Case Presentation

A 62 year-old woman with dyspnea for 4 months

R3 배병주

History

62/F

- **Chief Complaint** : Dyspnea (remote onset : 5 YA)
  (recent aggravation : 4MA)
- **Present illness**
  - 5YA - generalized edema, dyspnea
  - 4MA - aggravation
  - O/S hospital w/u : Thoracentesis, Echocardiography (Normal)
  - **Med & Tx** : digoxin, carvedilol, diuretics(furosemide, spironolactone) but continued to experience leg swelling and required two thoracenteses over the years for relief of dyspnea

- **Review of systems ：**

G/W (-) Fatigue (-) Fever/Chill (-/-)
Poor oral intake (+) Wt. loss (+) 7kg/ 4mon

HA/ Dizz (-/-) Sore throat (-)

Cough/ Sputum/ Rhinorrhea (+/+/-) Dyspnea (+)
A/N/V/D/C (-/-/-/-/-) Abdominal pain (-) H/M (-/-)

Frequency/Urgency/Dysuria (-/-/-)
Oliguria/Polyuria/Hematuria (+/-/-)

Physical examination

V/S : 136/65mmHg – 84/min – 20/min - 36.0°C

G/A : Chronic ill looking appearance, Alert mentality,
Afebrile state

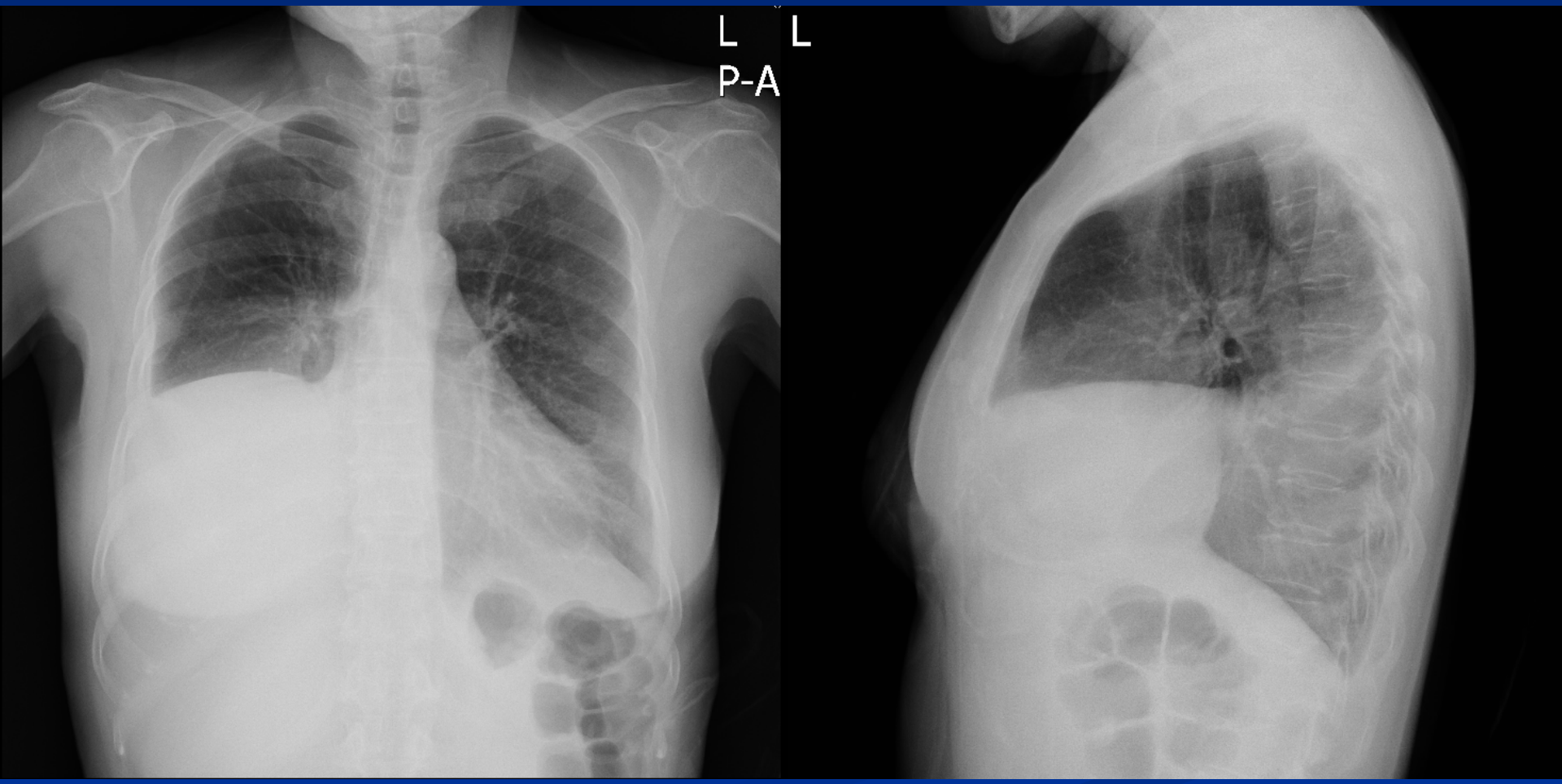
HEENT : Anicteric sclera, Not pale conjonctiva, No
dehydrated tounge & lips, No tonsilar hypertropy
s exudate, No pharyngeal inject, No JVD, No carotid bruit

Chest : Decreased BS, RLL
Dullness with decreased fremitus on the right
No wheezing
RHB s murmur

Abdomen : Free

Back & extrimity : No cyanosis or clubbing, 1+ pretibial pitting edema
Thick & short nails with color change,
cross-ridging and onycholysis

Initial CXR (2009.3.30)



