SNUH
SEOUL NATIONAL UNIVERSITY HOSPITAL

# Approach to patients with acute-subacute onset interstitial lung disease

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# Disclosure

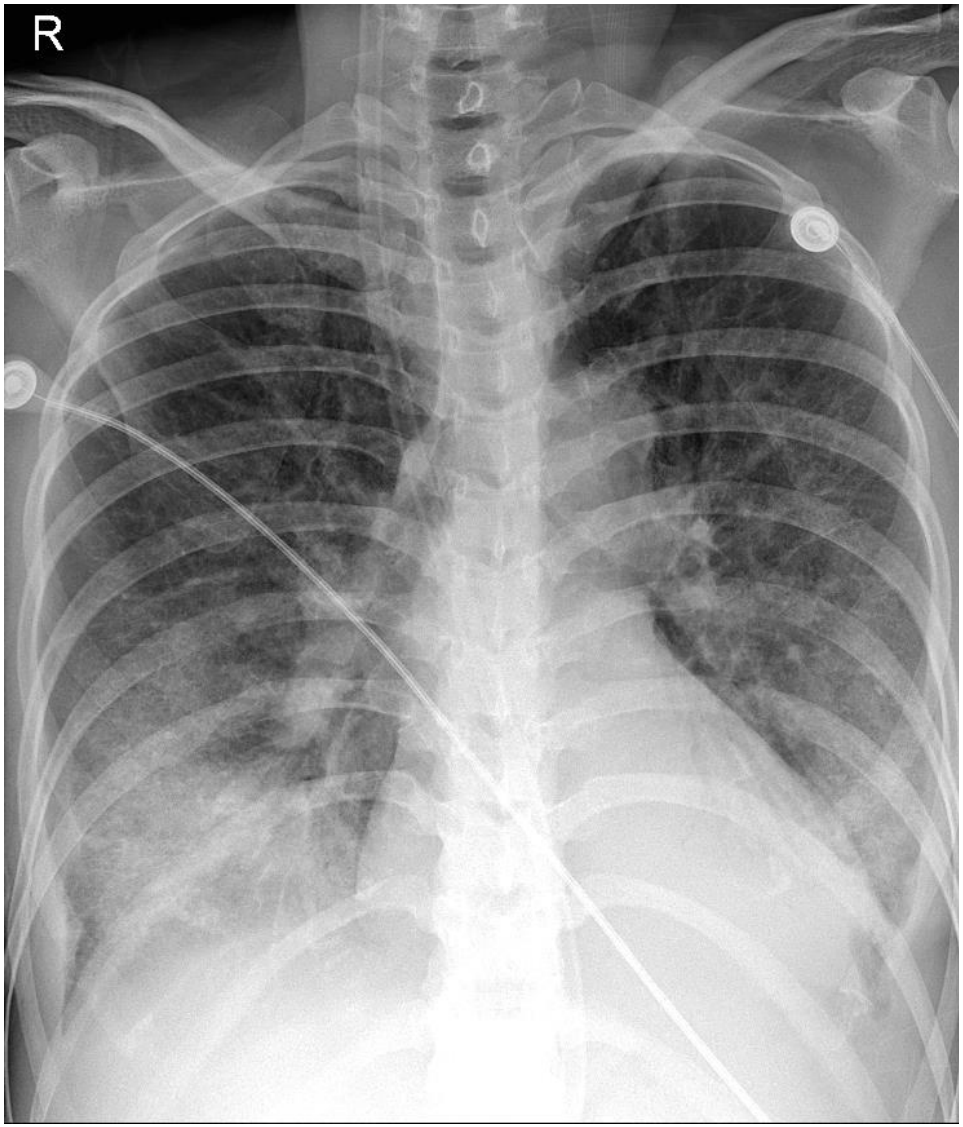
**I have no actual or potential conflict of interest in relation to this presentation**

# Case 54/F

Previous healthy

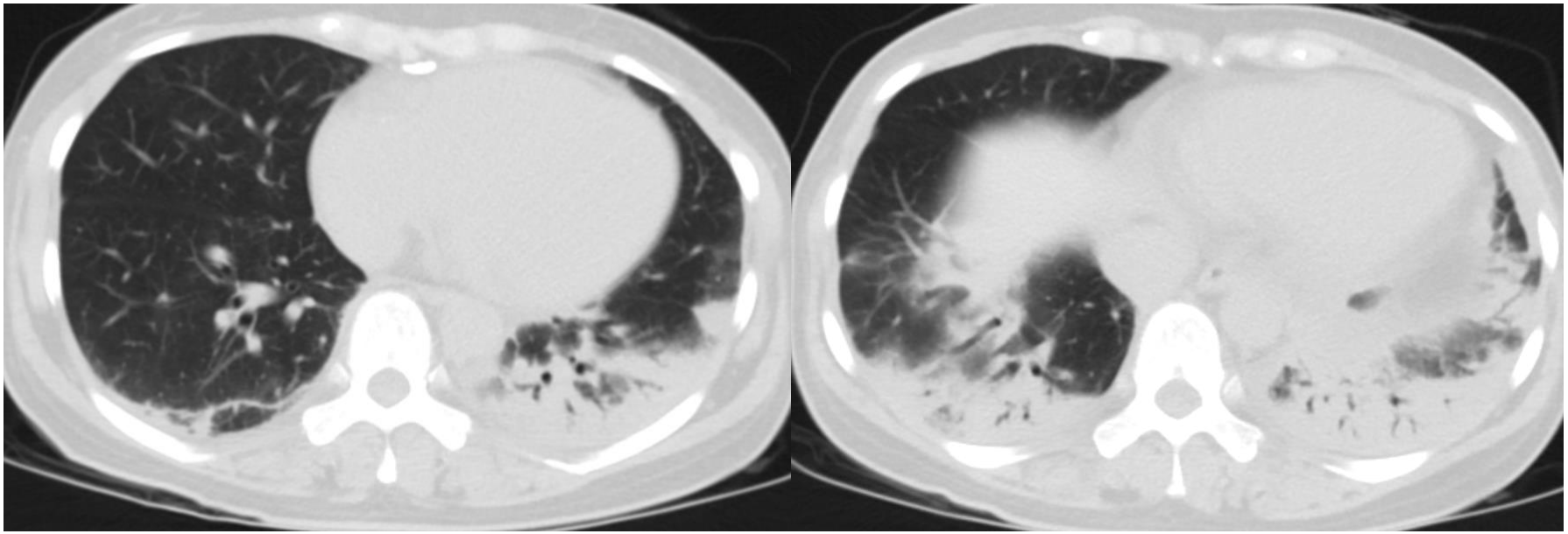
1달 전부터 기침 발생하여 인근 병원  방문, Chest X ray상 폐렴 의심되어 입원하여 IV 항생제 치료 받음. ( Gentamycin + Cefotaxime )

10일간 항생제 치료하였으나 임상적으로 호전 없어 전원함.



입원하여 시행한 Chest CT상 양하엽에 pneumonic consolidation 및 소량의 bilateral pleural effusion이 동반되어 IV 항생제 (Tazocin + azithromycin) 사용 시작함.

