



# Interstitial lung disease pattern turned out to be a predominantly lepidic lung adenocarcinoma



Irena Hammen, Dr. Med

Sdr Boulevard 17, 5000 Odense, Denmark

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## ABSTRACT

We report a case of a 46-year-old woman without any medical history who presented to our Respiratory Department with exertional dyspnoea for the last 6 weeks associated with non-productive cough. Chest radiography showed bilateral diffuse interstitial opacity. Bronchoalveolar lavage and transbronchial biopsies performed during flexible bronchoscopy as a step in the diagnostic workup of idiopathic interstitial pneumonia showed cells of pulmonary adenocarcinoma.

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## 1. Background

Diffuse interstitial lung opacities is a presentation of a heterogeneous group of diseases with the similar pathogenic mechanism: affection of the interstitial alveolar structures. The etiology and differential diagnosis are extremely broad, including f.e. heart failure, atypical pneumonia, diffuse pulmonary haemorrhage, military tuberculosis, lymphangitis carcinomatosa and a big group of interstitial lung diseases, like f.e. idiopathic interstitial pneumonias, granulomatous diseases, pulmonary manifestation of collagen and vascular diseases [1,2]. That presents several diagnostic challenges and requires wide diagnostic approach.

## 2. Case presentation

A 46-year-old woman, presented with a 6 weeks history of exertional dyspnoea and non-productive cough. She denied fever and weight loss and had no medical history. Family medical history was unremarkable as well. She was a recent ex-smoker with 10 pack-year history. Physical examination didn't reveal any abnormalities.

## 3. Investigations

Chest X-ray at the first visit showed bilateral reticular opacity (Fig. 1). Admission blood results including cell count, liver function tests serum electrolyte panel and C reactive protein were

within normal limits. Because the patient's radiological, clinical and laboratory findings were compatible with diffuse interstitial lung disease (DILD), further diagnostic work-up was set in this direction.

A full autoimmune screen, including antinuclear, antineutrophil cytoplasmic and double-stranded antibodies, was carried out and found to be negative as well as immunoglobulin levels. Only lactate dehydrogenase 251 U/L (105–205 U/L) was slightly elevated. Body plethysmography showed decreased diffusing capacity (DLCO) of 57.8% but normal lung volumes. High-resolution computed tomography revealed ground-glass opacities and interlobular septal thickening (Fig. 2). As the next step bronchoscopy was performed. Bronchoalveolar lavage fluids as well as transbronchial lung biopsy revealed adenocarcinoma with lepidic growth pattern, positive for thyroid transcription factor-1 (TTF-1) expression and negative for anaplastic lymphoma kinase (ALK) and epidermal growth factor receptor (EGFR) mutations.

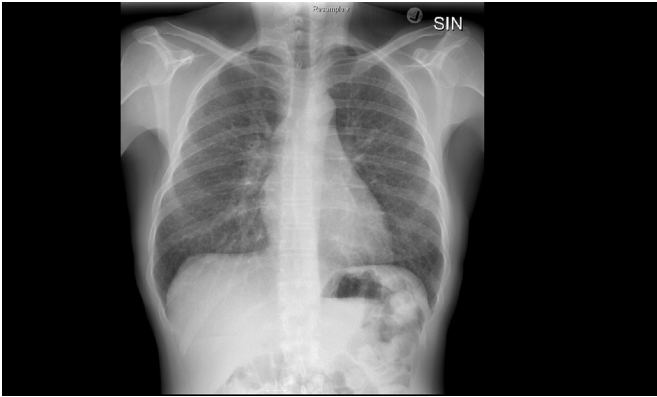
After diagnosing lung cancer we proceeded with Fluorodeoxyglucose positron emission tomography scan (18F FDG PET/CT), which revealed increased uptake of fluorodeoxyglucose in the bilateral interstitial infiltrations with SUV max 2.7 (Fig. 3).

Because of the bilateral pulmonary involvement staging of lung cancer was defined as T4N0M1a.

## 4. Differential diagnosis

Diffuse interstitial lung disease (DILD) has numerous differential diagnoses: idiopathic interstitial pneumonias, occupational/environmental disorders, granulomatous diseases, connective tissue

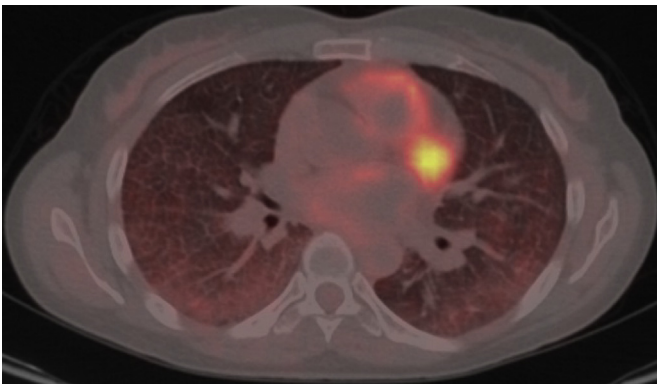
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**Fig. 1.** Chest X-ray at the first visit showing bilateral reticular opacity.



**Fig. 2.** High-resolution computed tomography revealing ground-glass opacities and interlobular septal thickening.



**Fig. 3.** 18F FDG PET/CT showing high uptake of fluorodeoxyglucose in the bilateral interstitial infiltrations.

and vasculitis-related diseases, pulmonary alveolar proteinosis, infection (miliary tuberculosis, atypical pneumonia), drug- and physical agents related disorders, malignancies, heart failure, diffuse pulmonary haemorrhage.

## 5. Treatment

The patient was referred to oncology and palliative systemic therapy in form of immunotherapy with cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) Tremelimumab was initiated.

## 6. Outcome and follow-up

Evaluation with Chest CT Scan taken 6 month after therapy start revealed a stable disease.

## 7. Discussion

6 weeks history of exertional dyspnoea and non-productive cough in a relatively young patient without any medical history is a non-specific presentation of lung involvement. Bilateral reticular opacity pattern on the chest X-ray led to the diagnostic considerations regarding interstitial lung disorders. The possibility of infectious etiology was unlikely (absence of fever and normal leukocyte count, as well as CRP-level). In addition, there were no involvement of other organs, like we could expect in case of f.e. collagen, vasculitis and granulomatous diseases. The patient neither had the history of dust exposure nor drugs intake, which ruled out pneumoconiosis, allergic alveolitis and drug-induced interstitial lung disease. Bronchoalveolar lavage didn't present any typical features of pulmonary alveolar proteinosis, like milky appearance or positive periodic acid-Schiff staining.

Malignancy is one of the important differential diagnoses in case of diffuse interstitial opacities. Pulmonary lymphangitic carcinomatosis presents spread of tumour cells to the lymphatic system of the lungs. It is known as metastatic infiltration in many neoplastic diseases, like colon, pancreas, lung, breast, renal cancer [3–5].

Lung adenocarcinoma, the most common subtype of lung cancer, includes heterogeneous group of malignancies with different pathological and radiological presentations. In most of the cases mixed growth patterns can be found. Studies have shown that predominant growth pattern (solid, acinar, papillary or lepidic) differs in radiological presentation as well as treatment outcome and prognosis [6,7]. For example, solid pattern is associated with higher 18F FDG uptake and poorer prognosis [6].

Predominantly lepidic adenocarcinoma (LPA) is defined with invasion into vessels, pleura or lymphatics [8]. That can lead to the radiological presentation in form of diffuse interstitial opacities [9]. LPA shows in ca 80% of the cases lower 18-F-FDG uptake as tumors with solid growth pattern with maximum standardized uptake value (SUV max) < 2.0 [7].

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