

Idiopathic Pulmonary Fibrosis: a case report

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ABSTRACT

Introduction: Idiopathic pulmonary fibrosis (IPF) is a specific form of fibrosing interstitial lung disease (ILD) primarily occurring in older adults and limited to the lungs. Histopathologic and radiologic findings are not pathognomonic, and the diagnosis can be quite challenging even after careful clinical evaluation, imaging, and pathological tests. An often-implemented multidisciplinary discussion takes place, a process that increases the accuracy of the diagnosis and impacts management. There is, unfortunately, no established optimal therapeutic approach.

Case Presentation: A 58-year-old female presented to the emergency room because of dyspnea and shortness of breath that progressively worsened over the past two weeks. Her history included chronic bronchitis and left breast cancer status-post mastectomy five years prior. Chest X-ray revealed diffuse bilateral hazy opacities, and, after multiple failed attempts of treating her symptoms, was admitted to ICU for further treatment and investigation. High-resolution computed tomography (HRCT) showed features of reticular abnormality, indicating a “possible usual interstitial pneumonia” (UIP). Biopsy of the affected lung showed diffuse moderate fibrotic changes in a honeycombing appearance suggesting underlying point fibrosis. Bronchial lavage found no malignant cells, ordered to rule out lymphangitic pulmonary metastases secondary to breast cancer. A multidisciplinary, dynamic discussion was necessary to narrow down and rule out other etiologies and lead to the diagnosis of interstitial pulmonary fibrosis (IPF).

Discussion: The identification of idiopathic pulmonary fibrosis (IPF) requires a multi-step diagnostic approach, involving a combination of histopathological and radiologic patterns of usual interstitial pneumonia (UIP), and a multidisciplinary discussion needed to diagnose a ‘definite IPF.’ Our patient with ‘possible IPF’ prompted additional steps to rule out all possibilities of other differential diagnoses.

Conclusion: The guideline recommendations in the diagnosis of idiopathic pulmonary fibrosis are a significant improvement and have helped assist clinicians to navigate under a disciplined approach to what was once a previously undisciplined field. This case focuses on the value of making an accurate diagnosis of IPF, ruling out other possible etiologies of interstitial lung diseases. This is a true clinical concern as prognoses of other diagnoses show more promise in terms of therapeutic approach compared to IPF in which prognosis is often grim.

Keywords: interstitial pulmonary fibrosis (IPF), usual interstitial pneumonia (UIP), bronchoalveolar lavage (BAL), interstitial lung disease (ILD), surgical lung biopsy (SLB), multidisciplinary, definite IPF, probable IPF

Idiopathic Pulmonary Fibrosis: a case report

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a common form of interstitial lung disease (ILD). The lung interstitium, the supportive connective tissue in the lung's parenchyma, is found between the alveolar epithelium and the pulmonary capillary endothelium. Patients with interstitial lung diseases have compromised lung parenchyma, impairing gas exchange, and places these patients under the functional category of restrictive lung disease.

The diagnosis of IPF has a multi-step approach, including the exclusion of other known causes of ILD (e.g. domestic and occupational environmental exposures, connective tissue disease, and drug toxicity), the presence of a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) in patients not subjected to surgical lung biopsy, and specific combinations of HRCT and surgical lung biopsy pattern in patients subject to surgical lung biopsy [Raghu et. al]

We want to present a case of an older woman with a past medical history of chronic bronchitis and left breast cancer (status post-mastectomy) who presented to the Emergency Room (ER) complaining of dyspnea and shortness of breath. As we work up our patient for suspected IPF, we found ourselves taking additional steps to rule out other possible etiologies of our patient's case presentation.

CASE PRESENTATION

A 58-year-old Caucasian female with a medical history of diabetes mellitus and hypertension developed progressive shortness of breath and dyspnea over two weeks. She denied any fever, chest pain, or sputum production at the time. She had recently returned from a trip to Florida, where she noticed her symptoms getting worse. With these concerns, she went to visit her primary care physician (PCP) at the clinic. Her pulse oximetry readings showed an oxygen saturation around 50% and her PCP immediately sent her to the emergency room.

In the ER, levels of oxygen saturation remained low (~50%) with signs of cyanosis around the mouth and the use of accessory muscles. She was treated with supplemental oxygen and nebulizer treatment, which began to improve her symptoms. A chest X-ray was ordered revealing diffuse bilateral hazy opacities, with a questionable left perihilar mass. After multiple attempts of treating her symptoms, and with concerning arterial blood gases revealing pO₂ = 60.4 mmHg and her O₂ saturation remaining around 87%, she was admitted to ICU to continue treatment where they prescribed her with azithromycin (500 mg).

