Complications of Inflammatory Myopathy: Lung Disease

Dana Ascherman, M.D.
Division of Rheumatology

MILLER
SCHOOL OF MEDICINE
UNIVERSITY OF MIAMI

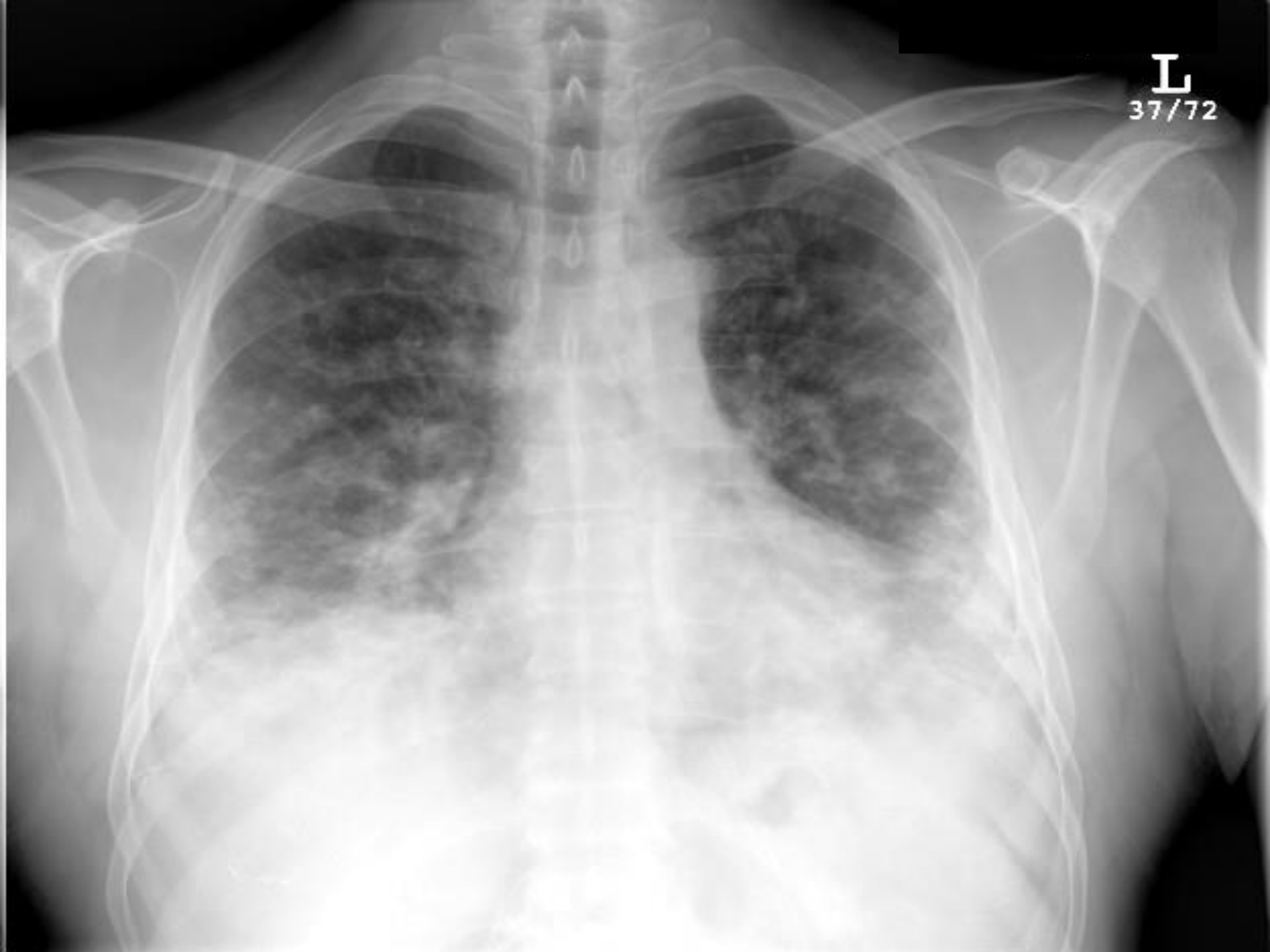
Case Presentation

