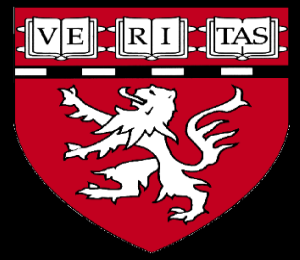
Radiology for the Pulmonary and Critical Care Physician

Andetta R. Hunsaker, M.D.

Chief of Thoracic Imaging

Department of Radiology
Brigham and Women's Hospital
Associate Professor
Harvard Medical School

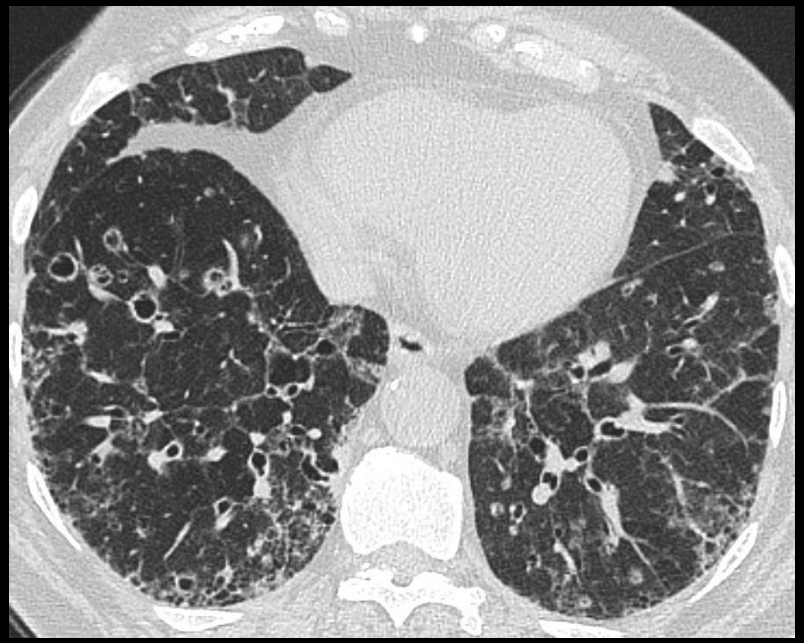


Disclosure of Conflict of Interest

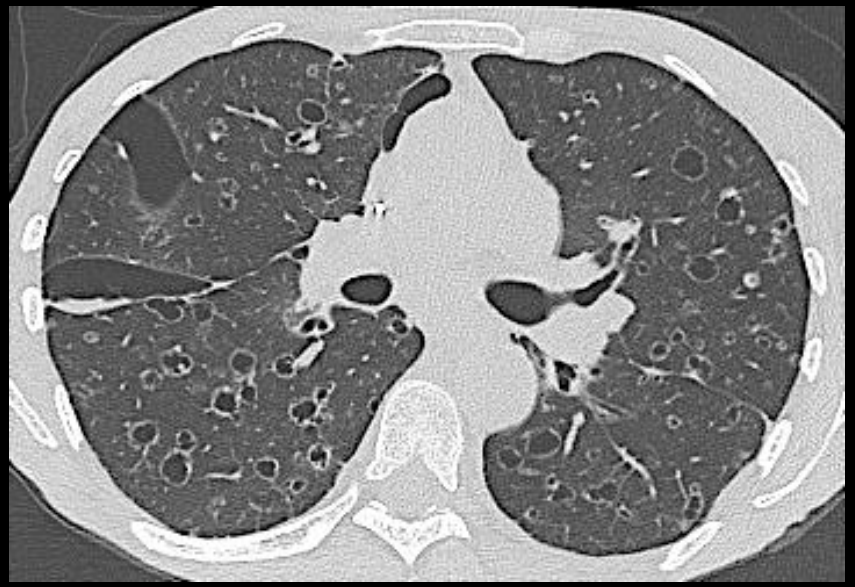
I receive royalties from Wolters Kluwer for a text book: Computed Body Tomography with MRI Correlation

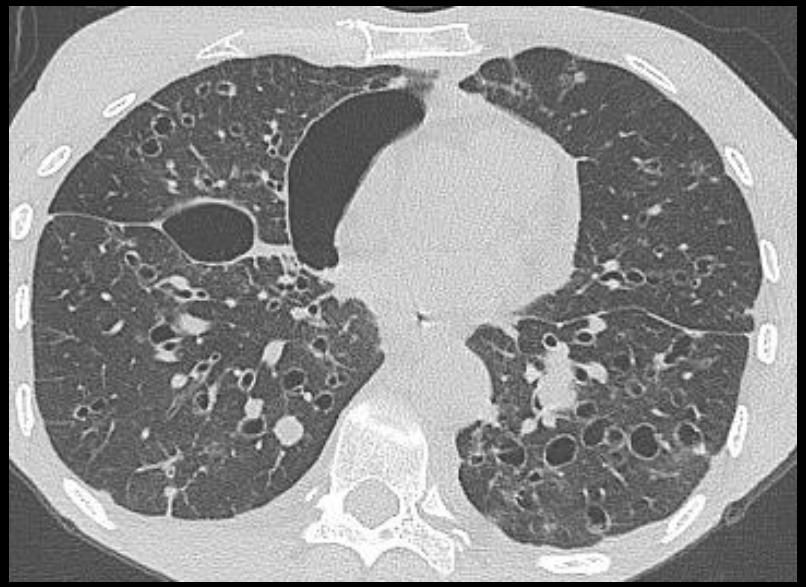
Quiz one:
63 y/o man.
What is the diagnosis?

Quiz Two. No History: What is the diagnosis?



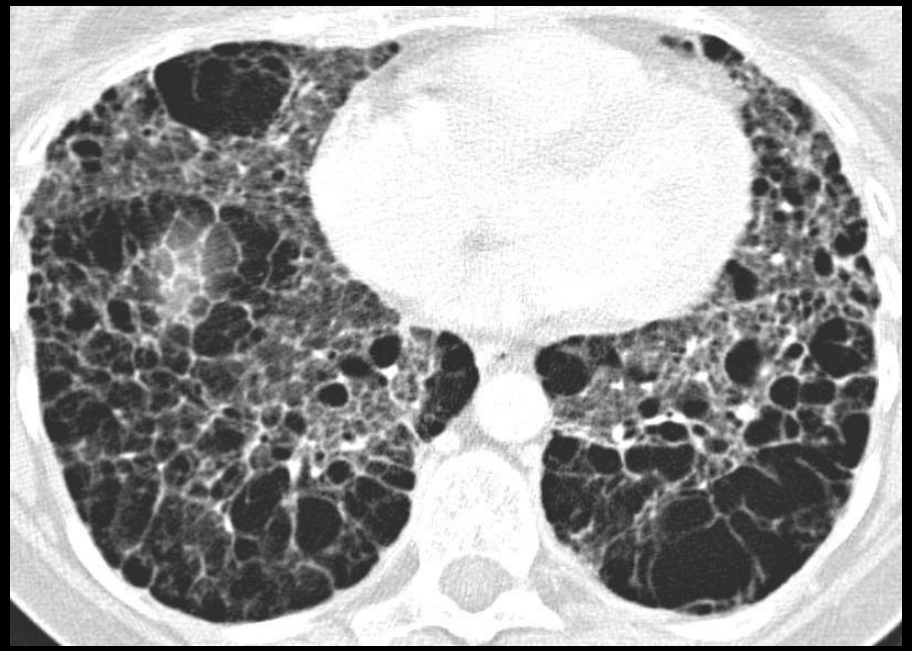
- Top patient is a smoker PLCH
- Bottom, patient has uterine sarcoma: Metastasis

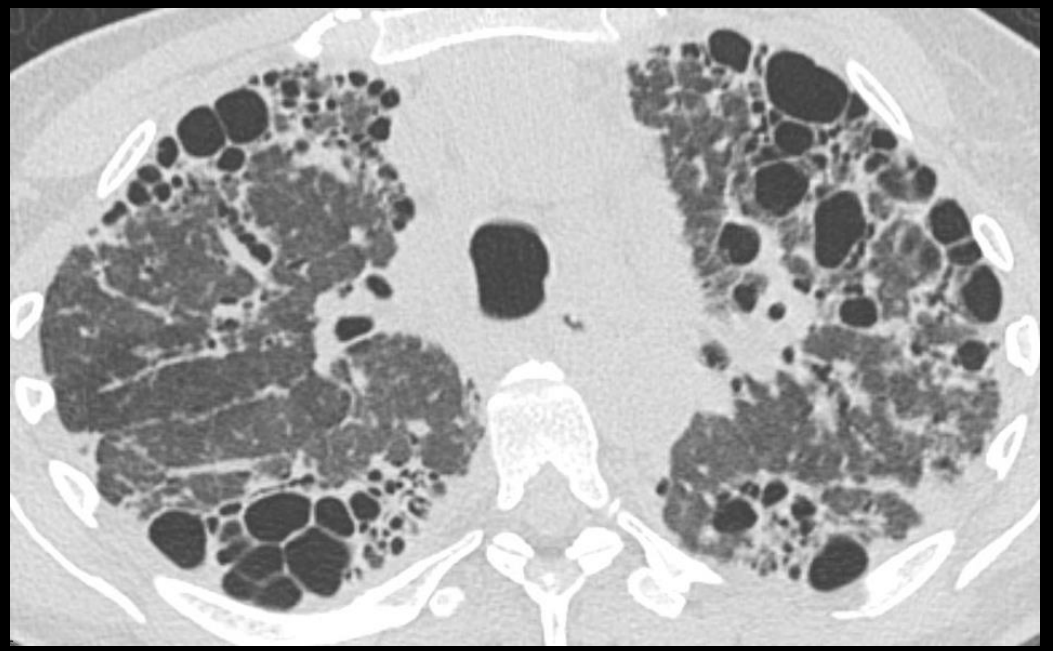




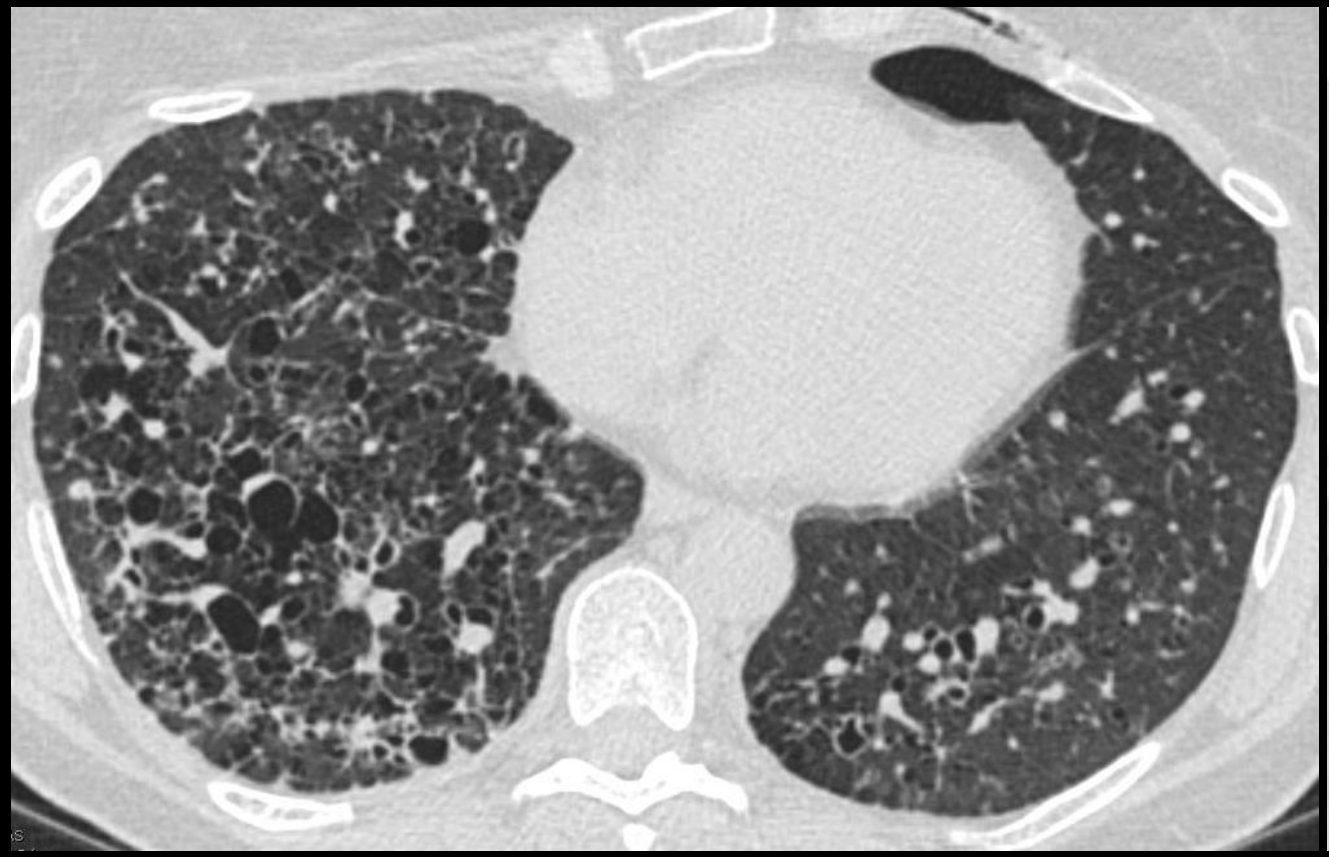
Quiz Three. What is the diagnosis?

