

## A Case of Early Interstitial Abnormalities and Obstructive Sleep Apnea

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### Abstract

**Introduction:** Interstitial lung abnormalities (ILA) have been associated with early and mild forms of pulmonary fibrosis and is defined as a precursor stage of idiopathic pulmonary fibrosis (IPF).

ILAs are linked to with age environmental and genetic risk factors, and pulmonary symptoms of IPF. Identifying patients with IPF at the earliest opportunity remains one of the most urgent challenges in the effective management of this disease.

IPF is associated with obstructive sleep apnea (OSA) and several studies suggest that initiating treatment in the early stages of pulmonary fibrosis will slow the decline in pulmonary function and prevent early mortality. We describe a case report of a patient with ILA and OSA.

**Case Report:** CZ, a 71 year- old obese male and ex asphalterist, underwent a pulmonary examination on suspicion of OSA. The pneumological examination revealed digital hippocratism and fine Velcro-like crackles at the bases bilaterally. A computed tomography (CT) scan demonstrated the presence of ILA. He was subjected to cryobiopsy for diagnostic completion: the biopsy specimens were examined for evidence of usual interstitial pneumonia (UIP) pattern; thus, the definite diagnosis on establishment of a consensus by a multidisciplinary team was of IPF. The suspicion of OSA was confirmed by nocturnal cardiorespiratory monitoring: the patient had a severe positional OSA and we has treated with positional therapy, and antifibrotic drug.

**Conclusion:** This clinical case underscores the importance of the early identification of IPF that is obscured by the features of ILA. An earlier diagnosis of IPF is needed for timely treatment and, potentially, improves the long-term clinical outcomes of this progressive and ultimately fatal disease. All associated comorbidities in IPF must be recognized and treated early, such as OSA.

**Keywords:** *Interstitial Lung Abnormalities; Obstructive Sleep Apnea; Idiopathic Pulmonary Fibrosis*

### Introduction

The term interstitial lung abnormalities (ILAs) defines a precursor stage of idiopathic pulmonary fibrosis (IPF); these radiological changes aren seen in several interstitial lung diseases (ILDs) [1,2]. ILAs are more prevalent with increasing age and in smokers [1,3-5]. Arraki and colleagues demonstrates that the development and progression of ILAs were common in those aged over 50 years who bear promoter polymorphisms in the MUCB promoter and that these patients experience accelerated decline in lung function and increased mortality [6].

Idiopathic pulmonary fibrosis (IPF) is one of the most frequent and most severe forms of interstitial lung diseases [7,8]. It is characterized by a progressive heterogeneous course, with a median survival of 2.5 to 4.5 years and few treatment options. The diagnosis of IPF entails a combination of a clinical history, radiological imaging and examination of histopathological samples in appropriate cases.

Guidelines suggest that the diagnosis of IPF comprise a clinical history, radiological imaging, performing BAL to exclude an alternative diagnosis, and an examination of histopathological samples in appropriate cases. When it is present in the clinical history and high resolution computed tomography (HRCT scan) with definite pattern of UIP-ie, the fibrosis that has a subpleural and basal distribution with visible honeycomb cysts- a diagnosis of IPF is possible. If honeycomb cysts are not seen but the distribution is typical and other features of fibrosis are present, such as reticulation and traction bronchiectasis/bronchiolectasis, the pattern can only be described as "probable UIP". Less typical patterns would be described as "indeterminate" or not UIP ("alternative diagnosis") if features of an alternative ILD are seen. Guidelines recommend that histological sampling, by surgical biopsy, transbronchial lung biopsy, or cryobiopsy, should be considered in any case in which a definite UIP pattern is not seen on HRCT. A multidisciplinary discussion is also recommended [8].

IPF is characterized by the progressive worsening of lung function, significantly affecting health-related quality of life, and has been associated with many comorbidities such as pulmonary hypertension, emphysema, lung cancer, coronary artery disease, diastolic dysfunction, gastroesophageal reflux disease, sleep disorders - in particular obstructive sleep apnea (OSA) - endocrine disorders and psychiatric disturbances [9].

OSA is a form of sleep-disordered breathing that is characterized by the repetitive partial or total collapse of the upper airway during sleep, affecting nocturnal sleep quality and causing daytime fatigue and sleepiness [10]. Recurrent episodes of complete or partial airway obstruction are associated with intermittent arterial oxygen desaturation [11].