- 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_LCO
  - HRCT with basilar ground glass, minimal honeycombing
  - Serology: -ANA, +SS-A, -Jo-1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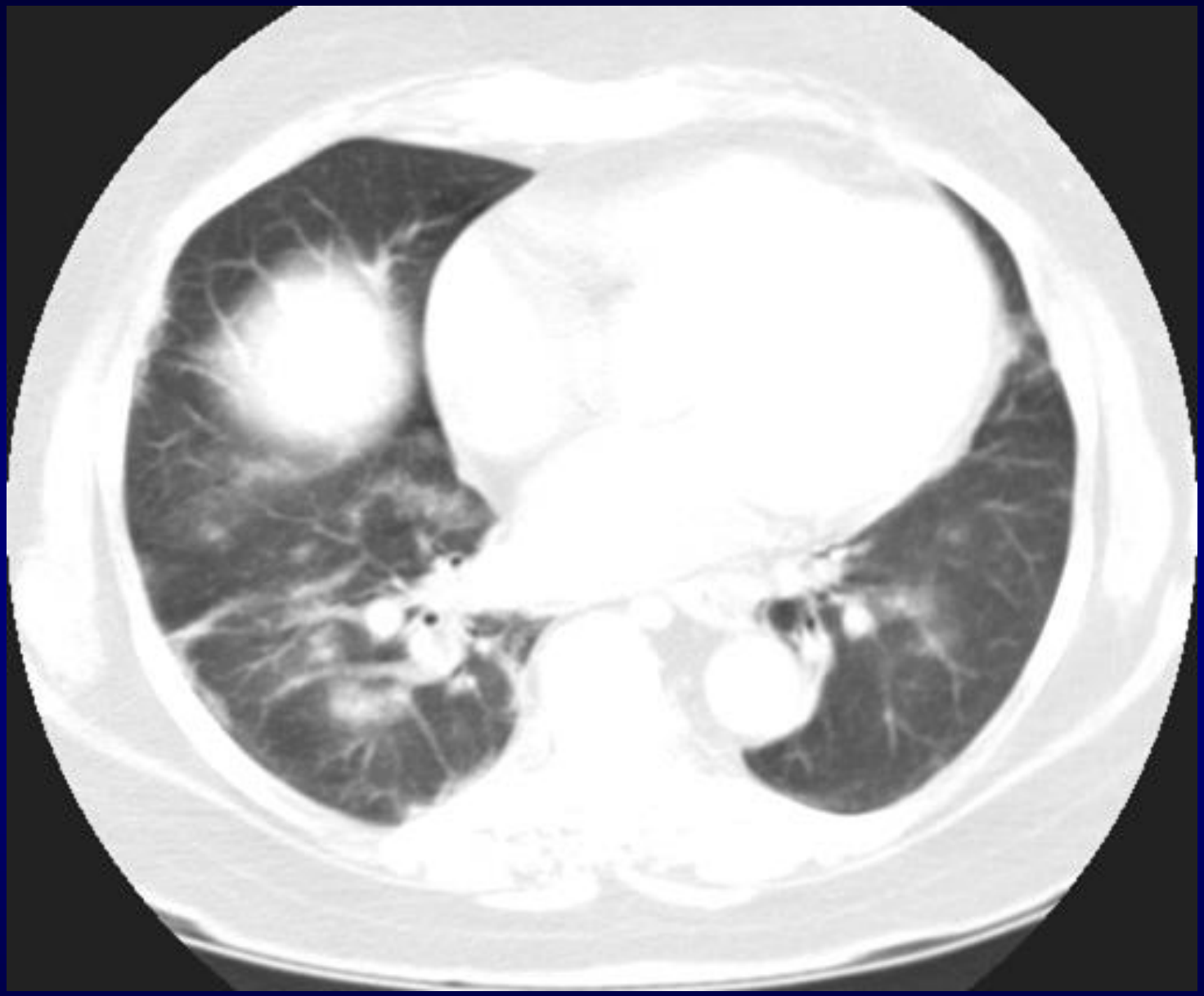