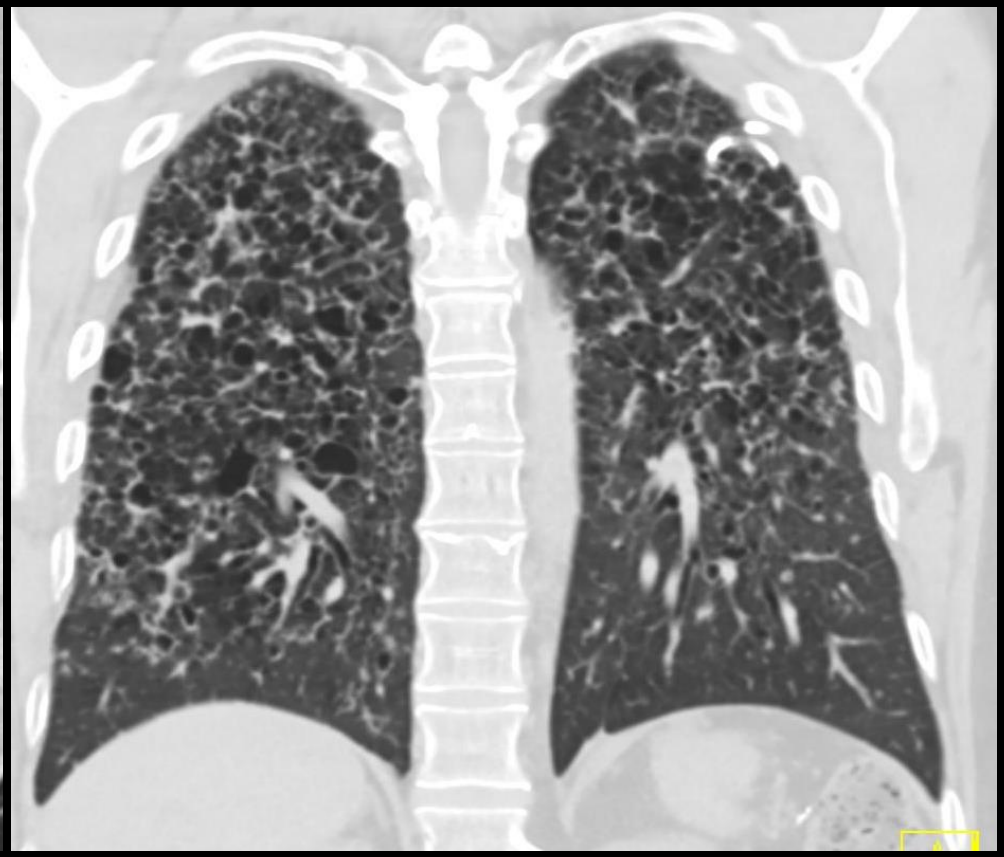
- Top right CTD UIP
- Bottom right Hermansky Pudlak
- Bottom left Smoking related ILD Unclassifiable



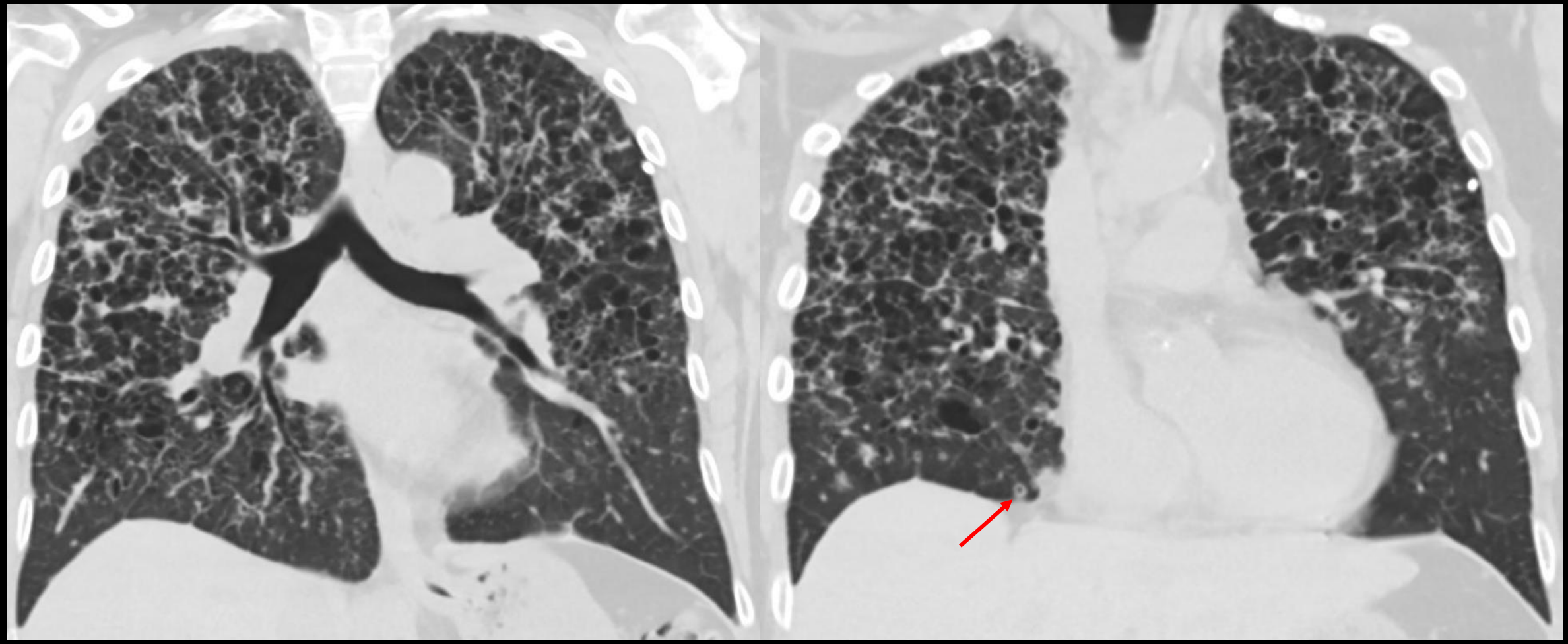


53 y/o woman with a 25-pack year smoking history who presented with a two-month history of fatigue, exertional dyspnea, and cough





Diagnosis: Pulmonary Langerhans cell histiocytosis



Goals

- Describe Radiographic features of various IIP with DDx
- Discuss Cystic Lung diseases
- Review smoking related lung diseases

Pulmonary Langerhans cell histiocytosis

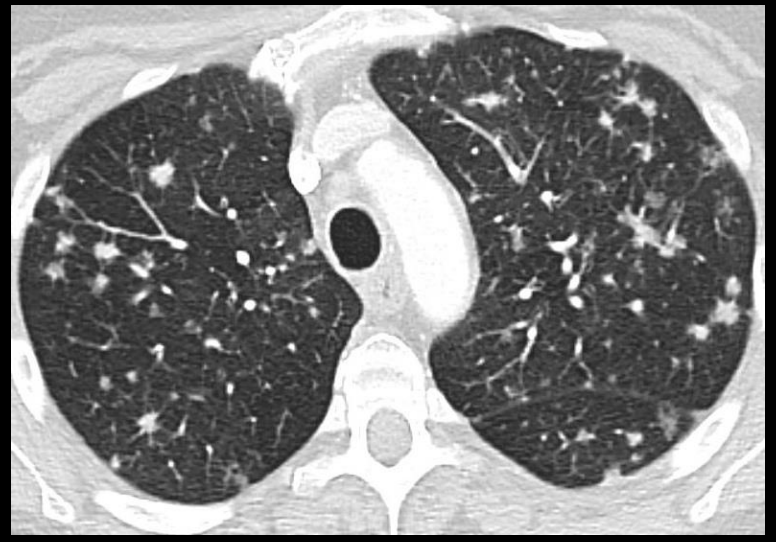
- Patients are 3rd to 4th decades of life; affects men and women equally
- >90% pts have smoking history
- Only a small percentage develop PLCH
- Mechanism of pathogenesis: possibly due to proliferation of Langerhans cells due to abnl immune reaction directed at components of cigarette smoke
- May also be a genetic predilection

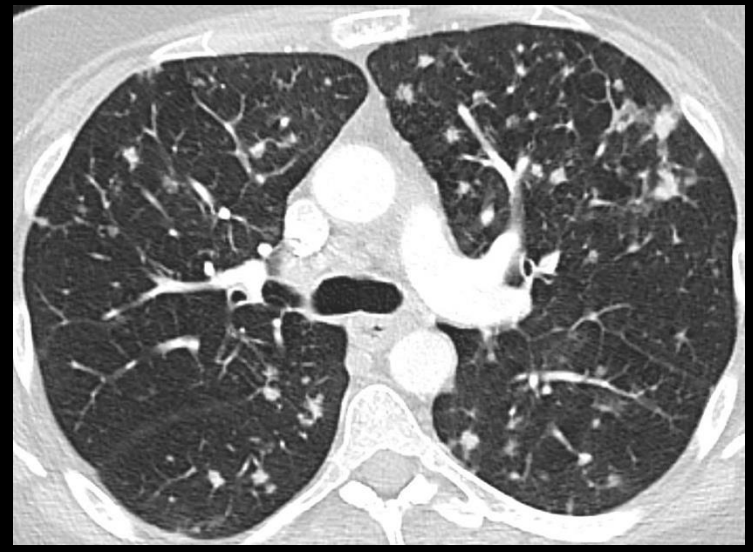
Symptoms of PLCH

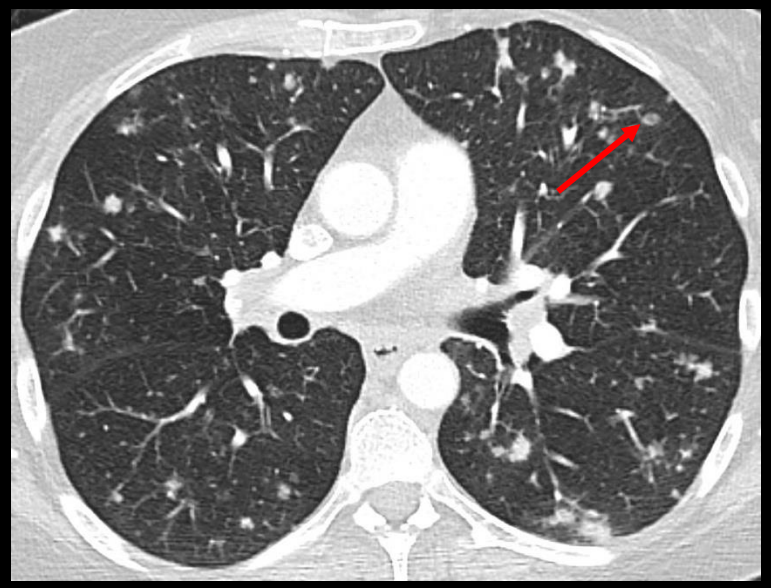
- Fatigue
- Weight loss
- Exertional dyspnea
- Non-productive cough
- PTX may be first sign in ~ 15-20% of patients
- ~20% no symptoms

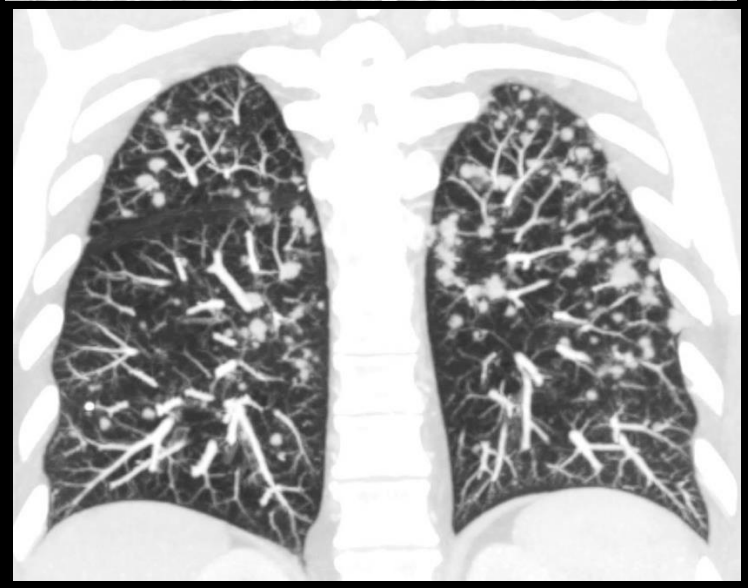
Radiologic Findings

- Nodules and cysts frequently in the upper and mid zones
- Nodules typically 1-10 mm but can be much larger
- Nodules may cavitate







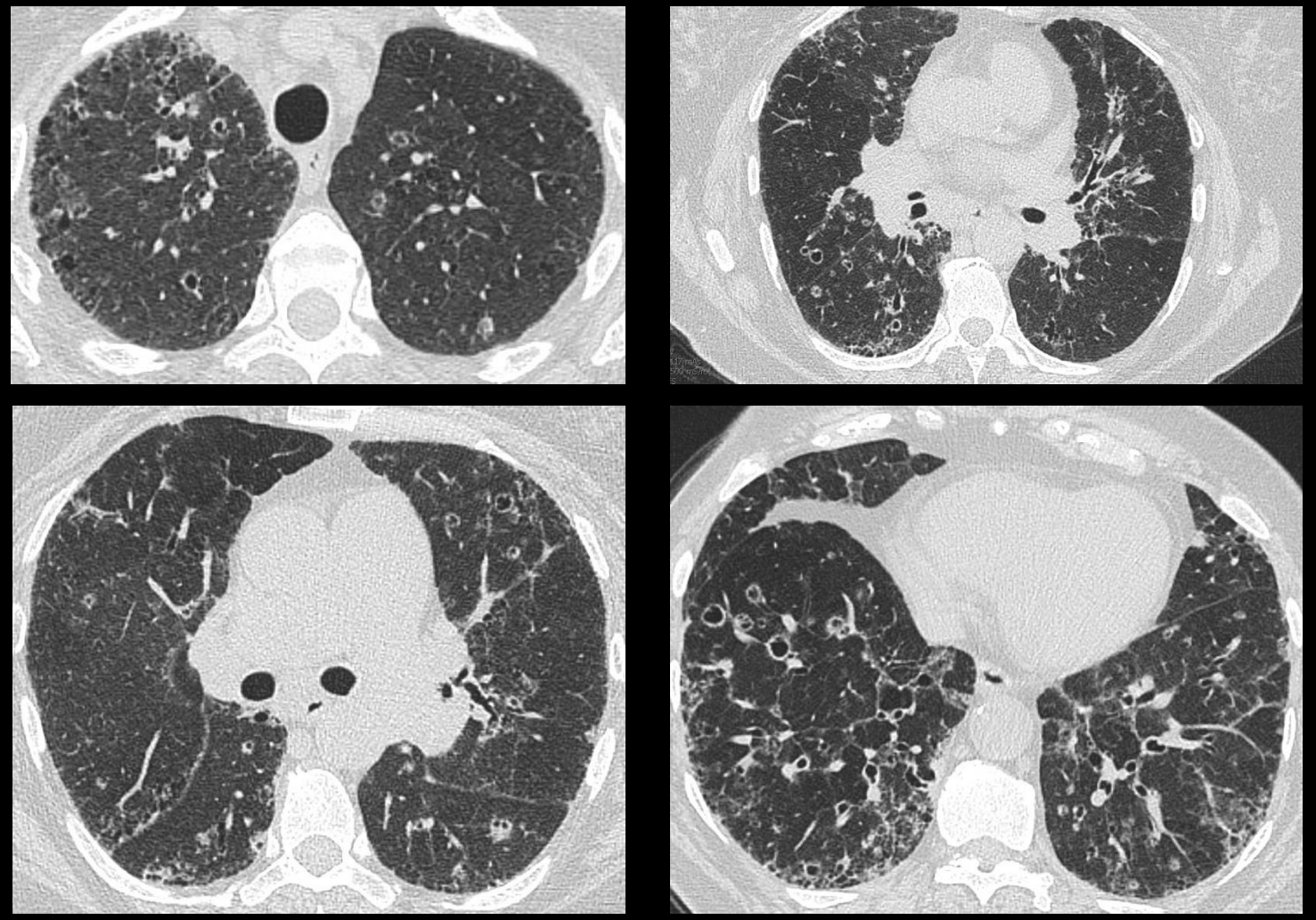


Additional Radiologic Features

- Nodular interstitial infiltration of Langerhans cells
- Peribronchiolar distribution of stellate nodules
- Fibrosis can be seen