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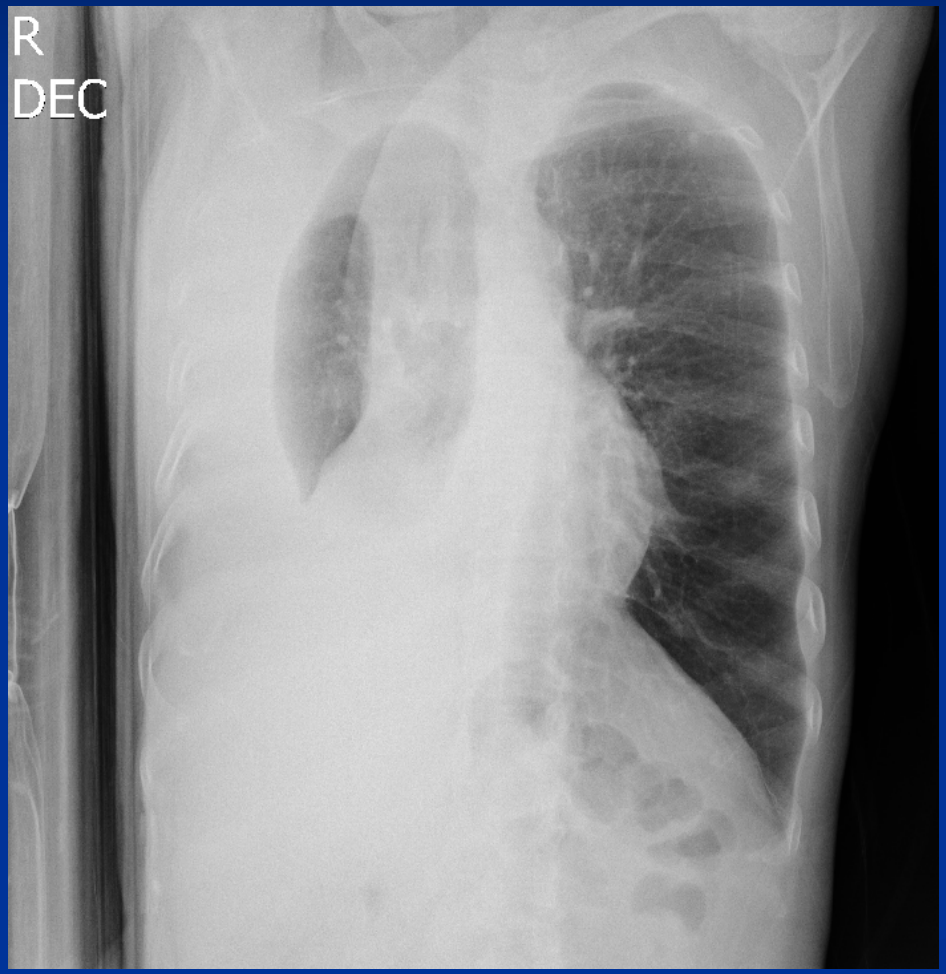


Initial assessment

- Exudative pleural effusion
  - #1. R/O Malignant pleural effusion
  - #2. R/O Rheumatoid pleurisy (SLE..)
  - #3. R/O Hypothyroidism
  - #4. R/O Transdiaphragmatic movement (ascites, hepatic and pancreatic diseases)
- Transudative pleural effusion
  - #5. R/O CHF
  - #6. R/O Nephrotic syndrome

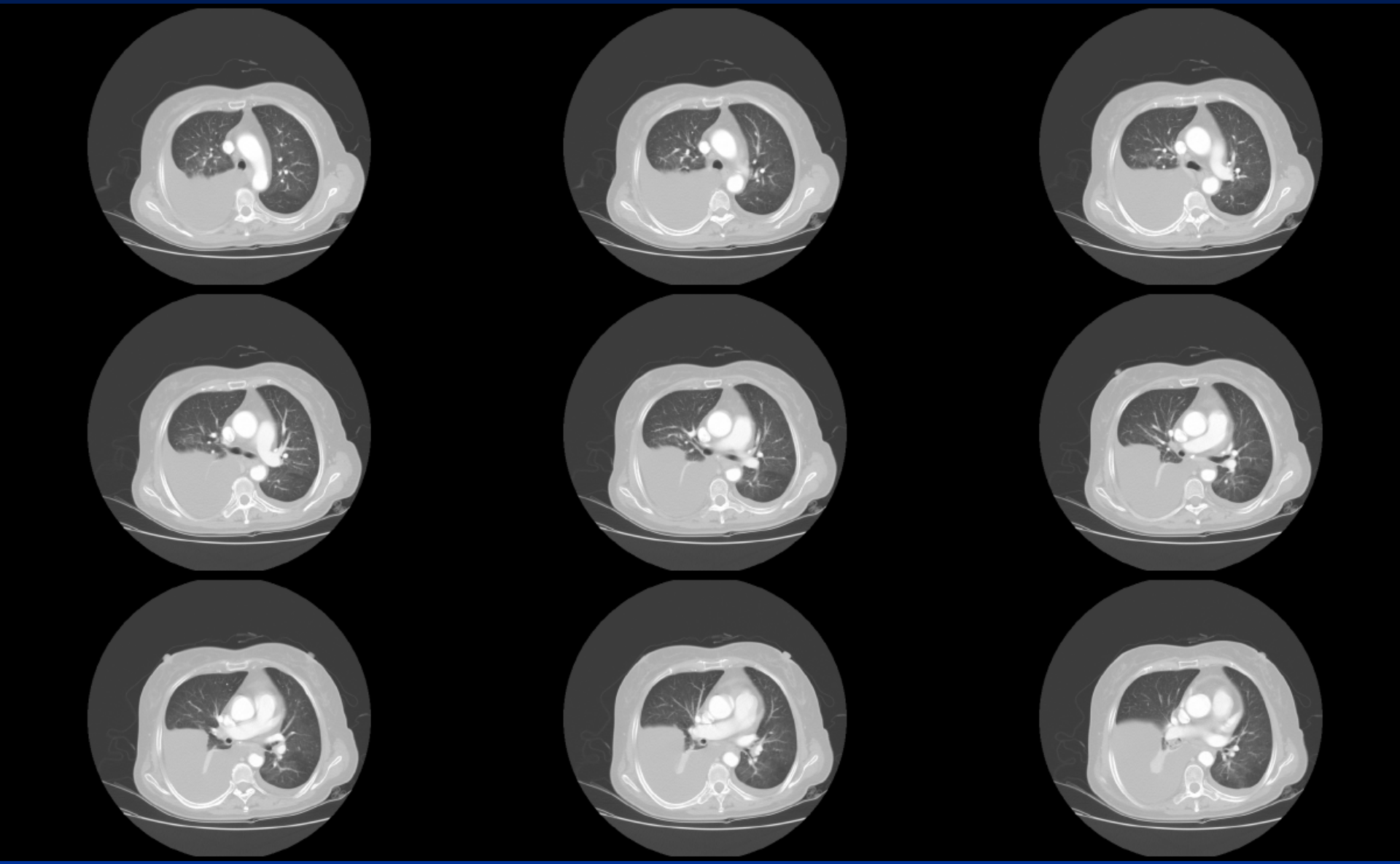
Initial plan

- #1. → Pleural fluid analysis, Chest CT, Bronchoscopy, Pleural biopsy, PET CT
- #2. → Rheumatologic serology
- #3. → TFT
- #4. → Abdomen CT, LFT, Amyalse, Lipase
- #5. → Echocardiography, NT-pro BNP
- #6. → Serum albumin level, Urine analysis, 24hr urine collection