Identifying patients with IPF and all of its comorbidities at the earliest opportunity remains one of the most urgent challenges in the effective management of this deadly disease.

### Case Report

CZ, a 71 years old obese man, ex asphalterist (tobacco ex-smoker at 30 pack/yrs, no alcohol use) was admitted to our Sleep Surgery department for long-standing history of snoring.

His medical history revealed a 6-year history of arterial hypertension and a dyslipidemia syndrome, coronary artery disease. He was not aware of any respiratory disease in his family.

On clinical examination the findings were: a BMI (body mass index) of 30,5 kg/m<sup>2</sup>: neck circumference 43 cm and an enlarged abdomen with adipose tissue (abdominal circumference 111 cm) The Epworth sleepiness scale showed a high degree of sleepiness, with a score of 16 [12] and the 6-point STOP Bang questionnaire revealed a suspicion of OSA [13].

On evaluation the patient had digital hypocratism, his pulse pressure was normal, rapid and regular and his blood pressure was 150/80 mmHg, His HR was 80/min, RR was 12 a/min, and SpO<sub>2</sub> was 95% in room air The arterial blood gas analysis showed: pH 7.45 PaO<sub>2</sub> 78 mmHg, PaCO<sub>2</sub> 43 mmHg pH, SatO<sub>2</sub> 94% HCO<sub>3</sub> 25 mmoli/L). The physical examination showed inspiratory and basal crackles. The Muller maneuver was performed to reveal the tracheal collapse.

Pulmonary function tests (PFTs) showed a forced vital capacity (FVC) of 117 per cent of the predicted level, forced expiratory volume in one second (FEV1) of 100 per cent of the predicted level and a diffusion capacity of carbon monoxide (DLco) 82 per cent of the predicted level.

Chest X-ray showed normal lung parenchyma. The TCHR showed slight thickening of the interlobular septa in both the upper and lower lobes, with associated widespread thickening of the bronchial walls in relation to non-specific alterations of the bronchitis and peribronchitis type, initial reticular linear scar, subpleural lines (Figure 1).