In the ICU, she mentioned working as a Home Depot cashier, with a history of smoking (20 pack-year), hypothyroidism, hyperlipidemia, chronic bronchitis, and left breast cancer. Following a left mastectomy five years ago, she revealed that she refused radiation/chemotherapy and had not been following up with her oncologist. She also provided us with her medication list (Table 1), none of which were of concern to associate with her current symptoms.

A high-resolution computed tomography (HRCT) of our patient's lungs produced images showing diffuse moderate fibrotic changes and honeycombing patterns, suggesting underlying point fibrosis. This brought attention to the pulmonologist and a suspected diagnosis of underlying pulmonary fibrosis.

The pulmonologist initially diagnosed the patient with acute respiratory failure with hypoxia, starting the patient on bronchodilators. The chest X-ray with the questionable left perihilar mass also prompted obtaining serum angiotensin converting enzyme (ACE) levels. However, as the results of the serum ACE levels came back normal, and with the failure of the pulmonary infiltrates to resolve, bronchoscopy with biopsy was recommended.

After consultation with the surgeon, a pre-operative diagnosis was made between idiopathic pulmonary fibrosis versus lymphangitic pulmonary metastases secondary to breast cancer. Clearing her pre-operative evaluation, the patient underwent bronchoscopy with transbronchial biopsy and bronchoalveolar lavage with fluoroscopic guidance. The procedure involved surgical lung biopsies (SLB) as well as bronchoalveolar lavage (BAL), in which samples were sent to the laboratory and studied. Biopsy showed evidence of marked fibrosis as well as a honeycombing pattern. The BAL showed the presence of macrophages, bronchial epithelial cells, and mixed inflammatory cells. The pathologist also noted that no malignant cells were identified, ruling out the pre-operative diagnosis of pulmonary disease via breast cancer.

After an extensive workup involving clinical evaluation, imaging, and pathological tests, it was suspected the patient had IPF. As a diagnosis of exclusion, a multidisciplinary discussion was the final step. This involved the collaborative expertise of the Surgeon, Pulmonologist, Pathologist, and Radiologist, and was essential to accurately diagnose the patient with idiopathic pulmonary fibrosis (IPF).

Table 1. List of Medication

List of Medication	Alprazolam, Lovenox, Novolog, Proventil, Rocephin, Atorvastatin, Enalapril, Glucagon, Ibuprofen, Levothyroxine, Nicotine
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Table 2. Timeline of Case

Date (mo/d/y)	Status	Tests/Results	Treatment/misc.
3/13/17 Emergency Room	Patient arrives at ER for dyspnea, SOB	Pulse oximetry – 50% EKG – no abnormalities CXR – diffuse bilateral hazy opacities (possible atypical pneumonia); questionable left perihilar mass	Supplemental oxygen, nebulizer treatment without resolution Admitted to ICU for the failure of treatment in ER
3/13/17 ICU	CTA chest w/ contrast – main pulmonary artery dilated at 3.5 cm, no acute/chronic filling defects, thoracic aorta normal without dissection or aneurysm, normal cardiac size without pericardial effusion, multiple mediastinal/bilateral hilar lymph nodes (1.8 cm), extensive interstitial changes with associated areas of bronchiectasis	pO2 – 60.4 mmHg O2 sat – 87% D dimer – 642 ng/mL Glucose – 284 mg/dL Neutrophil – 79.1 %	Azithromycin (500 mg) added to regimen
3/14/17	HRCT – diffuse moderate fibrotic changes, honeycombing suggesting underlying point fibrosis	CXR – diffuse reticular infiltrates predominantly on right side Serum ACE level – normal	Plan - bronchodilators - if pulmonary infiltrates fail to resolve, bronchoscopy with biopsy will be needed
3/16/17	Bronchoscopy with transbronchial biopsy and bronchial lavage with fluoroscopic guidance	Non Gyn Cytology Report – Bronchial lavage, right middle lobe; no malignant cells identified , evidence of macrophages, bronchial epithelial cells, mixed inflammatory cells	Pulmonary Report – Biopsy shows evidence of marked fibrosis, honeycombing pattern Surgeon Report – RUL, RML, and RLL with BAL. RUL – anterior segment biopsy, RUL – apical segment biopsy, RLL – lateral segment biopsy. Fragments of bronchial mucosa/ lung parenchyma
3/17/17	Fluoroscopy with CXR post bronchoscopy – no evidence of pneumothorax, relatively extensive infiltrate densities bilaterally		