입원 시부터 mild AST/ALT 상승 있었고, 입원 중 AST/ALT 451/246 로 상승되면서 LDH 2110, CPK 6055 되고 폐 병변 악화, 산소 요구량 증가하면서 폐렴 이외의 원인에 대한 감별 위하여 본원 응급실로 전원



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- Initial evaluation
  - Idiopathic vs non-idiopathic
- Idiopathic Interstitial pneumonia
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  - Acute interstitial pneumonia
  - Acute eosinophilic pneumonia
  - Acute exacerbation of unrecognized ILD
- Non-idiopathic interstitial pneumonia
  - CTD-ILD: focusing on antisynthetase syndrome
  - Diffuse alveolar hemorrhage syndrome
  - Others (Drug induced pneumonitis)
- Summary

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# Presentation of acute ILDs

- Worsening of respiratory symptoms during few days-weeks
- Chest imaging: usually diffuse bilateral infiltrates
- Possible scenarios
  - Acute exacerbation of known ILD
  - Acute exacerbation of unknown ILD
  - De Novo acute ILD

# Differential diagnosis of possible scenarios

- Acute exacerbation of known ILD
- Acute exacerbation of unknown ILD
  - Important to check previous x-rays or CT scans
  - An infectious event may reveal the underlying unknown ILD
- De Novo acute ILD

# Differential diagnosis of possible scenarios

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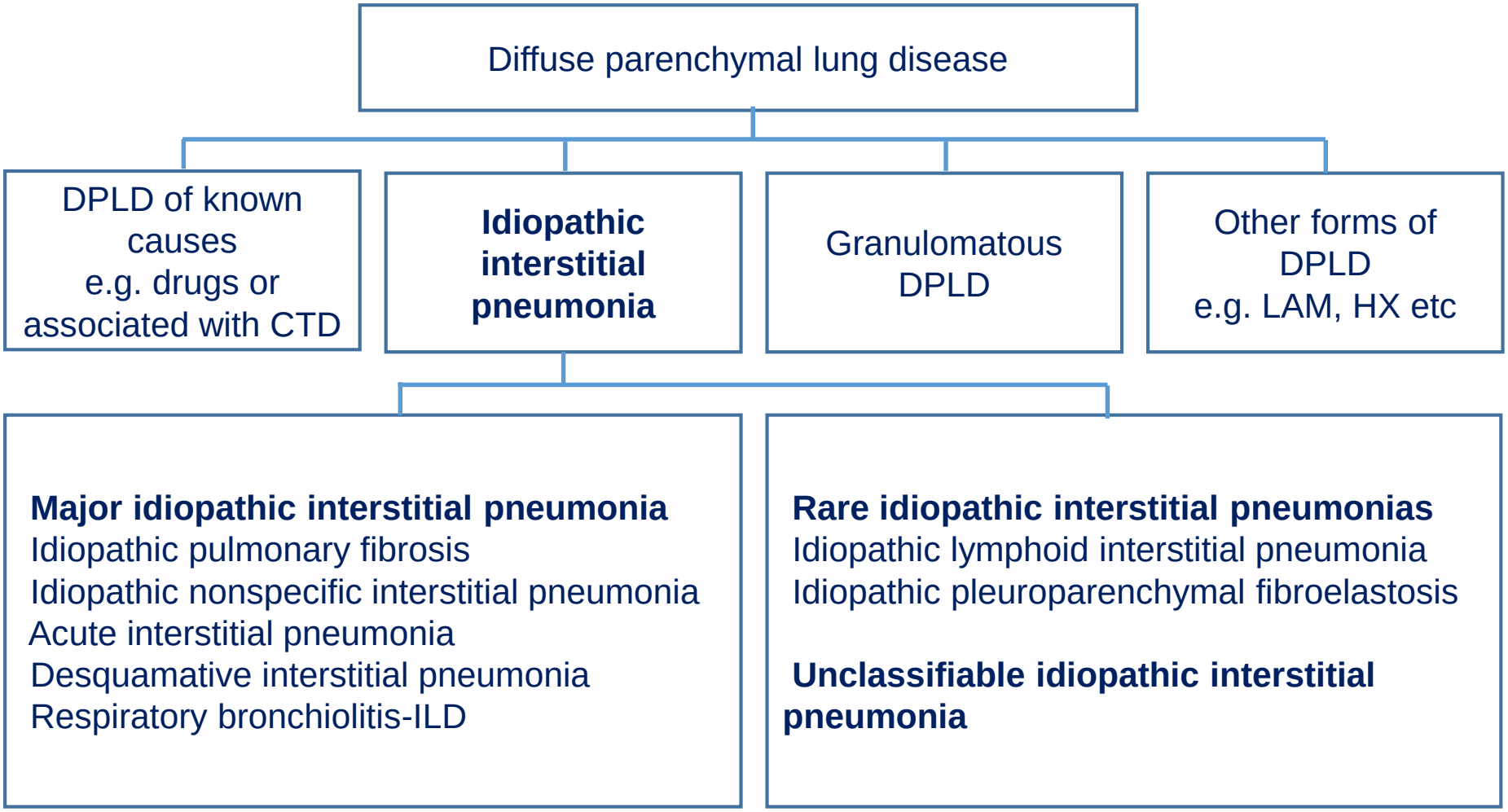
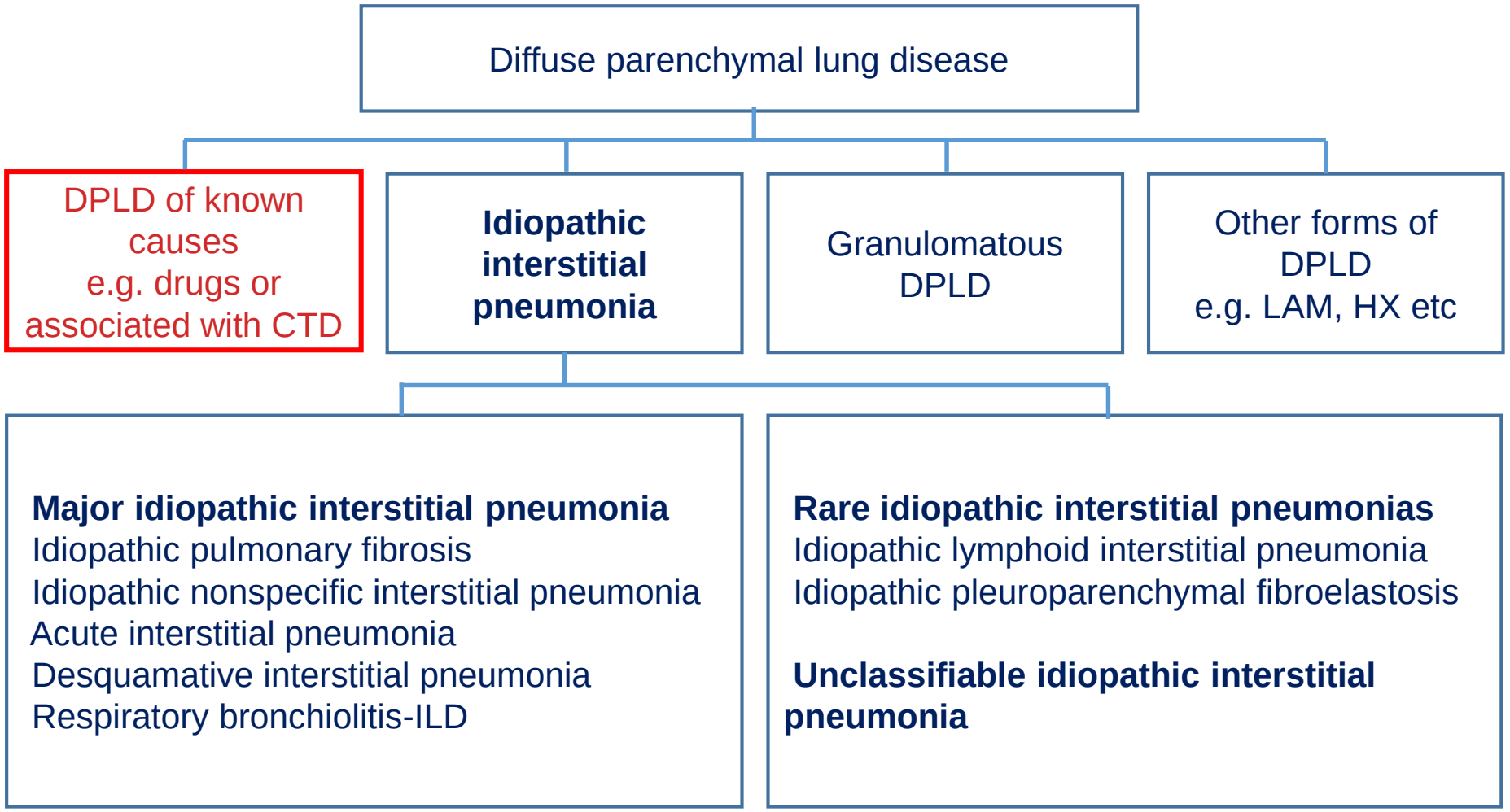
# Classification of diffuse parenchymal lung disease




