



## Idiopathic desquamative interstitial pneumonia diagnosed using transbronchial lung cryobiopsy: A case report

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### ABSTRACT

A 60-year-old Japanese man with a history of heavy smoking came to our hospital for a detailed examination, suspecting interstitial pneumonia because of gradually increasing dyspnea on exertion over a period of one year. Chest high-resolution computed tomography revealed ground-glass shadows with emphysematous changes. Pathological analysis of samples obtained using transbronchial lung cryobiopsy revealed an accumulation of alveolar macrophages with abundant eosinophilic cytoplasm in the alveolar space. Following a multidisciplinary discussion, the patient was diagnosed with desquamative interstitial pneumonia. To our knowledge, this is the first detailed report of desquamative interstitial pneumonia diagnosed using transbronchial lung cryobiopsy.

### 1. Introduction

Desquamative interstitial pneumonia (DIP) is characterized by the accumulation of alveolar macrophages in the alveolar lumen and septum [1]. Idiopathic DIP has been classified as smoking-related idiopathic interstitial pneumonia along with respiratory bronchiolitis–interstitial lung disease (RB-ILD) [2]. However, the prevalence of DIP is not known [3]. This may be due to not only the rarity of the disease but also the necessity of surgical lung biopsy (SLB) for its diagnosis [2].

Transbronchial lung cryobiopsy (TBLC) is a technique that has attracted much attention in recent years for its ability to obtain large samples with few crashes, and is useful for diagnosing diffuse lung disease, which has been difficult to diagnose with conventional forceps biopsy samples [4]. TBLC is safer and results in fewer complications and mortalities compared with SLB, although SLB is the gold standard for diagnosing diffuse lung disease [5]. The usefulness of TBLC has been demonstrated in a number of studies [5,6]. In those reports, a small number of cases of DIP were mentioned; however, the details of those cases were not described [6]. Here, we report a case of DIP diagnosed with TBLC.

### 2. Case presentation

A 60-year-old Japanese man with a history of arteriosclerosis obliterans visited our hospital. He had a history of smoking until a month before the visit (40 pack-years) and no history of environmental exposure. About a year prior to the visit, he became aware of dyspnea on exertion, which gradually increased. Approximately six months leading up to his visit, Raynaud's phenomenon appeared in his left index finger from time to time. His family doctor observed an abnormal shadow on the patient's chest radiographs and referred him to our hospital for further examination.

On the patient's first visit to our hospital, his vital signs were as follows: heart rate, 72 bpm; blood pressure, 134/93 mmHg; and body temperature, 35.9 °C. His percutaneous arterial blood oxygen saturation was 96% on room air, and his respiratory rate was 14 breaths/min. Chest examination revealed fine crackles in both lower lung fields. No skin rash, joint pain and swelling, muscle weakness, or other physical findings suggestive of connective tissue disease were observed. Laboratory testing on admission revealed a white blood cell count of 6300/μL, a hemoglobin concentration of 15.0 g/dL, and a platelet count of 21.6 × 10<sup>3</sup>/μL. The patient had a C-reactive protein concentration of 0.50 mg/