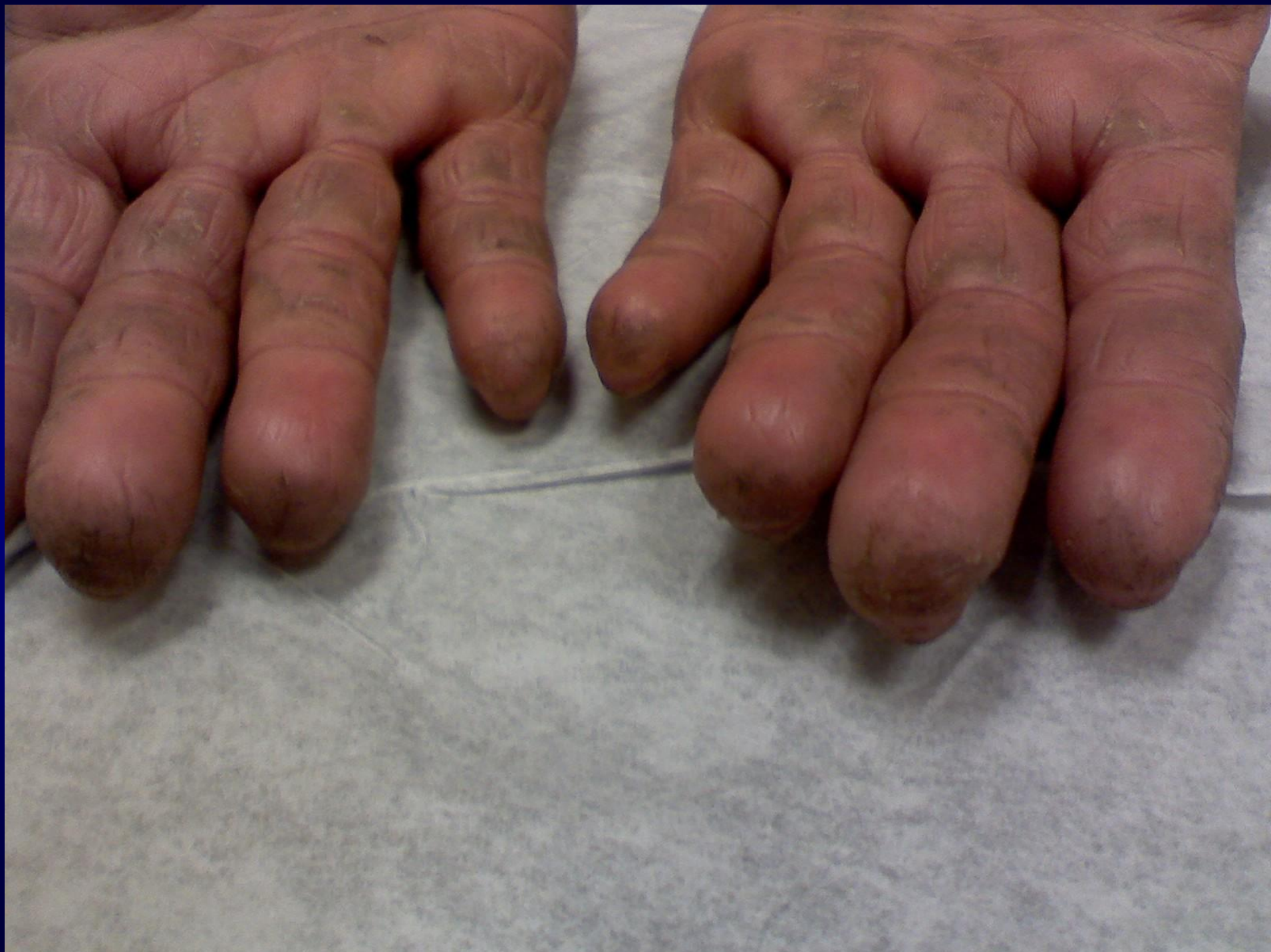
Bilateral lower lobe air space disease with ground glass opacities consistent with active alveolitis; minimal fibrosis in lung bases peripherally