Am J Repir Crit Care Med 2013; 188 : 733-748

# Classification of diffuse parenchymal lung disease

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# Evaluation of possible causes

- Drug  (amiodarone, chemo-agent, MTX etc)
- Radiation
- Smoking
- Occupational exposure
- Environmental exposure
- Connective tissue disease (CTD)

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# Evaluation of CTD

- Systemic symptom

- Arthralgia, myalgia, fever, fatigue, dry mouth, dry eyes

- Physical exam

- Muscle power, Raynaud phenomenon, mechanics' hands, skin lesion

- Laboratory findings

- Muscle enzyme, serologic tests, U/A (proteinuria, hematuria) etc.

- Other exam

- EMG/NCS, MRI, biopsy, shimmer test, nailfold capillaroscopy, etc.


HELP!

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# Categorization of major IIPs

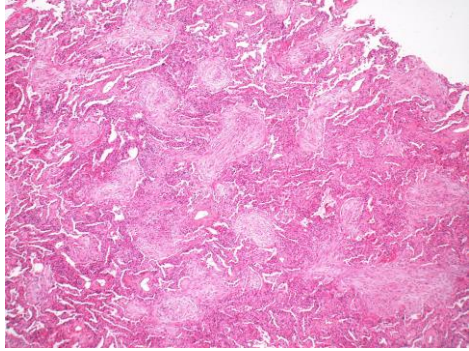
| Category | Clinical–Radiologic–Pathologic Diagnoses | Associated Radiologic and/or Pathologic–Morphologic Patterns |
|---|---|---|
| Chronic fibrosing IP | Idiopathic pulmonary fibrosis | Usual interstitial pneumonia |
| | Idiopathic nonspecific interstitial pneumonia | Nonspecific interstitial pneumonia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

2013 An Official ATS/ERS statement: Update of the International Multidisciplinary Classification of the IIPs

# Cryptogenic organizing pneumonia (COP)

- Formerly called bronchiolitis obliterans organizing pneumonia or BOOP
- Subacute-acute presentation (less than 2-3M)
- Characterized by a “pneumonia-like” illness
- Sometimes flulike illness characterized by cough, dyspnea, fever, malaise, fatigue
- Variable degrees of cough and dyspnea

# Diagnosis of COP



- Clinical and radiologic feature

- Pathologic finding of OP (Surgical lung biopsy>> TBLB)
  - Intraluminal fibrotic buds (Masson bodies) in respiratory bronchioles, alveolar ducts, and alveoli
  - Foamy cells in the alveolar spaces
  - Interstitial lymphoplasmacytic infiltrates and fibrinous exudates

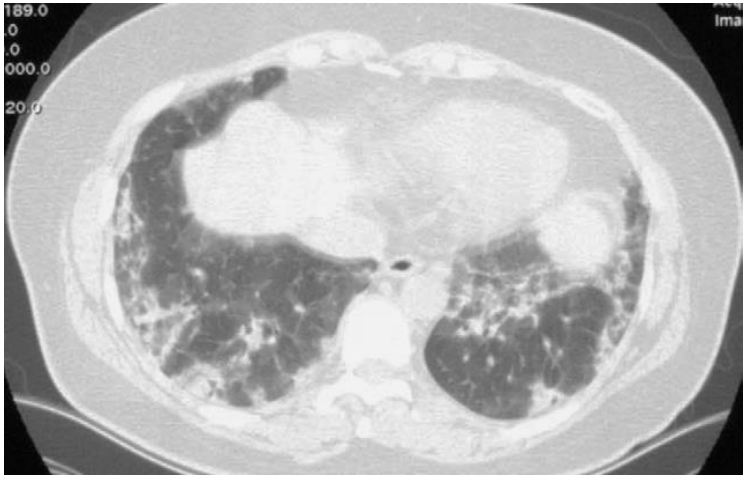
- Rule out
  - Infection (pneumonia)
  - Secondary OP - post-infectious, drug related, CTD related, HP, radiation, hematologic malignancy, etc.

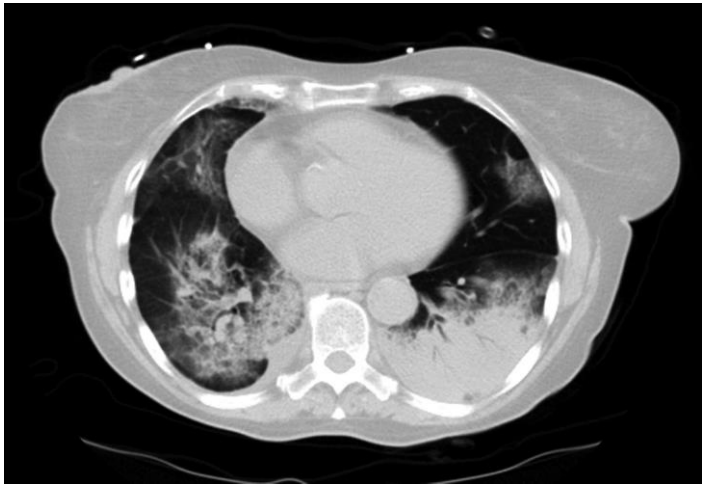
  → Cryptogenic OP

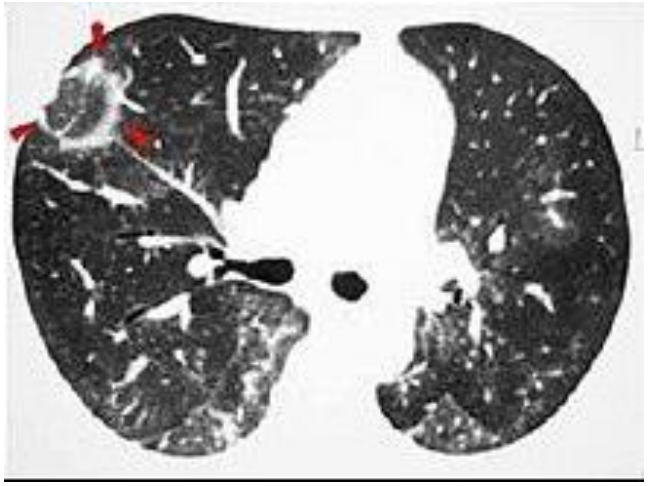
# HRCT of OP

- Patchy bilateral air-space consolidation (80-90%)
- Ground glass opacity (60%) or crazy paving
- Subpleural and/or peribronchovascular distribution (60-80%)
- Perilobular opacities (60%)
- The reverse halo sign (atoll sign) is considered to be specific, although only seen in ~ 20% of patients with COP
- Pleural effusion (10-30%)
- Can be spontaneously regression, migrating

# HRCT of OP







# Treatment and prognosis

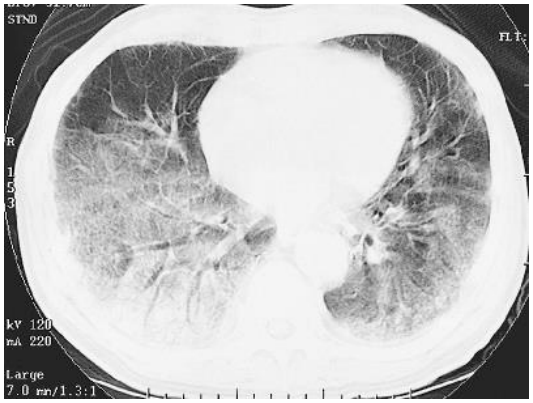
- Treatment of choice: steroid (0.5-1mg/kg for 6-12M)
  → results in complete recovery in 2/3 patients
- 1/3 patients – recurrent or persistent disease
- If reticular opacities (+), response of steroid treatment
- In general, clinical improvement is rapid (days - weeks)
- Relapse can occur
- Mortality < 5%

