# A Case of Pleuroparenchymal Fibroelastosis

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**Abstract:** Pleuroparenchymal fibroelastosis (PPFE) is a rare fibrotic lung disease with a poor prognosis. Some patients with PPFE have prominent lesions in one upper lobe. Due to the unilateral nature of lesions, similarities between some patients of PPFE and unilateral upper field pulmonary fibrosis (unilateral upper-PF) have been indicated. A 55-year-old man was referred to our hospital with PPFE, which had developed dyspnea 9 months previously. He had undergone resection of renal cancer 64 months prior to the onset of PPFE. He was administered the antifibrotic drug nintedanib, but passed away due to respiratory failure 43 months after the onset. What were impressive points in the clinical course of this PPFE patient was the similarity to unilateral upper-PF, including his medical history, and the poor prognosis. Although very rare, we do believe that the information on medical history and progression in this patient might provide suggestion into the treatment of future patients with a similar trajectory.

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## Introduction

Pleuroparenchymal fibroelastosis (PPFE) is a progressive disease that causes apical pleural thickening and pulmonary fibrosis in upper lobes of lungs. PPFE is a type of pulmonary fibrosis with a poor prognosis (Nakamura et al., 2021). Patients with PPFE include middle-aged and elderly men with a history of smoking (Nakamura et al., 2021). Although the etiology and pathology of this disease, like other pulmonary fibroses, remains unknown (Nakamura et al., 2021; Cottin et al., 2022), but it is known to occur in patients with a medical history of bone marrow or lung transplantation (Higo et al., 2019; Rasciti et al., 2019). Whereas some patients with PPFE have prominent lesions in one upper lobe. Due to the unilateral nature of lesions, similarities between some patients of PPFE and unilateral upper field pulmonary fibrosis (unilateral upper-PF) have been indicated (Sekine et al., 2017; Inafuku et al., 2022). Many patients with unilateral upper-PF have a history of thoracic surgery, and some studies have suggested