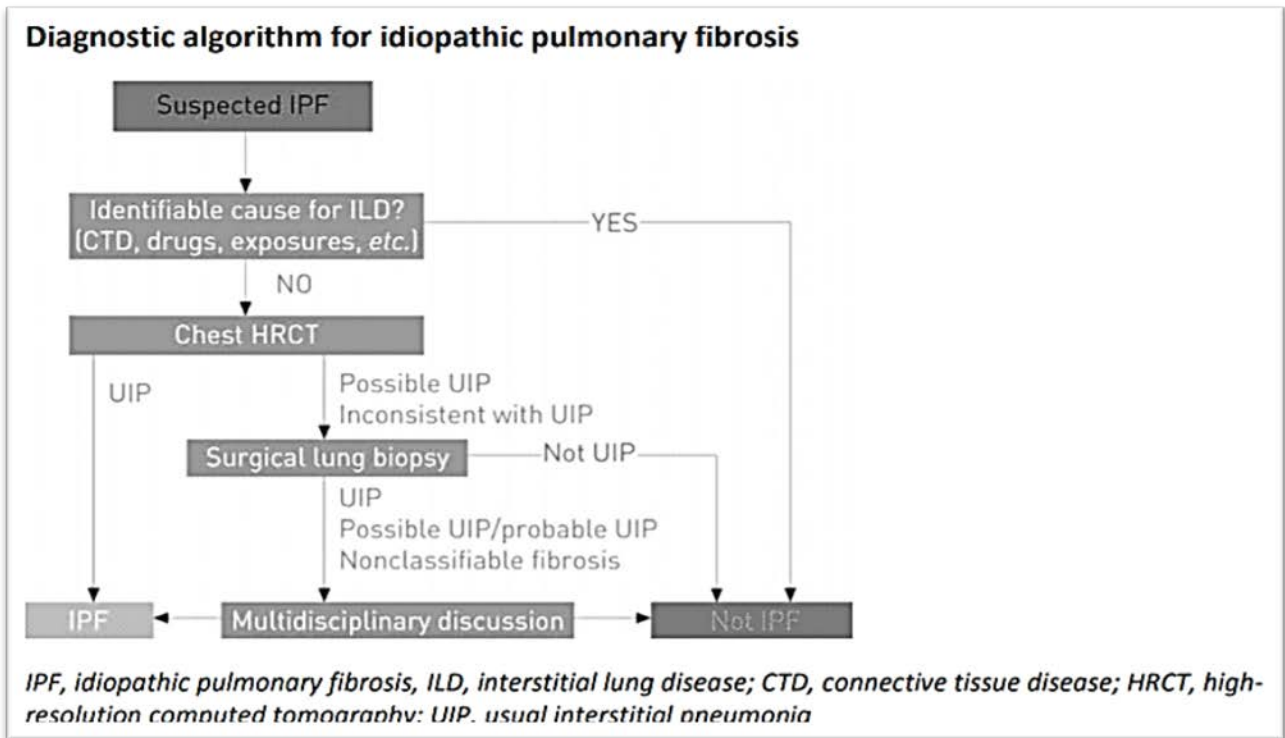
DISCUSSION

The initial radiologic evaluation of our dyspneic patient via chest X-ray is often a diagnostic challenge, as an extensive list of pulmonary, cardiac, muscular, hematological, or neuropsychiatric cases can present with dyspnea and shortness of breath [1]. It is difficult to be considered a primary imaging modality for evaluating patients with IPF, as approximately 10% of patients with histologically proven IPF have a normal chest X-ray [2].

A chest CT angiography with contrast was ordered for our patient (Table 2) to help narrow down our differential diagnoses. IPF is a progressive disorder, with almost half of the patients developing pulmonary arterial hypertension [3]. CTA imaging showed signs of main pulmonary dilation (3.5 cm) and extensive interstitial changes, with signs of diffuse moderate fibrotic changes in a nonspecific configuration. At this point, we recognized that our case most likely involved a patient with IPF.

Cases of suspected IPF require ruling out other etiologies of interstitial lung disease. Therefore, establishing an accurate diagnosis of IPF is often a challenging process. Not only does it involve extensive clinical evaluation, imaging, and pathological tests, but it also requires the exclusion of other known causes of ILD.

The following algorithm provided by *Raghu G. et al.* represents the diagnostic criteria for IPF.



Raghu G. et al., Am J Respir Crit Care Med, 183. pp 788–824, 2011

Identifiable cause of ILD?