# Acute interstitial pneumonia (AIP, Hamman-Rich syndrome)

- Acute presentation (days to weeks)
- Often preceded by a flu-like prodromal illness that lasts one to two weeks prior to presentation
- Rare, fulminant form of lung injury,  rapidly progressive hypoxemia
- Diagnosis: surgical lung biopsy
- Idiopathic ARDS+ diffuse alveolar damage on histology

# HRCT of AIP

- Bilateral, multifocal or diffuse areas of ground-glass opacity and consolidation
- Usually without pleural effusion
- Lower lobe, subpleural predominance
- GGO + consolidation




→ evolving fibrosis (traction bronchiectasis, reticular opacities, and architectural distortion)

# Treatment and prognosis of AIP

- No proven treatment
- Supportive and consists of mechanical ventilation and oxygen supplementation
- Corticosteroids might be effective in the early phase of disease in a subset of patients
- Mortality in 6M: > 50%

# Acute eosinophilic pneumonia (AEP)

- Acute dyspnea, cough, fever, malaise
  → Often misdiagnosed as infectious pneumonia

- Can be idiopathic, but identifiable causes including smoking, environmetal, occupational dust exposures, toxinc inhalations, infections, and medications

- More than half of patients present with acute respiratory failure

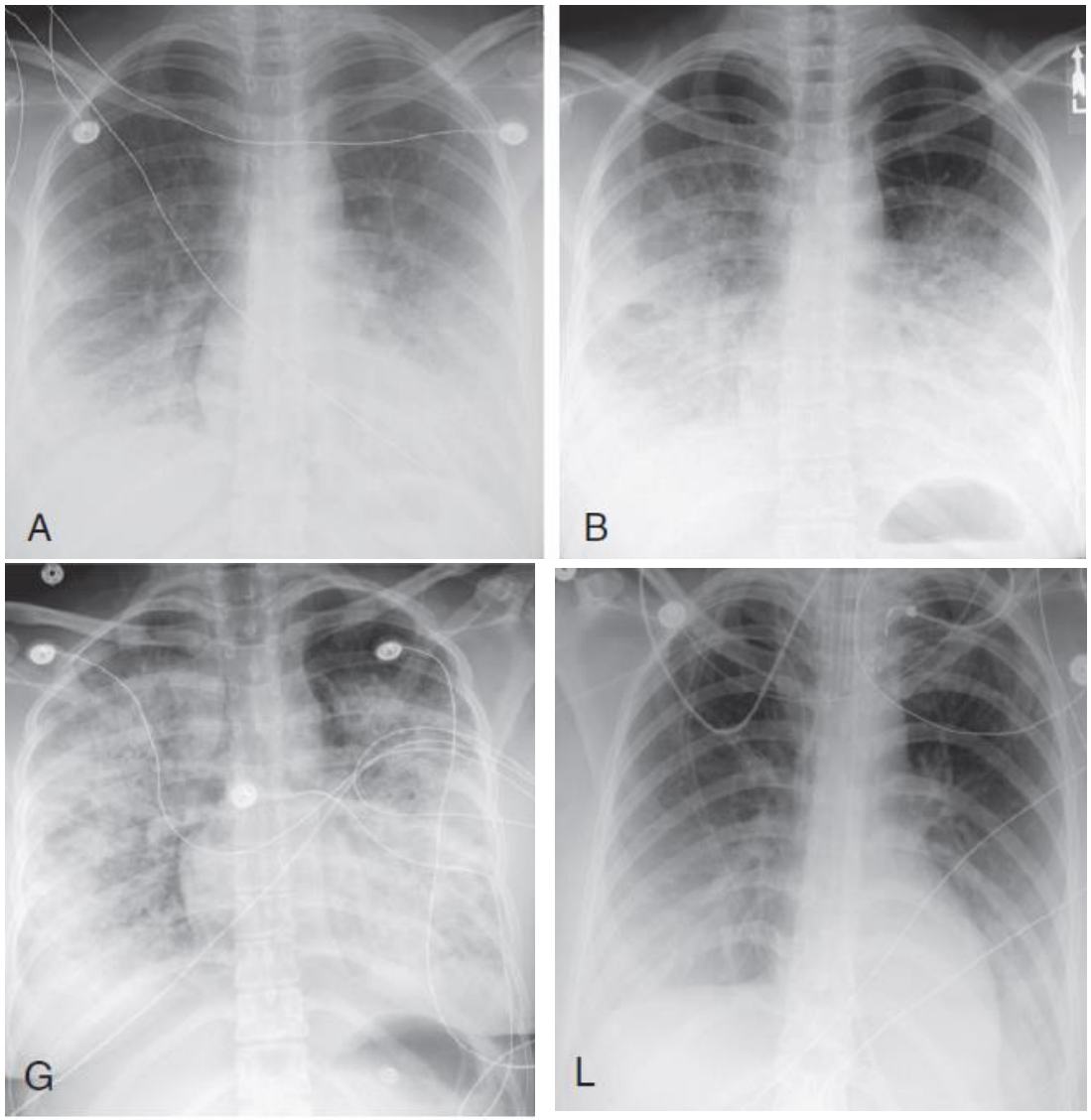
# Diagnosis of AEP

- Not always having peripheral eosinophilia
- Usually initial leukocytosis with neutrophilia → eosinophil count often rises to high values later during the course of disease
- Clincal diagnosis by BAL: Eosinophils > 25-40%
- HRCT: GGO, consolidations, interlobular septum thickening, pleural effusion → many of the features overlap with those found in cryptogenic organizing pneumonia
- Histology (if performed) : Eosinophils and diffuse alveolar damage

# Treatment and prognosis of AEP

- Good response to steroids (generally within 3days)
- IV MPd → changed to oral therapy that can be tapered over 2 to 4 weeks
- The chest radiograph usually normalizes within 1 wk in 85% of patients
- Recovery without corticosteroid treatment has been reported
- No relapse after stopping corticosteroid treatment

# Chest imaging of AEP




Murray and Nadel's Textbook of respiratory medicine

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# Antisynthetase syndrome (ASS)

- A group of related connective tissue disease characterized by
  - ✓ Inflammatory myopathy
  - ✓ Interstitial lung disease (ILD) – 70%
  - ✓ Presence of antibodies to the aminoacyl-tRNA synthetase (anti ARS antibody)
  - ✓ Arthralgia – 62%
  - ✓ Skin hyperkeratosis (mechanic's hands) – 28%
  - ✓ Raynaud phenomenon – 47%
  - ✓ Fever – 43%

Lega et al. Autoimmunity Reviews 13 (2014) 883–891

# Antisynthetase antibodies

- Targeted against cytoplasmic enzymes responsible for the formation of complex between aminoacyl-tRNA and its aminoacid which is a key step in protein synthesis

