 m. Oxygen saturation commenced at 97 %, reaching its nadir at 96 % during 6MWT. Chest X-ray revealed mild reticular opacities in both lower lung areas (Fig. 1). Chest CT revealed subpleural GGO and traction bronchiectasis mostly in both lower lungs. No nodules or cysts were present in the upper or middle lung areas (Figs. 2–3).

Video-assisted thoracoscopic (VATS) biopsies were performed at the superior and laterobasal segments of the right lower lobe on September 1. Biopsy specimens exhibited patchy interstitial bronchiolocentric fibrosis with chronic inflammation and focal aggregation of mononuclear cells and eosinophils in the fibrotic area. On immunostaining, the infiltrating mononuclear cells were positive

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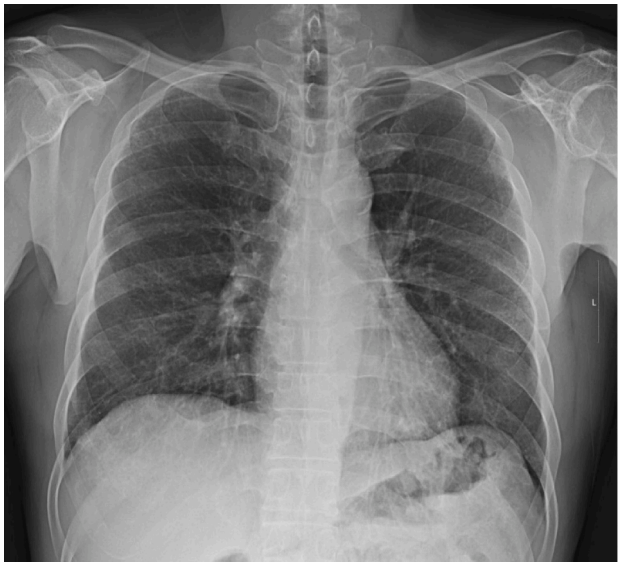

Fig. 1. Chest radiograph. Mild reticular opacities in both lower lung areas were observed.

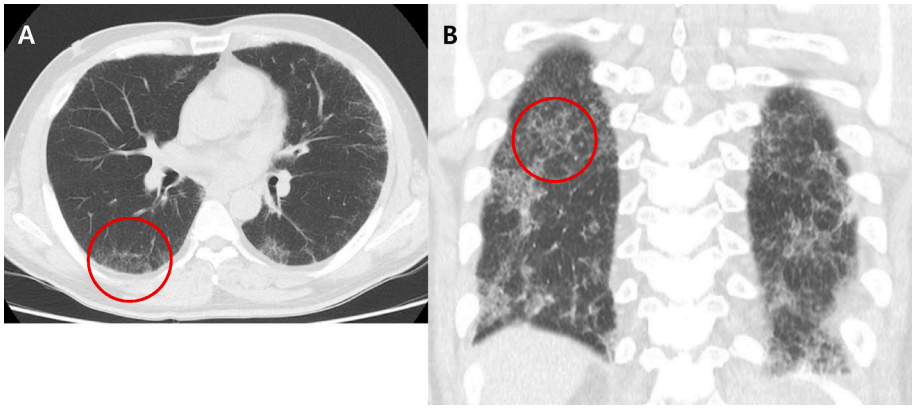

Fig. 2. Chest CT in the lower area. Subpleural GGO with reticular opacities was noted. Biopsy was performed at the right lower lobe superior segment (red circles in axial (A) and coronal (B) views, each). (CT = computed tomography, GGO = ground glass opacity).

