

CHALLENGES IN THE CLASSIFICATION OF FIBROTIC ILD: PATIENT CASE 2

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PATIENT PRESENTATION AND DIAGNOSTIC WORK-UP

The patient is a 72-year-old man presenting with dyspnoea on exertion. He is a former heavy smoker (40 pack-years) and his father, now deceased, had rheumatoid arthritis (RA). On physical examination he had mild bi-basilar crackles but no finger clubbing. Autoimmune serology was positive for rheumatoid factor (RF: 25 IU/ml). Lung function tests showed normal FVC, a FEV₁/FVC ratio of 72% and a TL_{CO} of 49% predicted. Lung CT showed centrilobular and paraseptal emphysema, subpleural fine reticulation and traction bronchiolectasis, with no clear basal predominance (Figure 1). BAL cytology showed 83% alveolar macrophages, 12% lymphocytes, 3% neutrophils, and 2% eosinophils.

DIAGNOSTIC CONSIDERATIONS

Patient had a mildly elevated RF and a father with RA. In the general population, the likelihood of developing rheumatoid arthritis increases with increasing levels of RF, with the greatest incidence seen in people with RF levels above 100 IU/ml (1). In patients with ILD, the 2011 guideline states that there are no reliable data on the role of screening serology in patients with suspected IPF (2). A recently published cohort study involving 526 patients with IPF found that 13.2% tested positive for RF – a much higher proportion than in the general popu-

lation. Over a median follow-up of 33.6 months, RA was diagnosed in 5.2% of RF-positive and in 2.3% of RF-negative patients (3). The patient was assessed by a rheumatologist, who found no evidence of rheumatoid arthritis.

The CT was inconclusive and could have been interpreted as showing either emphysema in combination with 1) (fibrotic) NSIP, 2) fibrosis in underlying RA, 3) possible UIP pattern or 4) inconsistent with UIP pattern due to absence of clear basal predominance. A lung biopsy was not performed in view of the patient's age. In a study of 135 patients with fibrotic IIP and without honeycombing on CT, more than 95% of patients older than 65 years who had moderate reticulation were subsequently found to have UIP at biopsy (4). Limitations of this study are that patients with hypersensitivity pneumonitis were under-represented and also these findings have not been prospectively validated.

MANAGEMENT AND FOLLOW-UP

In the multidisciplinary team review, a diagnosis of unclassifiable fibrosis was made and trial of steroids was started to see if there was a response. This treatment had no effect on pulmonary function parameters and a deleterious effect on wellbeing with severe psychological side effects. The treatment was discontinued and the patient was managed with a "wait and see" strategy. He was stable for one year but then experienced a rapid decline within a few weeks, with his FVC falling from 102% to 83% and TL_{CO} falling from 48% to 25% predicted. Infection, pulmonary embolus and cardiac failure were exclud-

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ed. The CT scan showed progression of fibrosis with focal areas of increased ground glass opacity (Figure 2, panels a and b). The patient was considered to be having an acute exacerbation (AE) of his pulmonary fibrosis. In patients with IPF the 1-year incidence of AE is estimated 14%, but AEs have also been reported in combined pulmonary fibrosis and emphysema (CPFE) and CTD ILD (5-7).

Following management of the exacerbation, the patient was started on pirfenidone due to progressive

IPF-like disease behavior. His lung function stabilised and remained so for one year (Figure 3). Unfortunately, 42 months after his initial diagnosis, he developed a growing intra-pulmonary lesion, strongly suspect to be a malignancy, and signs of pulmonary hypertension (Figure 2, panel c). Together with the patient we decided not to pursue further diagnostic tests or treatment trials because of his deteriorating condition and lack of good treatment options. He died at home.