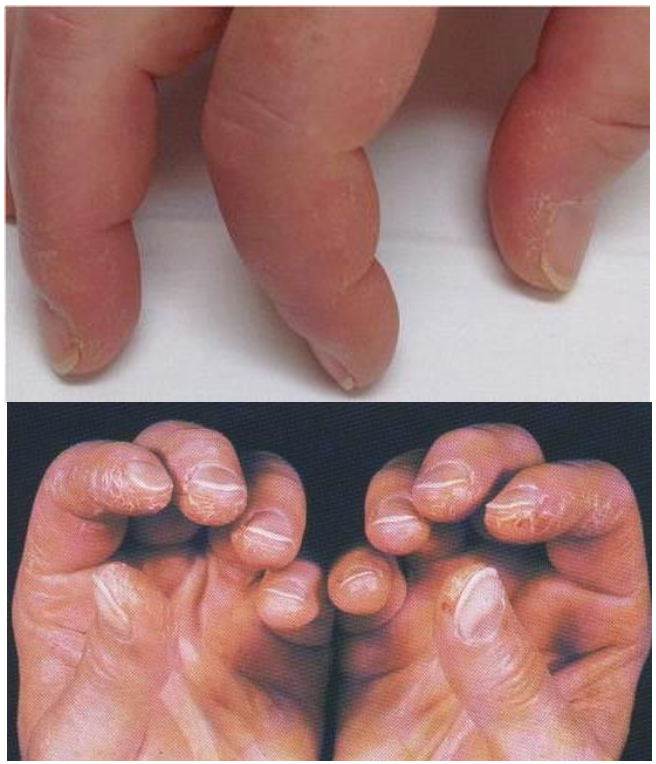
- Anti-Jo-1 antibody
  - (+) in approximately 75% of patients with ASS
  - Strong predictor for the development of ILD in patients with inflammatory myopathies

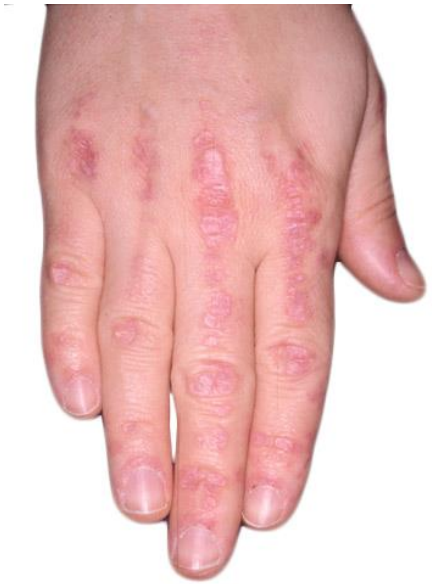
- Other common antibodies: anti-PL-12  and anti-PL-7

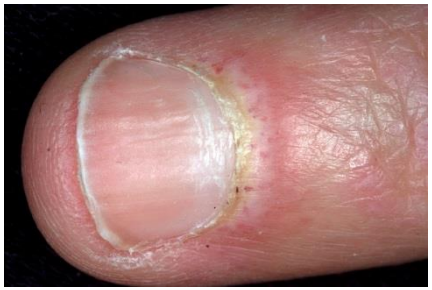
# Inflammatory myopathies

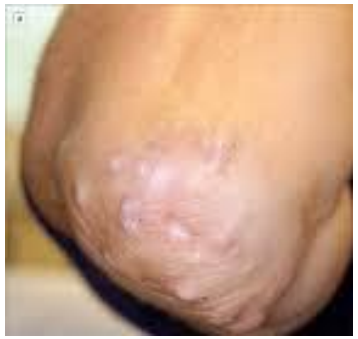
- Dermatomyositis: skin involvement (+)
- Polymyositis: skin involvement (-)
- Proximal and symmetric muscle weakness, muscle tenderness and muscle pain or myalgia
- Amyopathic dermatomyositis:
  - ✓ skin change only
  - ✓ no evidence of myositis

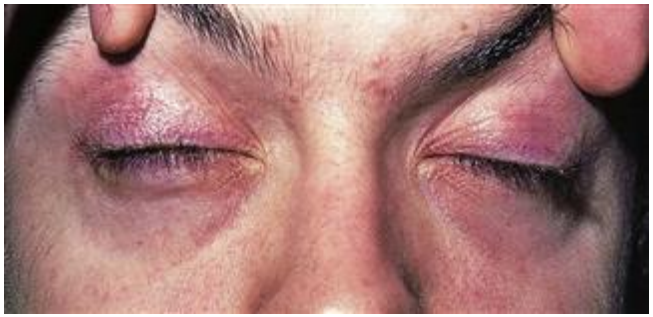
# Skin lesions of dermatomyositis





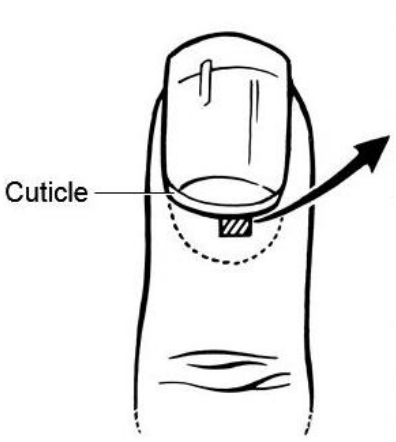


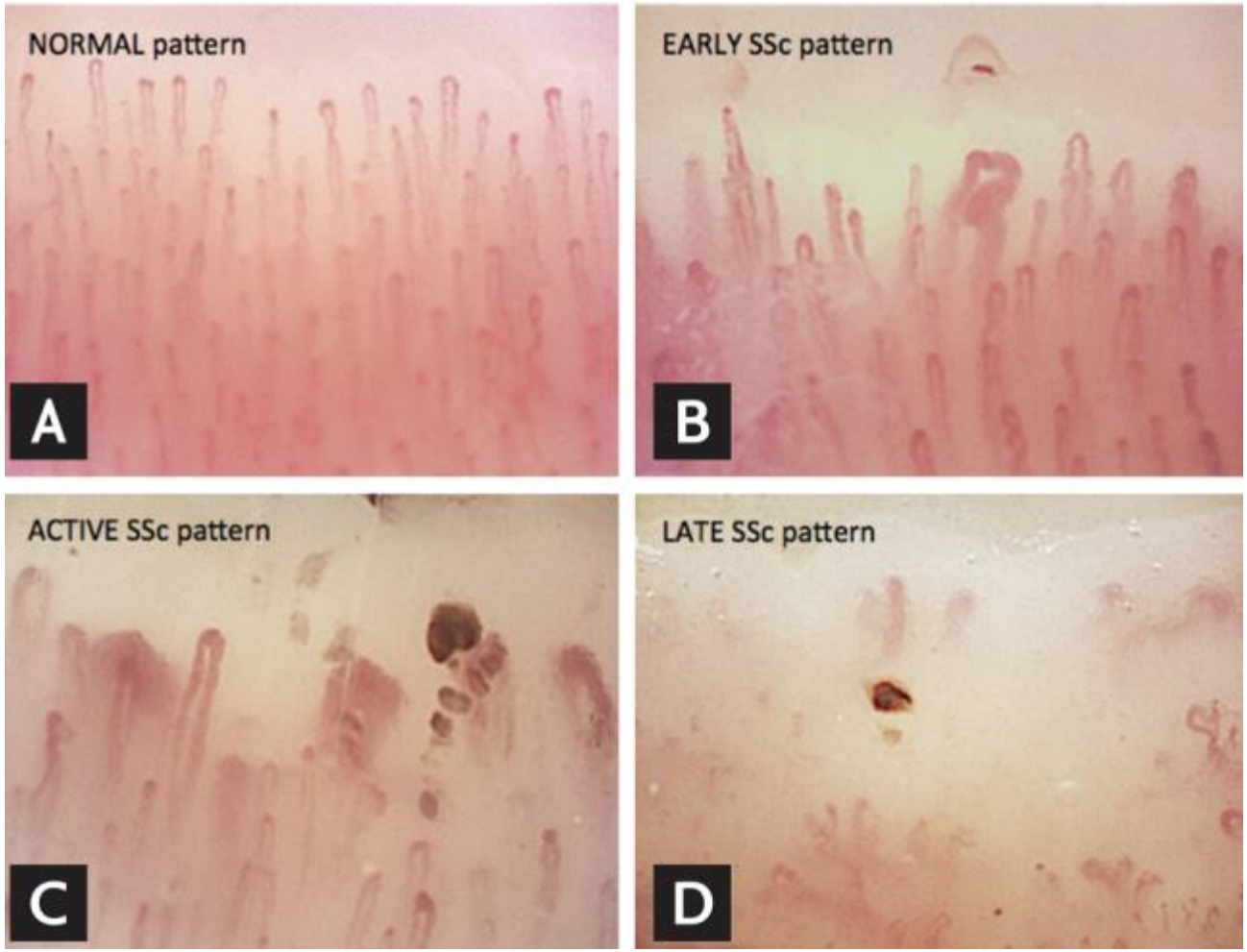




- Heliotrope rash: over eyelids (seldom seen in adults)
- Gottrons papule: erythema over MCPs, PIPs, MTP, knees, elbows
- V-neck rash
- Periungal erythema (periungual telengiectasis)
- Calcinosis

# Nailfold capillaroscopy




- SSc 82-94%
- DM 90-100 %
- SLE: 2-92 %
- MCTD: 54 %

Ruaro et al. KJIM 2015;30(1):1-5.