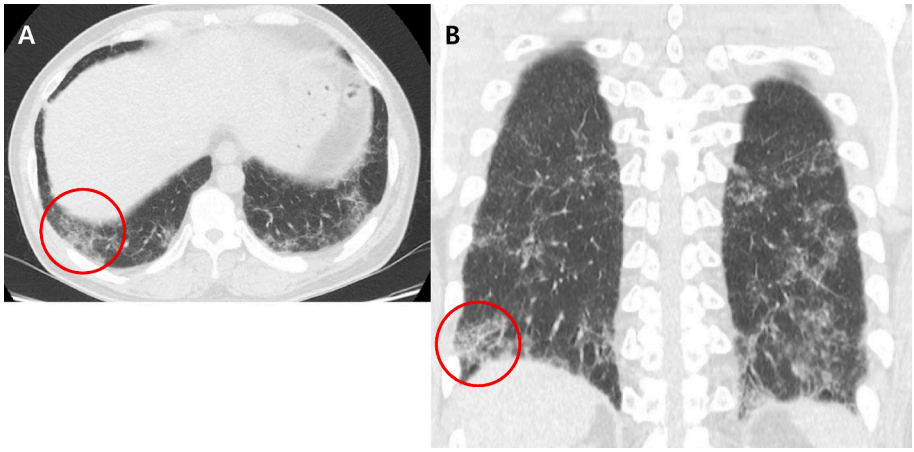

Fig. 3. Chest CT in the lower area. Subpleural GGO with traction bronchiectasis/bronchiolectasis was noted. Biopsy was performed at the right lower lobe laterobasal segment (red circles in axial (A) and coronal (B) views, each). See Fig. 2 for expansion of abbreviations.

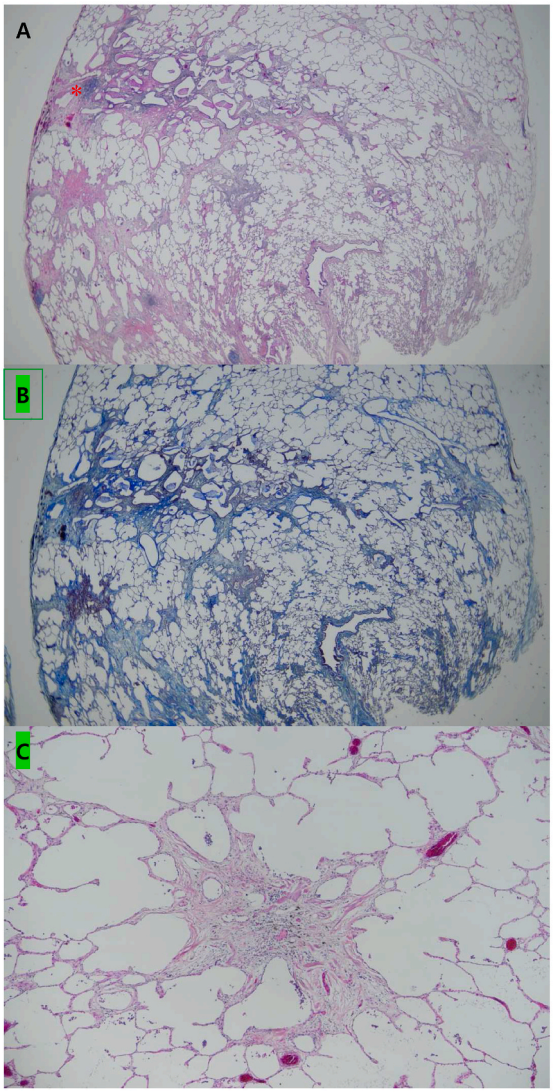

Fig. 4. Scanned power view of the biopsy specimens. (A) Patchy irregular or satellite-shaped bronchiolocentric fibrotic lesions were scattered throughout the specimen. Some fibrotic lesions on the upper portion (marked as a red asterisk) were associated with cellular infiltration and enlarged airspaces (x10). However, these infiltrates consisted solely of inflammatory cells and lacked Langerhans cell. (B) Masson trichrome stain highlighted the patchy peribronchiolar fibrosis (blue-colored areas) (x10). (C) Stellate-shaped scar-like fibrosis was evident (x40).