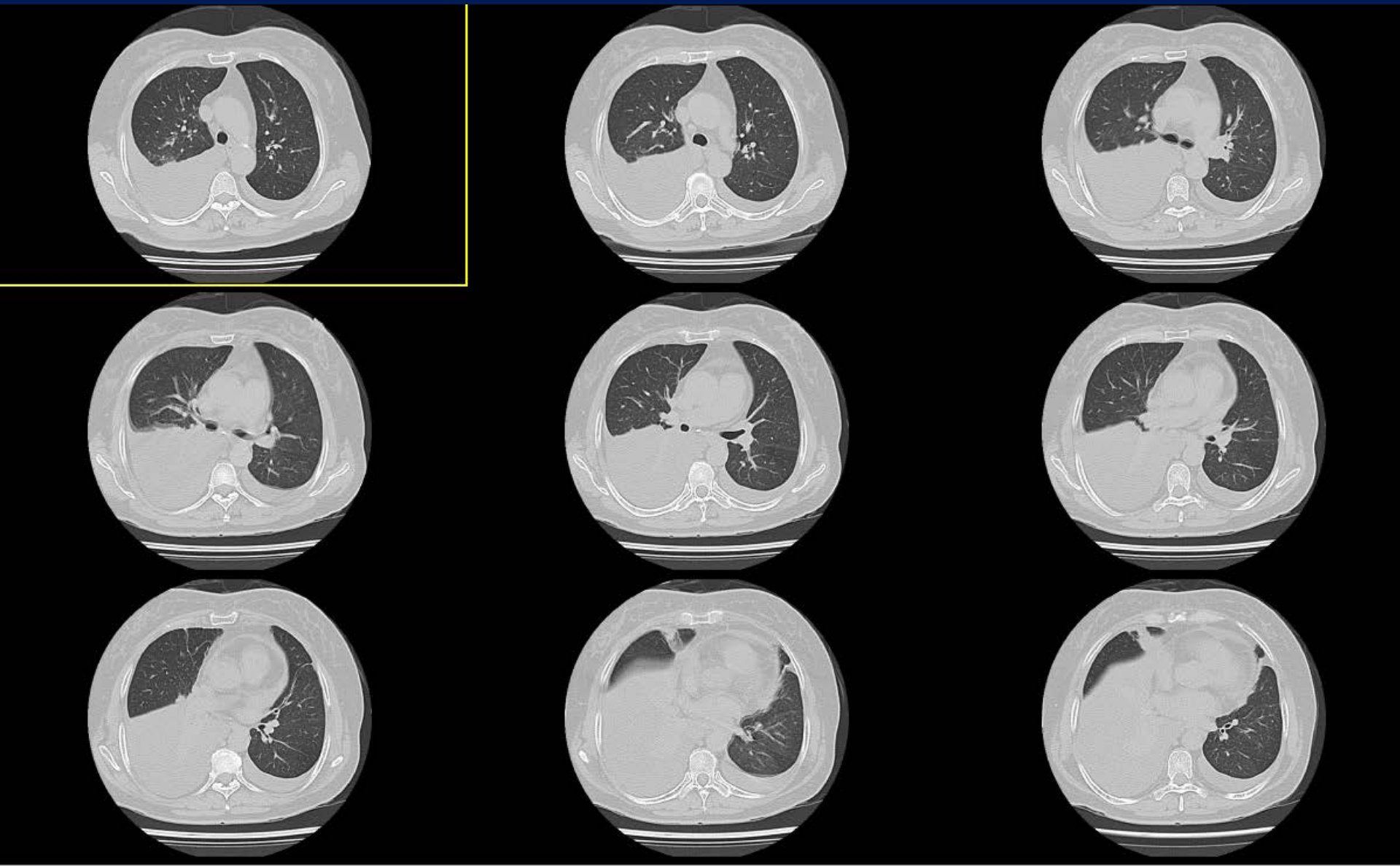
- **Initial laboratory finding :**
  - CBC : 6660-13.9/39.0-358k (Seg. 75.5%)
  - T.prot/alb 8.1/4.5 AST/ALT 29/14 ALP 88
  - BUN/Cr 39.8/1.3 Na/K/Cl 133/5.4/101
  - ESR : 57mm/h
  - CRP : 0.26mg/dl
  - PT INR 1.07, PT 90%, aPTT 37.0sec
  - U/A : Straw color, S.G. 1.020, pH 6.5, Prot trace
  - NT-pro BNP : 108.8pg/ml
  - TFT : Free T4 1.90ng/dl, TSH 0.760 μIU/ml

- Pleural fluid analysis : Exudate
  - pH 7.5
  - Yellow, clear
  - RBC 0, WBC 458 (Nø 1%, Lø 66%)
  - Prot 6.0, Glu 83, LDH 149
  - ADA : 33.4IU/L, CEA : 1.42 ng/mL, Amylase : 30
  - Cytology : No malignant cell
  - M. TB PCR : Negative, AFB Sm (-)

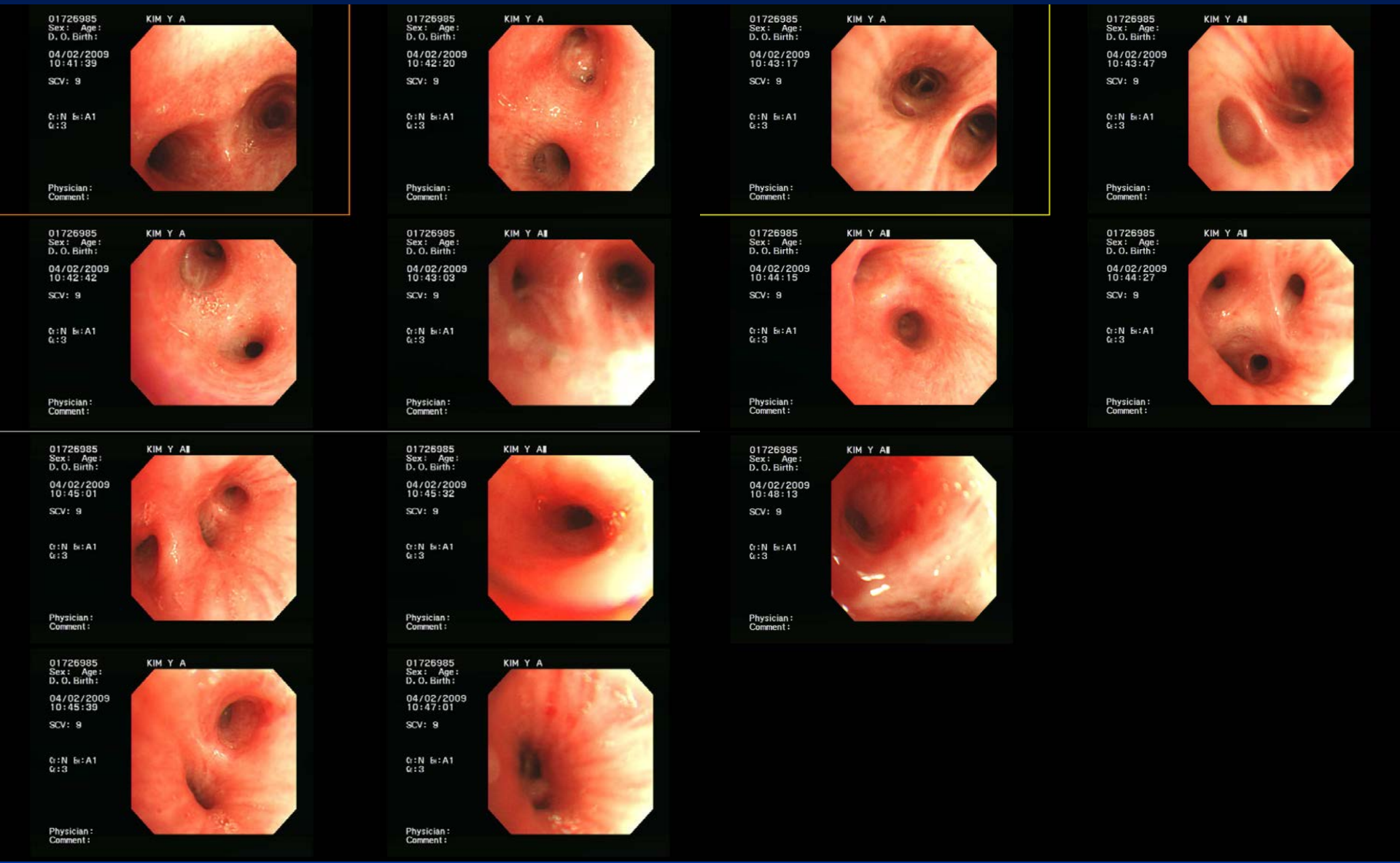
Initial CT (2009.3.30)