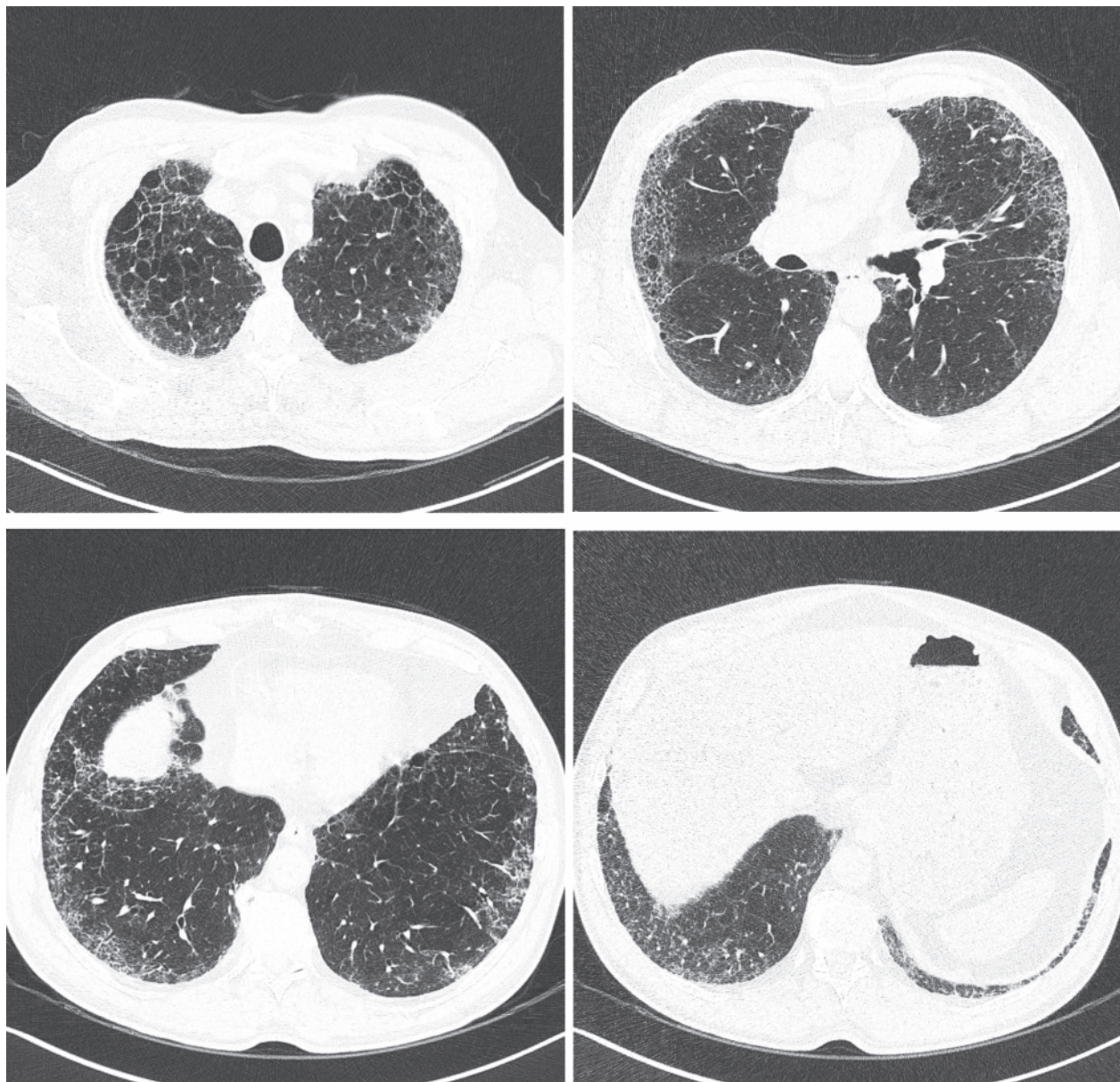
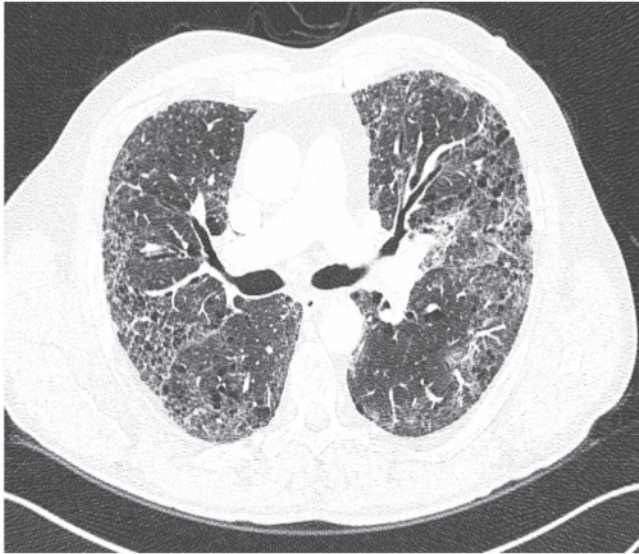
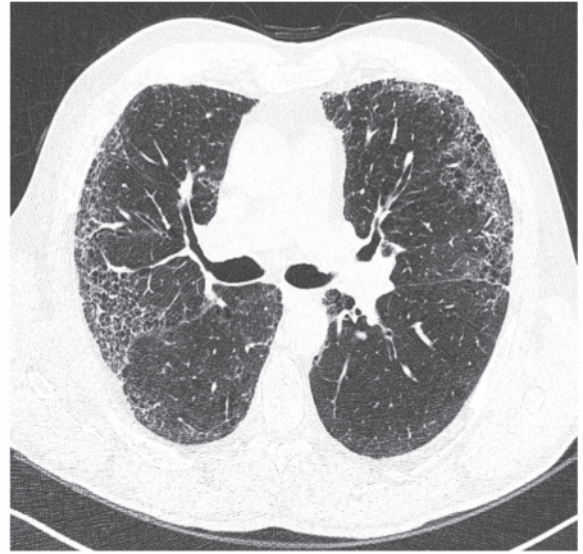


Fig. 1. Presenting HRCT showed centrilobular and paraseptal emphysema, subpleural fine reticulation and traction bronchiolectasis

Panel a



Panel b



Panel c

**Fig. 2.**

Panel a. Progression of fibrosis with focal areas of increased ground glass opacity suggesting acute exacerbation.