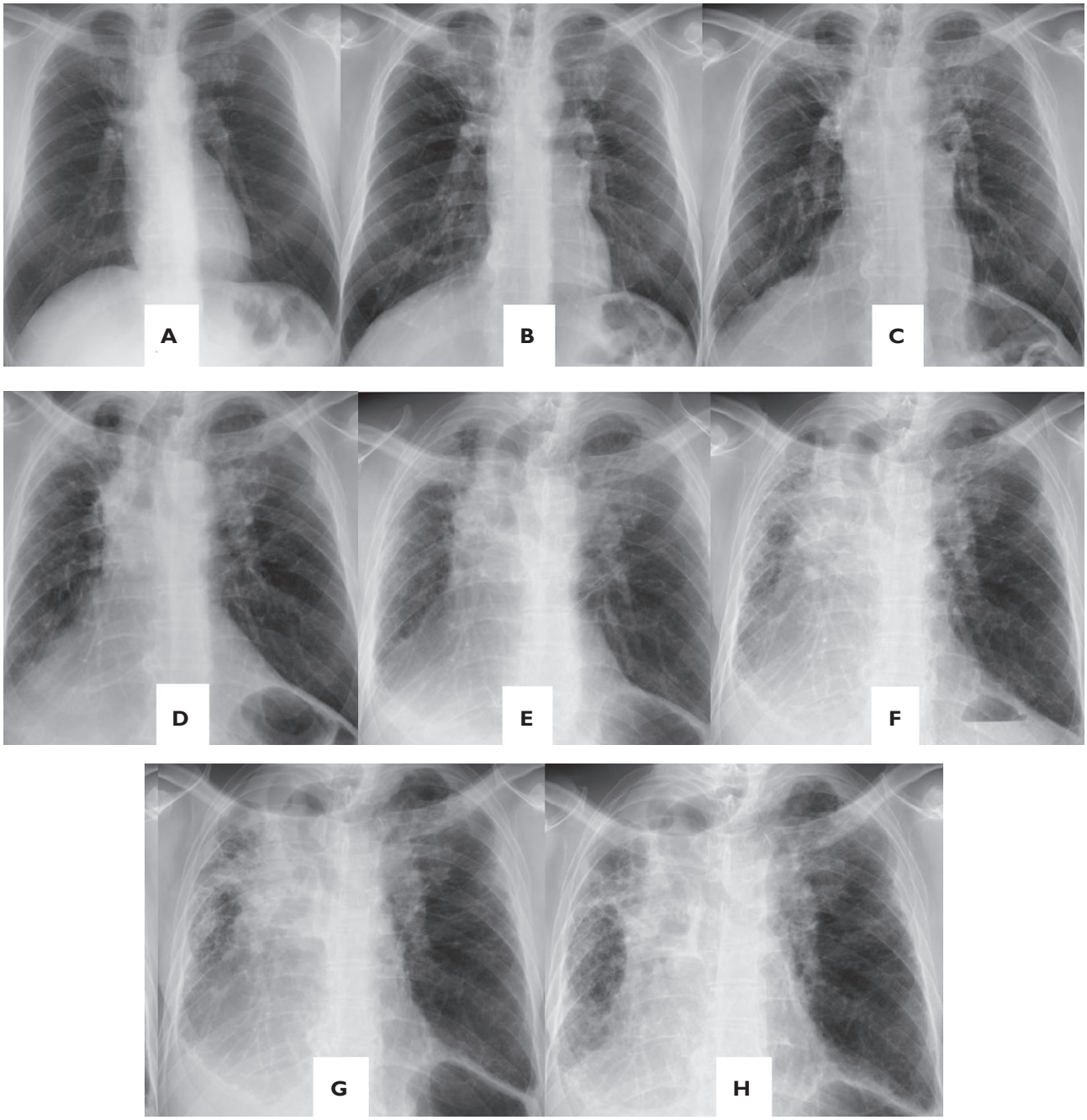


*Figure 1: Changes in chest radiographs over time. Chest radiograph taken just before resection of renal cancer 64 months before onset (A); chest radiograph taken 34 months before onset (B); chest radiograph taken 8 months before onset (C); chest radiograph taken at onset of pleuroparenchymal fibroelastosis (D); chest radiograph taken 8 months after onset (E); chest radiograph taken 18 months after onset (F); chest radiograph taken 25 months after onset (G); and chest radiograph taken 36 months after onset (H).*

Prague Medical Report / Vol. 126 (2025) No. 1, p. 30–35

a relationship between the onset of fibrosis and this medical history (Sekine et al., 2017; Inafuku et al., 2022).

This time, we treated a patient with PPFE who had prominent lesions on the right side. This patient had no history of thoracic surgery, but had undergone surgical treatment for renal cancer 64 months before the onset of PPEF. Although the mechanism of onset of PPFE was unknown, we do believe that this clinical course would provide some suggestive information on treatment for patients with a similar course in the future.

## Case report

A 55-year-old man was referred to our hospital after moving. He had a 10-pack-year smoking habit but no history of occupational inhalation of particulate matter. Laparoscopic left nephrectomy for renal cell carcinoma (clear cell subtype, G1>G2, pT3a, V+) had been performed 64 months before the onset of respiratory symptoms, but a chest radiograph taken at the time of the surgery showed no abnormal findings. Preoperative forced vital capacity (FVC) was 4.17 l (108.3%) and forced expiratory volume in one second