Previous CT (2008.11.14)



Bronchoscopy (2009.4.2)



Echocardiography (2009.4.2)

- LVEDd/s 38 / 17mm, LVEF 87 % by M-mode
- Normal LV systolic function
- No regional wall motion abnormality
- Normal LV wall thickness
- Small amount of pericardial effusion (posterior only, depth 10mm)

VATS (2009.4.3)

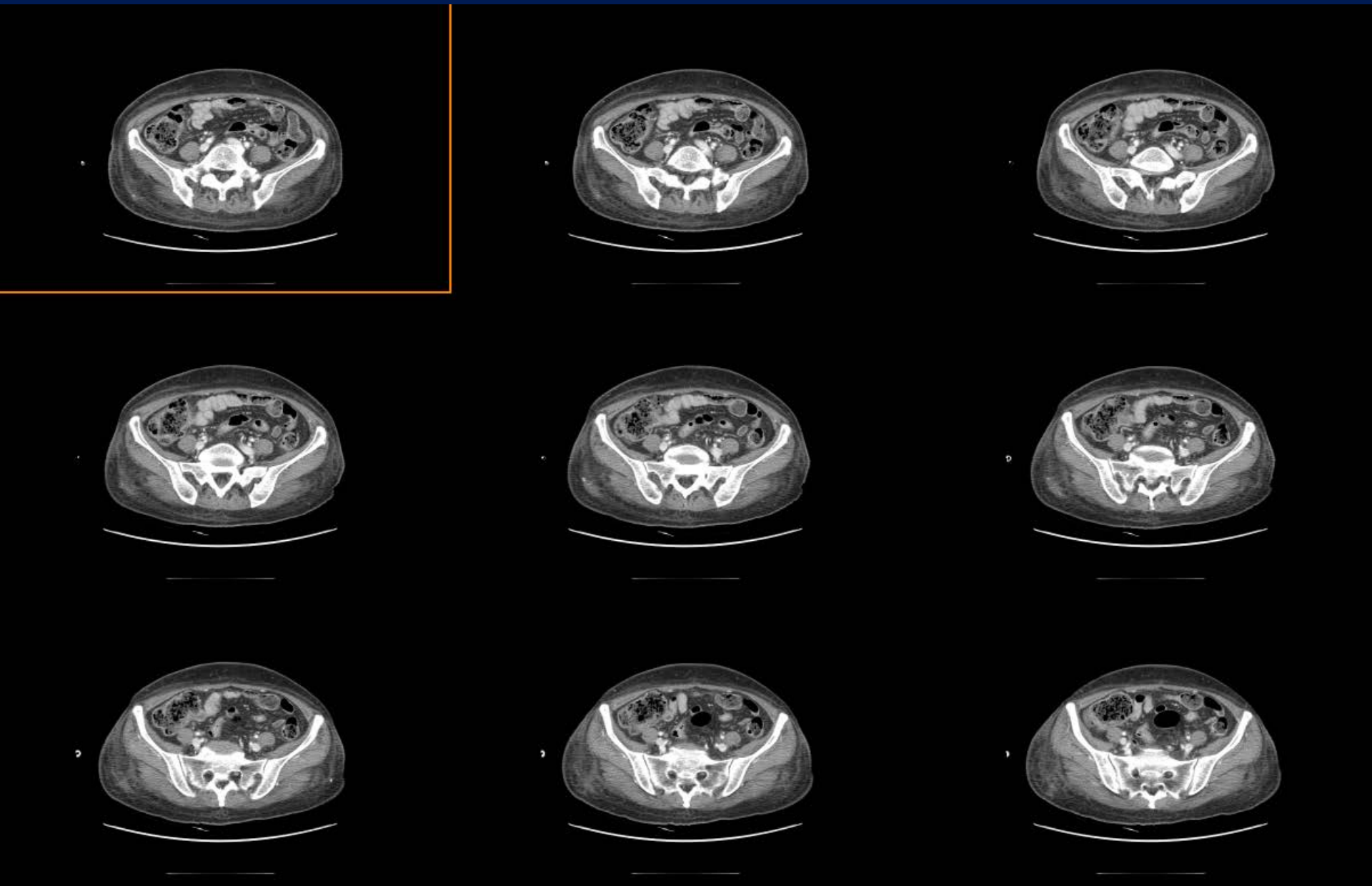
- Pleural biopsy

Inflamed pleura with focal myxoid degeneration

Rheumatologic Lab

- Anti-nuclear Ab : (+), 1:40(Speckled)
- Anti-ds-DNA Ab : (-)
- Anti-CCP Ab : (-)
- RA : 3 IU/mL
- ANCA : (-)
- HLA B27 : (+)
- C3/C4 : 101/ 40.20 mg/dl
- CH 50 (Complement Hemolytic Activity) : 45.0
- Ig A / M / G : 144.0 / 115.0 / 1569.0 mg/dl

Abdomen CT(2009.4.6)