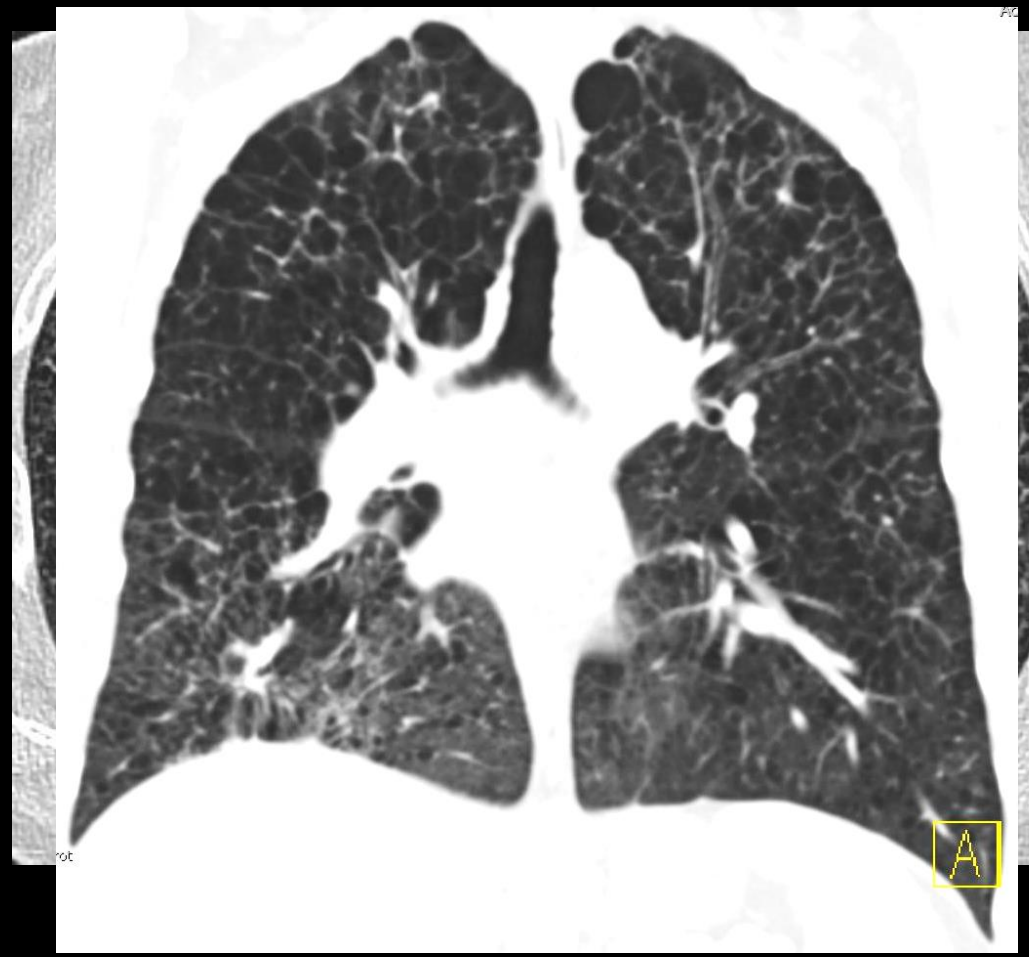
Radiologic Findings

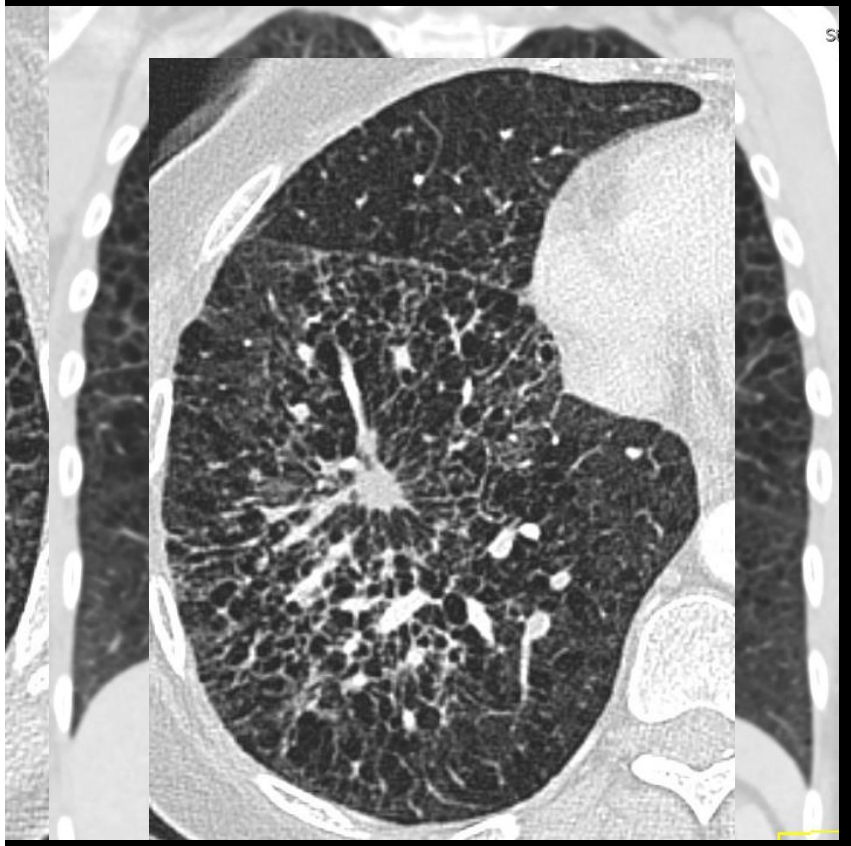
- Large nodules can be transformed to thick-walled cysts, then later to thin-walled cysts
- Cysts are varied in wall thickness and can be bizarre shaped



Radiologic Findings

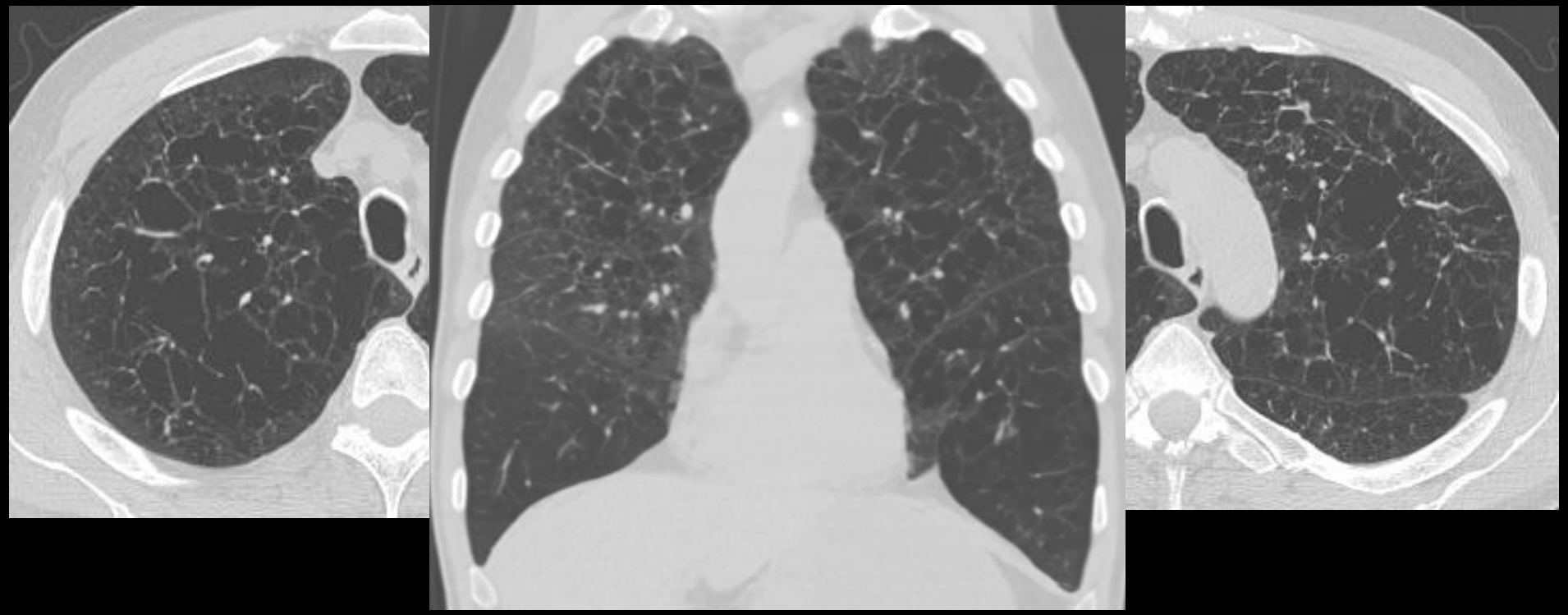
- Cysts may coalesce and be indistinguishable from de novo emphysema





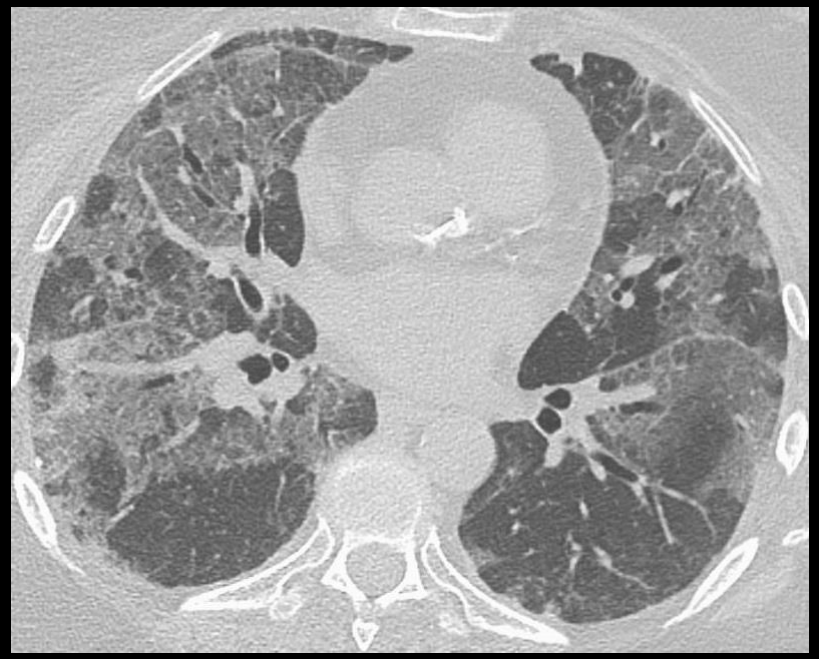
Radiographic Findings in LCH

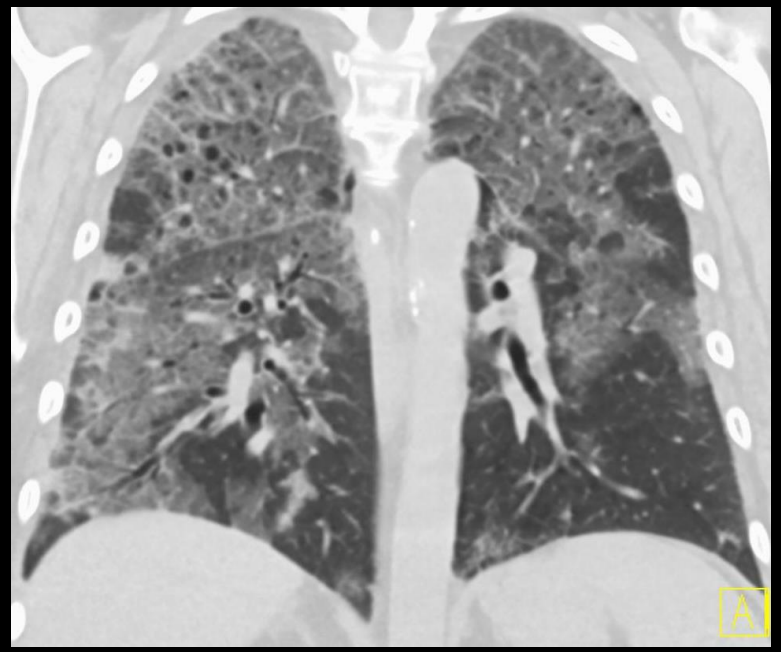
- Upper and mid lung predominance
- Spares CP sulci
- Preserved or increased lung volumes



