


Spontaneous improvement of interstitial pneumonia with autoimmune features: A case report

Hirotsugu Ohkubo¹  | Akiko Nakano¹ | Kohei Fujita¹ | Yoshiyuki Ozawa² | Takayuki Murase³ | Akio Niimi¹

¹Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

²Department of Radiology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

³Department of Pathology and Molecular Diagnostics, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Correspondence

Hirotsugu Ohkubo, Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya City University Graduate School of Medical Sciences, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya, Aichi 467-8601, Japan. Email: hohkubo@med.nagoya-cu.ac.jp

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Abstract

Interstitial pneumonia with autoimmune features (IPAF) was proposed to describe patients with interstitial lung disease who do not meet the classification criteria for a defined connective tissue disease. Here, we report a spontaneous improvement case of IPAF. A 58-year-old man developed dry cough and dyspnoea. Positive result was obtained for the anti-centromere antibody. High-resolution computed tomography (HRCT) showed reticular abnormalities and ground-glass opacities. Cryobiopsy specimens revealed cellular non-specific interstitial pneumonia. The patient displayed peri-ungual erythema and nail fold bleeding, but no sclerosis. He did not meet the criteria for systemic sclerosis, but did meet those for IPAF. Because symptoms slightly improved, the patient declined immunosuppressive treatment. After 6 months, repeated HRCT showed an apparent reduction in the area of ground-glass opacities. The forced vital capacity improved from 2.72 to 3.47 L and serum Krebs von den Lungen (KL)-6 decreased from 1977 to 531 U/ml, and symptoms disappeared.

KEYWORDS

interstitial pneumonia with autoimmune features, non-specific interstitial pneumonia, transbronchial cryobiopsy

INTRODUCTION

Interstitial pneumonia with autoimmune features (IPAF) is a term proposed in 2015 to describe idiopathic interstitial pneumonias that have clinical features of connective tissue disease (CTD), but do not meet the established criteria for CTD.¹ One of the morphological domains in the criteria for IPAF include the pathological pattern observed in surgical lung biopsy (non-specific interstitial pneumonia [NSIP], organizing pneumonia [OP], NSIP with OP overlap, lymphocytic interstitial pneumonia, interstitial lymphoid aggregates with germinal centres or diffuse lymphoplasmacytic infiltration). Li et al. suggested that IPAF should receive early immunosuppressive treatment.² However, how and when to treat IPAF has not been determined. Here, we report a spontaneous improvement case of IPAF.

CASE REPORT

A 58-year-old man developed dry cough and dyspnoea prior to presentations at our hospital. Three weeks before, he had developed symptoms of elevated fever and visited a local clinic, but the rapid flu test yielded negative results. He visited another hospital due to cough and progressive dyspnoea, and high-resolution computed tomography (HRCT) of the chest showed reticular regions and ground-glass opacities, predominantly in bilateral lower lung lobes (Figure 1A). He was then referred to our hospital. He had no history of exposure to asbestos and had previously smoked 1.25 packs of cigarettes a day for 37 years. He had no history of bird rearing or drug allergies and no family history of interstitial lung disease. Physical examination revealed periungual erythema, periungual epithelial extensions and nail fold bleeding, but no sclerosis. Fine crackles were

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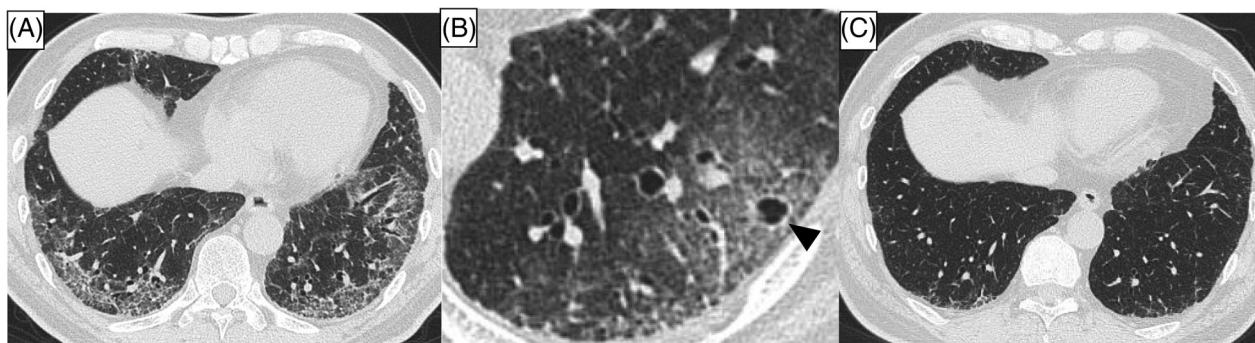