Assessment

- R/O Diuretics induced edema & pleural effusion
  - Diuretics use for long-term

  → Mild hypovolemia

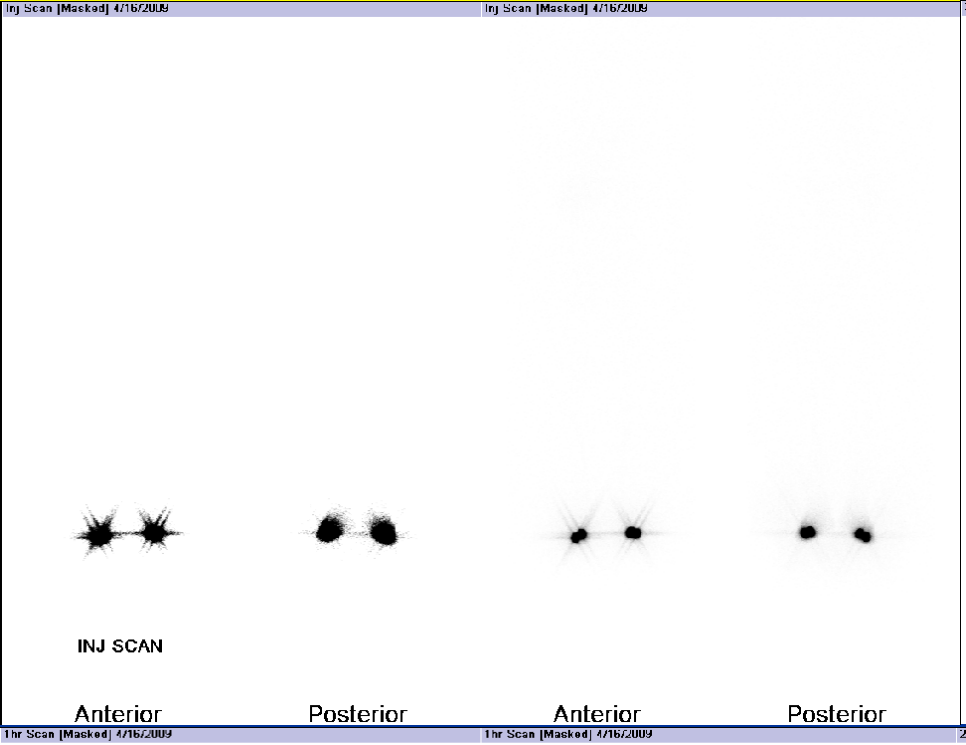
  → Renin ↑ → Aldosterone ↑

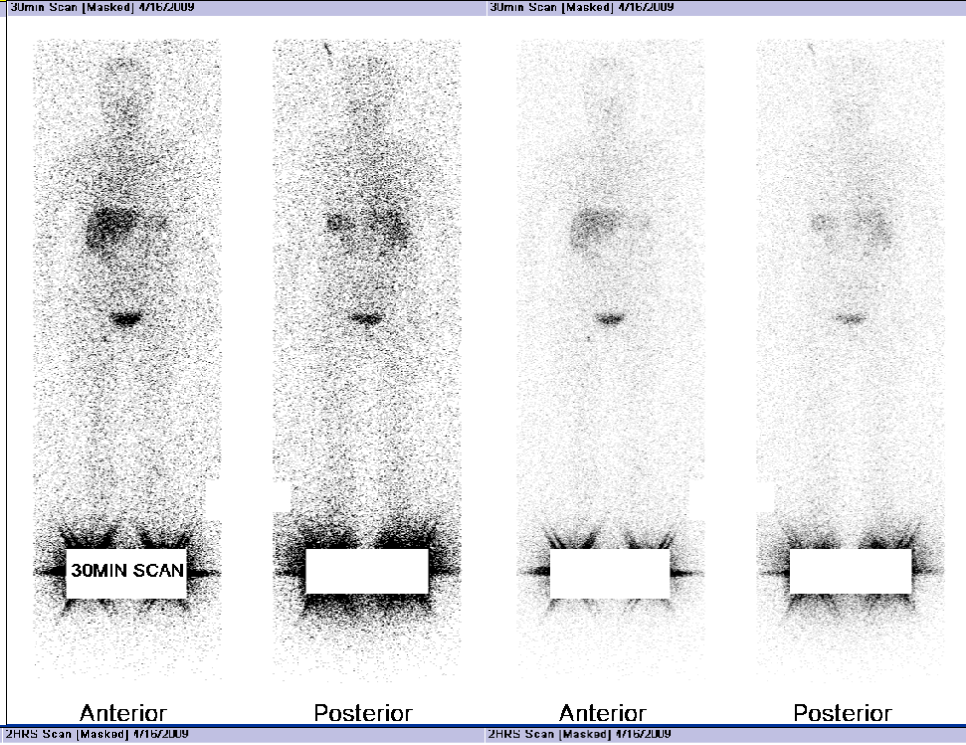
  ** Secondary aldosterism

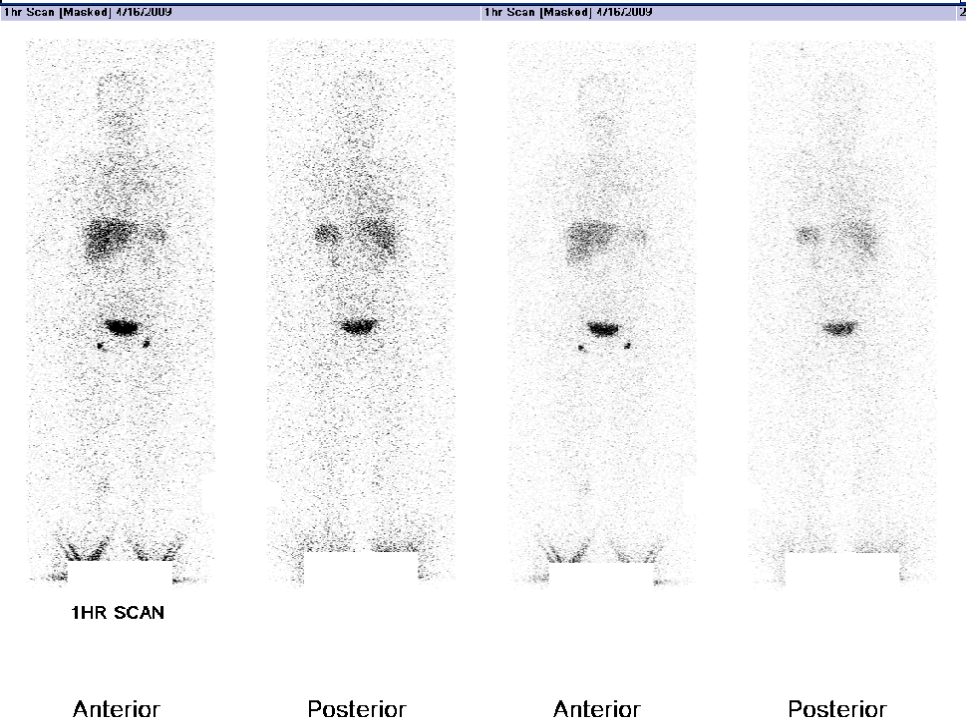
  → Aggravation of edema due to diuretics cessation

