Pulmonary Fibrosis Case Studies

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Mr. H.
- 62 year old man
- Dry cough
- Slowly progressive dyspnea on exertion
- Exercise limitation
- Dry inspiratory crackles
- Clubbing

Questions
- What do I do with this patient?
  - Diagnosis
  - Prognosis
  - Management
    - Pharmacologic therapy
    - Non-pharmacologic therapy
    - Transplantation

Normal Lung

Mechanisms of fibrosis
- Inflammation
- MMP/TIMP
- TGFβ

Pulmonary Fibrosis
Clinical Classification

Pulmonary Fibrosis

Exposure-related:
- Occupational
- Environmental
- Avocational
- Medication

Idiopathic interstitial pneumonia (IP)

Connective tissue disease:
- Scleroderma
- Rheumatoid arthritis
- Sjogrens
- UCTD

Other:
- Sarcoidosis
- Vasculitis/Diffuse alveolar hemorrhage (DAH)
- Langerhans cell histiocytosis (LCH)
- Lymphangioleiomyomatosis (LAM)
- Pulmonary alveolar proteinosis (PAP)
- Eosinophilic pneumonias
- Neurofibromatosis
- Inherited disorders
- Chronic aspiration
- Inflammatory bowel disease

Don't stop with “pulmonary fibrosis”

- Reasons for a specific diagnosis:
  - Many forms are treatable
  - Treatments depend on diagnosis
  - Prognosis varies
  - Clinical trial eligibility requirements

Diagnostic Algorithm

Suspected PF

Detailed history + PFTs/Labs + HRCT

Smoking history
Occ/Env history
Autoimmune ROS
Family history

Spirometry
Lung volumes/DLCO
ANA, RF

High-resolution CT (HRCT)

- 1-1.5 mm collimation
- Images taken every 10 mm
- Supine, prone and expiratory images

Case 1

Diagnostic Algorithm

Suspected PF

Detailed history + PFTs/Labs + HRCT

Smoking history
Occ/Env history
Autoimmune ROS
Family history

Spirometry
Lung volumes/DLCO
ANA, RF

Non-diagnostic

Lung biopsy

Diagnostic

1. IPF
2. Sarcoidosis
3. CV-ILD
4. Hypersensitivity pneumonitis
5. Rare disease (LAM, PAP)
Case 1

- 60 year old man
- Shortness of breath for one year
- Occasional nonproductive cough
- PMH: atrial fibrillation, GERD
- Meds: metoprolol, omeprazole
- SH: h/o tobacco, quit 10 years ago
- OH: retired school teacher, woodworker

Case 1

- Physical examination
  - Desaturates to 86% with walking
  - Bibasilar inspiratory crackles
  - Irregularly irregular, no murmur
  - Digital clubbing, no edema, rashes
- Pulmonary function tests
  - FVC 65% predicted, FEV1/FVC 0.85
  - TLC 70% predicted
  - DLCO 32% predicted

Case 1: HRCT

Case 1: HRCT

Diagnosis?

- A) Sarcoidosis
- B) Hypersensitivity pneumonitis
- C) Idiopathic Pulmonary Fibrosis
- D) Cryptogenic Organizing Pneumonia
- E) Connective Tissue Related ILD
- F) Requires more information
**Diagnosis?**

- A) Sarcoidosis
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- C) Idiopathic Pulmonary Fibrosis
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**IPF: HRCT diagnosis**

**Clinical Classification**

**Pulmonary Fibrosis**

- Exposure-related:
  - Occupational
  - Environmental
  - Avocational
  - Medication
- Idiopathic interstitial pneumonia (IPF)
- Connective tissue disease:
  - Scleroderma
  - Rheum. arthritis
  - Sjögrens
  - CTD
- Other:
  - Sarcoidosis
  - Vasculitis/Diffuse alveolar hemorrhage (DAH)
  - Langherhans cell histiocytosis (LCH)
  - Lymphangiomyomatosis (LAM)
  - Pulmonary alveolar proteinosis (PAP)
  - Eosinophilic pneumonias
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  - Inherited disorders
  - Chronic aspiration
  - Inflammatory bowel disease