# ILD in ASS

- ILD may precede / coincidence/ develop after the occurrence of inflammatory myopathy
- Acute or subacute (~ 40%) / gradual / no symptom
- ILD is often the dominant symptom in patients with ASS, and drives the prognosis and response to therapy.
- Symptom: cough, dyspnea, fever, fatigue, weight loss
- Anti-CADM-140 Ab: severe ILD
- Worse prognosis than patients with ASS without ILD

# Evaluation of ASS

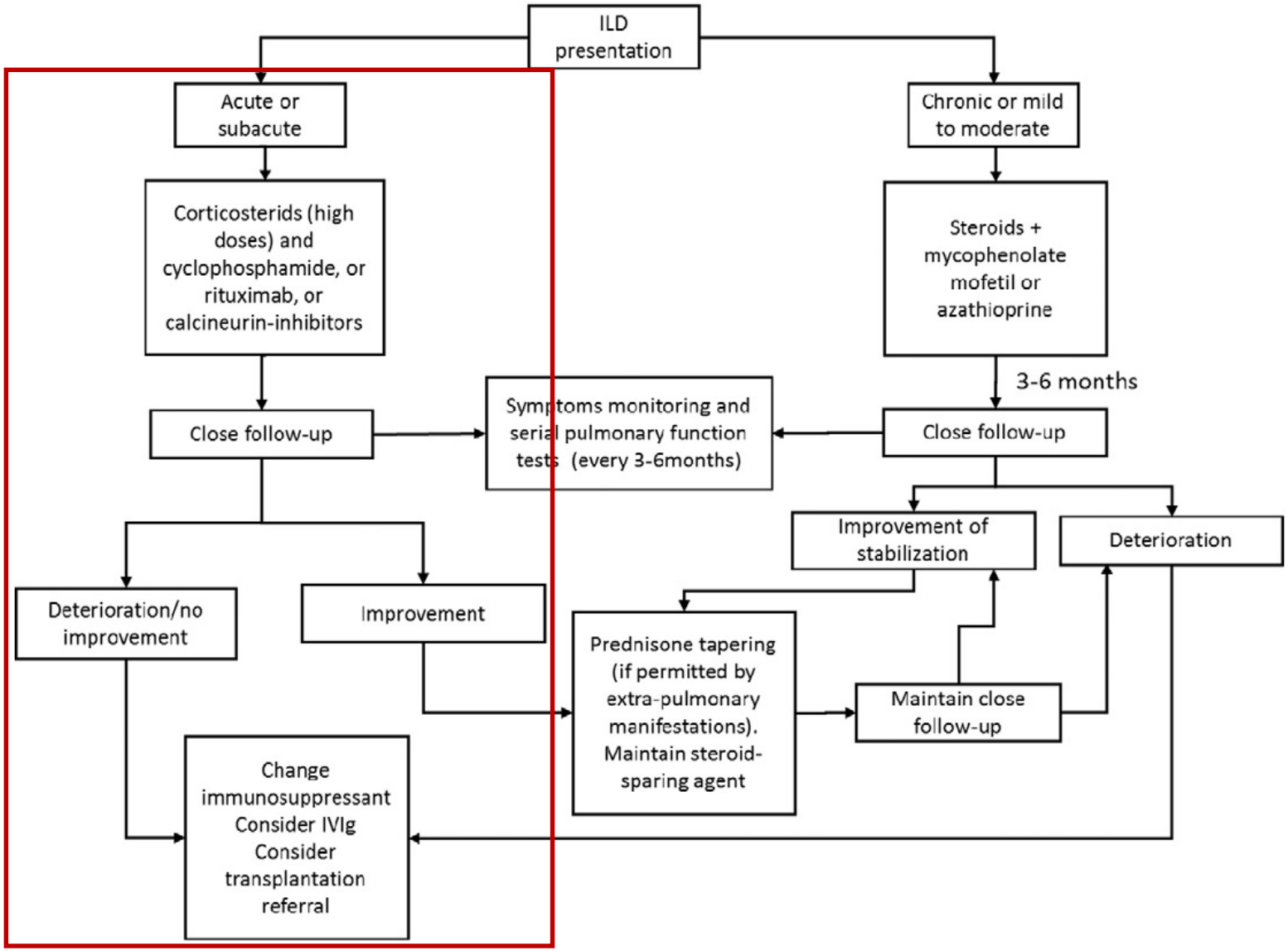
- Presence of anti ARS Ab

- Laboratory finding suggesting myositis
  - Elevated CK, aldolase, AST, ALT, LDH
  - CKMB and troponin T can be elevated
  - The degree of muscle enzyme elevation doe snot correlate with overall prognosis and response to treatment

- Electromyography (EMG), MRI, biopsy for myositis

- HRCT: nodules, linear opacities, GGO, consolidation, fibrosis, bronchiolectasis, etc

# Treatment of ASS




Morisset J et al. Management of myositis-related ILD . Chest 2016;150:1118–28.

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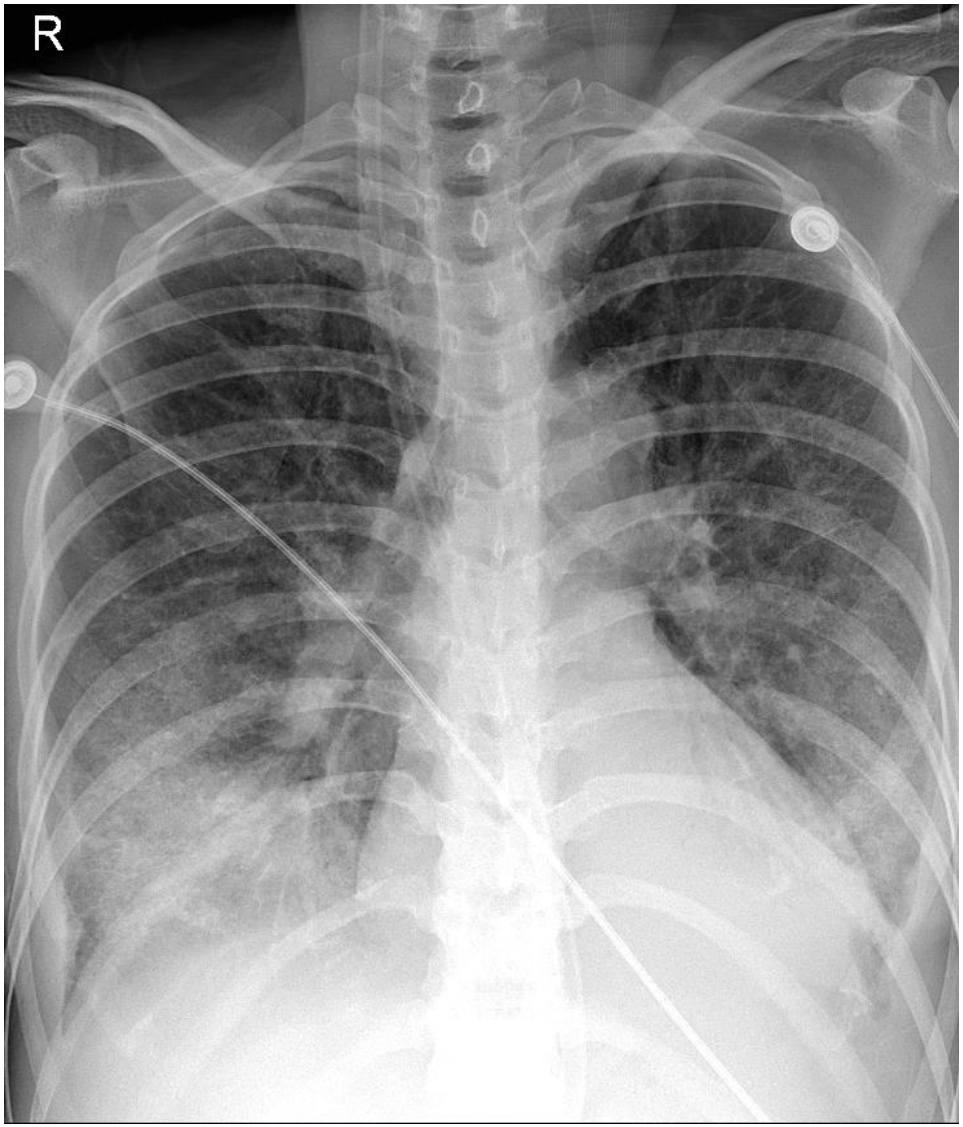