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**

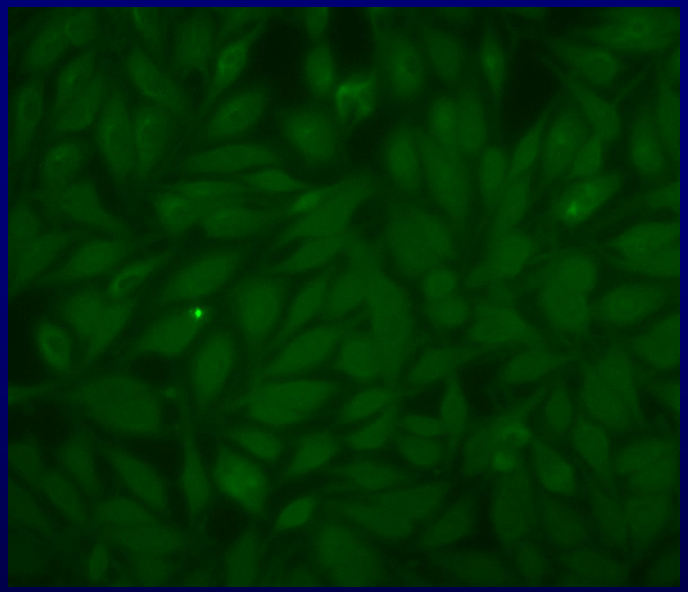
Case Presentation

- **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/wheezing**
  - **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 hypertenison (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

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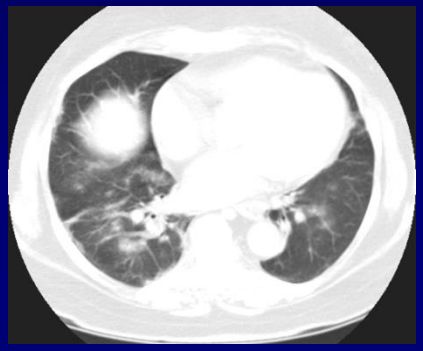
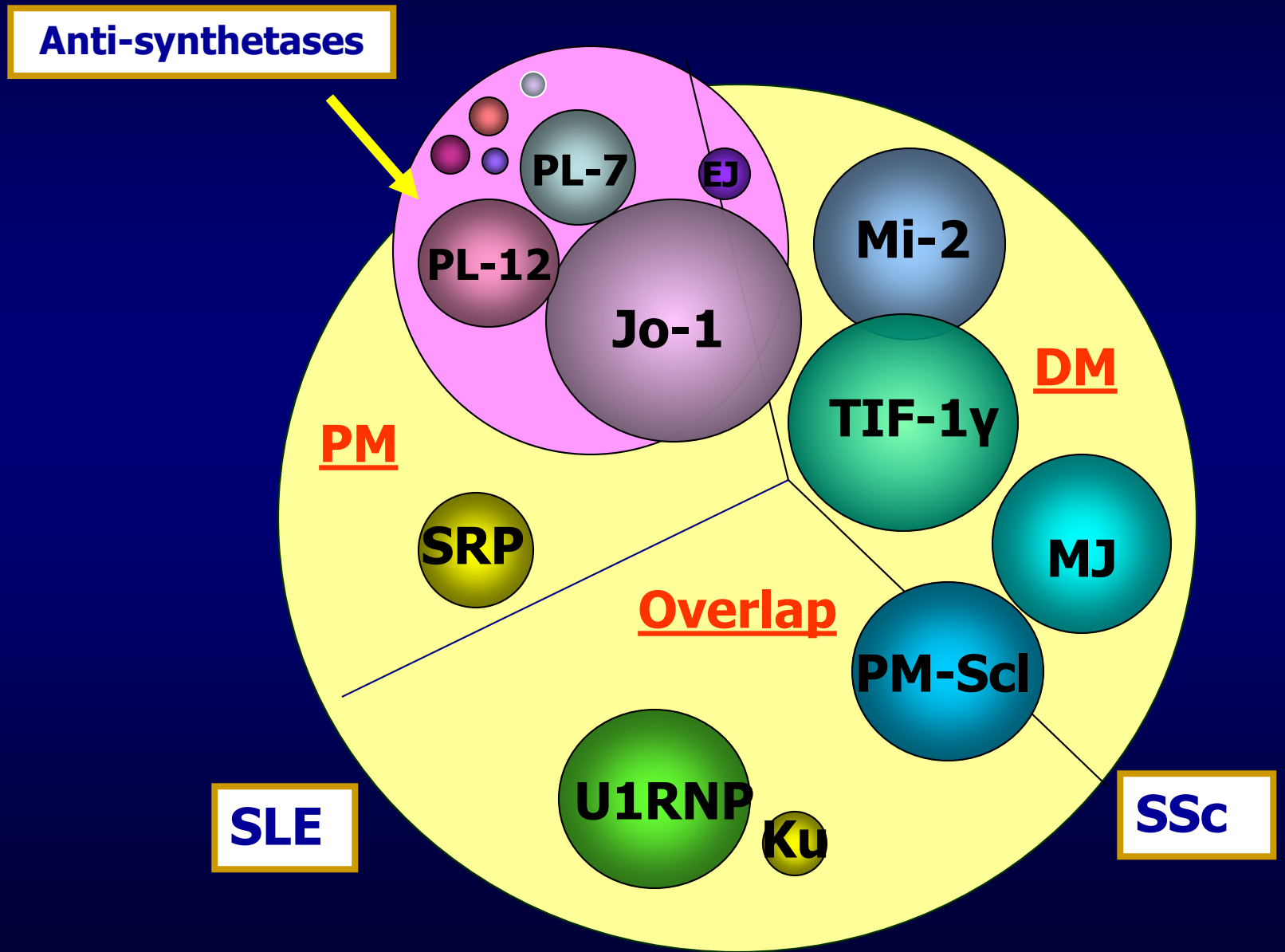
Diagnosis