59-year-old male presents with this CT scan obtained for SOB

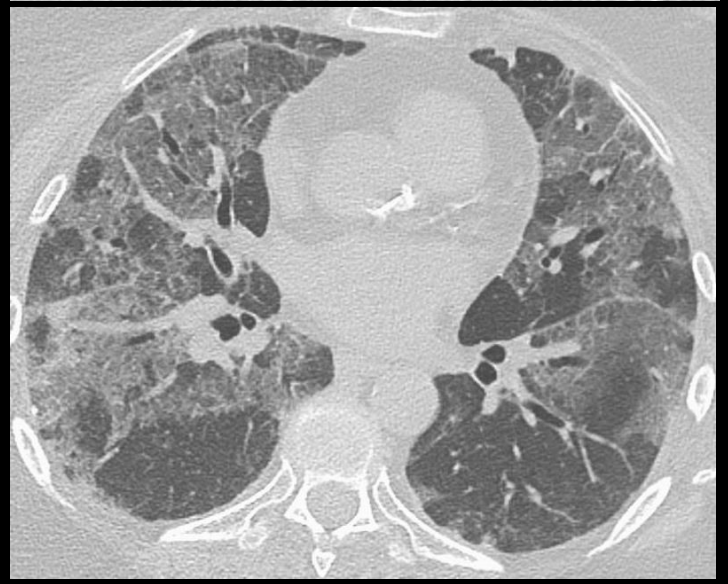
Additional History: Patient has a 60 pack-year history

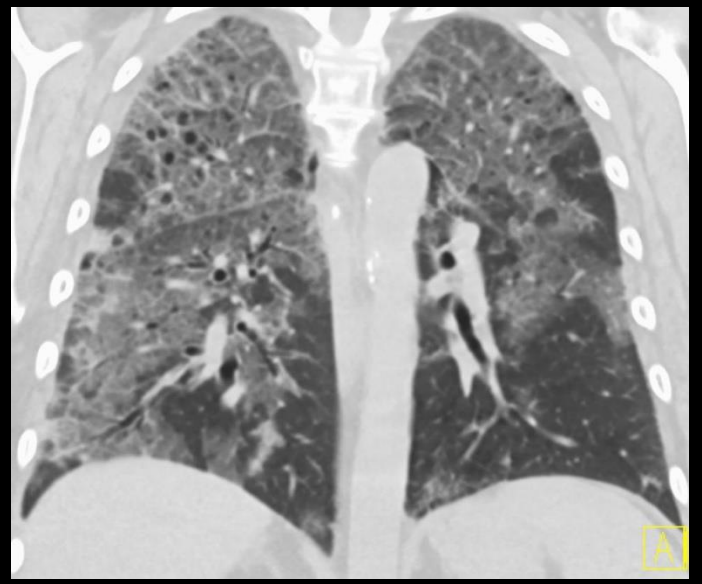




Imaging in DIP

- Widespread GGO in mid and lower lung zones
- Can be peripheral
- May see centrilobular nodules, possibly due to coexistent RB
- Cysts may represent dilated alveolar ducts or pulmonary cysts

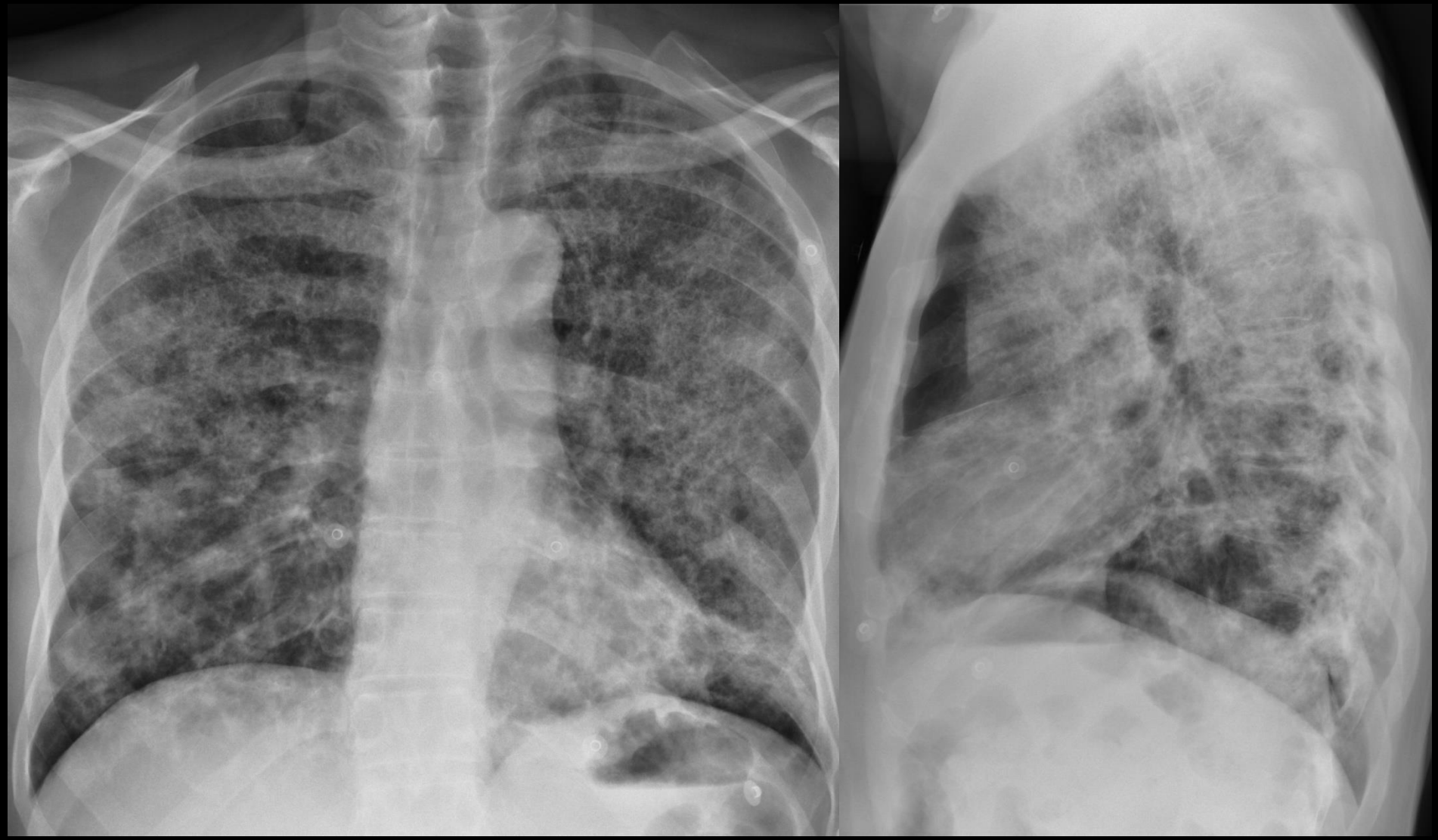




Desquamative interstitial pneumonia (DIP)

- On a spectrum with RB-ID
- Compared with RB-ILD, the diffusing capacity for carbon monoxide (DLCO) may be severely reduced
- Pigmented macrophages fill alveoli diffusely due to immune-mediated response to smoking
- Diffuse alveolar septal thickening

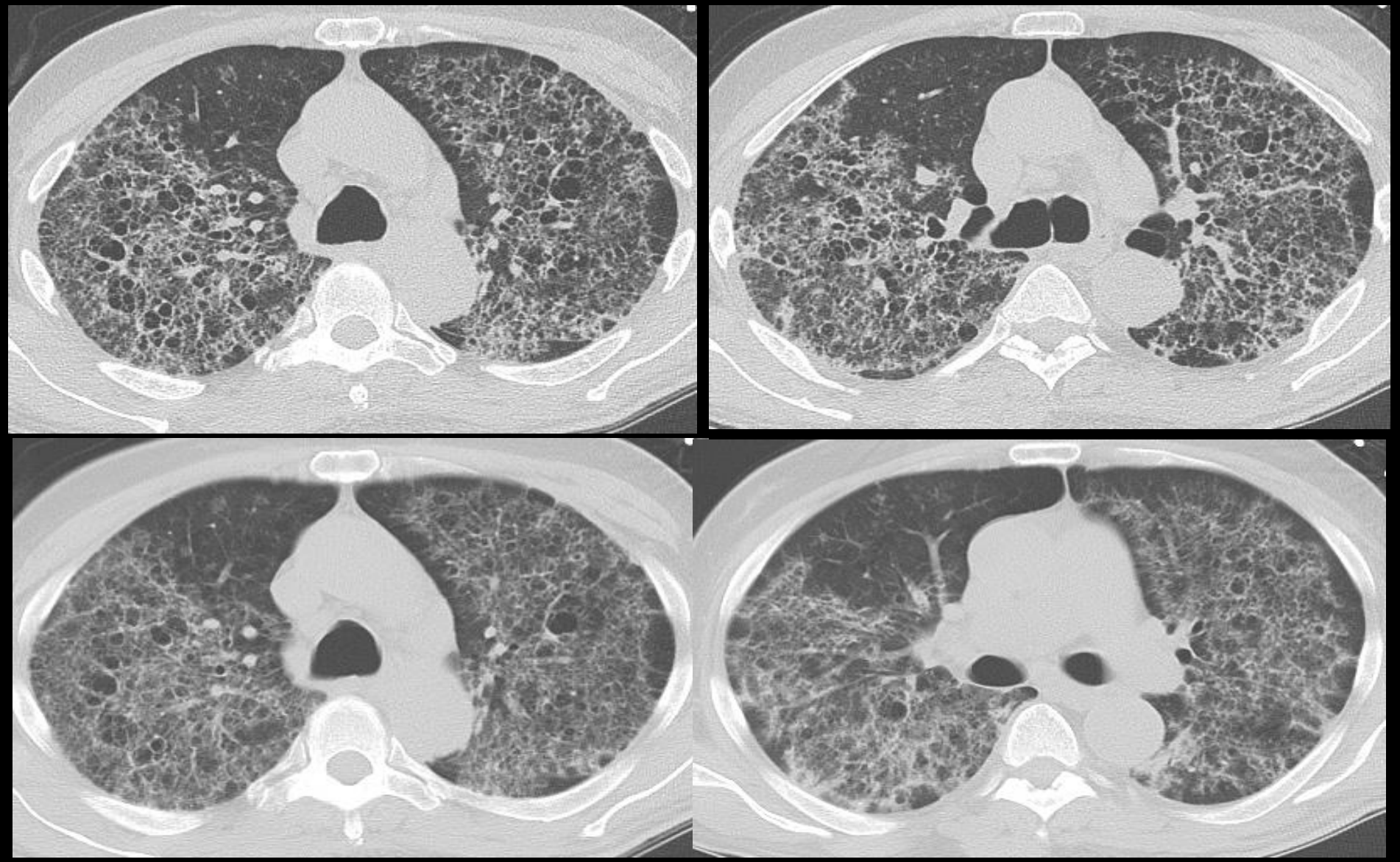
63 y/o man presented to ED with chronic cough and weight loss



Pneumocystis Jiroveci Pneumonia

Additional History:

Homeless IVDU

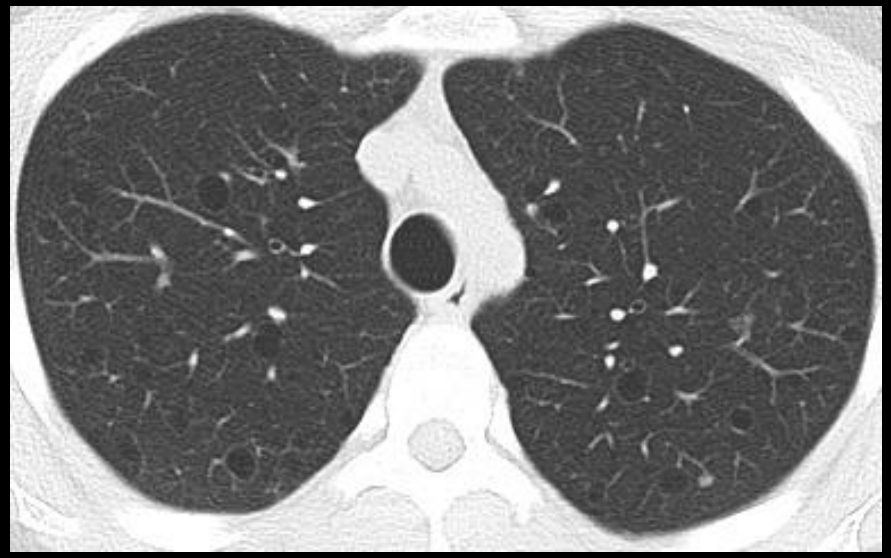


Diagnosis:Sporadic LAM

Lymphangioleiomyomatosis

- Women of childbearing age
- Mean age at presentation 30-35 yrs
- May be related to female hormone secretion
- Onset and exacerbations sometimes coincide with pregnancy and parturition
- The abnormal smooth muscle commonly has estrogen/progesterone receptors

Diagnosis Please





Tuberous Sclerosis Complex with sclerotic bone lesions and Renal angiomyolipomas

Lymphangioleiomyomatosis: TSC-LAM

- TSC-LAM
  - Autosomal dominant neurocutaneous syndrome (seizures, mental retardation, and adenoma sebaceum)
  - Hamartomatous multi-organ disease
  - Lymphangiogenesis – plays central pathogenetic role
  - Allows for LAM cells to invade and spread through lymphatics to distant sites
  - Hence elevated VEGF-D