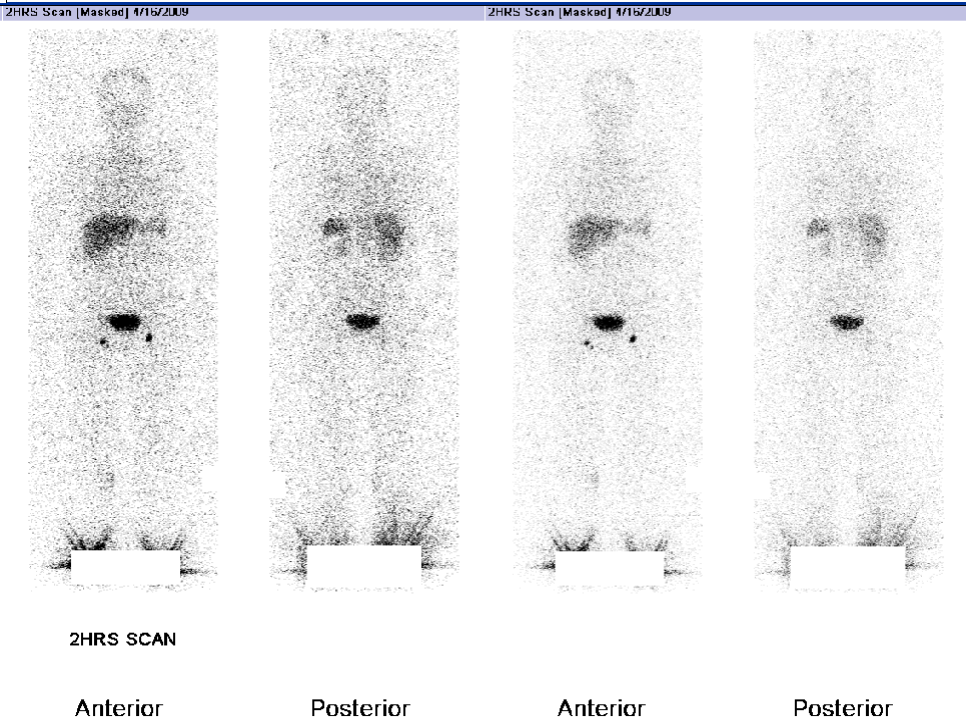
Assessment

- Yellow & thick nails
- Generalized edema
- Recurrent pleural effusion



Inj Scan [Masked] 4/16/2009
Inj Scan [Masked] 4/16/2009
INJ SCAN
Anterior
Posterior
Anterior
Posterior


30min Scan [Masked] 4/16/2009
30min Scan [Masked] 4/16/2009
30MIN SCAN
Anterior
Posterior
Anterior
Posterior


1hr Scan [Masked] 4/16/2009
1hr Scan [Masked] 4/16/2009
1HR SCAN
Anterior
Posterior
Anterior
Posterior


2HRS Scan [Masked] 4/16/2009
2HRS Scan [Masked] 4/16/2009
2HRS SCAN
Anterior
Posterior
Anterior
Posterior

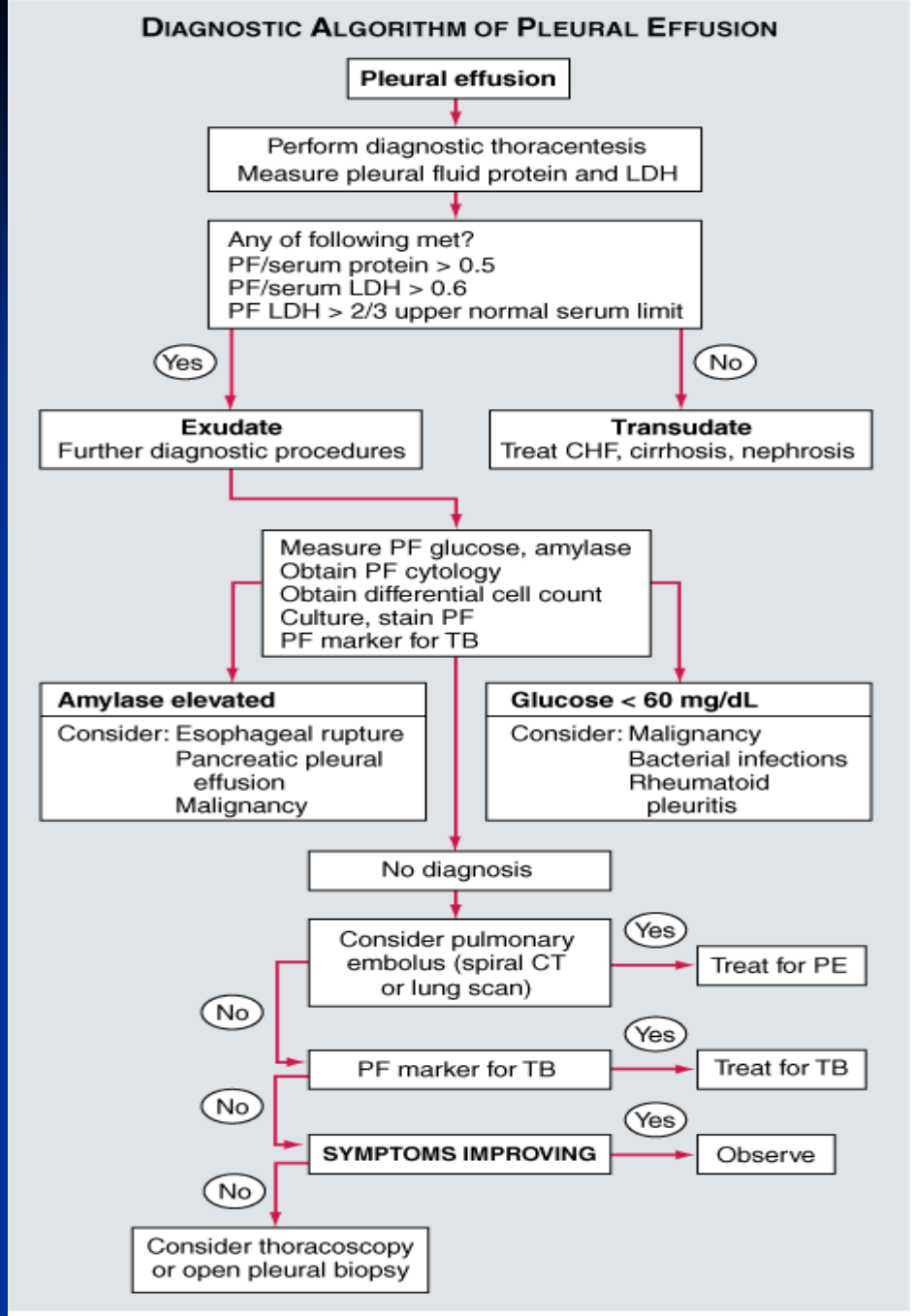
Final Diagnosis & Plan

- **Final Diagnosis**
  - Yellow nail syndrome
- **Plan**
  - Symptomatic Pleural effusion
    - Drainage via chest tube
    - Pleurodesis
  - Lymphedema management
  - Nail menifestation

Topic Review

Undiagnosed Pleural Effusion

R3 배병주



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Transudate

- Congestive heart failure
- Hepatic hydrothorax
- Nephrotic syndrome
- Peritoneal dialysis
- Hypoalbuminemia
- Urinothorax
- Constrictive pericarditis
- Trapped lung
- Superior vena caval obstruction

