Pleuropulmonary Pathology of Autoimmune Connective Tissue Diseases

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I have no relevant actual or potential conflict of interest in relation to this presentation
Learning Objectives

At the end of this session, participants will be able to:

– understand the differences between the histologic patterns of pleuropulmonary diseases associated with connective tissue diseases (CTDs)

– distinguish the most frequent forms of interstitial lesions seen in patients with CTDs
Clinical Background

• CTDs
  – group of autoimmune disorders that affect mainly (but not exclusively) joints and muscles
    • rheumatoid arthritis (RA)
    • systemic lupus erythematosus (SLE)
    • Sjögren syndrome
    • systemic sclerosis (SSc)
    • inflammatory myopathies
    • systemic vasculitides
    • ankylosing spondylitis
Clinical Background

- CTDs
  - diagnosis can be difficult
  - ~50% remain “undifferentiated” one year after presentation
Clinical Background

• Pulmonary involvement in CTDs
  – incidence variable, but increasing
  – may be secondary
    • infection
    • drug toxicity
    • amyloidosis
    • aspiration
    • musculoskeletal dysfunction
    • neoplasia
    • paraneoplastic
Clinical Background

• Pulmonary involvement in CTDs
  – may be initial CTD presentation
Clinical Background

- Pulmonary involvement in CTDs

<table>
<thead>
<tr>
<th>CTD</th>
<th>Pulmonary involvement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>40</td>
</tr>
<tr>
<td>SLE</td>
<td>50-70</td>
</tr>
<tr>
<td>Sjögren</td>
<td>9-75</td>
</tr>
<tr>
<td>SSc</td>
<td>40-60</td>
</tr>
<tr>
<td>PM/DM</td>
<td>60</td>
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</tbody>
</table>
Clinical Background

• Pulmonary involvement in CTDs
  – may affect any of the anatomical compartments
    • airways
    • alveolated parenchyma
    • vasculature
    • pleura
  – reflects clinical presentation
Anatomic Pulmonary Compartments

- Interlobular septa
- Pleura
- Airways
- Alveolated parenchyma
- Pulmonary lobule
- Vasculature

Mills SE, *Histology for Pathologists*, 3rd Ed, Figure 18-13B
Parenchymal lesions

- Overlap with idiopathic lung diseases

<table>
<thead>
<tr>
<th>Category</th>
<th>Clinical–Radiologic–Pathologic Diagnoses</th>
<th>Associated Radiologic and/or Pathologic–Morphologic Patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic fibrosing IP</td>
<td>Idiopathic pulmonary fibrosis</td>
<td>Usual interstitial pneumonia</td>
</tr>
<tr>
<td></td>
<td>Idiopathic nonspecific interstitial pneumonia</td>
<td>Nonspecific interstitial pneumonia</td>
</tr>
<tr>
<td>Smoking-related IP*</td>
<td>Respiratory bronchiolitis-Interstitial lung disease</td>
<td>Respiratory bronchiolitis</td>
</tr>
<tr>
<td></td>
<td>Desquamative interstitial pneumonia</td>
<td>Desquamative interstitial pneumonia</td>
</tr>
<tr>
<td>Acute/subacute IP</td>
<td>Cryptogenic organizing pneumonia</td>
<td>Organizing pneumonia</td>
</tr>
<tr>
<td></td>
<td>Acute interstitial pneumonia</td>
<td>Diffuse alveolar damage</td>
</tr>
</tbody>
</table>

Parenchymal lesions

• Usual interstitial pneumonia (UIP)
  - can be seen with any of the CTDs
  - most common ILD pattern in RA
    - often men, smokers
    - 1 - 4% of RA patients
Parenchymal lesions

- Usual interstitial pneumonia (UIP)
  - poor prognosis, but better than in patients with idiopathic UIP

![Graph showing survival curves for CVD-UIP and IPF/UIP patients.]

*Figure 1. Comparison of the survival curves for CVD-UIP and IPF/UIP patients.*

Parenchymal lesions

- Usual interstitial pneumonia (UIP)
  - serology recommended to evaluate for the possibility of associated CTD
    - RF, anti-cyclic citrullinated peptide, ANA

Right lung (autopsy specimen, sagittal)
59F with RA
UIP pattern
Parenchymal lesions

• Histopathology of UIP
  ▪ key features
    ▪ architectural distortion
    ▪ temporal heterogeneity
    ▪ spatial heterogeneity
Parenchymal lesions

- Histopathology of UIP
  - Clues to CTD association
    - germinal centres
    - fewer fibroblast foci
    - smaller honeycomb spaces
    - more inflammation

Parenchymal lesions

• Non-specific interstitial pneumonia (NSIP)
  ▪ can be seen with any of the CTDs
  ▪ most common ILD pattern in majority of CTDs
  ▪ better prognosis than UIP
Parenchymal lesions

• Non-specific interstitial pneumonia (NSIP)
  ▪ some routinely perform serology in NSIP patients to evaluate for CTD association
Parenchymal lesions

• Histopathology of NSIP
  ▪ two subtypes: cellular and fibrosing
  ▪ key features
    ▪ temporal uniformity
    ▪ spatial uniformity
    ▪ relatively preserved architecture
Fibrosing NSIP
Fibrosing NSIP
Parenchymal lesions

• Organizing pneumonia (OP)
  ▪ can be seen with any of the CTDs, albeit less commonly than fibrosing ILD
  ▪ good prognosis
    ▪ responds to corticosteroids
Parenchymal lesions

- Histopathology of OP
  - key features
    - intraluminal organizing fibrosis in airspaces
    - patchy distribution
    - preserved architecture
    - mild chronic interstitial inflammation
Parenchymal lesions

- Diffuse alveolar damage (DAD)
  - can be seen with any of the CTDs, albeit less commonly than fibrosing ILD
  - poor prognosis
  - may occur alone, or as an acute exacerbation of pre-existing fibrosing ILD
Parenchymal lesions

• Histopathology of DAD
  ▪ acute, organizing, and fibrosing phases
  ▪ key features
    ▪ diffuse distribution
    ▪ temporal uniformity
    ▪ alveolar septal thickening by organizing fibrosis
    ▪ hyaline membranes
Parenchymal lesions

- Lymphoid interstitial pneumonia (LIP)
  - rarely encountered
  - several reclassified as cellular NSIP or lymphoma
  - classically in Sjögren
Parenchymal lesions

• Histopathology of LIP
  ▪ key features
    ▪ diffuse distribution
    ▪ non-granulomatous chronic inflammation
    ▪ alveolar septa predominantly involved