FIGURE 1 High-resolution computed tomography (HRCT) images and histological findings. (A) HRCT image at first visit. (B) HRCT image after transbronchial cryobiopsy. Arrowhead shows a cavity by cryobiopsy. (C) HRCT image after 6 months

audible on his back. Resting and ambulatory percutaneous oxygen saturation percentages in room air were 94% and 82%, respectively. Laboratory data showed leucocytosis (8100/ μ l) with neutrophilia (71.2%). C-reactive protein was 0.75 mg/dl. Serum lactate dehydrogenase concentration was elevated to 328 IU/L (normal range, 120–220 IU/L) and serum Krebs von den Lungen (KL)-6 level was elevated to 1977 U/ml (normal range, <500 U/ml). The anti-nuclear antibody (1:640 titre, discrete speckled) and the anti-centromere antibody were positive. Pulmonary function testing results showed a forced vital capacity (FVC) of 2.72 L (69.4% of predicted value) and diffusing capacity of the lung for carbon monoxide was 8.62 ml/min/torr (40.5%). The patient met neither the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for systemic sclerosis,³ nor the very early diagnosis of systemic sclerosis (VEDOSS) criteria.⁴ We performed transbronchial cryobiopsy from the left lower lung lobe using flexible bronchoscope under deep sedation, revealing a cavity in the left lower lung lobe on HRCT after the procedure (Figure 1B). A predominance of lymphoid cells was confirmed in bronchoalveolar lavage fluid (BALF) from the inferior lingular segment; lymphocytes, 50%;

neutrophils, 1%; eosinophils 8%; macrophage, 41%; and CD4/CD8 ratio, 0.20. No microorganisms were cultured in BALF. A cryobiopsy specimen obtained from the left lower lung lobe revealed mild thickening of the alveolar wall without vasculitis (Figure 2). The histology was compatible with cellular NSIP. Symptoms and ground-glass opacities slightly improved, and the patient declined immunosuppressive treatment. Repeated HRCT after 6 months showed an apparent reduction in the area of ground-glass opacities (Figure 1C). The FVC improved from 2.72 to 3.47 L, representing a 16.2% improvement. Serum KL-6 decreased from 1977 to 531 U/ml, and cough and dyspnoea disappeared. Furthermore, periungual erythema and nail fold bleeding improved.

DISCUSSION

This patient met the IPAF criteria,¹ and pathological analysis of cryobiopsy specimen demonstrated cellular NSIP. The diagnostic criteria for systemic sclerosis were revised in 2013 by the ACR/EULAR.³ The present patient met neither the ACR/EULAR criteria nor the VEDOSS criteria,⁴ but showed

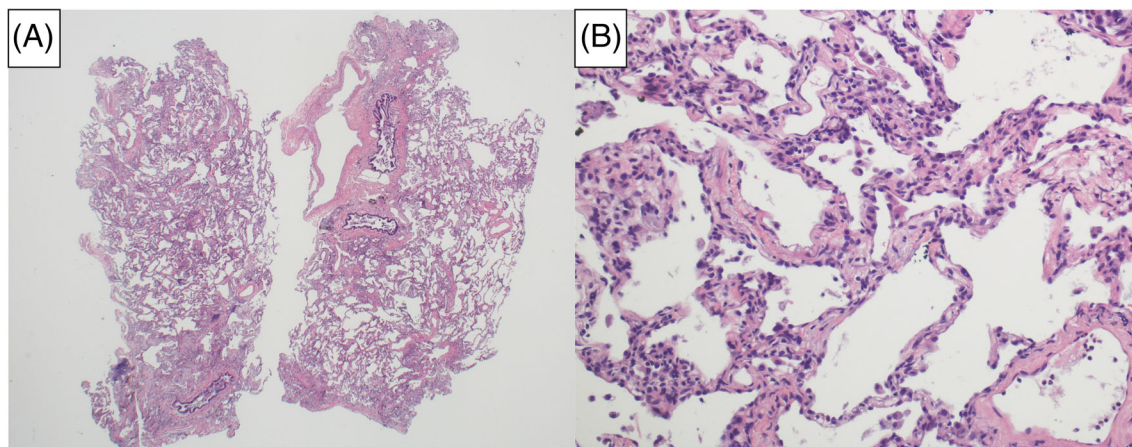


FIGURE 2 Histological findings for transbronchial cryobiopsy specimen of the left lower lobe. Images show moderate thickening of the alveolar walls (haematoxylin and eosin staining). (A) Low magnification, (B) High magnification

positive results for the anti-centromere antibody, presence of periungual erythema, periungual epithelial extension and nail fold bleeding.

In the present case, FVC and KL-6 improved spontaneously without administration of corticosteroids and immunosuppressants, while transbronchial cryobiopsy led to the diagnosis of cellular NSIP. The natural courses of cellular NSIP that meet the criteria for IPAF are not yet fully understood. To the best of our knowledge, this is the first report that cellular NSIP spontaneously improved that meet the criteria for IPAF with positive result for the anti-centromere antibody. It is important for the physician to consider the appropriate indications for the administration of corticosteroids and immunosuppressants in patients who meet the IPAF criteria.

Periungual erythema and nail fold bleeding sometimes improve, but usually do not improve in patients with systemic sclerosis. In the present case, these finger abnormalities and interstitial lung disease improved simultaneously. It is unknown how often IPAF progress to CTD, and what differences are present in the pathogenesis between IPAF and CTD. The temporal deteriorations of symptoms and signs might be caused by aberrant immune reactions for viral infection or environmental triggers. However, further research is needed to confirm such hypothesis.

The present case is categorized as idiopathic NSIP according to the current guidelines and improved spontaneously. IPAF remains a research diagnosis with little consensus on optimal treatment strategies. Accumulation of more cases is necessary for understanding and treating IPAF.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

Hirotsugu Ohkubo and Akiko Nakano equally contributed to the study. They drafted the submitted article and take responsibility for the integrity of the data and the accuracy

of the data analysis. Kohei Fujita, Yoshiyuki Ozawa and Akio Niimi contributed to the interpretation of the manuscript. Takayuki Murase contributed as a pathologist.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this case report and accompanying images.

ORCID

Hirotsugu Ohkubo  <https://orcid.org/0000-0002-8538-1150>

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