**Survival**

- Median survival for IPF is 2-3 years
- Others better

**IPF: Published Definition**

*American Thoracic Society*

**Idiopathic Pulmonary Fibrosis: Diagnosis and Treatment**

*International Consensus Statement*

For joint statement of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) issued at the ATS/ERS Joint Conference, May 1999 and in the JBRP Interstitial lung disease 2000.2000;161:646

"A specific form of chronic fibrosing interstitial pneumonia limited to the lung and associated with the histologic appearance of usual interstitial pneumonia on surgical lung biopsy."
Conventional therapy
- Ineffective (and often harmful)

Collard Chest 2004;125:2169

Adding Acetylcysteine

Colard Chest 2004;125:2169

Novel therapies
- Interferon γ 1b
- Pirfenidone
- Bosentan
- Etanercept

Treatment
- Enroll in a clinical trial
- Consider therapy:
  - prednisone/azathioprine/acetylcysteine
  - Pulmonary rehabilitation
  - Lung transplantation evaluation

Case 2
- 50 year old woman
- Progressive cough and dyspnea over 6 months

PMH: “arthritis”
Meds: ibuprofen as needed
SH: former smoker, quit 1 year ago
OH: Clerical work, “dusty office”
Case 2

- Physical examination
  - No desaturation with walking
  - Scattered expiratory wheezes
  - Regular rate, rhythm
  - No clubbing, edema

- Pulmonary function tests
  - FVC 75% predicted, FEV1/FVC 68%
  - TLC 75% predicted
  - DLCO 65% predicted

Case 2: HRCT

Diagnosis?

- A) Sarcoidosis
- B) Hypersensitivity pneumonitis
- C) Idiopathic Pulmonary Fibrosis
- D) Cryptogenic Organizing Pneumonia
- E) Connective Tissue Related ILD
- F) Requires more information
Diagnosis?
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Surgical Lung Biopsy
- VATS is preferred approach
- Requires single lung ventilation
- Several disparate biopsies taken

Surgical Pathology

Surgical Pathology

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Clinical Classification

Pulmonary Fibrosis

Exposure-related ILD
- Inorganic agents (= pneumoconiosis)
  - asbestosis
  - silicosis
- Organic agents (= hypersensitivity pneumonitis)
  - Fungal spores (water damage, moldy hay)
  - Animal proteins (birds!)
- Medications
  - Amiodarone, Nitrofurantoin, Methotrexate

Hypersensitivity Pneumonitis

Case 2: Expiratory images

Treatment
- Removal from antigen
- Immunosuppression
  - Corticosteroids
  - Azathioprine
- Pulmonary rehabilitation
- Lung transplantation evaluation
Case 3

40 year old man
Persistant cough and dyspnea over 6 months
PMH: asthma
Meds: albuterol MDI
SH: active smoker
OH: Machinist for aerospace company

Physical examination
- No desaturation with walking
- Scattered crackles
- Skin nodules at site of tattoo
- No clubbing, edema

Pulmonary function tests
- FVC 80% predicted, FEV1/FVC 75%
- TLC 70% predicted
- DLCO 55% predicted

Diagnosis?
- A) Sarcoidosis
- B) Hypersensitivity pneumonitis
- C) Idiopathic Pulmonary Fibrosis
- D) Cryptogenic Organizing Pneumonia
- E) Connective Tissue Related ILD
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Sarcoidosis

- Idiopathic disease affecting all organ systems

### Treatment

- **Stage 1 disease**: often no therapy
- **Stage 2-3 disease**:
  - Prednisone
  - Methotrexate
  - Hydroxychloroquine
  - Azathioprine
  - Infliximab
- **Stage 4 disease**: transplantation