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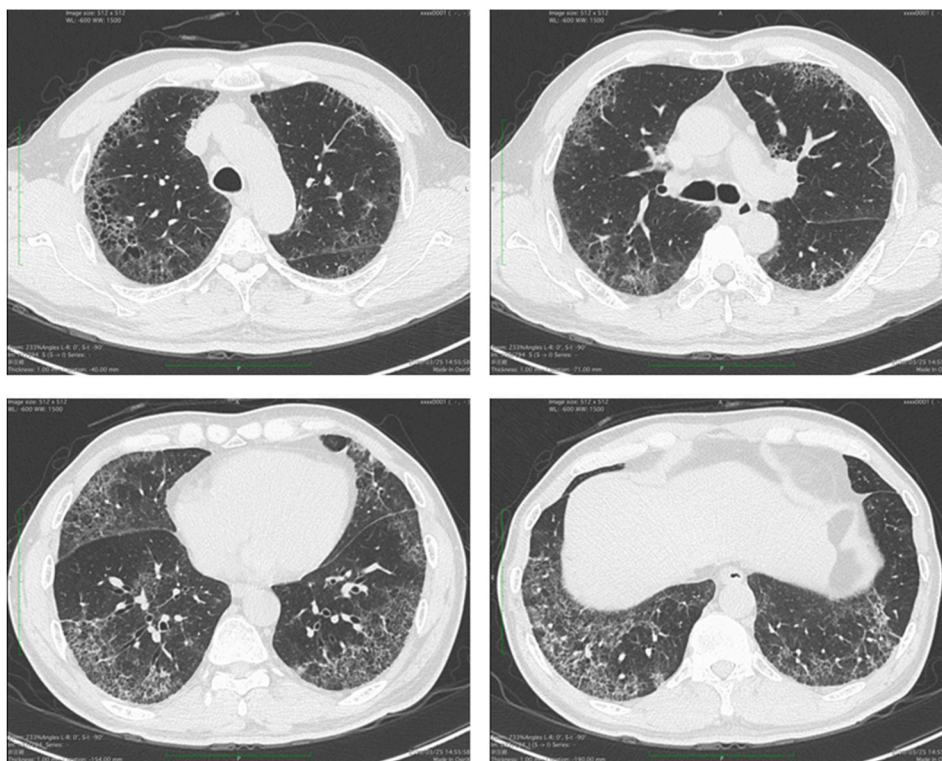
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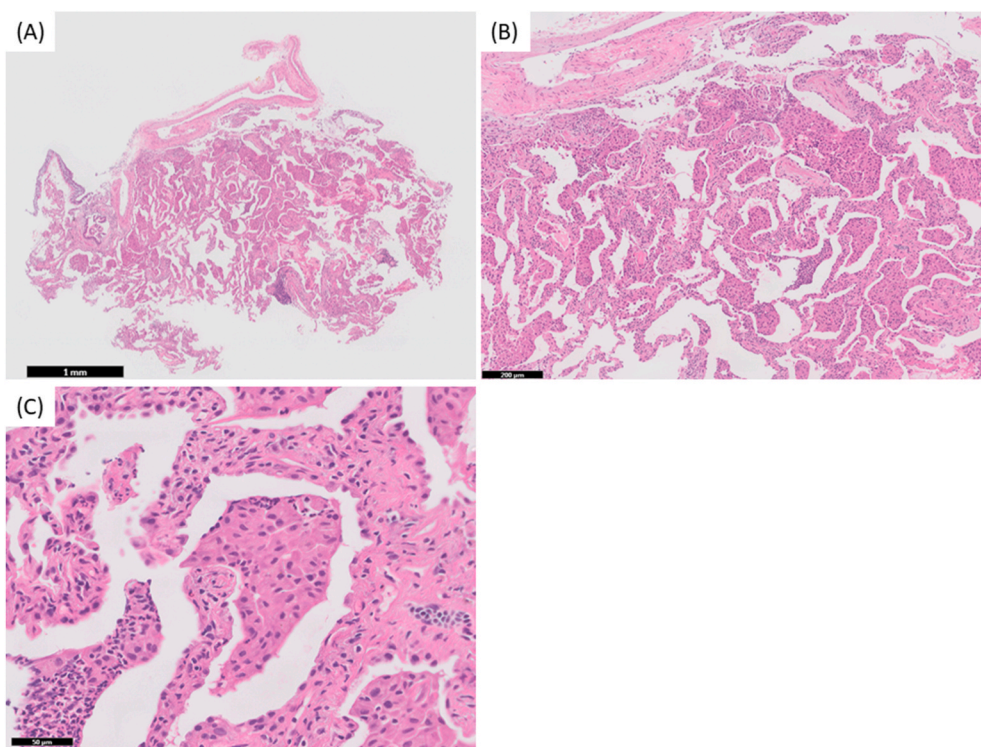
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**Fig. 1.** High-resolution computed tomography findings. Chest computed tomography revealed wide-ranging ground-glass attenuation and reticulation with traction bronchiectasis. Ground-glass attenuation was distributed mainly in the peripheral areas and partially along with the bronchovascular bundles.



**Fig. 2.** Histological findings of the lung (hematoxylin and eosin staining). (A) Macrophages are widely accumulated in the alveolar space (Scale bar = 1mm). (B) Thickening of the alveolar walls by fibrous tissue can be observed, showing a uniform appearance (Scale bar = 200µm). (C) Type II alveolar epithelial cells have proliferated, and alveolar macrophages with abundant eosinophilic cytoplasm, eosinophils, and neutrophils have accumulated in the alveolar spaces (Scale bar = 50µm).

dL and a lactate dehydrogenase concentration of 351 IU/L. His Krebs von den Lungen-6 concentration was 526 U/mL, and that of his surfactant protein-D was 166 ng/mL. Antinuclear antibodies were detected at a titer of 1:320 (with a cytoplasmic pattern), although no antibodies specific for connective tissue disease or markers of vasculitis were

detected.

High-resolution computed tomography (HRCT) of the patient’s chest revealed patchy, bilateral ground-glass opacities and reticular abnormalities in the upper to lower lobes. In addition, there were cystic spaces in the ground-glass opacities (Fig. 1). Pulmonary function tests

demonstrated neither restrictive impairment nor airway obstruction; however, a reduced diffusing capacity of the lung for carbon monoxide (DLCO) was observed (59% of the predicted capacity). Bronchoalveolar lavage fluid from the right middle lobe (B5) revealed a total cell count of  $5 \times 10^5$  cells/mL (82% macrophages, 7% lymphocytes, 6% neutrophils, and 5% eosinophils). TBLC was performed on S8a and S8b of the right lung. The biopsy specimens were  $5.5 \times 2.5$  mm (S8a) and  $4.4 \times 3.0$  mm (S8b) in size. Histologically, alveolar macrophages with abundant eosinophilic cytoplasm uniformly fill the air spaces. The alveolar and interlobular septa were infiltrated with inflammatory cells (Fig. 2). The fibrosis was mild, and the alveolar architecture was relatively well maintained. The lesion was compatible with a histological diagnosis of DIP.