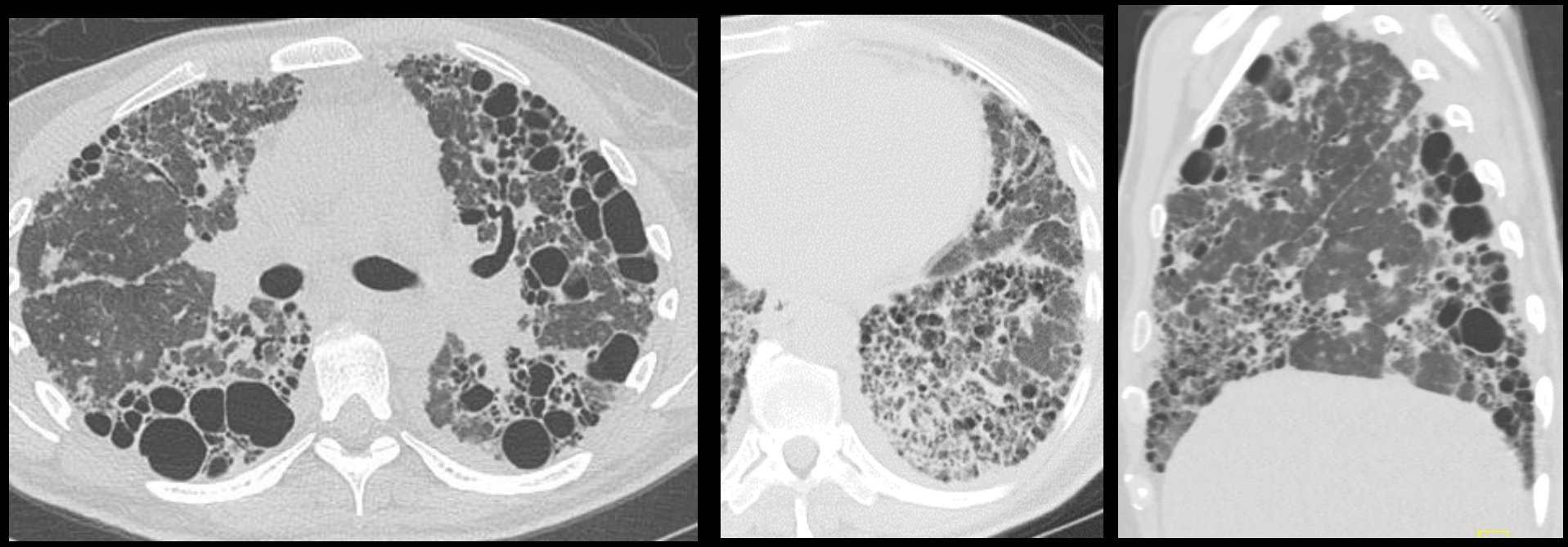
Lymphangioleiomyomatosis: TSC-LAM

- TSC-LAM
  - 5-10 X more common than S-LAM
  - Less severe than sporadic form
  - LAM occurs in ~ 1/3 pts with TSC
  - HRCT may show diffuse nodular (MMPH) changes with thin-walled cysts
  - Nodules are peripheral and UL predominant
  - May see sclerotic bone lesions (enostoses)

43-year-old female with renal failure

Findings

- Peripheral cysts
- Diffuse GGO
- Traction bronchiectasis
- Fissural and septal thickening



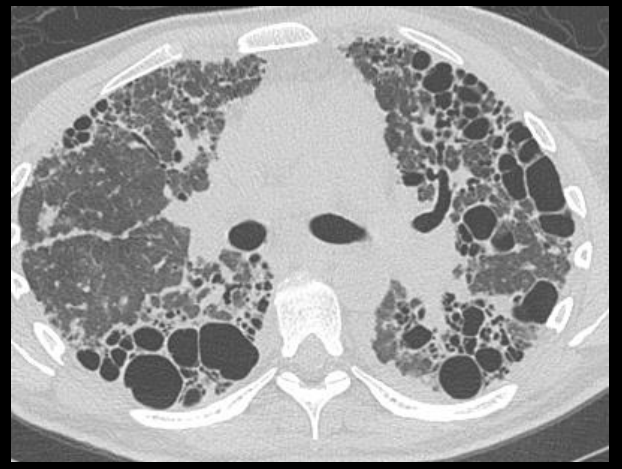
Differential Diagnosis

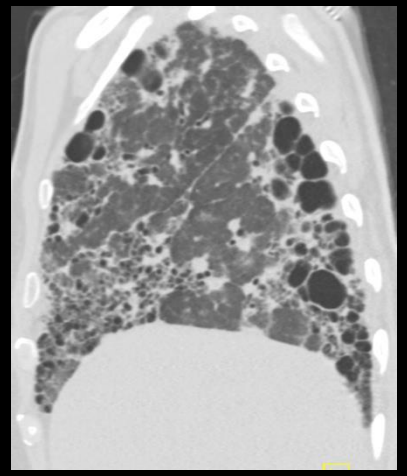
A. Typical UIP pattern with exacerbation

B. Lymphocytic Interstitial Pneumonia

C. Connective Tissue Disease - ILD

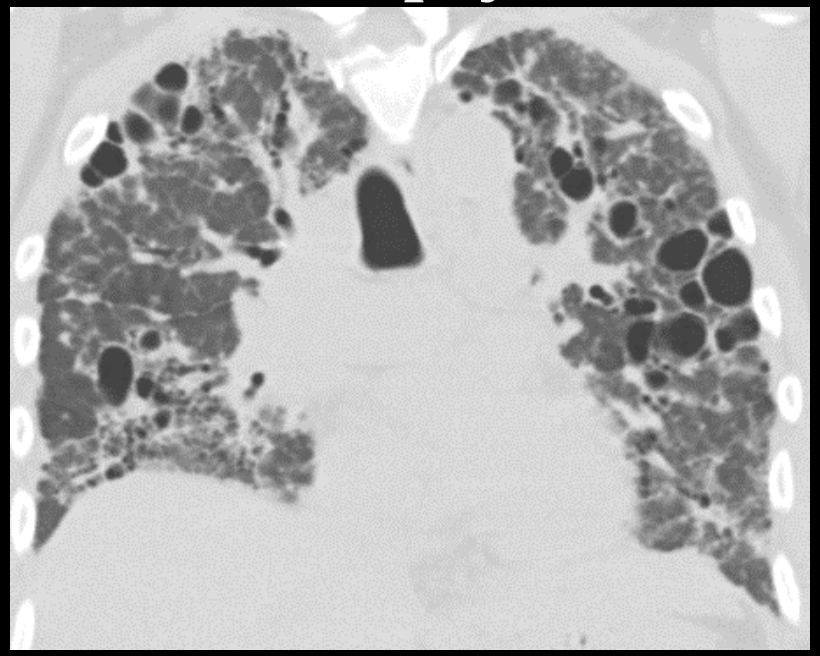
D. Hermansky-Pudlak

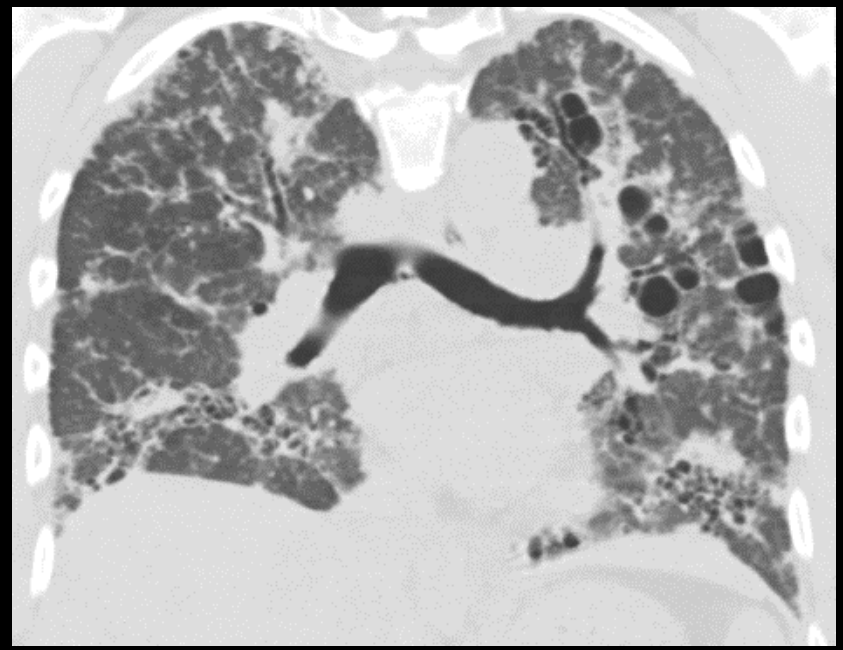




Hermansky-Pudlak Syndrome

43 y/o female, never smoker from Puerto Rico who is blind, albinism, HTN, renal failure. Had retroperitoneal bleed following renal biopsy





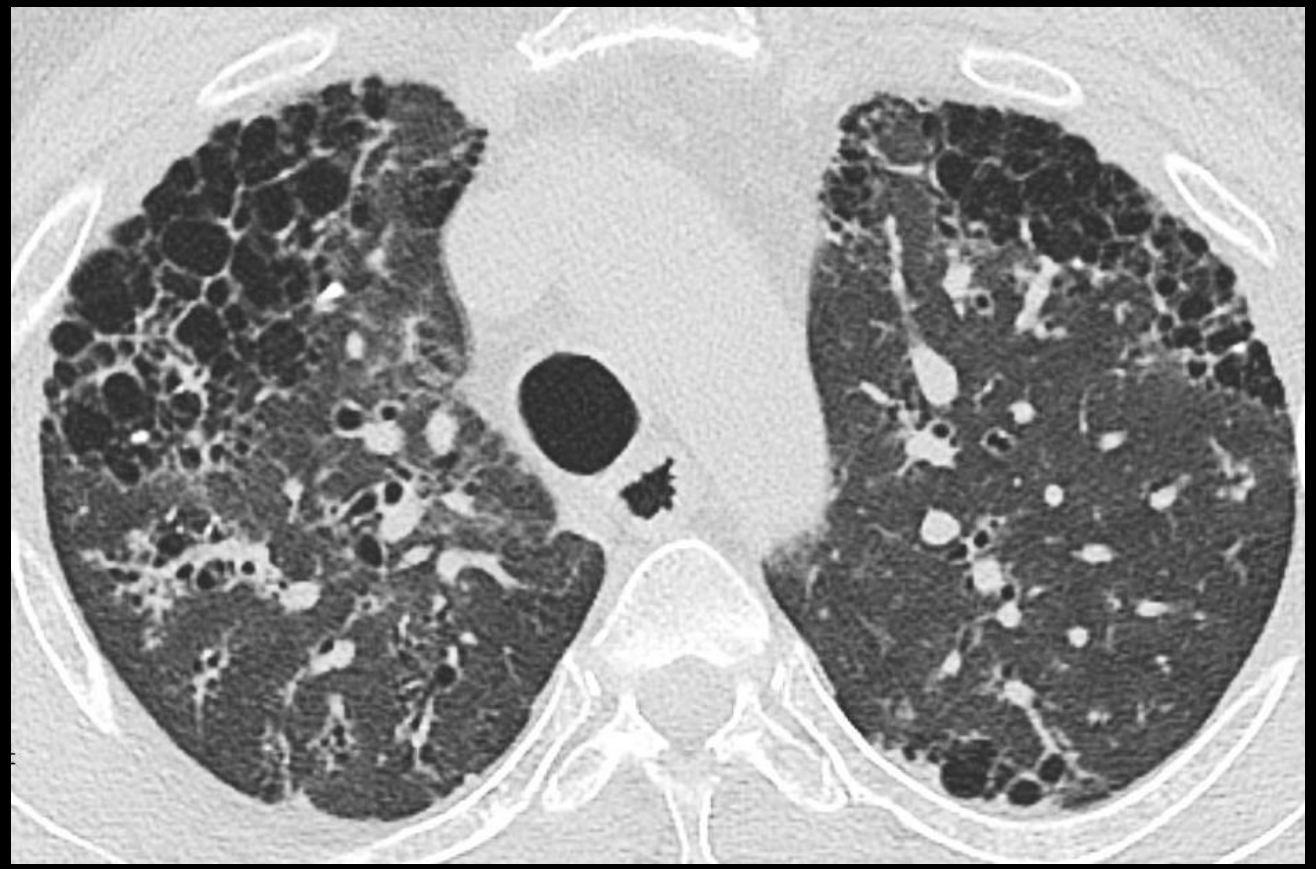
Teaching Points

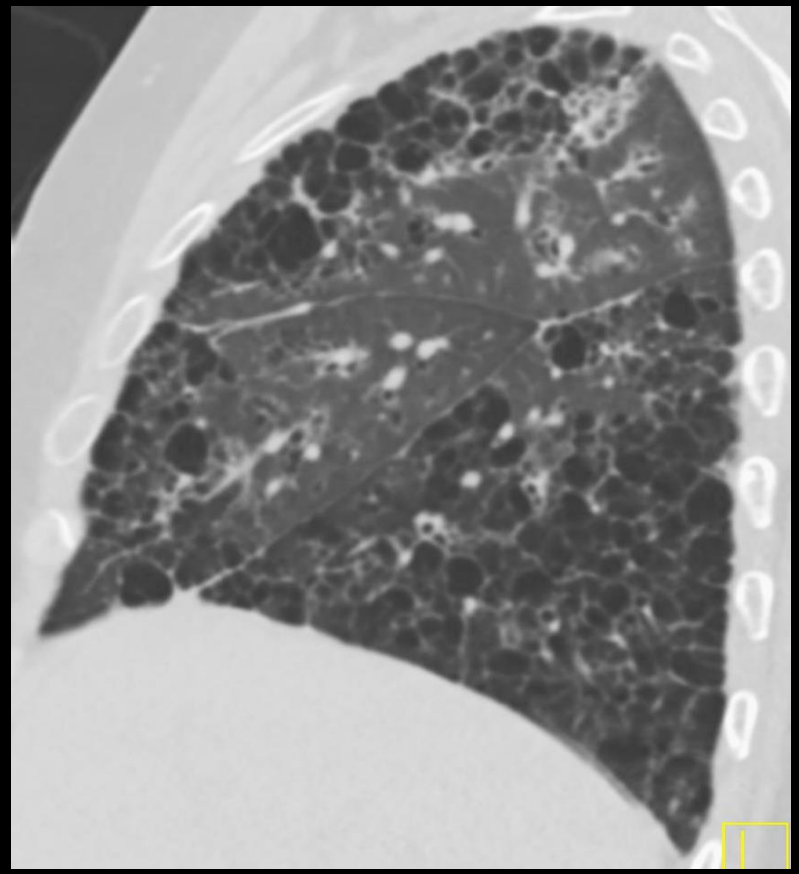
Hermansky-Pudlak

- Important to differentiate from UIP as it does not respond to UIP treatment
- Clue is Puerto Rican, blindness, albinism, platelet dysfunction
- Avoid aspirin products
- Traction bronchiectasis
- Subpleural cysts
- Septal thickening