As we suspected IPF with the patient in our case presentation, it was essential to rule out any other identifiable causes of ILD. Causes of consideration involve connective tissue diseases, drug toxicities, and environmental exposures. Given her list of medications (Table 1), there were not any offending agents identified with increased association with ILD. It was also noted that her long-time occupation as a cashier for Home Depot limited any serious harmful environmental exposure - leading to possible pulmonary disease.

The significance of circulating autoantibodies in patients with IPF has been of clinical and scientific interest for many years. Published guidelines suggest patients with suspected IPF be screened with rheumatic factor (RF), anti-cyclic citrullinated peptide (CCP), and anti-nuclear antibody (ANA) testing. The primary concern is that occasionally 'IPF autoantibody-positive patients' do not have IPF, but some unrecognized and occult connective tissue disease (CTD) [4].

Our patient, although revealing no history of chronic autoimmune disease or CTD, was not tested for any circulating autoantibodies. This decision may have resulted from a lack of awareness of recent guideline autoimmune screening. Although unusual, this did not hinder progression in working up our patient. One differential diagnosis of interest was sarcoidosis as the chest x-ray image showed a questionable left perihilar mass, prompting us to obtain serum ACE levels. The absence of abnormal serum ACE levels supported ruling out the differential and, with that, ruling out identifiable causes of ILD.

Chest HRCT

In recently updated guidelines, high-resolution computed tomography (HRCT) scanning now has a central role in the IPF diagnostic pathway with formal designation of criteria for an HRCT pattern of UIP. [1] Our case presentation shows our patient's HRCT scan revealing a honeycombing pattern, and diffuse reticular infiltrates predominantly on the right side. Following the criteria for UIP, these results place our patient under 'possible UIP pattern' (*Raghu et al.*).

In some patients, surgical lung biopsy (SLB) is unnecessary as the diagnosis of IPF is secure, based on typical clinical and HRCT features [1]. Our patient does not show a 'definite UIP pattern,' and following the guidelines suggested additional testing.

Surgical Lung Biopsy (plus bronchial lavage)

The prognosis of IPF is overall poor, with a 5-year survival worse than several cancer types [5]. Although the incidence is higher, other interstitial lung diseases, such as idiopathic interstitial pneumonia, require different therapies and better prognoses. The pathological confirmation of IPF rules out other possible conditions with better therapeutic options and prognoses. This shows the value of biopsy affecting therapeutic management. [5]. The histopathological criteria for our patient's biopsy revealed a 'possible UIP pattern.' The combination of our patient's HRCT and surgical lung biopsy would categorize her under 'Probable IPF' and with a multidisciplinary discussion, appropriately diagnose her with IPF.

However, our patient's case presentation momentarily imposed on a 'definite IPF' and required further testing.

Our patient underwent bronchoscopy with transbronchial biopsy and bronchial lavage (BAL) via fluoroscopic guidance. Studies show additional testing of BAL in the diagnosis of IPF is controversial. The most critical application of BAL is to increase the index of suspicion for alternative disorders [1].

In the British Thoracic Society (BTS) guidelines, the diagnostic use of BAL was reserved for patients in whom the diagnosis is uncertain after clinical assessment and HRCT scanning [1]. Demonstrating the clinical importance of history taking, obtaining information about her breast cancer, and the refusal of radiation/ chemotherapy, revealed another differential diagnosis imperative to rule out: lymphangitic pulmonary metastases secondary to breast cancer. Our patient underwent additional testing of bronchial lavage (BAL) with the results of this test, revealing no evidence of malignant cells.

Multidisciplinary team decision

After a thorough work-up, including ruling out other possible etiologies of ILD (sarcoidosis, breast cancer metastases), as well as HRCT and pathological features showing a 'UIP pattern,' the diagnostic pathway for identifying IPF must undergo a multidisciplinary approach. With several fields of expertise involved, including pathologists, pulmonologists, radiologists, and surgeons, combined with histopathological and radiologic patterns associated with UIP, the confirmed diagnosis of IPF was determined.

CONCLUSION

The guideline recommendations in the diagnosis of idiopathic pulmonary fibrosis are a major improvement and have helped assist clinicians in navigating under a disciplined system to what was once a previously undisciplined field. This case focuses on the value of making an accurate diagnosis of IPF. This is an important concept, keeping in mind considering the many possible etiologies of interstitial lung diseases. The guidelines, therefore, offer a systematic,

efficient approach as IPF is a true clinical concern knowing prognoses of other diagnoses show more promise in terms of therapeutic approach in contrast to IPF. We hope this case presentation provides insightful information that will offer new or strengthen existing data.

RESOURCES

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