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## Case Report

# Usual interstitial pneumonia progressing to nonspecific interstitial pneumonia-like pattern on high-resolution CT with histologic confirmation ☆☆☆

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## ABSTRACT

Idiopathic pulmonary fibrosis (IPF) is a progressive and fatal disease. Although high-resolution computed tomography (HRCT) is important for the diagnosis of IPF, the changes in the HRCT findings in IPF are not fully understood. The patient was a 66-year-old man. His HRCT findings had atypically developed from a probable usual interstitial pneumonia pattern to a nonspecific interstitial pneumonia (NSIP) like pattern over 6 years. On the basis of the histologic examination and multidisciplinary discussion, IPF was diagnosed, and nintedanib, administered. This case can be useful for the differential diagnosis of IPF and NSIP.

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## Introduction

Idiopathic pulmonary fibrosis (IPF) is a progressive and fatal disease. IPF differs from nonspecific interstitial pneumonia (NSIP) in terms of the treatment and prognosis [1]. According to the 2018 ATS/ERS/JRS/ALAT guidelines, the diagnosis

of IPF should be based on a combination of high-resolution computed tomography (HRCT) and surgical lung biopsy with multidisciplinary discussion [2]. This IPF guideline sets a high value on scrutinizing the HRCT images for honeycombing, which is the major criterion for the usual interstitial pneumonia (UIP) pattern. If there is no honeycombing, a surgical lung biopsy is necessary for the diagnosis of IPF. However, it is

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sometimes difficult for even skillful radiologists to distinguish between IPF and NSIP on the CT images. The changes in the CT findings of IPF patients are not fully understood and make the differential diagnosis more difficult. Here, we present a rare case of IPF that atypically developed from a probable UIP pattern without honeycombing to a fibrotic NSIP (f-NSIP) like pattern, as shown on the chest CT.

## Case report

The patient was a 66-year-old man. Since receiving a diagnosis of and undergoing surgery for left ureteral cancer in 2010, he had been informed of the presence of interstitial lung abnormalities (ILA) as shown on the chest CT images. In 2015, he was recommended further investigation because the ILA had worsened. However, he refused because he had no symptoms. In 2016, he experienced dry cough and dyspnea on exertion and presented to our hospital. He was hospitalized for further investigation and treatment.

The patient had a medical history of alcoholic cirrhosis and hives. He was a former smoker (30 pack years). He had allergies to Japanese cedar, Japanese cypress, and house dust. He had worked in the fishing industry and had no dust inhalation. He had no exposure to potential antigens associated with hypersensitive pneumonia. On admission, his temperature was 36.2°C; blood pressure, 121/73 mm Hg; pulse rate, 77 bpm; and saturation of percutaneous oxygen (SpO<sub>2</sub>) in room air, 96%. His 6-minute walk distance (6MWD) was 458 m, and the SpO<sub>2</sub> was reduced to 89%. The physical finding was fine crackles in both lower lung fields. There was no finding of rash or arthritis.

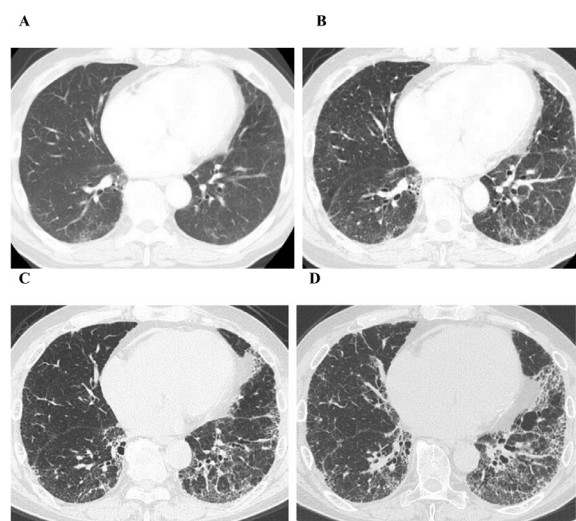
The laboratory findings demonstrated increases in lactate dehydrogenase (LDH, 258 IU/L. Reference range: 119–229 IU/L), C-reactive protein (CRP, 0.58 mg/dL. Reference range: <0.3 mg/dL), and KL-6 (1141 U/mL. Reference range: <500 U/mL). The autoantibody test findings for connective tissue disease were all negative. Anti-*Trichosporon asahii* antibody was slightly increased (0.81. Reference range: <0.15). Pulmonary function testing showed decreases in vital capacity (VC, 2.54L, 78.9%. Reference range: >80%), forced vital capacity (FVC, 2.42L, 75.2%. Reference range: >80%), total lung capacity (TLC, 3.71L, 72.3%. Reference range: 80–120%) and diffusing capacity of the lungs for carbon monoxide (7.19 mL/min/mm Hg, 44.6%. Reference range: >80%).

