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Case report

Transbronchial lung cryobiopsy in idiopathic acute fibrinous and organizing pneumonia

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ABSTRACT

A 53-year-old Japanese female was admitted to our hospital with 3-week history of cough and worsening dyspnea. Chest computed tomography revealed unilateral focal consolidation in the right lower lobe. She underwent transbronchial lung cryobiopsy (TBLC) and histology showed acute fibrinous and organizing pneumonia (AFOP). High-dose methylprednisolone treatment improved her respiratory condition and radiological findings. AFOP is a rare histologic interstitial pneumonia pattern and has been diagnosed by surgical lung biopsy or autopsy in most cases. To our knowledge, this is the first detailed report of AFOP diagnosed by TBLC. TBLC can be performed safely with less invasion and be a useful diagnostic technique for rapidly progressive diffuse lung disease such as AFOP.

1. Introduction

Transbronchial lung cryobiopsy (TBLC) is a novel technique which allows to obtain large biopsy samples of lung parenchyma that surpass the size and quality of forceps biopsy samples [1,2]. Specimens from endobronchial forceps biopsies are generally too small to diagnose diffuse lung diseases. TBLC is safer and has lower complication and mortality rates compared to surgical lung biopsy (SLB) [3,4].

Acute fibrinous and organizing pneumonia (AFOP), first reported in 17 patients with acute respiratory failure, is a histologic pattern associated with a clinical picture of acute lung injury [5]. In 2013 American Thoracic Society/European Respiratory Society statement, AFOP was classified as a rare histologic interstitial pneumonia pattern [6]. To date, the diagnosis of AFOP has been made by SLB or by autopsy in most cases [7], and there were no reports on the diagnosis of idiopathic AFOP confirmed by TBLC. Here, we report a case of idiopathic AFOP with progressively worsening symptoms diagnosed by mean of TBLC and then successfully treated.

2. Case report

A 53-year-old Japanese female with a history of cervical cancer and vocal cord papilloma visited to our hospital for evaluation of three weeks history of progressive dry cough and dyspnea. She was a past smoker (1 pack/day for 8 years) and had no history of environmental exposure. Although she was treated with azithromycin as an outpatient, she presented with right chest pain, fever and hemoptysis on three days after the first visit and admitted to our hospital.

On hospital admission, her vital signs were as follows: heart rate 125 bpm, blood pressure 114/81 mmHg, body temperature 39.0 °C. Percutaneous arterial blood oxygen saturation was 94% on room air and respiratory rate was 24/min. Chest examination revealed unilateral coarse crackles in the right lower lung fields. Skin rash, joint pain and swelling, muscle weakness, and other physical findings suggestive of connective tissue disease were not observed. Laboratory testing on admission showed a white blood count of 11,180/μL, hemoglobin of 14.2 g/dL and platelet count of 327,000. Erythrocytes sedimentation rate was 98 mm/h and C-reactive protein was 5.3 mg/dL. Lactate dehydrogenase, Krebs von den Lungen-6 and surfactant protein D were within the normal range. Work up for respiratory disease including sputum cultures, urinary *pneumococcal* and *Legionella* antigen were all negative. Serologic studies for connective tissue disease, vasculitis were also unrevealing.

High-resolution computed tomography (CT) of the chest revealed

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Abbreviations list

AFOP	Acute fibrinous and organizing pneumonia
COP	Cryptogenic organizing pneumonia
CT	Computed tomography
SLB	Surgical lung biopsy
TBLC	Transbronchial lung cryobiopsy

unilateral focal consolidation with halo sign in the right lower lobe (Fig. 1A–D).

Despite that ceftriaxone and minocycline were started on the first day, her clinical condition did not improve. On the third day of admission, the patient underwent flexible bronchoscopy with bronchial wash and TBLC from the right lower lobe B^9 and B^{10}. The biopsy specimens of 4 mm × 5 mm size were collected by TBLC. Histological study of these specimens showed intra-alveolar fibrin balls, involving more than three quarters of alveolar space and mononuclear cells infiltration without eosinophils and formation of hyaline membranes (Fig. 2A–C), indicating AFOP. Bacterial culture was negative.

After TBLC, high dose of methylprednisolone was initiated, resulting in rapid clinical improvement. On the twenty five day of admission, she was discharged home on 25 mg prednisone daily. She has remained free of pulmonary symptoms and finished taking prednisone ten months later. There was no evidence of collagen tissue disease, vasculitis, and other etiology during the disease course. We diagnosed her with idiopathic AFOP.

