Interstitial Lung Disease: An Overview

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Overview

- Presentation and Evaluation
- Idiopathic Interstitial Pneumonias
  - Focus on IPF and NSIP
- Granulomatous Lung Disease:
  - Sarcoidosis
  - Hypersensitivity Pneumonitis

Presentation

- Presenting symptoms
  - SOB
  - Cough
  - Chest pain
  - Duration of symptoms
- Presenting physical signs
  - Hypoxia
  - Tachypnea
  - Inspiratory crackles
  - Clubbing
  - Cor pulmonale

Imaging

- Radiological features:
- Pattern:
  - Reticular (lines)
  - Nodular ("dots")
  - Combined: Reticulonodular
- Location:
  - Upper lobe
  - Lower lobe
  - Homogenous vs. heterogenous

Radiographic Features: Reticular Pattern
Radiographic Features: Nodular Pattern

CT Features

CT Features

Pulmonary Function Testing

- Restrictive ventilatory defect:
  - Symmetric decrease in FEV1 and FVC
  - Decrease in TLC
  - Decreased diffusion capacity
- Mixed restriction and obstruction

Further Evaluation

- Bronchoscopy:
  - Rule out infection
  - Cell counts
  - Transbronchial biopsies:
    - Rule out other causes
    - Granulomatous disease
- Surgical lung biopsy
- Neither

The Idiopathic Interstitial Pneumonias

ATS/ERS Joint Statement, AJRCCM 2000; 165: 277
**Diagnosis**

![Diagnosis Diagram]

**The Idiopathic Interstitial Pneumonias**

<table>
<thead>
<tr>
<th>CRP Diagnosis</th>
<th>Histology</th>
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<tbody>
<tr>
<td>IPF</td>
<td>UIP</td>
</tr>
<tr>
<td>NSIP</td>
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</tr>
<tr>
<td>AIP</td>
<td>DAD</td>
</tr>
<tr>
<td>DIP</td>
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<tr>
<td>RB-ILD</td>
<td>Respiratory Bronchiolitis</td>
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**IPF and NSIP**

**Pathophysiology of IPF**

- **Potential Risk Factors**
  - Cigarette smoking
  - Environmental exposures
  - Microbial agents
  - GERD
  - Genetic factors

![Pathophysiology of IPF Diagram]

![IPF - Potential Risk Factors Diagram]
Differential Diagnosis of IPF:
- Other idiopathic interstitial pneumonias
- Hypersensitivity pneumonitis
- Sarcoidosis
- Bronchiolitis obliterans organizing pneumonia
- Eosinophilic pneumonia
- Malignancy
- Infection

IPF versus NSIP - Clinical Features:

<table>
<thead>
<tr>
<th>IPF</th>
<th>NSIP</th>
</tr>
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<tbody>
<tr>
<td>Age 50-70</td>
<td>Age 40’s-50’s</td>
</tr>
<tr>
<td>M&gt;F</td>
<td>M&gt;F</td>
</tr>
<tr>
<td>Symptoms 6-24 months</td>
<td>Symptoms 6 months to 3 years</td>
</tr>
<tr>
<td>Cough, dyspnea</td>
<td>Cough, dyspnea, fatigue, weight loss, fever</td>
</tr>
<tr>
<td>BAL - neutrophils, mild to moderate eosinophils</td>
<td>BAL - Lymphocytes</td>
</tr>
<tr>
<td>Insidious onset</td>
<td>Subacute onset</td>
</tr>
<tr>
<td>Mortality 68%</td>
<td>Mortality 11%</td>
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HRCT Features of IPF:

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<tr>
<td>Radiographic features</td>
<td></td>
</tr>
<tr>
<td>Basal-predominant reticular abnormality, ground glass and reticular opacities</td>
<td>Ground glass and reticular opacities</td>
</tr>
<tr>
<td>CT distribution</td>
<td></td>
</tr>
<tr>
<td>Peripheral, subpleural basal, symmetric</td>
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</tr>
<tr>
<td>CT findings</td>
<td></td>
</tr>
<tr>
<td>Reticular, honeycombing, traction bronchiectasis, architectural distortion, focal ground glass</td>
<td>Ground glass, irregular lines, consolidation</td>
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Histologic Features of IPF:

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**IPF versus NSIP – Histologic Features**