Despite three continuous months of cessation of smoking, the patient's dyspnea on exertion worsened, and his DLCO deteriorated to 45% of the predicted capacity. Subsequently, we started immunosuppressive treatment with prednisolone (30 mg/day; 0.5 mg/kg/day), with gradual tapering of the dose, which led to an improvement in pulmonary symptoms. Moreover, HRCT performed 3 months later confirmed this improvement, and the patient's DLCO had improved to 75% of the predicted capacity, and no adverse or unexpected events had occurred.

### 3. Discussion

This case report indicates that TBLC may be useful in the diagnosis of DIP. Currently, SLB is required for the diagnosis of not only DIP but also many other diffuse lung diseases [2]. However, because of its invasiveness, it is not practical to implement SLB in all cases. TBLC has gained widespread attention in recent years [7]. Because it can be performed during bronchoscopy, it is expected to be applicable to a larger number of patients than SLB is. In fact, it has been reported that the widespread use of TBLC has led to a decrease in the number of SLBs performed [8]. There have been vigorous efforts to validate the usefulness of TBLC. Romagnoli et al. [9] reported a low concordance between TBLC and SLB in terms of histological diagnosis of diffuse lung disease, while Troy et al. [10] reported that their concordance in terms of histological and multidisciplinary discussion (MDD) diagnoses was 70.8% and 76.9%, respectively. Zaizen et al. [11] reported that TBLC is useful in the diagnosis of usual interstitial pneumonia (UIP). UIP patterns are easier than other patterns of lung disease to evaluate using HRCT. If the lesion tissue is properly harvested, it is easier to confirm pathologic findings characteristic of UIP, such as fibroblastic foci and abrupt changes, than for other patterns.

The pathological features of DIP are often difficult to distinguish from those of RB-ILD, its most striking feature being the accumulation of pigmented macrophages in the small airways and alveoli [12]. The main feature distinguishing DIP from RB-ILD is the higher intensity of fibrotic changes in the former [13]. In addition, it can be difficult to distinguish DIP cases from cases of non-specific interstitial pneumonia if the patients are smokers [3]. Because macrophage aggregates in the alveoli are particularly common in smokers, the degree of fibrosis and the diffuse appearance of macrophage aggregates are important points of distinction. Therefore, a TBLC-based diagnosis requires a proper collection of lesions and confirmation of the alveolar structure over a relatively large area. In the pathology of this case, pigmented alveolar macrophages filled the alveolar space over a wide area, and the surrounding alveolar septum was conspicuous for the growth of type II alveolar epithelial cells, with extensive fibrosis extending to the margins of the lobes. Together, these findings strongly suggested DIP. However, DIP cannot be diagnosed using only the initial histological examination; it is important that the diagnosis also takes into account HRCT findings and the clinical background.

MDD is vital in making the best use of the information obtained by TBLC [14]. In fact, in this case, there were clinical features of severe smoking history, Raynaud's symptoms, and elevated antinuclear antibodies. Interstitial pneumonia with autoimmune features is another

common finding in DIP cases [15,16]. In addition, HRCT revealed emphysematous changes, ground-glass attenuation, and cystic changes, predominantly in the periphery of the lower lobe. The imaging features of the present case were also typical of DIP. After discussion among a respiratory physician, radiologist, and pathologist, the patient was diagnosed with DIP.

### 4. Conclusion

DIP may be diagnosed using MDD if an appropriate sample is obtained via TBLC, thereby reducing the need for SLB in making such a diagnosis.

#### Informed consent

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

We have received written consent for publication from this patient.

#### Availability of data and materials

Not applicable.

#### Competing interests

The authors declare that they have no potential competing interests.

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#### Authors' contributions

H.I. and N.S. conceived, designed, and drafted the article. M.O. contributed to the pathological diagnosis. S.T. contributed to the radiological diagnosis. A.H., T.K., H.Y., T.M., Y.O., Y.I. and H.M. made critical revisions. All authors have read and agreed to the published version of the manuscript.

#### Declaration of competing interest

The authors declare that there is no conflict of interest.

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#### List of abbreviations

TBLC	transbronchial lung cryobiopsy
DIP	desquamative interstitial pneumonia
RB-ILD	respiratory bronchiolitis–interstitial lung disease

SLB	surgical lung biopsy
MDD	multidisciplinary discussion
HRCT	high-resolution computed tomography,
DLCO	diffusing capacity of the lung for carbon monoxide
UIP	usual interstitial pneumonia

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