Panel b. Initial CT for comparison.

Panel c. A growing lesion developed in the left upper lobe, strongly suspected of being a malignancy.

CONCLUSION

Fibrotic disease is not always classifiable due to overlapping diagnostic boundaries with connective tissue disease – interstitial lung disease (CTD-ILD),

idiopathic pulmonary fibrosis (IPF) and coexisting pulmonary fibrosis and emphysema (CPFE). A pragmatic approach to treatment based on disease behaviour might be chosen.

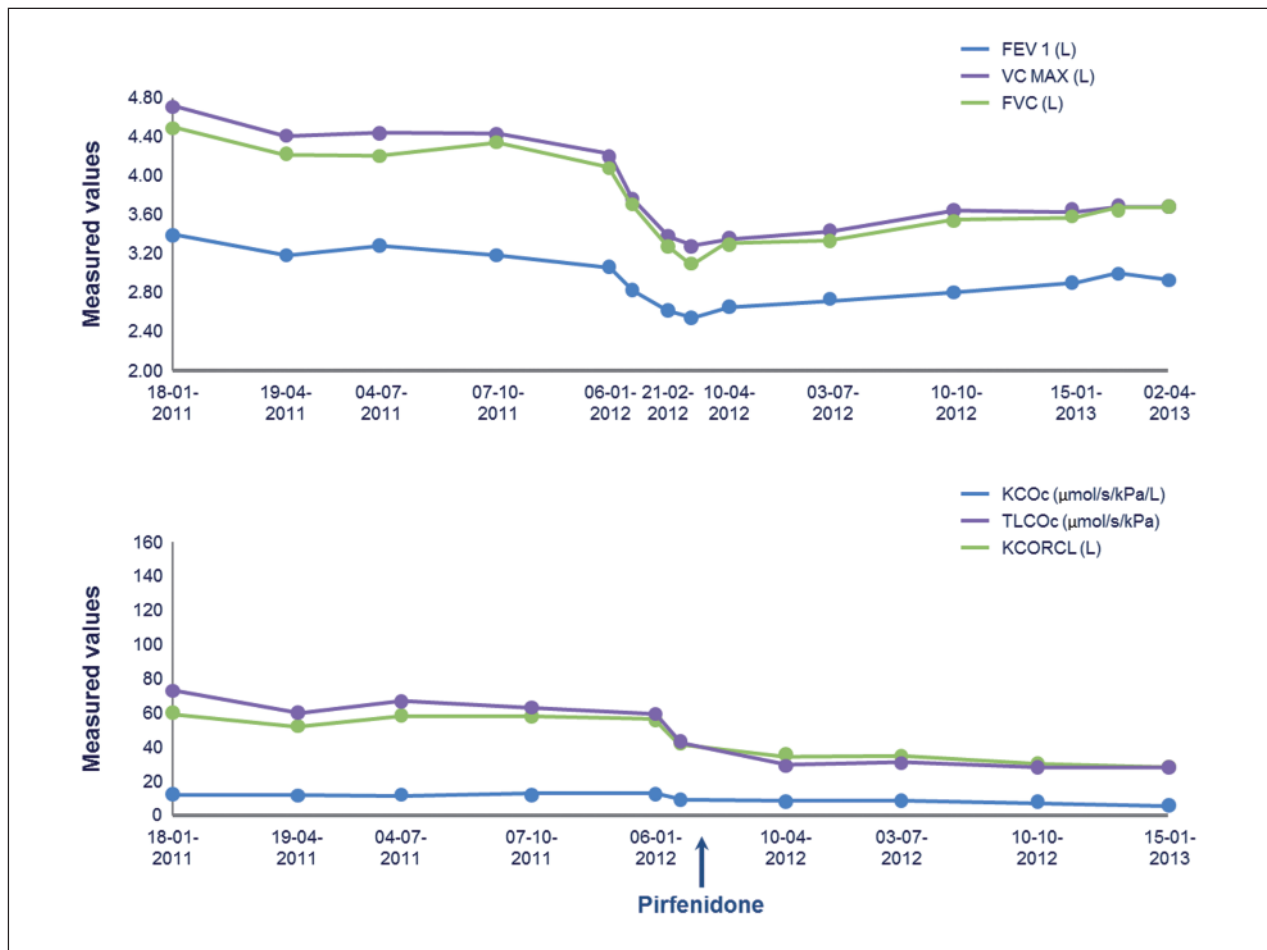


Fig. 3. Lung function parameters before and during pirfenidone treatment

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