Exudate

- Infection ; Pneumonia, Tuberculosis
- Iatrogenic causes ; Drug…
- Malignancy
- Other inflammatory disorders
- Increased negative intrapleural pressure
- Connective tissue disease
- Endocrine dysfunction
- Lymphatic abnormalities
- Movement of fluid from abdomen

Introduction

- **Undiagnosed pleural effusion**
  - Up to 25 percent of patients
- **Attention**
  - Patient's history
  - Drugs
  - Occupational exposures
  - Risk factors
    - Pulmonary embolism
    - Tuberculosis
    - Comorbid conditions

Differential diagnosis by time course

- **Persistent**

1. Malignant pleural effusion

- **Several months ~ years**

1. Rheumatoid pleurisy (SLE..)
2. Asbestos exposure
3. Radiation pleuritis

- **Several years**

1. Lymphatic abnormality (Yellow nail syndrome, Pulmonary lymphangiectasia)
2. Trapped lung

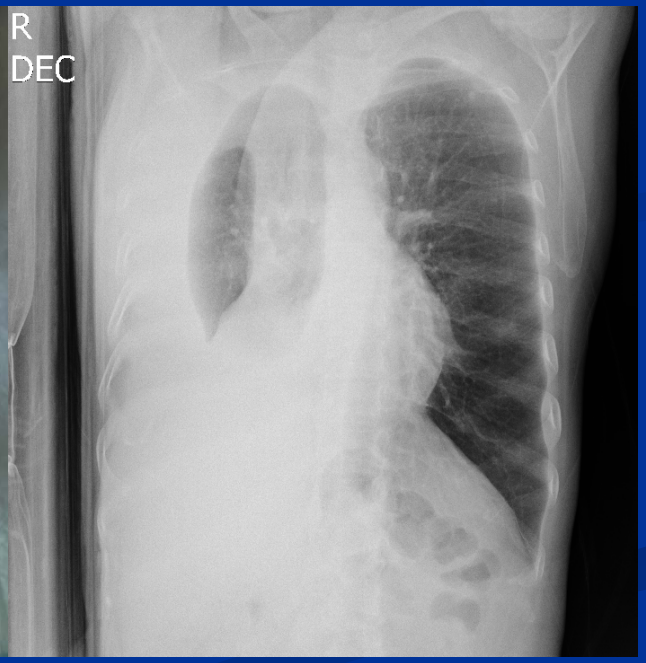
- **Others**

1. CHF
2. Hypothyroidism
3. Transdiaphragmatic movement
4. Drug : Nitrofurantoin, Amiodarone, Ovarian stimulation therapy

Diagnostic evaluation

- **Reanalysis of Pleural fluid**
  - Most undiagnosed pleural effusions : exudative
  - ADA, Interferon-γ
- **Imaging**
  - Enhanced CT, CT angiography, PET/CT
- **Pleural biopsy**
  - Closed/ CT-guided/ VATS/ Open pleural biopsy

Yellow nail syndrome



Introduction

- **Samman and White** first described "yellow nail syndrome" in 1964.

- **Clinical Triad**
  - **Yellow nails**
  - **Lymphedema**
  - **Chronic respiratory manifestations**

Clinical presentation

- **Characteristics of the nails**
  - Thickening
  - Slow growth (< 0.25mm/week)
  - Transverse ridging
  - Increased curvature with a "hump"
  - Onycholysis
  - Pale yellow to greenish color

Clinical presentation

Clinical presentation

- **Respiratory manifestations (60%)**
  - Pleural effusion (36%)
  - Bronchiectasis
  - Rhinosinusitis
  - Chronic cough or shortness of breath
  - Recurrent lung infections (Pneumonia)

Clinical presentation

- **Lymphedema (80%)**
  - Slowly progressive
  - Symmetric >> Asymmetric
  - Pitting or Non-pitting
  - Induration and hyperkeratosis extending to the thighs
  - Periodic lymphangitis
  - Contribute to the swelling

Demographic and Clinical Features

Table 1—*Demographic and Clinical Features of 41 Patients With YNS**

Characteristics	Data
Age, yr	
Median	61
Range	18–82
Gender	
Male	20 (49)
Female	21 (51)
Manifestations	
Yellow nails	41 (100)
Lymphedema	26 (63)
Chronic cough	23 (56)
Pleural effusions	19 (46)
Bronchiectasis	18 (44)
Chronic sinusitis	17 (41)
Recurrent pneumonias	9 (22)

