Complications of Inflammatory Myopathy: Lung Disease

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Case Presentation

- 43 year old male referred for evaluation of ILD and possible autoimmune disorder
- Developed “pneumonia” in 2007—no response to antibiotics
- Diagnosis revised to “pulmonary fibrosis”
  - treated with prednisone for 1 year with clinical, functional, and radiologic improvement
- Pulmonary evaluation:
  - restrictive PFTs with reduced FVC, TLC, D\textsubscript{L}CO
  - HRCT with basilar ground glass, minimal honeycombing
  - Serology: -ANA, +SS-A, -Jo-1
Bilateral lower lobe air space disease with ground glass opacities consistent with active alveolitis; minimal fibrosis in lung bases peripherally.
Case Presentation

- Review of Systems:
  - no constitutional symptoms (F/C, NS, weight loss)
  - denies dry eyes/dry mouth, Raynaud’s
  - denies skin thickening or rashes beyond patchy hyperpigmentation of palms
  - currently no cough or shortness of breath
  - no difficulty swallowing, no heartburn/reflux
  - no joint pain/swelling/stiffness
  - mild proximal upper extremity aching, but no proximal weakness
Case Presentation

Physical Examination:

- afebrile, normal blood pressure, respiratory rate
- grossly adequate tear, salivary pools
- no detectable lymph nodes
- lungs with good air movement, no use of accessory muscles, no rales/rhonchi/wheezeing
- normal pulses
- musculoskeletal exam without synovitis
- normal proximal, distal muscle strength
- skin without Gottron’s rash/papules
Case--Summary

- “mechanic’s hands,” no muscle weakness
- steroid-responsive ILD
- ANA, -Jo-1, +SSA → cytoplasmic staining

Anti-Synthetase Syndrome (incomplete)
Objectives

- Types of Lung Involvement
- Diagnosis of Lung Disease
- Management of Lung Disease
Lung Involvement

- multiple forms of lung involvement in myositis

  - “Extrinsic”
    - weakness of respiratory muscles
    - aspiration (due to swallowing impairment)
    - opportunistic infection
    - congestive Heart Failure (rare)
    - pulmonary hypertension (rare)

  - “Intrinsic”
    - Interstitial Lung Disease (ILD)
Lung Involvement

- at least 30% myositis patients have ILD
  - most commonly involved extramuscular organ system

- Anti-Jo-1 Ab found in 50–75% myositis-ILD
  - strong association of ILD with all anti-synthetase Ab in myositis

- **lung disease may precede muscle involvement**

- significant contribution to morbidity/mortality
  - 5 year survival with ILD ~70% (vs. ~ 85%)
  - likely depends on subtype of ILD

No correlation between extent/severity of muscle or skin disease and activity of ILD
Lung Involvement: Symptoms

- shortness of breath with or without nonproductive cough

- pleurisy and pleural effusion are unusual (unlike SLE)

- variable presentation of ILD:
  - acute (ARDS) or subacute [Clawson, A&R, 1995]
  - chronic and more slowly progressive
  - asymptomatic (usually with basilar fibrosis)
Objectives

• Types of Lung Involvement

• Diagnosis of Lung Disease

• Management of Lung Disease
Diagnosis

1. Clinical suspicion

2. Imaging

3. Pulmonary Function Tests (PFTs)

4. Biopsy—rule out alternative processes
Diagnosis: Autoantibodies

- Anti-synthetases
- PL-7
- PL-12
- Jo-1
- MP
- SRP
- U1RNP
- Ku
- Mi-2
- TIF-1γ
- DM
- MJ
- PM-Scl
- SLE
- SSc
- Overlap
# Autoantibodies