A chest X-ray image in 2016 showed ground-glass opacities (GGO) and reticular shadows in both the middle and the lower lung fields (Fig. 1).

The chest HRCT images in 2010 showed mild subpleural predominant GGO and reticular shadows in both lower lobes (Fig. 2A). In the HRCT images in 2013, the shadows had worsened slightly and were now accompanied by peripheral traction bronchiectasis (Fig. 2B). There was no honeycombing. At that point, the shadows had the probable UIP pattern. In 2015, peribronchovascular GGO and reticular shadows appeared (Fig. 2C). In 2016, the patient's status clinically worsened and the HRCT pattern progressed to NSIP-like pattern. The HRCT images revealed peribronchovascular GGO and reticular shadows with traction bronchiectasis predominantly in both lower lobes (Figs. 2D and 3). These shadows looked like f-NSIP pat-



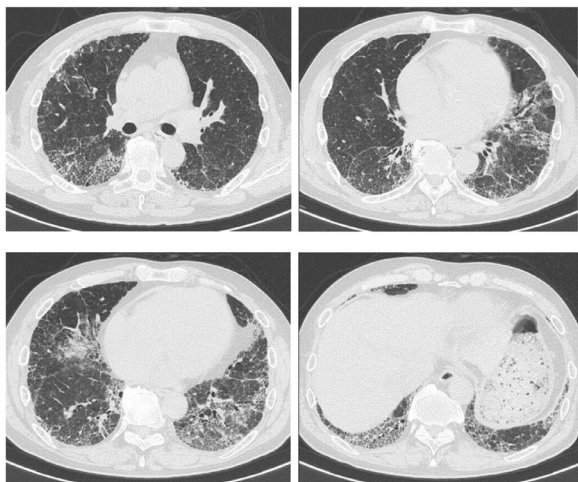
**Fig. 1** – Chest X-ray image in 2016 showing ground-glass opacities (GGO) and reticular shadows in both the middle and the lower lung fields.



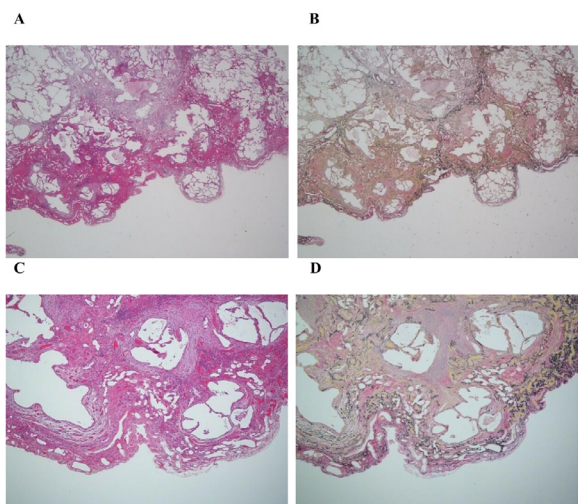
**Fig. 2** – (A) HRCT images showing mild subpleural predominant GGO and reticular shadows in both lower lobes in 2010. (B) In 2013, the shadows worsened slightly and peripheral traction bronchiectasis was also present, which were a probable UIP pattern. (C) In 2015, peribronchovascular GGO and reticular shadows appeared. (D) In 2016, the shadows worsened and looked like the f-NSIP pattern, especially in the left lung.

tern, especially in the left lung. However, the findings had been asymmetrical between the right and left lungs since 2010.