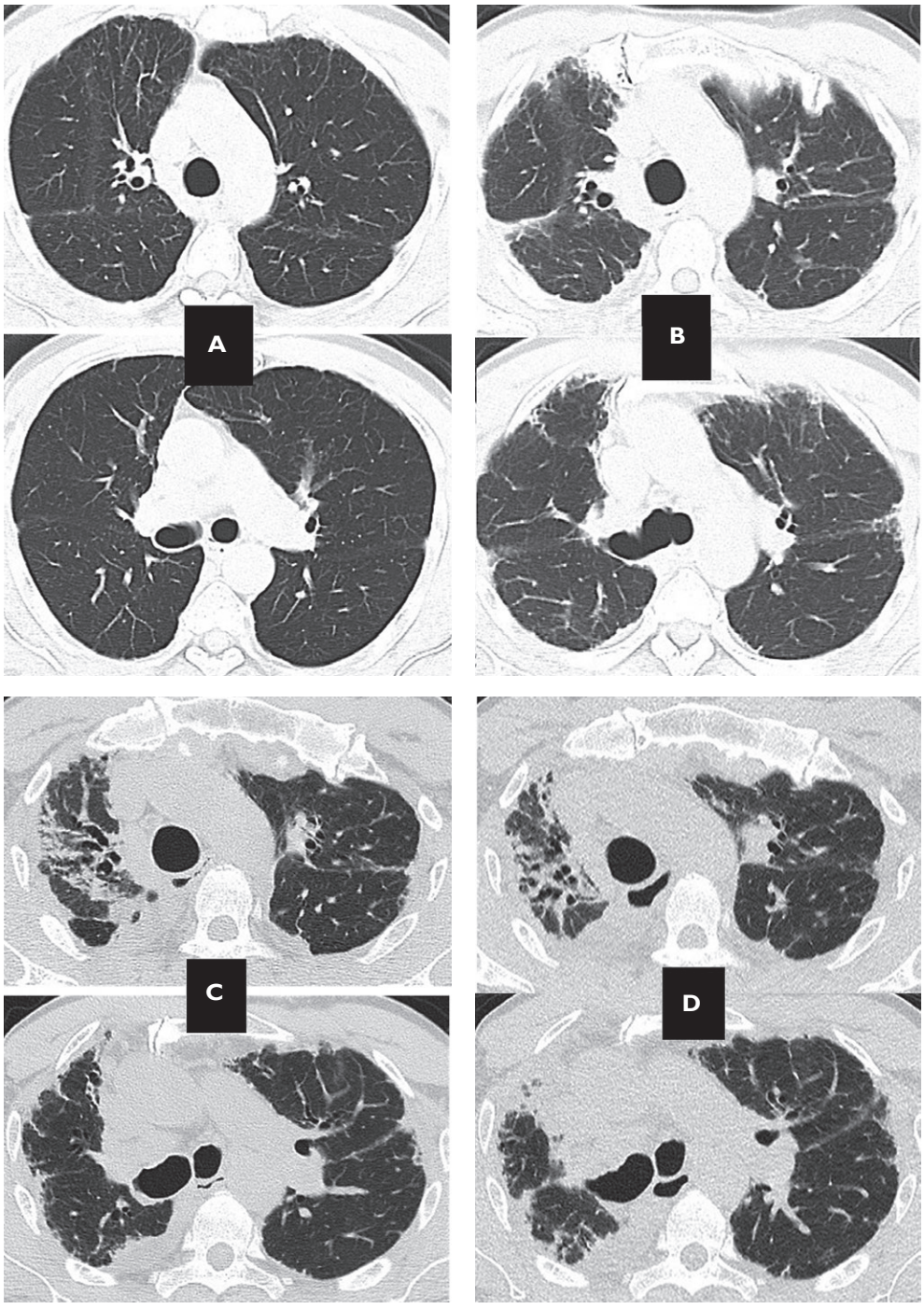


*Figure 2A: Changes in chest CTs (computed tomography) at the level of upper lobes and carina over time. Chest CT taken just before resection of renal cancer 64 months before onset (A); chest CT taken 6 months before onset (B); chest CT taken 9 months after onset (C); and chest CT taken 16 months after onset (D).*

($FEV_1$) 3.14 l (100.2%). There was no recurrence of the renal cancer thereafter, but approximately one year after the operation, the patient began to have dyspnea on exertion and dry cough. A chest radiograph taken around this time showed fibrosis predominantly in the upper lobes, with the lesion on the right side being prominent, and the shadow gradually intensified. Based on the radiological findings and clinical course, the patient was diagnosed with PPFE at another medical institution. When the patient was referred to our hospital 3 years after the onset of respiratory symptoms, he was thin, with a height of 163 cm, weight of 53 kg, and body mass index (BMI) of 19.9. Chest auscultation revealed no heart murmurs, but fine crackles were heard in both lung fields. At the time of his initial visit to our hospital, blood examination showed hemoglobin 14.6 g/dl, platelet count of 263,000/μl, albumin l 4.0 g/l, creatine 1.09 mg/dl, lactate dehydrogenase 184 U/l (124–222 U/l) and C-reactive protein (CRP) level of 0.10 mg/dl. Respiratory function test showed FVC 2.16 l (58.7%) and $FEV_1$ 1.98 l (64.3%), confirming a significant decrease in FVC. Two years after onset, the antifibrotic drug nintedanib was initiated, but