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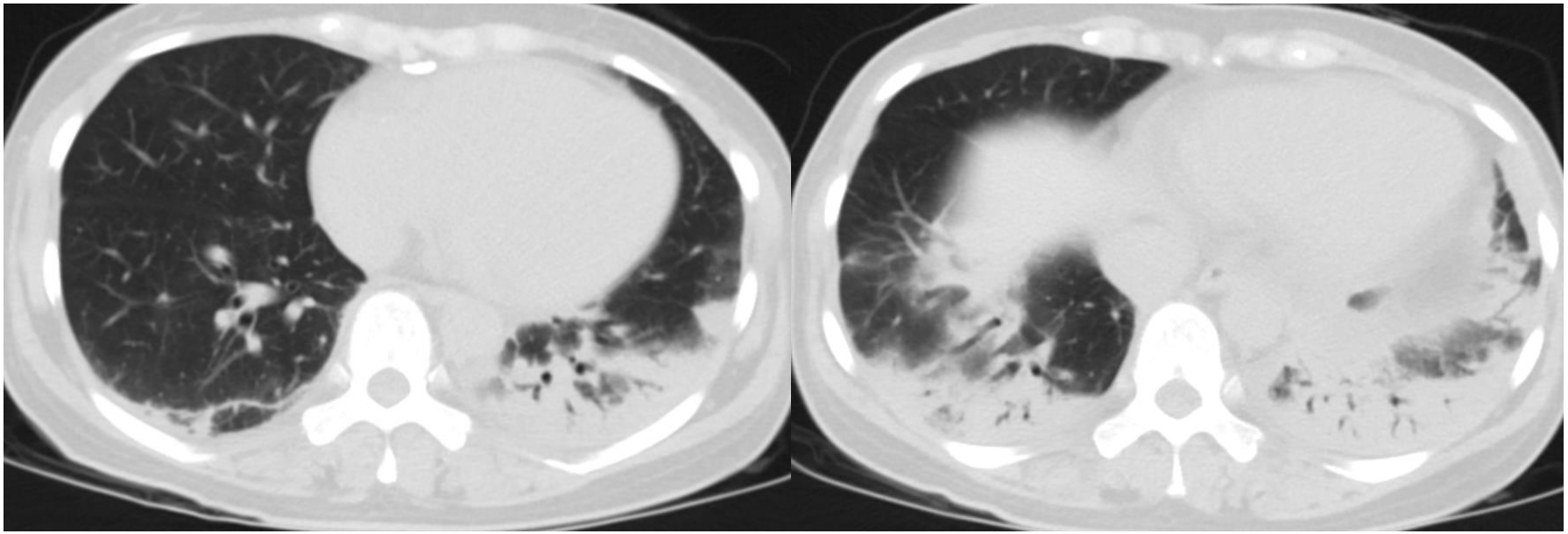
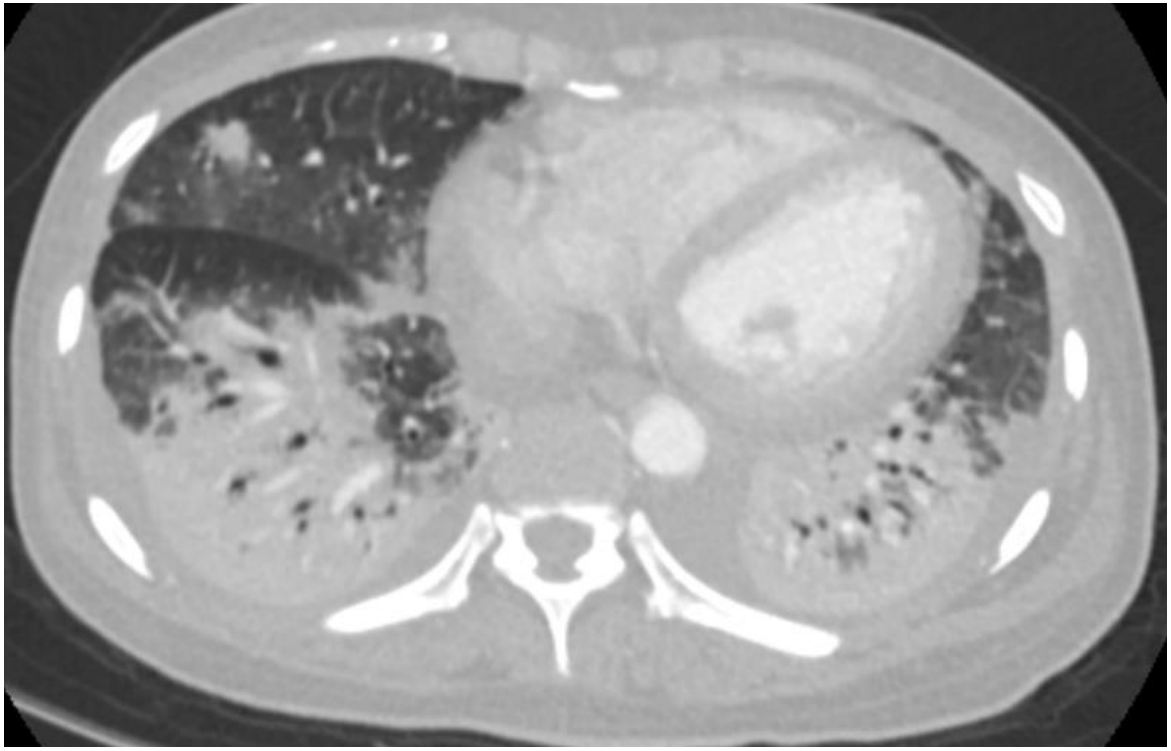


문진상 전신 관절통 및 근육통 있었음. 아침마다 38도의 발열 동반되었다고 함. 신체 검진상에서 피부의 rash는 관찰되지 않음. 손가락 측면에서 mild mechanic's hands소견이 관찰됨.