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Target</th>
<th>Subset</th>
<th>Phenotype</th>
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<tbody>
<tr>
<td>Mi-2</td>
<td>NuRD</td>
<td>DM</td>
<td>Shawl, V-neck, Gottron’s</td>
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<tr>
<td>CADM-140</td>
<td>MDA-5</td>
<td>DM</td>
<td>Amyopathic, ILD</td>
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<td>SAE</td>
<td>SUMO</td>
<td>DM</td>
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<tr>
<td>MJ</td>
<td>NXP-2</td>
<td>JDM</td>
<td>Calcinosis, Ulceration</td>
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<td>p155/140</td>
<td>TIF1-γ</td>
<td>DM, JDM</td>
<td>Severe skin, malignancy</td>
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<td>SRP</td>
<td>72, 54 kDa</td>
<td>PM</td>
<td>Severe/refractory myositis</td>
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<tr>
<td>p200/100</td>
<td>HMGCR</td>
<td>IMNM</td>
<td>Necrotizing myopathy</td>
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<tr>
<td>Jo-1</td>
<td>ARS</td>
<td>PM/DM</td>
<td>Anti-synthetase syndrome</td>
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### Anti-synthetase Autoantibodies

<table>
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<tr>
<th>Antibody</th>
<th>Antigen (tRNA synthetase)</th>
<th>Prevalence in IIM (%)</th>
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<tbody>
<tr>
<td>Jo-1</td>
<td>histidyl</td>
<td>20-30</td>
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<tr>
<td>PL-7</td>
<td>threonyl</td>
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<tr>
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<tr>
<td>Tyr</td>
<td>tyrosyl</td>
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</tr>
<tr>
<td>Zo</td>
<td>phenylalanyl</td>
<td>&lt;1</td>
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</tbody>
</table>
Myositis--Autoantibodies

**Jo-1** (histidyl-tRNA synthetase): 25%

- Defines clinically homogeneous patient population: anti-synthetase syndrome (fever, myositis, arthritis, Raynaud’s, mechanic’s hands, ILD)

- Gene linkage: B8, DR3 (DQA1*0501, DQA1*0401)
Anti-Synthetase Syndrome: Lung

- Anti-synthetase syndrome is being increasingly recognized within pulmonary medicine—even in absence of overt myositis.

- ILD is an important feature and critical determinant of prognosis in myositis patients.
Objectives

• Types of Lung Involvement

• Diagnosis of Lung Disease

• Management of Lung Disease
Myositis-ILD--Management

➢ Assessment and management of co-morbidities:
  ▪ gastro-esophageal reflux
  ▪ pulmonary hypertension
  ▪ infection

➢ Immunosuppressive medications
  ▪ corticosteroids
  ▪ anti-metabolites: Cellcept**, Imuran, Prograf
  ▪ cyclophosphamide
  ▪ biologic agents—Rituximab, TNF inhibitors
  ▪ anti-fibrotic agents?

➢ Cell-based therapy (e.g., stem cells)? Not yet!

➢ PJP prophylaxis
  ▪ Bactrim DS vs. Dapsone vs. Pentamadine

**Fischer, et. al. J Rheum, 2013**
Myositis-ILD--Management

- Oxygen
- Pulmonary rehabilitation
- Vaccination (influenza, Prevnar/Pneumovax)
- Serial monitoring of:
  - Pulmonary Function Tests/6MW
  - High Resolution Chest CT
  - ECHO
- Lung transplantation
Future Needs

- Multidisciplinary Approach—rheumatology, pulmonary

- Database development
  - clinical features—define key variables
  - standardize data collection—clinical indices, HRCT
  - parameters of treatment response—OMERACT

- Biological specimens—serum/cells, lung tissue
  - autoantibody screening
  - molecular profiling—serum proteins
  - gene array

- Data sharing—treatment regimens/responsiveness
Conclusions

- Lung disease is common in myositis
- Multiple forms of lung involvement—intrinsic, extrinsic
- Need to ascertain subtle rheumatologic features in patients with predominant involvement of lung (diagnosis can be missed)
- Critical role of: autoantibody assessment, imaging, biopsy
- Treatment: corticosteroids + MMF/tacrolimus/Cytoxan • address co-morbidities (infection, reflux, pulm HTN)
- Need for data sharing—between disciplines, institutions