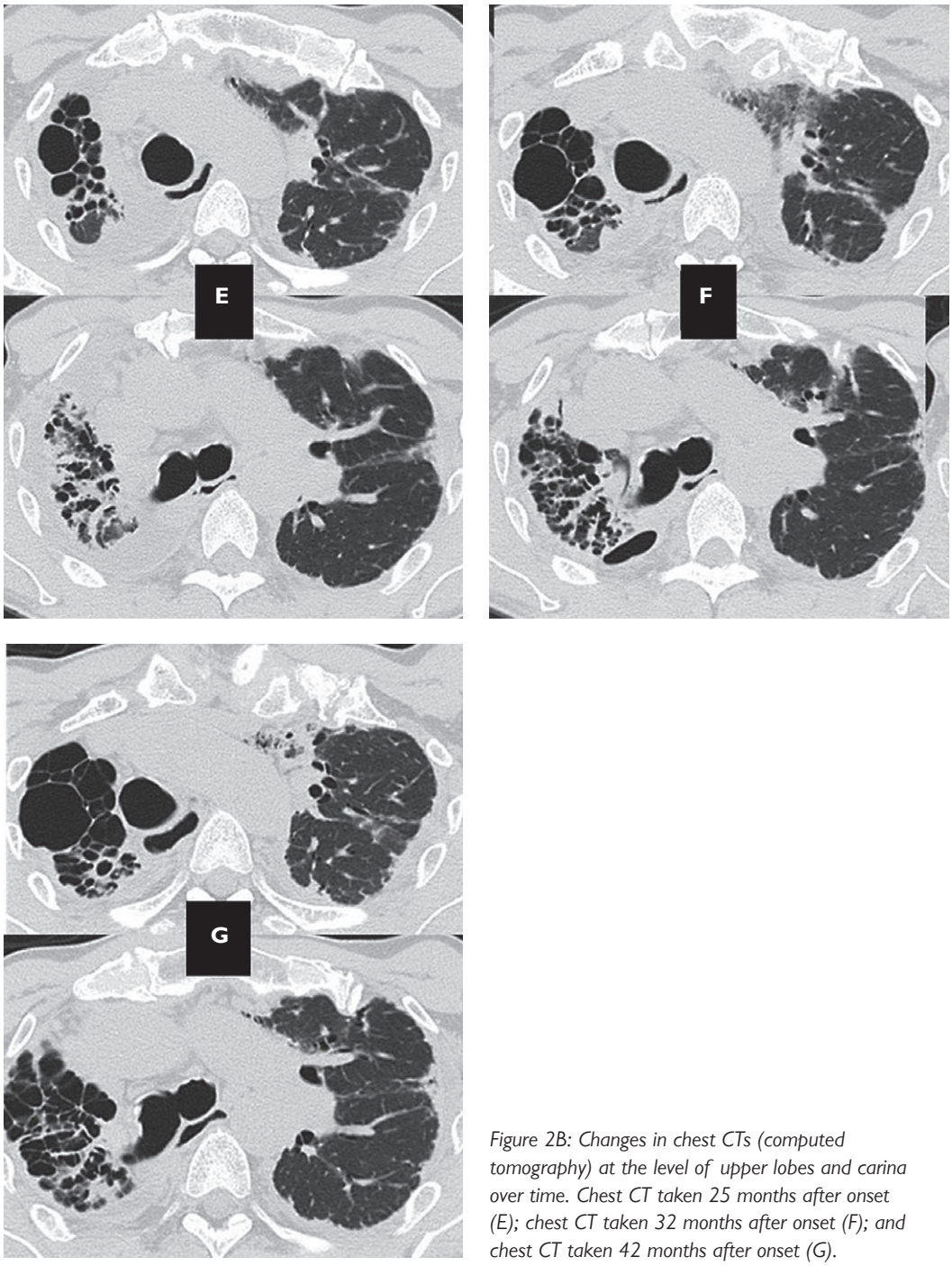


*Figure 2B: Changes in chest CTs (computed tomography) at the level of upper lobes and carina over time. Chest CT taken 25 months after onset (E); chest CT taken 32 months after onset (F); and chest CT taken 42 months after onset (G).*

Prague Medical Report / Vol. 126 (2025) No. 1, p. 30–35

three years after onset, hypoxemic respiratory failure progressed, and home oxygen therapy was initiated. At this time, the patient's body weight was 48 kg, and although there was no pretibial edema, there was a clear decrease in muscle mass of lower extremities. The time course of chest X-rays and computed tomography (CT) scans are shown in Figures 1 and 2. Two years later, the patient developed a right pneumothorax, but recovered conservatively. His hypoxemic respiratory failure then progressed further, and he passed away due to respiratory failure 43 months after the onset of PPFE.