Patient History

53 y/o female with lupus who presents with restrictive spirometry, DOE and dry cough





Findings

- Exuberant honeycombing
  - Lower and upper lobes
- Prominent anterior upper lobe honeycombing
- Traction bronchiectasis
- Demarcation nl/abnl lung

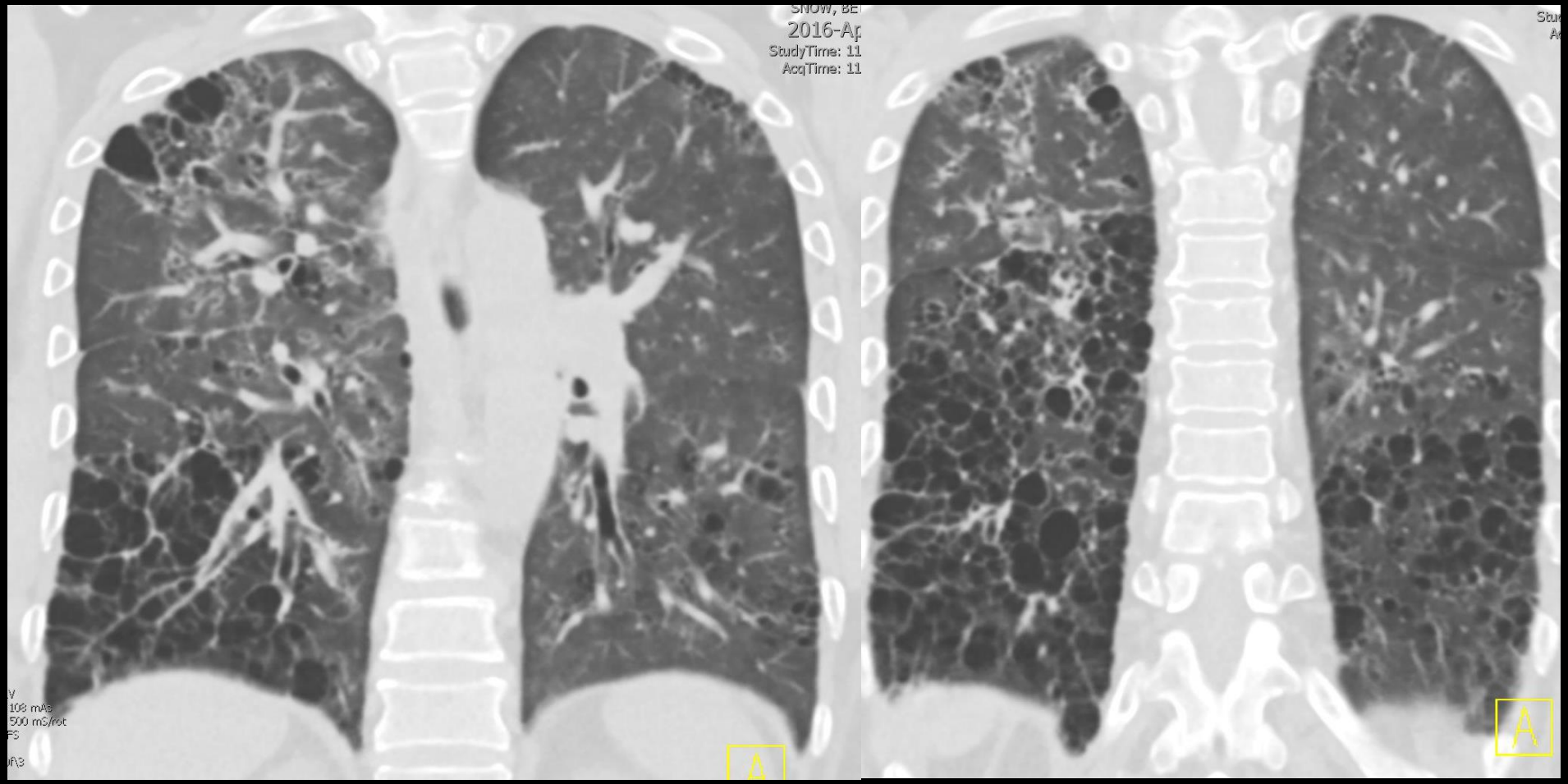
DDx CTD UIP

- Significant exuberant honeycombing in the anterior segments of the upper lobes is suggestive of CTD UIP
- The straight edge sign appears to be the most specific (highest positive likelihood ratio in one study)

Chung et al AJR 2018;210:307-313

CTD UIP

Straight edge sign



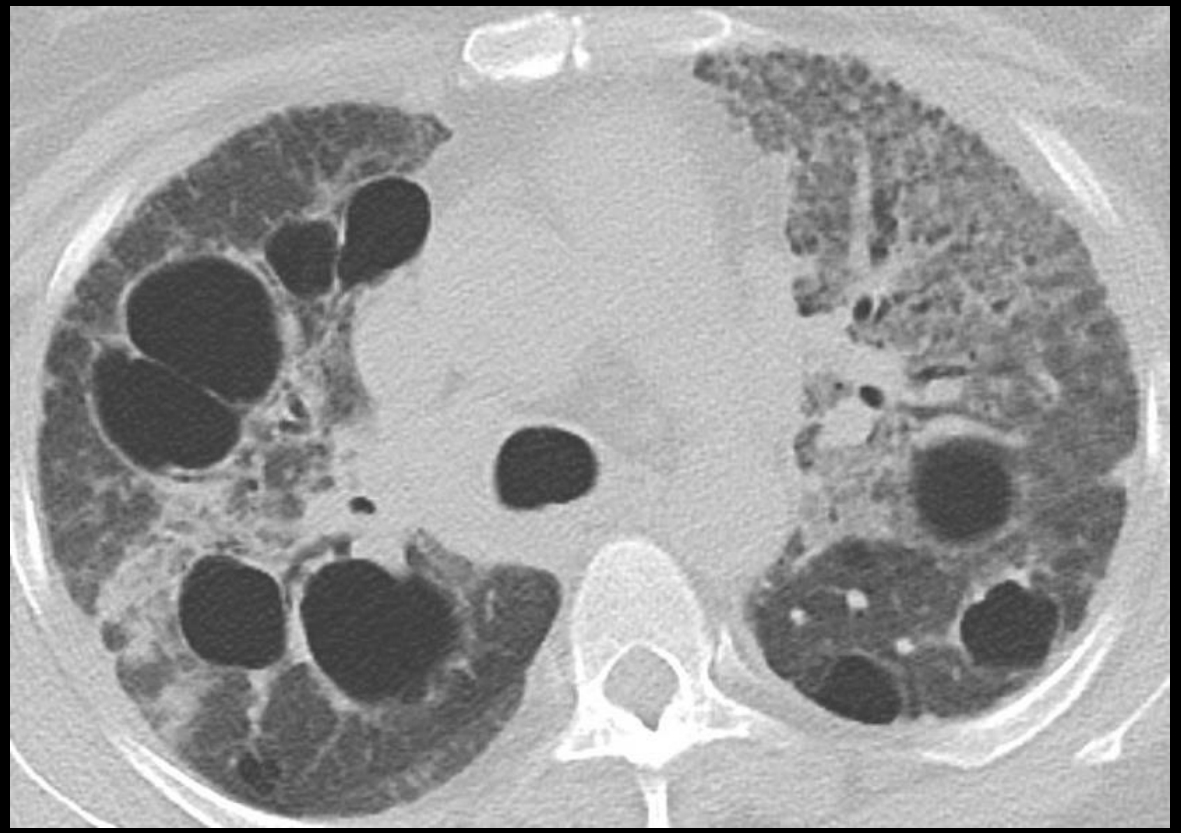
Teaching Points

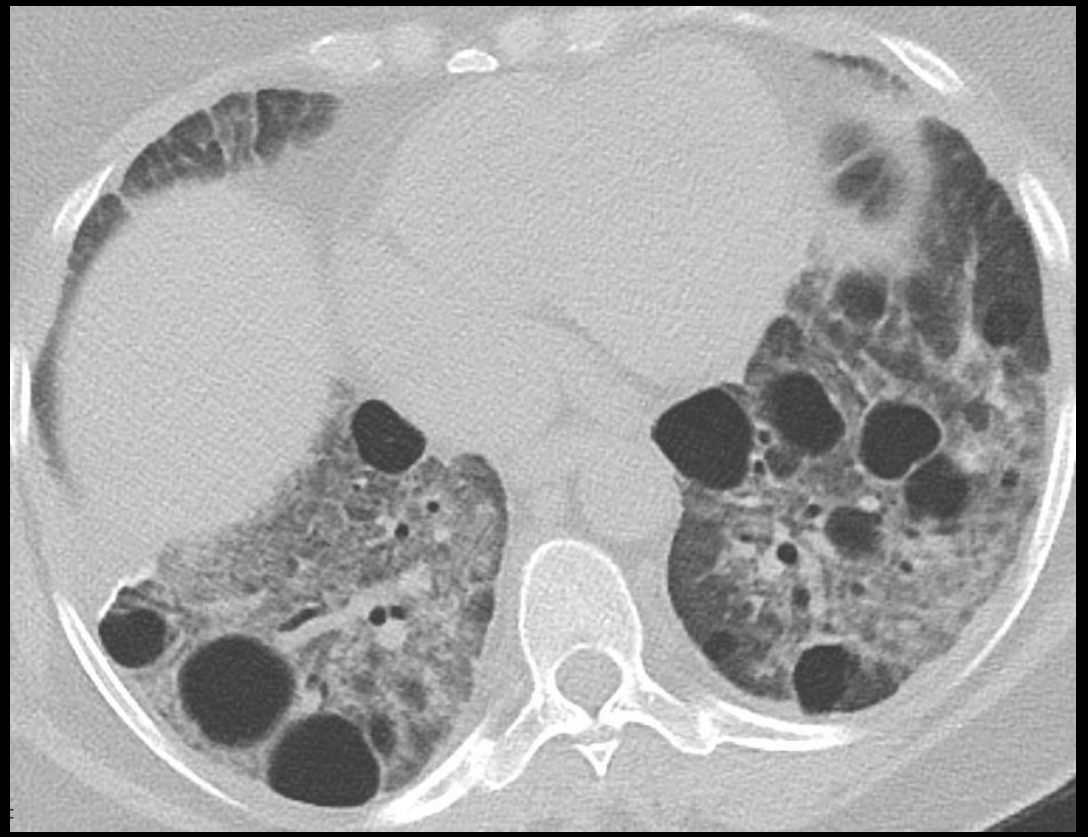
- Most common in patients with RA followed by systemic sclerosis, idiopathic inflammatory myopathies
- Have longer survivals than UIP IPF
- Patterns of fibrosis in CTD
  - UIP followed by NSIP in RA
  - NSIP in systemic sclerosis
  - NSIP + OP in myositis

Chung et al AJR 2018;210:307-313

Patient History

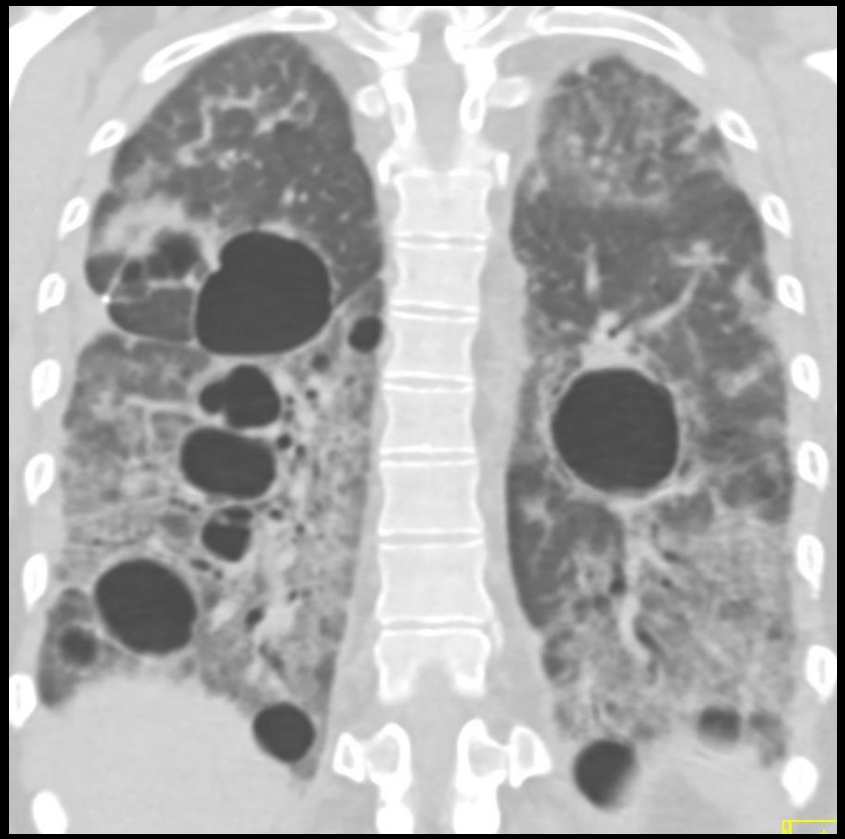
47 y/o female diagnosed with juvenile RA at age 2 and was later diagnosed with Sjogren's disease