3. Discussion

This case study implies two important clinical issues. First, TBLC can be a useful diagnostic technique for rapid progressive interstitial lung disease such as AFOP. Second, the CT image of idiopathic AFOP at early phase might be similar to that of cryptogenic organizing pneumonia (COP) in some cases.

This is the first report to show TBLC as a useful biopsy technique for diagnosis of idiopathic AFOP. Previous report referred AFOP case diagnosed with TBLC, though it was secondary AFOP and with no detailed description [8]. The diagnostic yield of TBLC is higher, attributable to the larger, higher quality samples harvested, than with conventional forceps in patients with interstitial lung diseases. TBLC seems to be a safe procedure, with lower complication and mortality rates compared to SLB [4]. SLB for interstitial lung disease can help clarify the diagnosis, however in-hospital mortality after elective lung biopsy was as low as 1.7%, it significantly rise to 16% in non-elective, urgent and emergency procedures [9]. SLB cannot be performed in the acute phase. No studies have compared the performance of TBLC with the gold standard of SLB incorporated into a multidisciplinary discussion. One study reported a pooled systematic review on diagnostic yield for TBLC of approximately 80% in patients being evaluated for suspected interstitial lung diseases [10]. On the other hand、although endobronchial forceps is the most used diagnostic biopsy technique, specimens are often too small and are associated with a relevant extent of artifacts in evaluating interstitial lung diseases. The histologic pattern of AFOP differs from the classic patterns of diffuse alveolar damage and organizing pneumonia in that organizing intra-alveolar fibrin constitutes the dominant histologic finding and differs from the pattern of eosinophilic pneumonia by the lack of prominent eosinophils. Intra-alveolar fibrin in the form of “fibrin balls” is to be found with an average of 50% airspace involvement without formation of hyaline membranes [5]. Taking this histologic finding into account, AFOP is difficult to diagnose with TBLB, which can harvest only a small amount of specimen. Pathologists suggest that adequate specimens should measure at least 5 mm in diameter since that corresponds to the size of full field seen with a 4 × objective on many microscopes. Such a field size allows pattern recognition in most cases [11]. In this case, AFOP was successfully diagnosed because of the specimens size of 4 mm × 5 mm could be collected by TBLC(Fig. 2).

Second, the CT image of idiopathic AFOP at early phase might be similar to that of COP in some cases. As chest CT in this case showed the consolidation with halo sign in the right lung, we diagnosed COP at her initial visit. Mostly, radiological findings in AFOP show diffuse patchy opacities and ground glass appearance of the lungs with both peripheral and bilateral distribution. This case is a rare case that present consolidation with halo sign in unilateral distribution. It has been reported that CT images of AFOP may show the lesion as a solitary nodule with air bronchograms with progression to diffuse lung opacities [12]. For the present, not a few cases of AFOP may be possibly misdiagnosed as