## Discussion

PPFE was included as one of the rare interstitial pneumonias in the International Classification of idiopathic interstitial pneumonias proposed in 2013 (Travis et al., 2013). It is a chronic, progressive pulmonary fibrosis, and its clinical and pathological condition are similar to idiopathic pulmonary fibrosis, but its histological characteristic is the proliferation of elastic fibers under the pleura of the bilateral upper lung fields (Kinoshita et al., 2017). PPFE is also a disease concept that overlaps with limited upper lobe pulmonary fibrosis (Amitani disease) reported in 1992 by Amitani et al. Most patients with PPFE develop bilateral apical pleural thickening and upper lobe fibrosis. Usual interstitial pneumonia, the most common type of pulmonary fibrosis, is characterized by prominent lesions in both lower lobes, traction bronchiectasis, thickening of broncho-vascular bands and honeycombing. However, in PPFE, lower lobe involvement is absent or mild, and these characteristic findings of idiopathic pulmonary fibrosis are usually not observed (Nakamura et al., 2021; Cottin et al., 2022).

The first noteworthy point in this case was that fibrotic change was prominent in right lung. Regarding the uneven distribution of fibrotic change, reports have pointed out the similarity between patients with unilateral upper lung PF (pulmonary fibrosis) and PPFE patients with prominent fibrosis in one lung (Sekine et al., 2017; Inafuku et al., 2022). In our patient's case, a progression was observed on images over time, from a time point when no fibrotic changes were evident. The progression of the fibrotic change over time in this patient was very similar to that observed in those with unilateral upper-PF (Sekine et al., 2017; Inafuku et al., 2022). The imaging course of this patient supported the notion that some PPFE patients had similar degrees of fibrosis on both sides and others had more prominent fibrotic change on one side.

The second point to be worthy of attention in our case was his medical history of surgery for renal cancer 64 months before the onset of PPFE. In previous reports by Sekine et al. (2017), the majority of patients with unilateral upper-PF had a medical history of thoracic surgery (Inafuku et al., 2022). Patients undergoing thoracic surgery included not only lung cancer patients but also patients with benign diseases, and this suggested that there was no direct association between unilateral upper-PF and malignant disease (Sekine et al., 2017; Inafuku et al., 2022). Our patient had no history of thoracic surgery but had undergone truncal surgery. Although we found no reports suggesting an association between abdominal surgery and unilateral upper PF, this medical history in our patient was intriguing.

The third notable point of the clinical course of this PPFE patient was the poor prognosis. The prognosis of PPFE remains poor at present, with the median survival time from diagnosis reported to be 3–8 years (Enomoto et al., 2017, Sekine et al., 2017; Ishii et al., 2018; Oda et al., 2021). No specific clinical factors have been found to be associated with a good or poor prognosis in this disease entity. In general, many patients with chronic respiratory disease have a poor prognosis due to weight loss or malnutrition, and these factors are also attracting attention in relation to the prognosis of interstitial lung diseases (Kinoshita et al., 2023; Suzuki et al., 2023). In our patient, the BMI was 19.9 at the time of his first visit to our hospital, and three years later, his BMI had decreased to 18.1. In relation to prognosis, in this patient, antifibrotic drug was initiated during the course of PPFE. It is unclear whether the course of the disease might have been different if this drug treatment had been initiated at the same time as the diagnosis of PPFE. Some studies have shown that PPFE is less responsive to antifibrotic drugs and has a poor prognosis (Sugino et al., 2021; Kinoshita et al., 2022). On the other hand, there are studies that show that antifibrotic drug treatment may slow the decline of lung function (Nasser et al., 2021; Cottin et al., 2022). As they were all small retrospective studies, further evaluation is required to determine whether the effectiveness of antifibrotic drugs in PPFE and other progressive pulmonary fibrosis is equivalent.

## Conclusion

We reported the course of a patient with pleuroparenchymal fibroelastosis. This patient had prominent right-sided lesions, suggesting similarity to unilateral upper pulmonary fibrosis. This patient had no history of thoracic surgery, but had undergone renal cancer resection, which was suspected to be related to the development of unilateral upper PF.

The prognosis for PPFE remains poor, as was the case in this patient. It is strongly expected that knowledge regarding the pathology and treatment of this disease will be accumulated, and thus the prognosis would be improved.

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