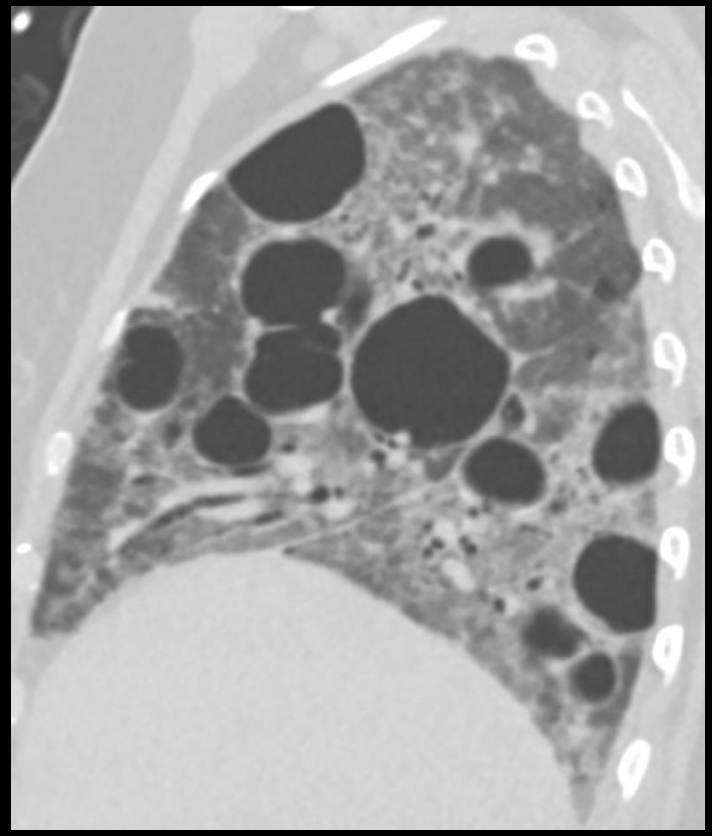




Findings

- Extensive ground glass attenuation
- Thin-walled cysts deep in the lungs
- Mild traction bronchiectasis





Lymphocytic Interstitial Pneumonia

- Reactive lymphoid hyperplasia
- Commonly affects middle-aged women
- Associated diseases: dysproteinemias, Sjogren's, SLE, Hashimoto's thyroiditis, HIV, infections
- Diffuse interstitial inflammatory infiltrate-lymphocytes and plasma cells

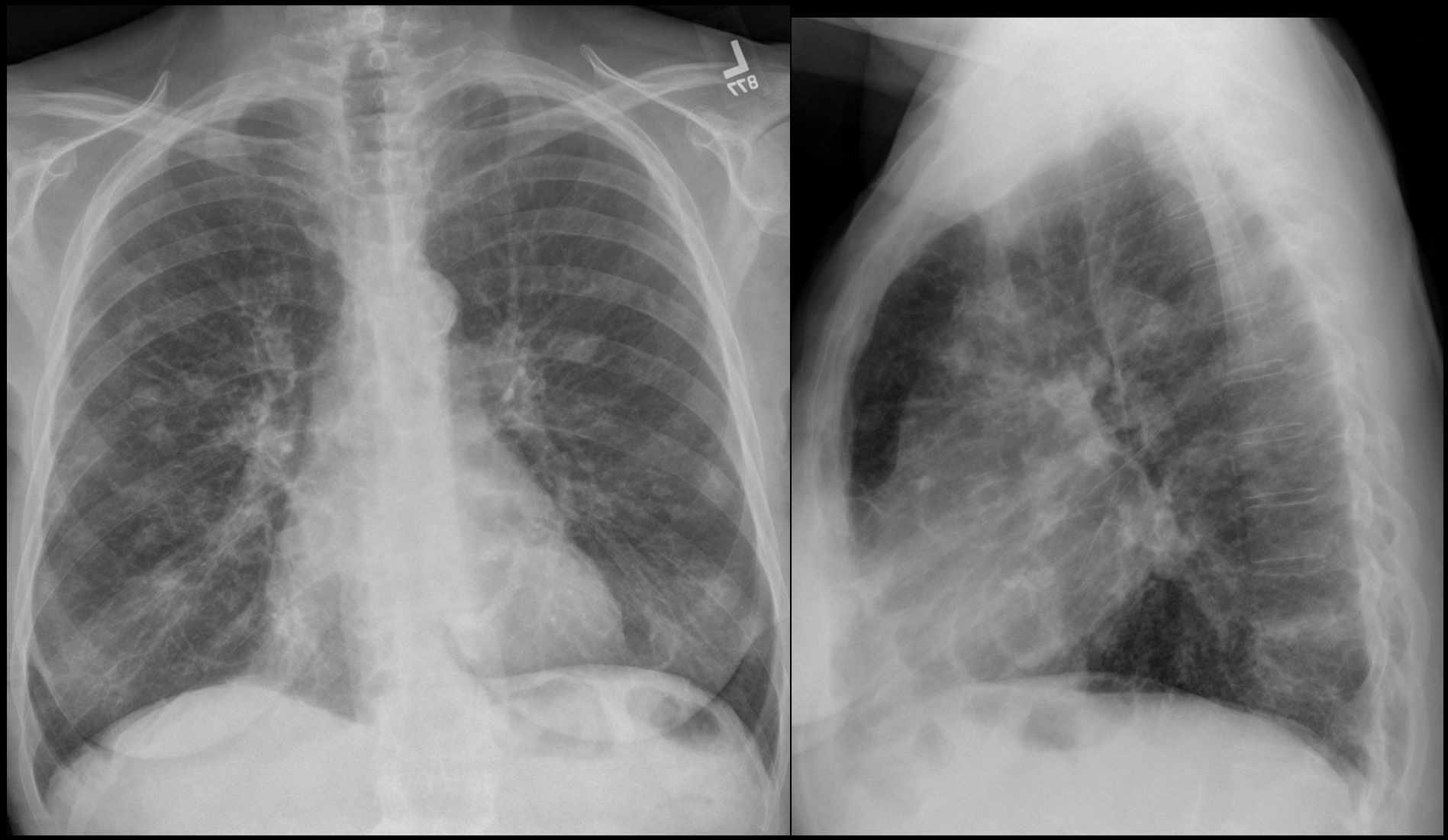
Lymphocytic Interstitial Pneumonia

- Diffuse or patchy ground-glass opacification
- Consolidation
- Centrilobular nodules
- Interlobular septal thickening
- Lung cysts in up to 80%
- Cysts typically large; basal predominance
- Cysts may be sole manifestation

Amyloidosis

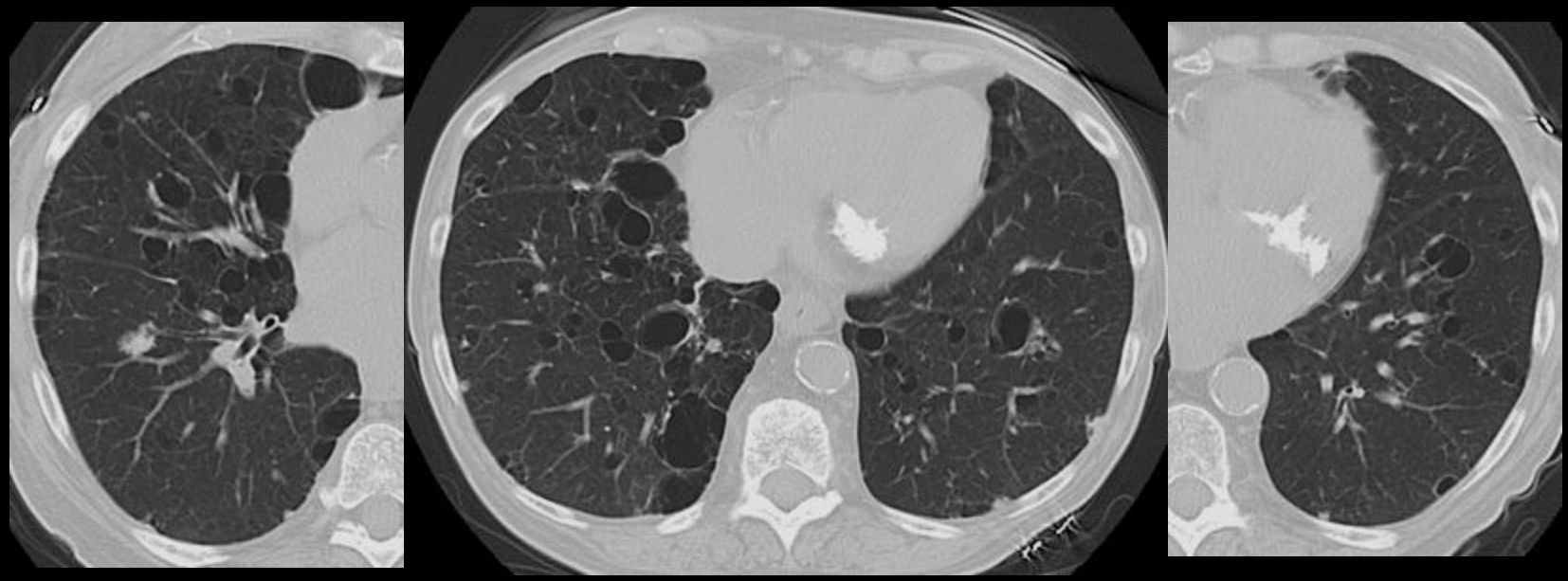
- Involvement of lung common in AL amyloidosis (70%-92%); rarely clinically sig
- Cardiac involvement commonly accompanies lung involvement
- Persistent radiologic changes of heart failure despite proper treatment think amyloid

Amyloidosis in patient with Sjogren's disease



HRCT in Amyloidosis

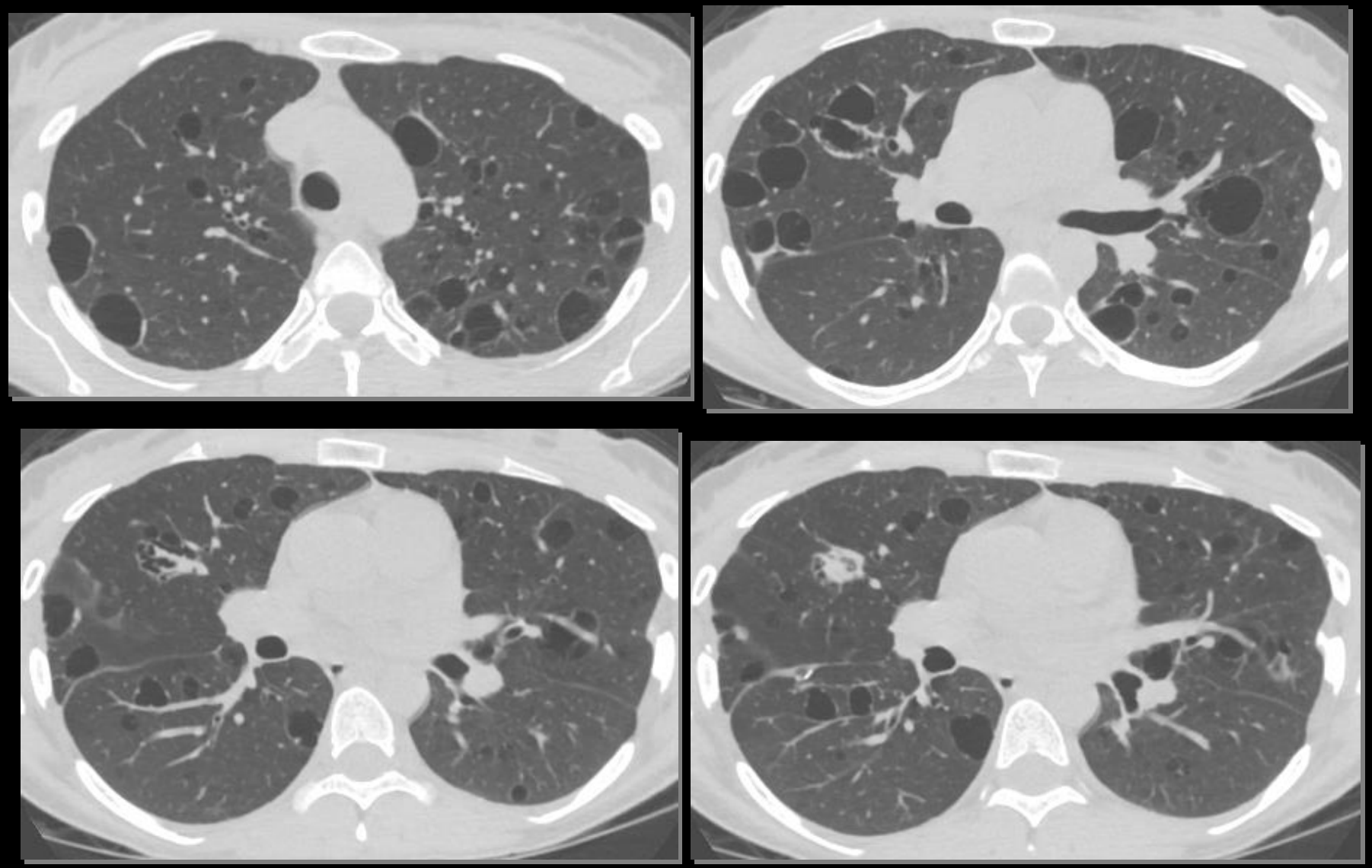
- Pulmonary nodules, GGO
- Interlobular septal thickening
- Honeycombing, LNE
- Cysts rare