Figure A

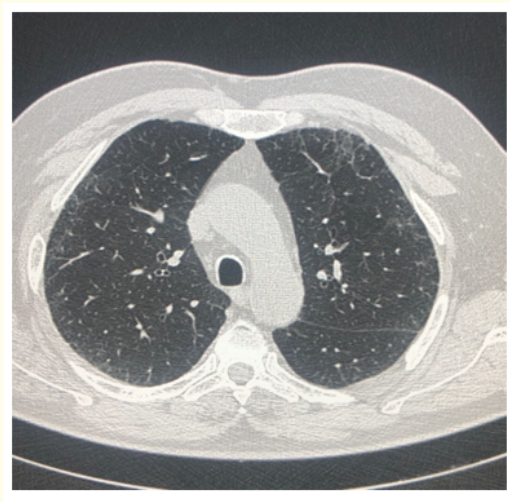


Figure B

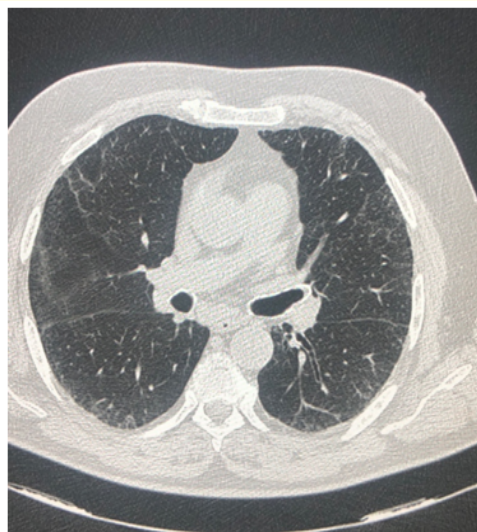


Figure C

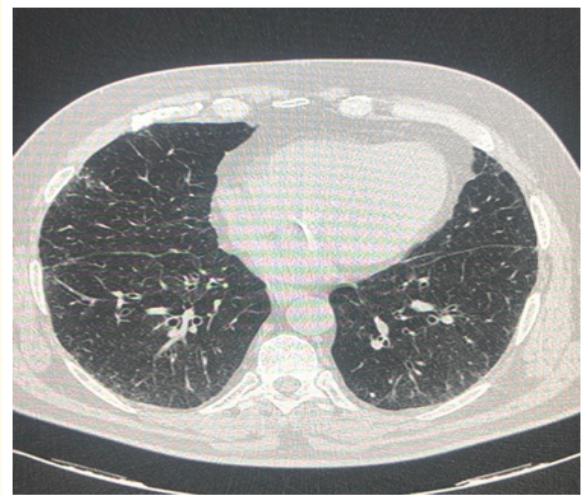


Figure D

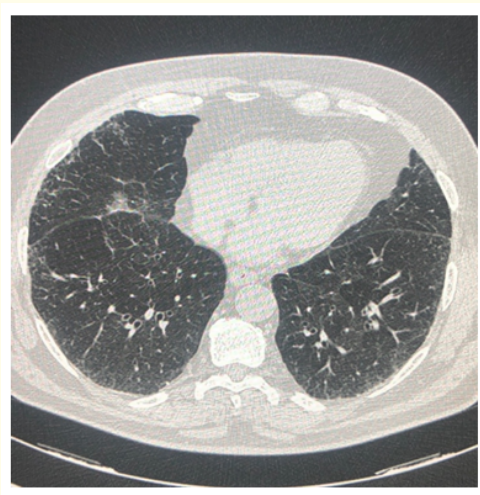


Figure E



Figure F

Figure 1: CT images.

These findings were consistent with ILA. At this time point, the patient was also screened for autoantibodies (including antinuclear antibodies and antineutrophil cytoplasmic antibodies) and HIV, all of which were negative.

Ecocardiography showed ejection fraction of 50%, moderate mitralic aortic insufficiency and moderate pulmonary hypertension.

The patient underwent bronchoscopy and BAL, again with, unremarkable findings. The case was discussed at a multidisciplinary team conference (MDC) and a decision to procede with cryobiopsy was made. The patient was sent to referral center for interstitial lung diseases.

Two biopsies, one each from the right lower lobes, showed a pattern of UIP. Thus MDC concluded that the case had IPF.

At the last examination, the patient underwent nocturnal cardiorespiratory monitoring in room air. Apneas, hypopneas, and apnea-hypopnea index (AHI) were defined according to current criteria. Other parameters that were analyzed were events of obstructive apneas (OA) and central apnea (CA), number and events of hypopnea (H) and average of arterial saturation (SpO<sub>2</sub> average%) with time of desaturation (T < 90%).

The examination revealed severe positional OSA (AHI 52.8/h) (Table 1). The patient received positional therapy (neck-worn vibrating device) and antifibrotic drugs [14].

	Diagnostic
Supine AHI (Events/h)	52.9
Prone AHI (Events/h)	0.0
Right AHI (Events/h)	3.3
Left AHI (Events/h)	2.5
AHI (Events/h)	11.2
OA - N° events	53
CA N° events	5
H N° events	11
SpO <sub>2</sub> average (%)	94
T < 90%	2.9

**Table 1:** Diagnostic nocturnal cardio-respiratory monitoring results.

## Discussion

ILAs are often incidental finding, affecting > 5% of lungs on CT scans. These abnormalities, as part of the spectrum of ILAs, colud be centrilobular nodules, ground-glass or reticular abnormalities, non-emphysematous cysts, traction bronchiectasis, and honeycombing. The most common localizations are: (1) predominant centrilobular ground-glass opacities; (2) predominantly subpleural abnormalities; (3) mixed centrilobular and subpleural abnormalities; and (4) imaging findings providing firm evidence of interstitial lung disease [15].

In the past several years, there has been increasing awareness of ILA features on CT scans by clinicians.

Several studies have described a clear association between ILAs and an increased risk of neoplastic alterations, histologic fibrosis, accelerate declines in pulmonary function and all-cause mortality [6,16,17]. The conclusion of Whittaker Brown., *et al.* supports that recognition of ILAs is clinically useful because it can allow timely diagnosis of IPF and lung cancer [18].

In our case report these initial radiographic abnormalities were the early manifestation of IPF: the correct diagnosis allowed us to start the treatment early. This case report also highlights the importance of investigating all comorbidities that are associated with IPF, as reported [8,9,19].



ILA is more common than IPF. The ILA subgroup must be determined in the development in IPF, particularly because identifying the earliest stage of IPF could have clinical implications with regard to the efficacy of treatment, as reported [20,21].

### Conclusion

This clinical case underscores the importance of identifying IPF and comorbidities in the optimal management. An earlier diagnosis needed for timely treatment and can improve the long-term clinical outcomes of this progressive and ultimately fatal disease.

### Conflict of Interests

All authors declare that they have no competing interests.

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