Fabien et. al. *Chest* 2008;134;375-381

Radiologic Findings

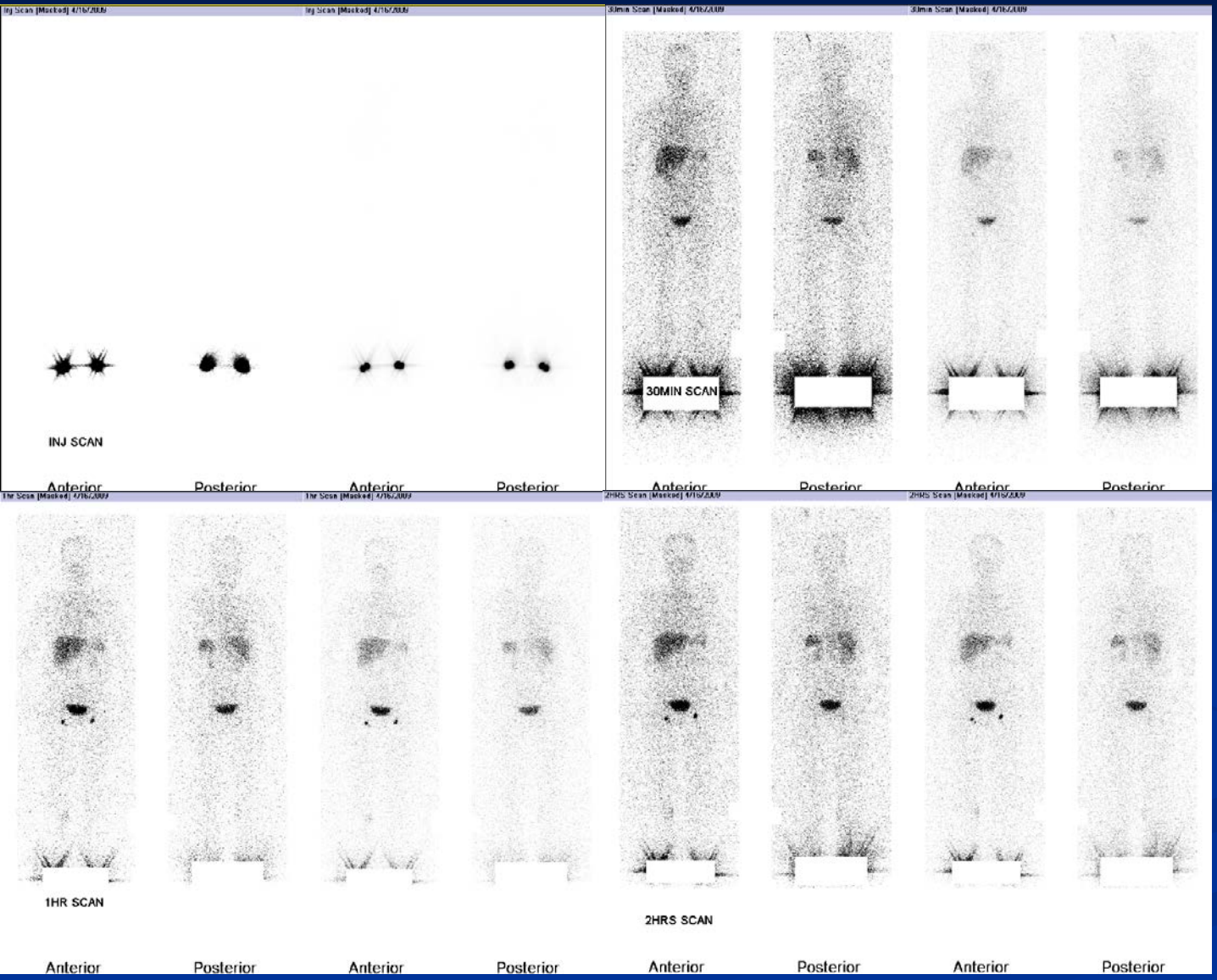
Table 2—*Chest CT Findings**

Characteristics	No. (%)
Bronchiectasis	18 (47)
Unilateral	3 (8)
Bilateral upper lobes	2 (5)
Bilateral lower lobes	11 (29)
All lobes	2 (5)
Pleural effusions	18 (47)
Bilateral	13 (34)
Unilateral	5 (13)
Localized parenchymal infiltrates	7 (18)
Intrathoracic lymphadenopathy	3 (8)
Pericardial effusion	3 (8)
Normal	3 (8)

*CT was not available in 3 of 41 patients.

Fabien et. al. *Chest* 2008;134;375-381

Radiologic Findings : Lymphoscintigraphy



Delayed
lymphatic drainage

Echocardiography

- Mild pulmonary hypertension
- Mild-to-moderate pericardial effusion
- Mild diastolic dysfunction
- Mild restrictive physiology
- Normal

Fabien et. al. *Chest* 2008;134;375-381

Pulmonary Function Studies

- Obstructive pattern : 43%
- Restrictive pattern : 14%
- Mixed obstructive-restrictive pattern : 6%
- Isolated decrease in the diffusing capacity : 6%
- Normal : 23%

Fabien et. al. *Chest* 2008;134;375-381

Bronchoscopy Results

- 12 patients (29%) → Bronchoscopy
  - 10 patients : Normal
  - 2 patients : Extrinsic compression.

Fabien et. al. *Chest* 2008;134;375-381

Prognosis

- Follow-up : 37 patients (90%)
- Mortality : 17 cases (46%), Median f/u interval : 82 months
- Patients with YNS had decreased survival (p=0.01)

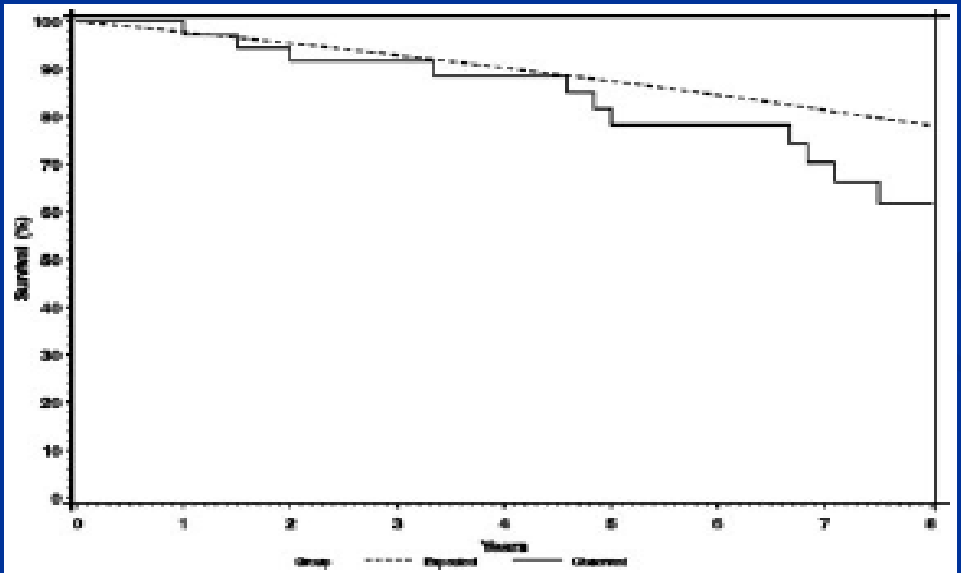


FIGURE 2. Kaplan-Meier survival curve of subjects with YNS compared general life expectancy.

Control ----------

YNS _____

Fabien et. al. *Chest* 2008;134;375-381

Pathophysiology

- **Unclear**
- Anatomic/ functional lymphatic drainage abn.
- Microvasculopathy with protein leakage
- Acquired >> Hereditary

Diagnosis

- **Classical triad**
  - **Yellow dystrophic and/or slow growing nails**
  - **Lymphedema**
  - **Respiratory manifestations**

  in the absence of other more likely explanations

- Presence of **two of them** has been judged to be **sufficient for diagnosis**.

Diagnosis

- Lymphoscintigraphy (radionuclide imaging) >> lymphangiography
  - Lymphatic abnormalities consisting mostly of hypoplasia of the lymphatic system
- MRI and CT

Multiple clinical associations

- **Connective tissue disease**
- **Malignancy**
- **Immunodeficiency states**
- **Drugs**
- **Several endocrine disorders (DM and thyroid dysfunction)**
- Obstructive sleep apnea
- Myocardial infarction
- Hemochromatosis
- Guillain-Barre´ syndrome
- Xanthogranulomatous pyelonephritis
- Tuberculosis
- Low serum protein states

Management

- **Bronchiectasis**
  - Bronchopulmonary hygiene measures
    - Postural drainage
    - Chest physiotherapy
    - Inhaled bronchodilator
  - Influenza and pneumococcal immunizations
  - Prompt Tx. of complicating respiratory infections

Management

- **Recurrent symptomatic pleural effusion**
  - Therapeutic thoracenteses
  - Pleurodesis
  - Surgical maneuvers (Pleurectomy)

- **Nail manifestation**
  - 'Barometer' of YNS
  - Better control of respiratory manifestations
  - Local steroid injection
  - Vitamin E

Management

- **Lymphedema**
  - Gradient pressure garments
  - Exercise
  - Bandage wraps
  - Manual lymphedema drainage
  - External pneumatic compression
  - Better control of respiratory manifestations

** Lymphedema and pleural effusions are persistent and spontaneous recovery has not been reported.