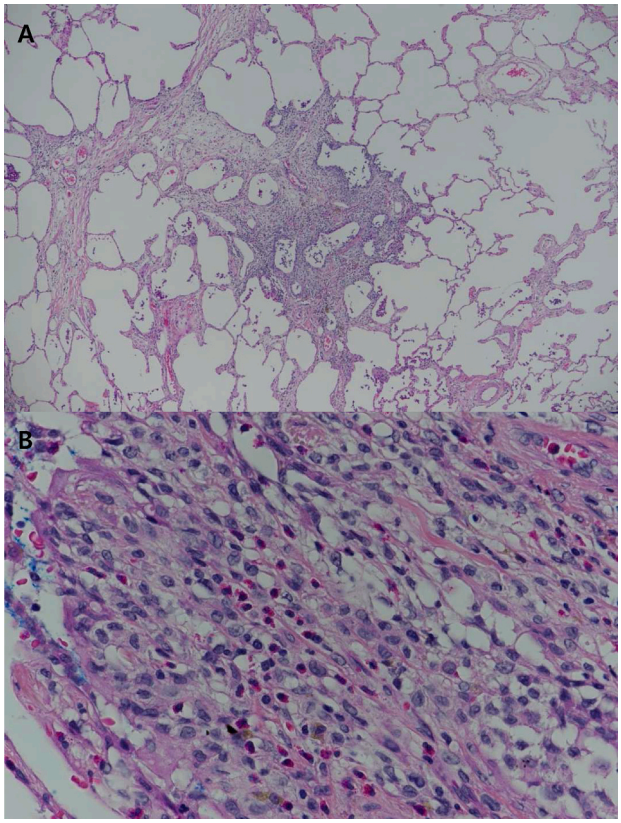

Fig. 5. Biopsy specimens with Langerhans cell infiltration.
(A) Patchy nodular vague stellate-shaped fibrosis and mononuclear cell infiltration in the peribronchiolar interstitium were noted (x40). (B) High power view demonstrated the infiltration of Langerhans cells showing folded nuclei and abundant ill-defined cytoplasm admixed with eosinophils (x400).

for CD1a and S-100, suggesting Langerhans cell infiltration. The infiltration was more prominent in the periphery of the stellate nodule (Figs. 4–7). All these findings were consistent with scarred PLCH.

The patient promptly quit smoking upon confirming the result of VATS biopsies. Although the patient was diagnosed with PLCH, because infectious causes were ruled out and the GGO lesion could have been reversible before progressing to fibrosis, oral prednisolone was administered at a daily dose of 30 mg from September 30 with gradual tapering over 21 weeks. A follow-up chest CT conducted on December 22 revealed no significant changes in interstitial lesions, including GGO. A follow-up PFT conducted on March 2, 2023 indicated FVC of 79 % (3.90 L) of the predicted normal value, and DLCO of 55 % (14.4 mL/min/mmHg). The patient remained under follow-up at an outpatient clinic. He reported no symptoms, such as cough or dyspnea on exertion.

3. Discussion

PLCH develops predominantly in young smokers. A confident clinical diagnosis can be made based on the characteristic clinical presentation and ill-defined nodules or bizarrely shaped cysts with upper lobe predominance on HRCT. Classic LCH is characterized by patchy nodular infiltrates of varying cellularity that have a distinct peribronchiolar distribution and are typically stellate shaped. Increased numbers of Langerhans cells are frequently observed in individuals who smoke or in a variety of other conditions, such as COPD, lung cancer and certain interstitial lung diseases; however, they typically appear as isolated entities rather than forming clusters. Therefore, the requisite diagnostic feature of LCH is the presence of clusters of Langerhans cells within the nodules, which stain positively for S-100 and CD1a [1,2].

In advanced LCH, fibrosis may predominate with only a few Langerhans cell clusters remaining at the edge of a scar, as observed in this case. Rather, the lesions of LCH comprise paucicellular fibrous scars that occasionally concentrate around respiratory bronchioles or display at least a centrilobular distribution. Old scarred LCH do not display the subpleural distribution of usual interstitial pneumonia or the homogeneous scarring of fibrotic non-specific interstitial pneumonia. Depending on the age of the lesion, small numbers

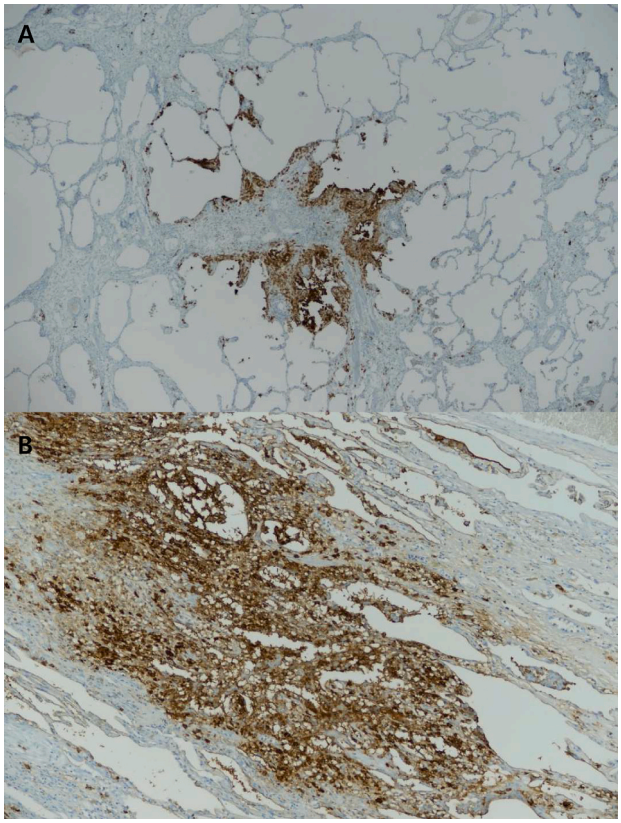

Fig. 6. Biopsy specimens with CD1a immunohistochemical
stain. (A) The infiltrating mononuclear cells were positive for CD1a immunostain, suggesting Langerhans cell infiltration. The infiltration of Langerhans cells was more prominent in the periphery of the stellate nodule (x40). (B) The mononuclear cells were positive for CD1a immunostain, suggesting Langerhans cell infiltration (x100).