Initial ER Lab> ABGA: 7.45-29-55-20.2-Spo2:90% (O2: NP 4L)
CBC: 20470-13.9-151K (Seg: 89%) CRP: 9.2
ALP 159 AST/ALT: 467/258 CK/CK-MB/TnI: 5781/85/0.11 LDH: 2189
PT INR: 0.99 D-dimer:69 ESR: 24 myoglobin 2213

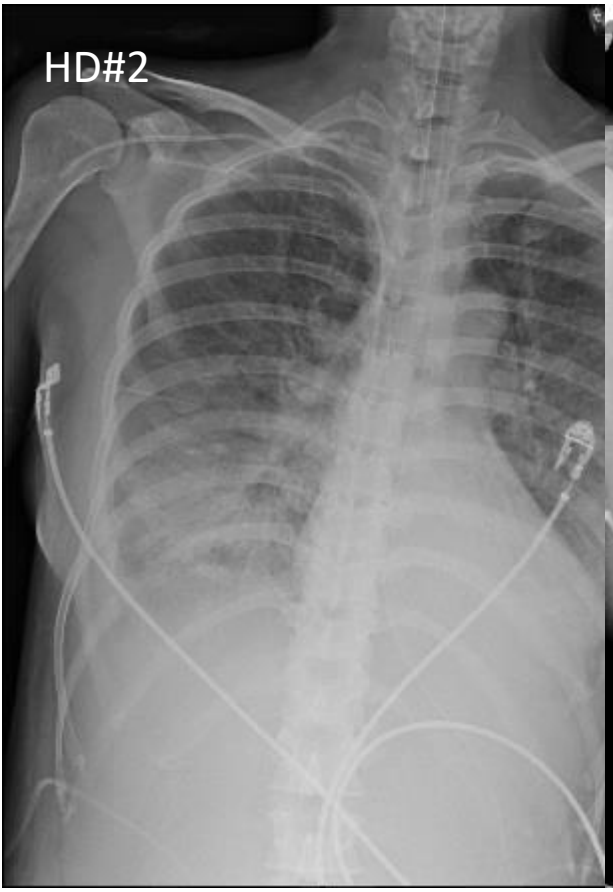


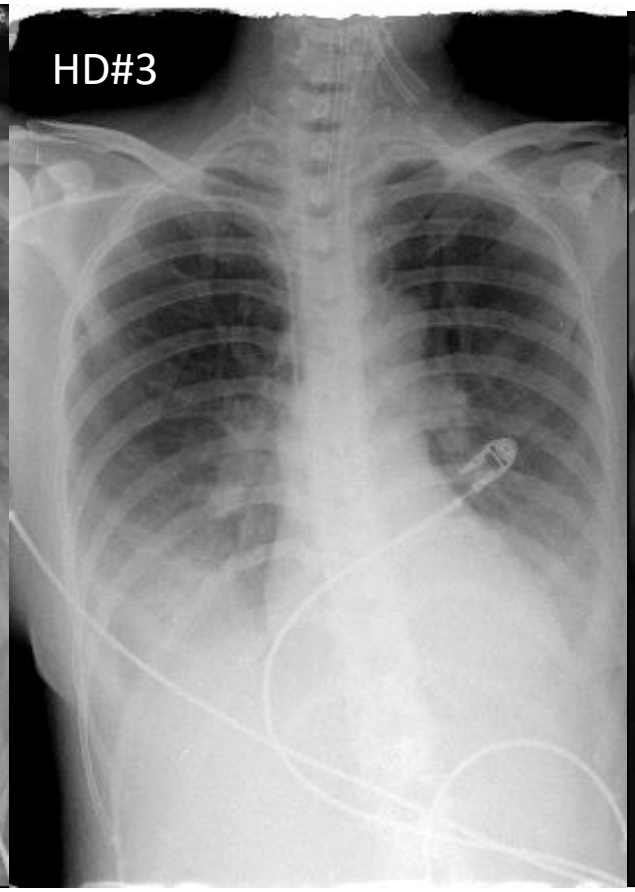
Chest CT
- R/O organizing pneumonia combined with pneumonia
Small amount of pericardial effusion.

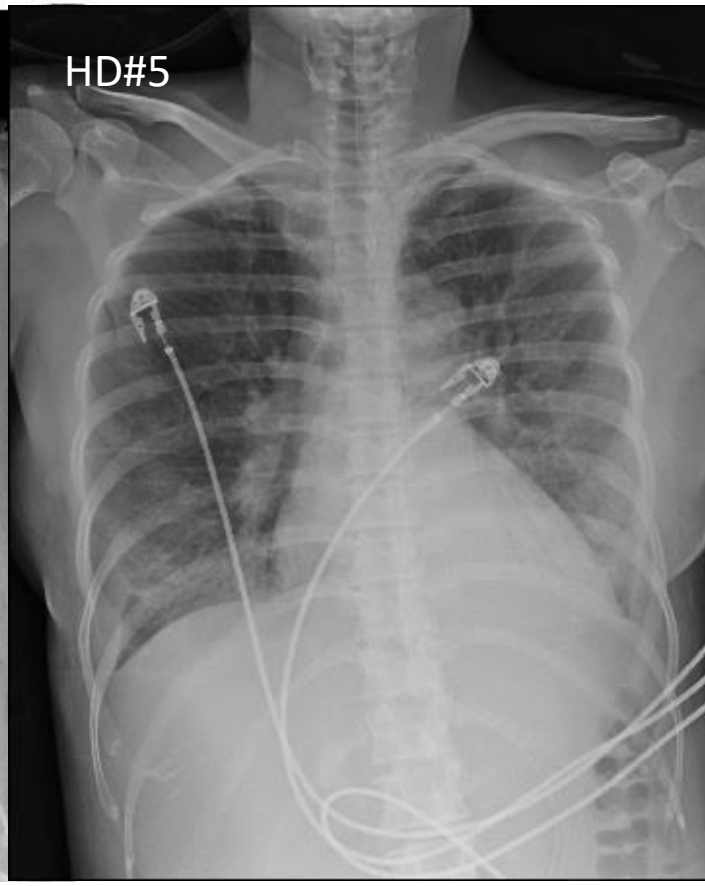
ER 내원 당일 type I respiratory failure 진행하여 Facial mask 10L에서 SpO2 89%소견 보여 ICU 입실, intubation및 MV 시작함.

elevated muscle enzyme, myalgia, arthralgia, fever, mechanic's hands
→ R/O antisynthetase syndrome

임상적으로 급격한 악화를 보이고 있어 류마티스 내과와 협진하여 검사를 진행하면서 steroid 투약을 시작함.




meropenem+ levofloxacin
MPd 125mg 투약 시작

Extubation

Anti-CCP +16.4 RF : +, 24
ANA : 1:80, Discrete speckled pattern (centromere)
Anti Jo1 + 4.6
Anti RNP, Smith, Ro/La : negative
Aldolase : 55.2 C3/C4 : 81/38 Anti ds DNA : 5.3
Anti cardiolipin IgM/IgG : -/-
Anti Scl 70 : negative

HD #6 2013.10.21 Thigh MRI
Diffuse left thigh abnormalities: scattered muscle edema and enhancement in random distribution - circumferential fascial enhancement of sartorius, gracilis and semitendinosus- mild subcutaneous septal accentuation->> More likely polymyositis

EMG/NCS:
There is electrophysiologic evidence of myopathy, which is compatible with inflammatory myopathy.

Muscle biopsy:
Consistent with myopathy with tubuloreticular bodies

# Contents

# Summary

When you see a patient with acute-subacute onset ILD..

- Thorough evaluation of possible causes of ILD is essential !!

- Idiopathic interstitial pneumonia
  - COP: pneumonia-like illness, good response to steroid
  - AIP: poor prognosis, no proven treatment
  - Acute eosinophilic pneumonia: BAL eosinophilia, good response to steroid

- Anti-synthetase syndrome
  - Triad: arthritis, myositis, ILD + fever, mechanic's hands
  - Evaluation: Anti-Jo 1 Ab, muscle enzyme, MRI, biopsy, etc.
  - Rapid progressive ILD requires aggressive treatment with high dose steroid + additional immunosuppressant

**Thank you for your attention**