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<tr>
<td>Distribution</td>
<td>Patchy, non-uniform</td>
<td>Diffuse, uniform</td>
</tr>
<tr>
<td>Temporal appearance</td>
<td>Variegated</td>
<td>Uniform</td>
</tr>
<tr>
<td>Alveolar septal inflammation</td>
<td>scant, patchy</td>
<td>Prominent</td>
</tr>
<tr>
<td>Collagen-type fibrosis</td>
<td>Characteristic, patchy</td>
<td>Variable, diffuse</td>
</tr>
<tr>
<td>Honeycomb change</td>
<td>Characteristic</td>
<td>Usually absent</td>
</tr>
<tr>
<td>Fibroblast proliferation</td>
<td>Fibroblast foci</td>
<td>Rare fibroblast foci</td>
</tr>
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**Histologic Features of UIP**

**Histologic Features of IPF**

**IPF - Role of Lung Biopsy**
- Definitive diagnosis requires surgical biopsy
- TB bx can rule out other diagnoses
- Patients with atypical features (age <45, extensive ground glass, sparing of bases, nodular pattern, absence of honeycombing, atypical PFT findings,) should be considered for biopsy if feasible

**ATS/ERS Prior Criteria for Diagnosis in Absence of Biopsy**
- **Major Criteria:**
  - Exclusion of other causes
  - PFT's consistent with IPF
  - Bibasilar reticular abnormalities, minimal ground glass on HRCT
  - TB bx or BAL not consistent with alternate diagnosis
- **Minor Criteria:**
  - Age>50 yrs
  - Insidious onset of otherwise unexplained DOE
  - Duration > 3 months
  - Bibasilar inspiratory crackles

**ATS/ERS New Criteria for Diagnosis**
- Exclusion of other known causes of ILD
- Presence of UIP pattern on HRCT in patients not subjected to surgical lung biopsy
- Specific combinations of HRCT and surgical lung biopsy pattern in patients subjected to surgical lung biopsy
**IPF - Therapy**

- No medical therapies proven to prolong survival
- The only therapy demonstrated to prolong survival is lung transplantation
- Ongoing/completed studies:
  - Pirfenidone
  - Endothelin receptor antagonists
  - Anticoagulation
  - N-Acetyl-Cysteine
  - Other

**PANTHER**

- Triple therapy vs. placebo
- Triple therapy arm closed early:
  - Increased mortality (11% vs 1%)
  - Increased hospitalization (29% vs 8%)
  - More SAE’s (31% vs 9%)

**Pirfenidone**

- Antifibrotic agent
- Studied in multiple clinical trials
- Statistically significant slowing of rate of decline in lung function
- Further study requested by FDA

**N-Acetyl-Cysteine**

- Precursor of antioxidant glutathione
- Randomized, placebo controlled trial of NAC in addition to "standard therapy"

**IPF - Therapy**

- Recommendation against the following:
  - Corticosteroid monotherapy
  - Colchicine
  - CSA
  - Combined corticosteroid and immune-modulator therapy
  - INF alpha
  - Bosentan
  - Etanercept

**IPF - Prognosis**

- Prognosis
  - 3 year 50% mortality
  - only 10-25% of patients respond to therapy
Sarcoidosis

- Clinical features - ACCESS database:
  - Non-caseating granulomas (Th1 reaction)
  - Symptoms: asymptomatic, cough, wheezing, DOE, SOB, chest pain
  - Race: 53% white 44% African American
  - Age: 46% < 40 yo 54% ≥ 40 yo
  - Gender: 64% female 36% male

(Saughtman et al. AJRCCM 2001; 164: 1754)

Sarcoidosis - Systemic Disease

- Organ involvement:
  - Lung (90%)
  - Skin (dermatitis, EN, LP)
  - Eyes (ant/post uveitis)
  - RES (liver, spleen)
  - Cardiac (Arrhythmias; cardiomyopathy)
  - Upper airways (Chronic sinusitis)
  - Hypercalcemia
  - Renal (stones, granulomas)
  - Neurologic (Psych/Thalamic pain)

Sarcoidosis - Pulmonary Staging

- CXR Abnormalities:
  - stage I - hilar adenopathy (80% remit)
  - stage II - adenopathy + interstitial (60%)
  - stage III - interstitial (30%)
  - stage IV - end stage upper lobe fibrosis
  - More acute presentation = better prognosis

Sarcoidosis - Stage I
Sarcoidosis - Stage II

Sarcoidosis - Pathology

Sarcoidosis - Syndromes

- Specific Syndromes
  - Lofgren’s syndrome - E. nodosum, fever, hilar adenopathy.
  - Heerfordt’s syndrome - uveitis, parotitis, fever

Sarcoidosis - Indications for Treatment

- Indications for treatment
  - Symptomatic pulmonary disease
    - DOE
    - Cough
    - Airway sarcoid
    - Worsening PFTs (DLco)
  - Cardiac involvement
  - Renal disease
  - Posterior uveitis
  - Neurologic involvement
  - Lupus pernio
  - Hypercalcemia

Sarcoidosis - Treatment

- Treatment plan
  - Corticosteroids 0.5-1.0 mg/kg/day x 6 wk
  - Taper 5 mg/wk to 0.25 mg/kg for 1 year total.