of Langerhans cells and/or eosinophils may be present; however, older lesions exhibit fewer of these cells, and immunohistochemistry may confirm the diagnosis. Very old lesions are almost completely acellular, and in some cases, stellate scars are the only clue to suggest the diagnosis of scarred LCH. Therefore, in the absence of Langerhans cell clusters, the diagnosis of LCH can be suggested when peribronchiolar stellate-shaped scars are present along with respiratory bronchiolitis (RB) [1,3,4].

Few cases of PLCH with GGO had been reported, wherein the GGO reflects desquamative interstitial pneumonia (DIP)- or respiratory bronchiolitis interstitial lung disease (RBILD)-like changes related to smoking [5,6]. However, all these reported cases were accompanied by nodules or cysts. Our case showed only GGO, and we diagnosed PLCH by biopsy at the GGO area in the lower lung. Our pathological examination revealed findings suggestive of RB (Fig. 7). Notably, no definite features resembling DIP were identified. Smoking can cause the whole spectrum of RB, DIP, and PLCH in predisposed individuals. LCH biopsies also reveal focal areas resembling DIP and smoker's RB, but the convention is that these lesions are ignored unless there is true widespread DIP and not just accumulation of smoker's macrophages in alveoli. Despite the presence of RB- and DIP-like changes in lung biopsy specimens, a diagnosis of DIP or RB-ILD is not established if other distinctive histopathologic features, as those seen in PLCH, are present [6]. In our case, the traction bronchiectasis, observed on chest CT, might correspond to advanced PLCH.

4. Conclusions

This case was unusual because PLCH presented as GGO. In addition, it developed in subpleural and lower lung areas. To the best of our knowledge, this is the first case of PLCH presenting as GGO in the lower lungs. Therefore, for findings that do not suggest a specific disease, biopsy should be considered as possible.

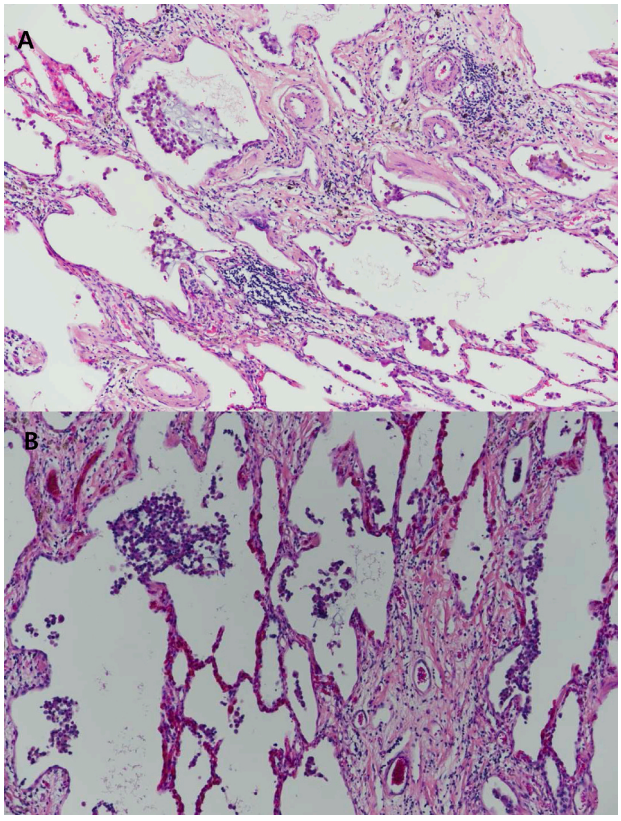

Fig. 7. Biopsy specimens showing RB pattern. Specimens
of the right lower lobe superior (A) and laterobasal segments (B) revealed intraalveolar macrophage accumulation in peribronchiolar lung parenchyma, where Langerhans cell infiltration was noted (x100, each). (RB = respiratory bronchiolitis).

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CRediT authorship contribution statement

Hong Lyeol Lee: Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Lucia Kim:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization. **Kyung Hee Lee:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization. **Cheol-Woo Kim:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests.

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