1. Clinical suspicion
2. Imaging



3. Pulmonary Function Tests (PFTs)
4. Biopsy—rule out alternative processes

Diagnosis: Autoantibodies



Autoantibodies

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

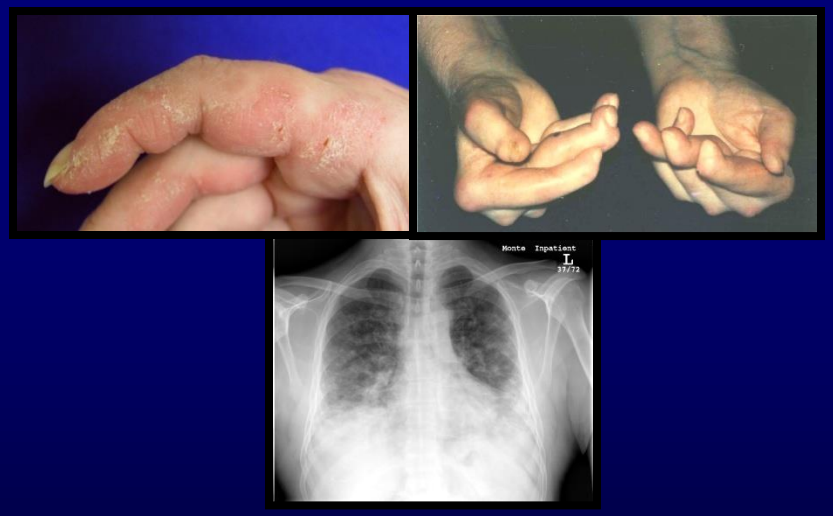
Anti-synthetase Autoantibodies

Antibody	Antigen (tRNA synthetase)	Prevalence in IIM (%)
Jo-1	histidyl	20-30
PL-7	threonyl	<5
PL-12	alanyl	<5
OJ	isoleucyl	<5
EJ	glycyl	<5
KS	asparaginyl	<1
Tyr	tyrosyl	<1
Zo	phenylalanyl	< 1

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

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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