- Alternative therapies
  - Methotrexate
  - Imuran
  - Cytoxan
  - Chlorambucil
  - Chloroquine
  - Leflunomide (Arava)
  - Cellcept (Mycophenolic acid)

Hypersensitivity Pneumonitis
Hypersensitivity Pneumonitis

- Can result from various antigen exposures
- Leads to variable presentations
- Lack of consensus on diagnostic criteria

<table>
<thead>
<tr>
<th>Table 1: Selected Causes of Hypersensitivity Pneumonitis</th>
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<tbody>
<tr>
<td>Exposure</td>
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<tr>
<td>---------</td>
</tr>
<tr>
<td>Flour</td>
</tr>
<tr>
<td>Fungi</td>
</tr>
<tr>
<td>House dust</td>
</tr>
<tr>
<td>Humidifiers, and air conditioning systems</td>
</tr>
<tr>
<td>Hot tubs</td>
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<tr>
<td>Medicating fluids</td>
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<tr>
<td>Vacuum cleaners</td>
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HP - Allergens

HP - Clinical Presentation

- Dyspnea
- Cough
- Crackles
- Acute, subacute, or chronic
- Allergen may be difficult to identify

<table>
<thead>
<tr>
<th>Table 2: Diagnostic Evaluation for Hypersensitivity Pneumonitis</th>
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</thead>
<tbody>
<tr>
<td>Diagnostic Indicators</td>
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<tr>
<td>-----------------------</td>
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<tr>
<td>Medical history</td>
</tr>
<tr>
<td>Occupational, hobbies, and environmental hazards</td>
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<tr>
<td>Physical examination</td>
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<tr>
<td>Chest radiograph</td>
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<tr>
<td>High-resolution computed tomography</td>
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<tr>
<td>Simple procedures</td>
</tr>
<tr>
<td>Antigen stimulation challenge tests</td>
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<tr>
<td>Bronchoalveolar lavage</td>
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</tbody>
</table>

HP - Imaging

- Upper lobe predominant
- Interstitial prominence
- Can present in fibrotic phase

Arch Pathol Lab Med 2008; 132: 195 – 198

AJRCM 2005; 171: 762-768

Arch Pathol Lab Med 2008; 132: 195 – 198

Arch Pathol Lab Med 2008; 132: 195 – 198

Arch Pathol Lab Med 2008; 132: 195 – 198
**HP - Pathology**
- Interstitial pneumonitis
- Cellular bronchiolitis
- Non-necrotizing granulomas

**HP - Management**
- Identification and elimination of offending allergen
- Minimization of exposure
- Systemic corticosteroids

**Approach to I LD**
- Confirm diagnosis of I LD
  - CXR, HRCT scan, Bronchoscopy, OLBx, "clinical picture"
- Assess function
  - PFTs, exercise oximetry testing, QOL tool (SF-36)
- Treatment plan
  - disease specific plus vaccines, exercise, nutrition, etc.

**Review Question 1**
The only treatment that has been show to improve survival in IPF is:
- Oxygen therapy.
- High dose steroids (Pred 2 mg/kg/day).
- Low dose steroids + Imuran.
- γ-IFN.
- None of the above.

**Review Question 2**
A key difference between IPF and NSIP on histologic evaluation is:
- a. The presence of subpleural interstitial fibrosis
- b. The finding of fibroblastic foci
- c. Presence of a prominent inflammatory infiltrate
Review Question 2

A key difference between IPF and NSIP on histologic evaluation is:

a. The presence of subpleural interstitial fibrosis
b. The finding of fibroblastic foci
c. Presence of a prominent inflammatory infiltrate

Summary

- Interstitial lung disease has a variety of causes
- A detailed history and targeted evaluation is warranted
- IPF is the most common IIP and carries a poor prognosis
- Other IIP’s may be more responsive to therapy

References