The bronchoalveolar lavage fluid (BALF) in the left middle lobe bronchus (B<sup>4</sup>) in 2016 showed total cells  $3.0 \times 10^5$ /mL and increases in neutrophils (5.0%. Reference range: <3%) and eosinophils (14.0%. Reference range: <1%). The bacterial and mycobacterial culture findings were negative. The histologic examination of the surgical lung biopsy in the left lung lobe (S6) in 2016 revealed dense fibrosis with architectural distortion of predominant subpleural and paraseptal distribution (Fig. 4A, B). There was also patchy fibrosis in the lung parenchyma. A higher magnification photomicrograph



**Fig. 3 – Chest HRCT images in 2016 showing peribronchovascular GGO and reticular shadows with traction bronchiectasis predominantly in both lower lobes. There was no honeycombing.**



**Fig. 4 – Histologic examination of the surgical lung biopsy in the left lung lobe (S6) in 2016. (A, B) Low magnification photomicrograph (magnification:  $\times 4$ ) revealing dense fibrosis with architectural distortion of the predominant subpleural and paraseptal distribution. There was also patchy fibrosis in the lung parenchyma. (C, D) Higher magnification photomicrograph (magnification:  $\times 20$ ) revealing subpleural destructive scarring with fibroblastic foci. (A, C) Hematoxylin and eosin stain. (B, D) Elastica van Gieson stain.**

revealed subpleural destructive scarring with fibroblastic foci (Fig. 4C and D). There was no finding suspicious for hypersensitive pneumonia and so on. Therefore, the histologic findings were the UIP pattern.

On the basis of a multidisciplinary discussion, IPF was diagnosed, and the patient was treated with an anti-fibrotic agent, nintedanib. He had been stable for a year and there was no change in FVC (1.96–1.90 L). However, his symptoms and FVC worsened gradually and he died of acute exacerbation of IPF in 2019.

## Discussion

In this report, we have described atypical changes in the chest CT images of a patient with histologic UIP. To our knowledge, this is the first reported case of an IPF patient whose probable UIP pattern developed to an NSIP like pattern.

Sumikawa et al reported that 21 of 98 patients (98%) with the histologic UIP pattern had the NSIP pattern on HRCT and 8 patients (8%) had unclassified CT findings [3]. Silva et al reported that 18 of 23 patients with NSIP diagnosed by use of surgical biopsy had the NSIP pattern on HRCT at the time of diagnosis [4]. Furthermore, in 5 patients (28%), the pattern developed to an UIP like one on HRCT. In these ways, it is sometimes difficult to distinguish between IPF and NSIP on the CT findings.

Yamauchi et al reported that 30 patients with IPF had no honeycombing and 12 patients (40%) developed traction bronchiectasis or cysts without honeycombing in the long-term observation of the HRCT images [5]. These findings mean that the probable UIP pattern can develop to an alternative diagnosis pattern, including the NSIP pattern. Moreover, no significant difference was found in the mean survival time with or without the appearance of honeycombing on HRCT. On the other hand, in the INPLUSIS study, no significant difference was found in the effect of nintedanib on IPF patients with or without honeycombing on CT [6]. Although honeycombing shown on HRCT is the key finding for the diagnosis of IPF, the clinical course and prognosis can be equivalent to those of IPF patients without honeycombing. Therefore, patients without honeycombing also need to be diagnosed and treated properly. Further investigation into the changes in the CT findings of IPF patients is required.

In our case, the HRCT findings in 2016 appeared to be the NSIP like pattern, however; since 2010, the findings were the asymmetrical between the right and left lungs. IPF with different degrees of the lesions in both lungs is called asymmetrical IPF [7]. The CT findings reflect the spatial heterogeneity that is one of the characteristics of IPF. Even if the HRCT images show an NSIP like pattern, asymmetrical findings may help with the diagnosis of IPF.

## Conclusion

IPF without honeycombing can develop to an NSIP like pattern. Although it is difficult to diagnose IPF on the basis of the CT findings in rare cases such as this one, the comparison with the past CT images can be useful. Furthermore, asymmetrical findings can be one of the rationales for the diagnosis of IPF.

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## Disclosure of COI

None of the authors have any financial conflicts of interest to disclose concerning this research.

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