Interstitial Lung Disease: An Overview

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Disclosures

- Grants to study Genomic Predictors of IPF Outcomes (NIH) and protein markers of non-IPF ILD outcomes (ACCP)

- Grant to study early ILD detection
  - UC-Davis Gordon Wong endowment

- IPF Consulting/Speaking
  - Genentech
  - Boehringer Ingelheim
Objectives

• Provide a framework for how the interstitial lung diseases (ILD) are organized

• Review the key components of the ILD evaluation
What is interstitial lung disease?
Inflammatory ILDs

Non-specific Interstitial Pneumonia

Organizing Pneumonia

Common in autoimmune ILD
Fibrotic ILDs

Peripheral fibrosis
(common in idiopathic pulmonary fibrosis)

Central fibrosis
(common in chronic hypersensitivity pneumonitis)

Selman et al. AJRCCM 2012
Inflammatory ILDs

Cellular non-specific Interstitial Pneumonia

Organizing Pneumonia

Usually indicates autoimmune ILD
Fibrotic ILDs

Usual Interstitial Pneumonia (usually indicates IPF)

Airway-centric fibrosis (usually indicates chronic hypersensitivity pneumonitis)
What types of ILD we see on a regular basis

**Interstitial Lung Disease**

- **Etiology Known**
  - Autoimmune disease
    - RA, SSc, Sjogrens, IIM
  - Environmental ILD
    - Hypersensitivity pneumonitis
  - Occupational ILD
    - Asbestosis/Silicosis
  - Drug-induced ILD
    - Amio/MTX/Chemo

- **Etiology Unknown (aka idiopathic)**
  - Smoking-related
    - Desquamative interstitial pneumonia
    - Respiratory bronchiolitis-ILD
  - Chronic Fibrosing
    - Idiopathic pulmonary fibrosis
    - Idiopathic NSIP

- **Unclassifiable**
  - None of the above
Interstitial Lung Disease

Inflammation

Inflammatory Predominant ILDs
- Autoimmune ILD (most)
- Hypersensitivity Pneumonitis (early)
- Cryptogenic Organizing Pneumonia
- Drug-induced ILD

Fibrosis

Fibrotic Predominant ILDs
- UIP due to Scleroderma or RA
- Hypersensitivity pneumonitis (late)
- Idiopathic pulmonary fibrosis
- Asbestosis
The ILD Evaluation

Goals

• Standardized work-up to improve diagnostic accuracy

• Avoid unnecessary lung biopsy

• Diagnose early in the disease course

• Treat the disease early to improve outcomes
The ILD Evaluation

History

- Environmental history (Birds, mold)? - HP
- Joint pain/swelling, rash, muscle weakness, skin tightening, dysphagia? - CTD-ILD
- New medication? - Chemo/Amio/MTX
- Job exposures? - asbestosis, silicosis
- Family history of ILD? – familial IPF
- Smoking history? – smoking-ILDs
- Early graying, bone marrow abnormality, liver disease? – short telomere-related ILD

Laboratory work-up
- Autoimmune serologies

Physical Exam
- Autoimmune features?
- Crackles? Location?

High-resolution CT Scan
The ILD Evaluation

- History unrevealing
- Physical exam non-specific
- Laboratory work-up negative
- Chest CT scan non-diagnostic

Unclassifiable ILD

Surgical Lung Biopsy
- Must have sufficient lung function
- Largely safe, but small and finite risk of death and exacerbation
The ILD Evaluation - PFT

- Helps characterize physiology
  - Forced vital capacity (FVC)
  - Diffusion capacity (DLCO)

- Can assist with prognostication
  - Baseline values
  - Longitudinal change over time

The ILD Evaluation - Bronchoscopy

• Generally of limited use with a few notable exceptions
  • Hypersensitivity pneumonitis – cellular analysis
  • Asbestosis – cellular analysis, biopsy
  • Drug toxicity – cellular analysis, biopsy

• Potential emerging utility in bronchoscopic biopsy to diagnose IPF
The ILD Evaluation – Multi-disciplinary Discussion

Multidisciplinary Approach

The process of achieving a multidisciplinary diagnosis in a patient with IIP is dynamic, requiring close communication between clinician, radiologist, and when appropriate, pathologist (1). Clinical data (presentation, exposures, smoking status, associated diseases, lung function, laboratory findings) and radiologic findings are essential for multidisciplinary diagnosis.

MDD
Pulmonologist
Chest Radiologist
Pulmonary pathologist

Consider ILD center referral for all patients with ILD
The ILD Center Experience

- Standardized evaluation
- Multi-disciplinary discussion
- Co-morbidity assessment and treatment
- Pulmonary rehabilitation referral
- Assessment for supplemental oxygen needs
- ILD support group
- ILD therapeutics
- Clinical trials
An accurate diagnosis is critical

>50% of patients diagnosed with autoimmune ILD will live >10 years

<50% of patients diagnosed with IPF will live >5 years
Appropriate ILD Therapy is Critical
Azathioprine response in patients with fibrotic connective tissue disease-associated interstitial lung disease

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autoimmune-ILD: steroids and immunosuppressive therapy probably helpful

Fig. 2. Longitudinal change in percent predicted FVC (a) and DLCO (b) in a cohort of patients with fibrotic CTD-associated ILD treated with azathioprine and mycophenolate mofetil.
Environmental ILD: steroids and immunosuppressive therapy probably helpful
IPF: steroids and immunosuppressive therapy harmful

Prednisone, Azathioprine, and N-Acetylcysteine for Pulmonary Fibrosis

The Idiopathic Pulmonary Fibrosis Clinical Research Network®
A Phase 3 Trial of Pirfenidone with Idiopathic Pulmonary Fibrosis

The efficacy and safety of Nintedanib, 150 mg twice daily, were compared to placebo in a Phase 3 trial for Idiopathic Pulmonary Fibrosis (IPF). The results showed that Nintedanib was likely helpful in improving lung function, as indicated by changes in forced vital capacity (FVC). The graph illustrates the mean observed change from baseline in FVC for patients in the Nintedanib and placebo groups over time. The adjusted mean difference of 109.9 (95% CI, 71.3-148.6) with Nintedanib suggests a significant improvement compared to placebo.

The table below summarizes the number of patients at risk for both the Nintedanib and Placebo groups:

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<thead>
<tr>
<th>No. at Risk</th>
<th>Nintedanib</th>
<th>Placebo</th>
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<tr>
<td>Pirfenidone</td>
<td>276</td>
<td>273</td>
</tr>
<tr>
<td>Placebo</td>
<td>262</td>
<td>225</td>
</tr>
</tbody>
</table>
Summary

• ILD subtypes progress at highly variable rates

• You will help some ILD subtypes by prescribing steroids/immunosuppression

• You will hurt some ILD subtypes by prescribing steroids/immunosuppression

• An early and accurate diagnosis is critical
Thank You!