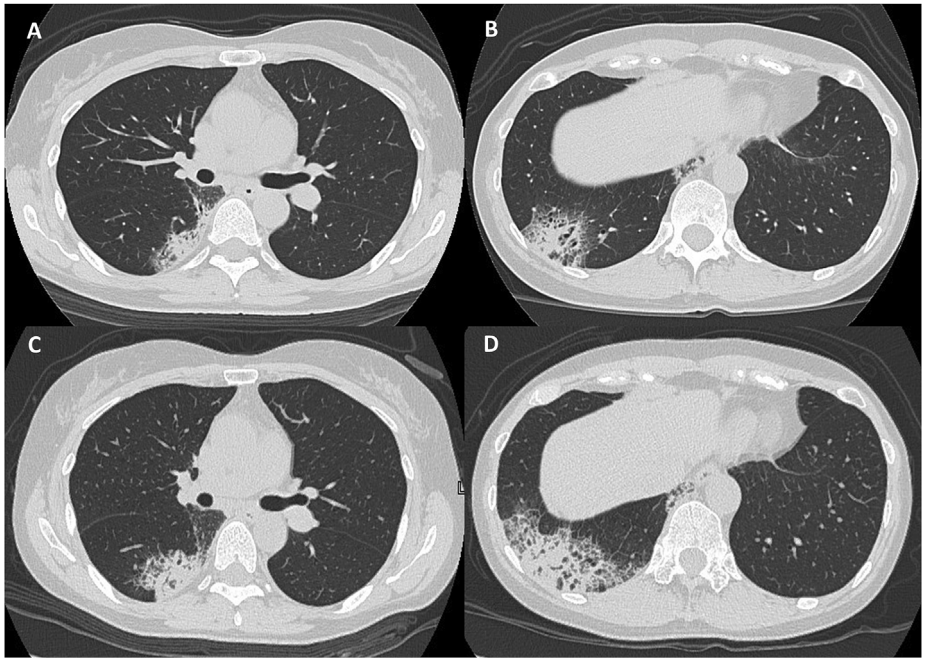

Fig. 1. (A,B) Chest computed tomography of the first visit showed consolidations with halo sign in the right lower lobe. (C,D) The shadow progressed six days later.

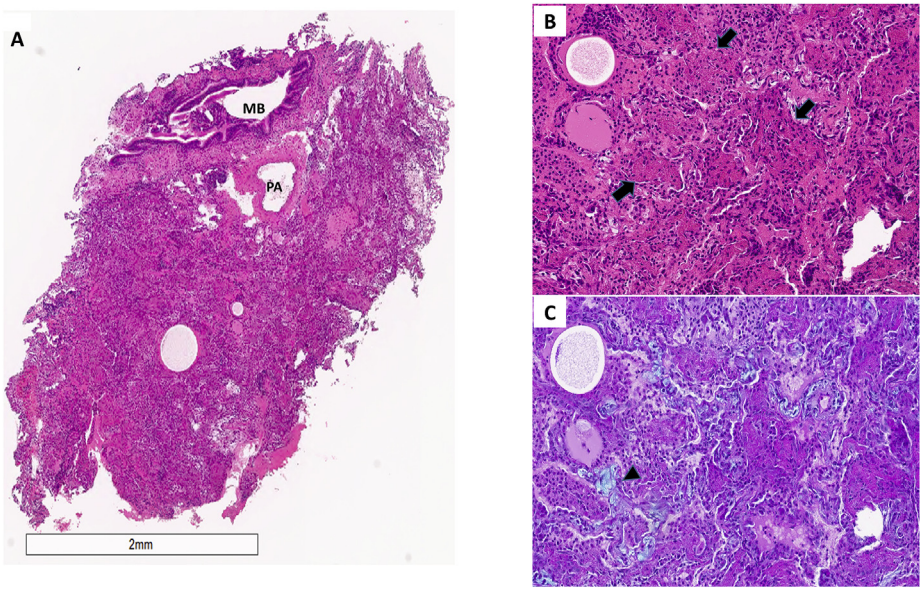

Fig. 2. Histological findings of the TBLC specimens.
(A) Intra-alveolar fibrin deposition within the alveolar spaces. Fibrin account for over three quarters of specimen (Hematoxylin and eosin staining, × 1). PA: pulmonary artery, MB: Membranous bronchioles
(B) This lesion was characterized by Intra-alveolar fibrin in the form of fibrin 'balls' and interstitial inflammation without formation of hyaline membranes (Hematoxylin and eosin staining, × 10). ➡fibrin balls
(C) This lesion showed accumulation of fibrin and occasional intra-alveolar polypoid fibrosis in alveolar spaces (Alcian blue and PAS staining, × 10). ▲polypoid fibrosis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

COP only with CT images without histology specimens.

In this case, right chest pain and blood sputum appeared suddenly, and the shadow extended in a short time, indicating serious and progressive condition.

AFOP patients can present with an acute and rapidly progressing form associated with poor prognosis. Among AFOP patients who died, the time from presentation of symptoms to death reportedly ranged from 6 to 36 days, with an average of 29 days [5]. The mortality rate associated with AFOP pattern was slightly over 50%, similar to DAD. Recommended treatment of AFOP has not been established. Some patients with AFOP require immunosuppressive agents such as cyclophosphamide, azathioprine, and mycophenolate mofetil in addition to corticosteroids [7]. In our case, early diagnosis seemed to contribute to an early choice of steroid pulse therapy and a good prognosis.

4. Conclusion

We successfully diagnosed and treated the case of progressively worsening idiopathic AFOP by virtue of TBLC. TBLC can be performed safely with less invasion and be a useful biopsy technique for rapidly progressive diffuse lung disease such as AFOP.

Conflicts of interest

The authors have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100888.

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