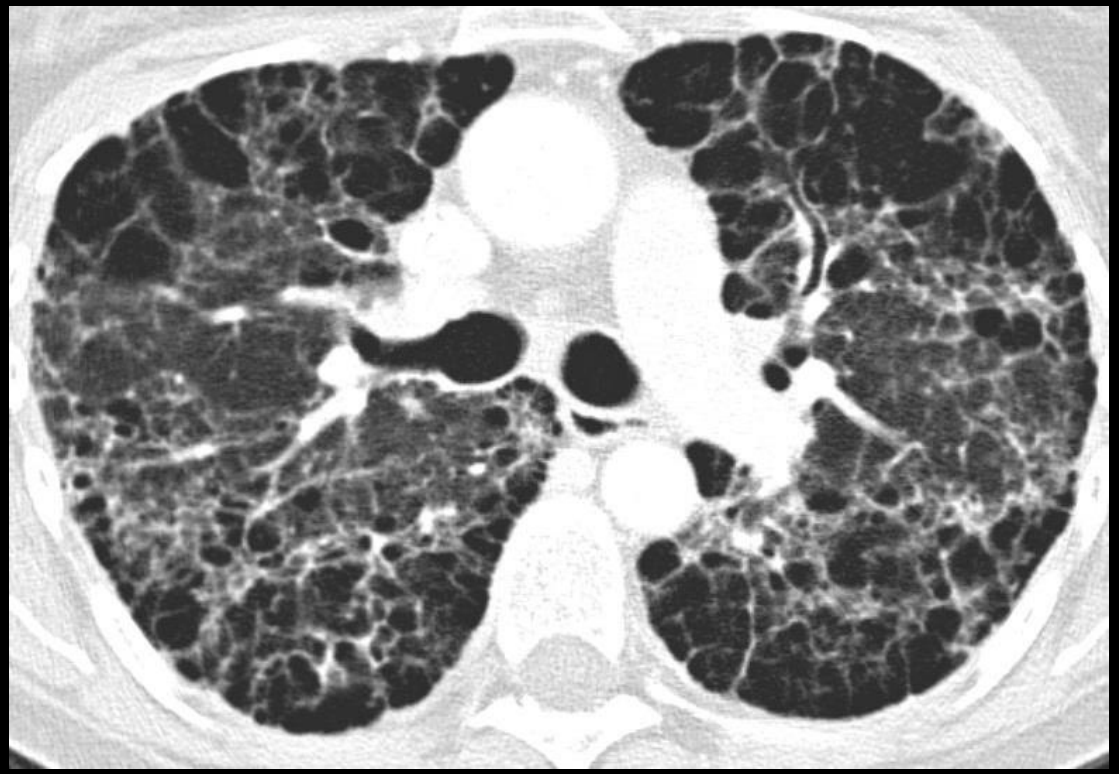
Light Chain Deposition Disease (LCDD)

- Middle age pts; mean age 67
- 70% associated with MM or macroglobulinemia
- Commonly involves kidneys
- Lung involvement rare
  - Light chains secreted by plasma cells and deposited in alveolar walls, small airways and vessels
  - Nodules, cysts, LNE
  - Cyst formation due to dilatation of small airways

Light Chain Deposition Disease



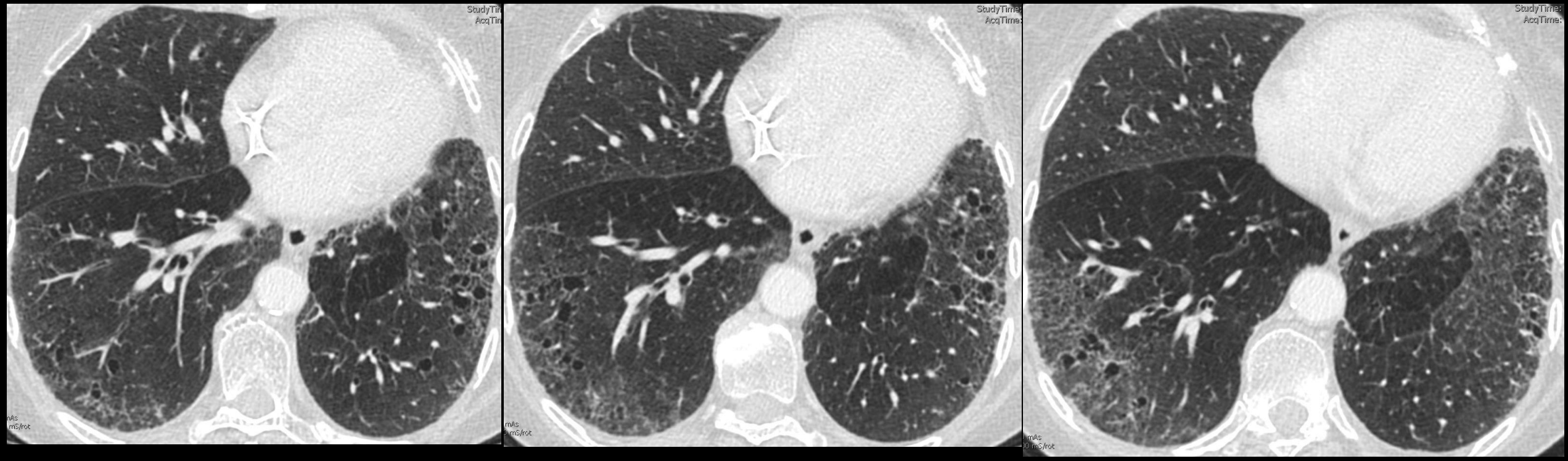
39 y/o woman with
27 pack year
smoking history and
RA and severe SOB
for several months



Fibrosis in smokers

- Smoking strongly associated with IPF
- Cysts with small dots are frequently seen on HRCT images of smokers
- These cysts are likely due to destruction of lung by emphysema
- In smokers, fibrosis of all types can be present including UIP pattern and collagenous type
- Both emphysema and fibrosis can be seen as multi-cyst pattern resembling IPF/UIP

Case four: 62 y/o woman with 40 pack yr smoking history presents with cough and dyspnea on exertion for about one year



Diagnosis: Airspace enlargement with fibrosis (AEF)

Airspace enlargement with fibrosis (AEF)

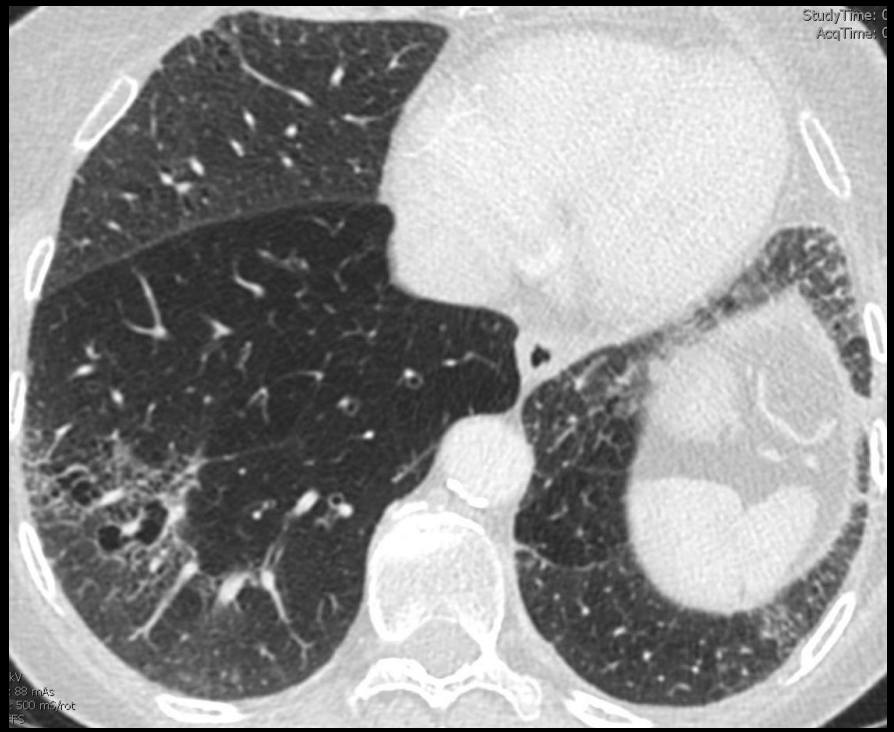
- Terms for emphysema coexisting with fibrosis have been variously called SRIF (Smoking related interstitial fibrosis) or AEF
- Cigarette smoke leads to alveolar wall fibrosis with time and severity of exposure
- Increased collagen concentration is found at histology

Airspace enlargement with fibrosis (AEF): Histology

- Emphysematous change
- Absence of fibroblastic foci
- Fibrosis is confined to the subpleural and peribronchovascular interstitium
- Clinical course is stable in most cases so must be distinguished from UIP and other IIPs if symptoms worsen over time

Imaging in AEF

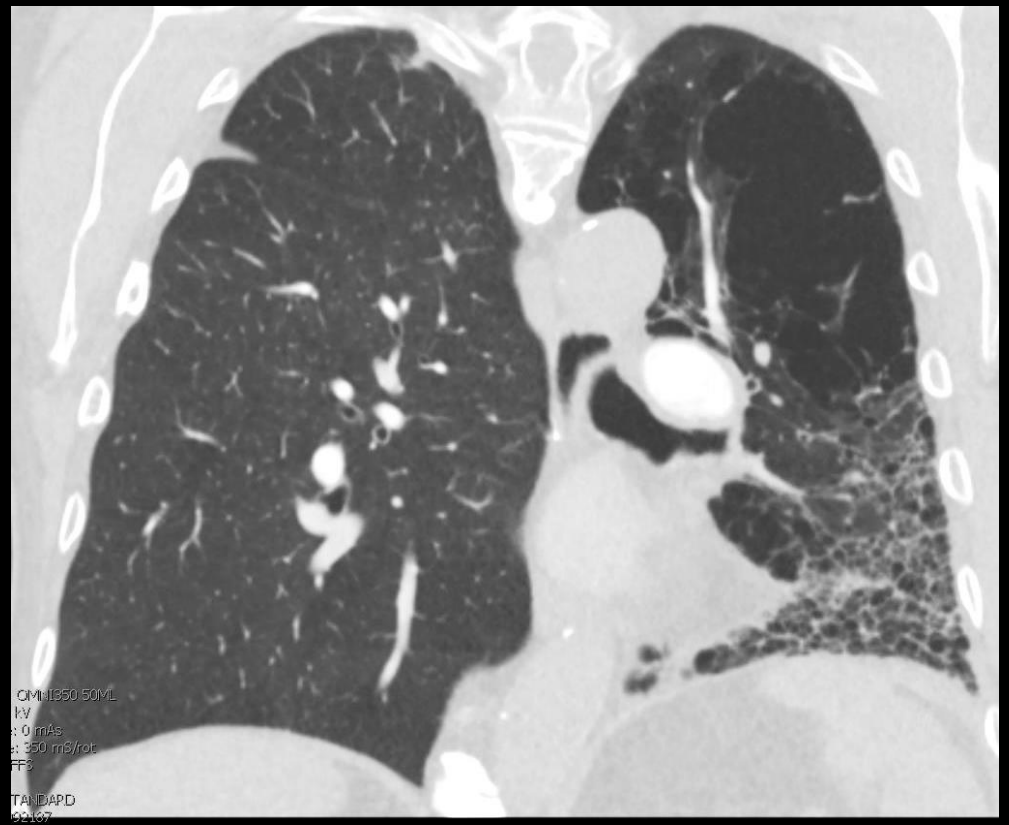
- Various sized thin-walled cysts
- May slightly spare subpleural regions
- Reticular and GGO

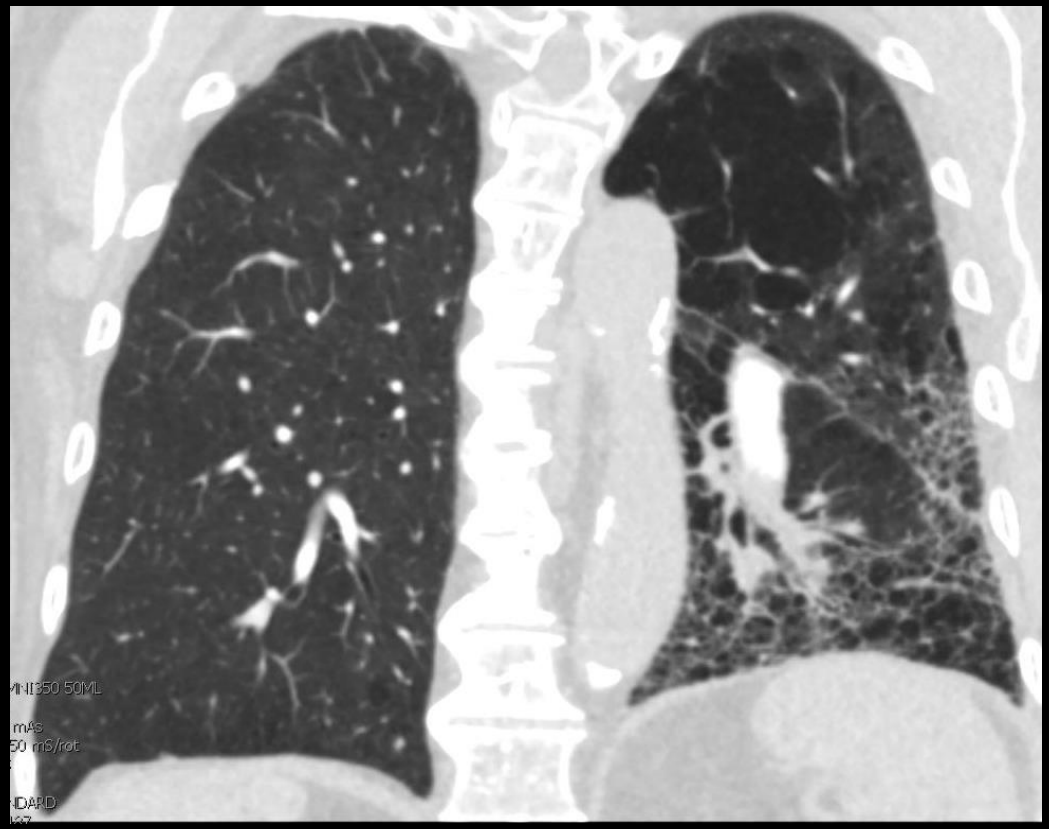


Case Five: 53 y/o man with 45 pack yr smoking history presents with severe SOB

Diagnosis: Combined Pulmonary Fibrosis Emphysema (CPFE)

Same patient S/P single lung transplant





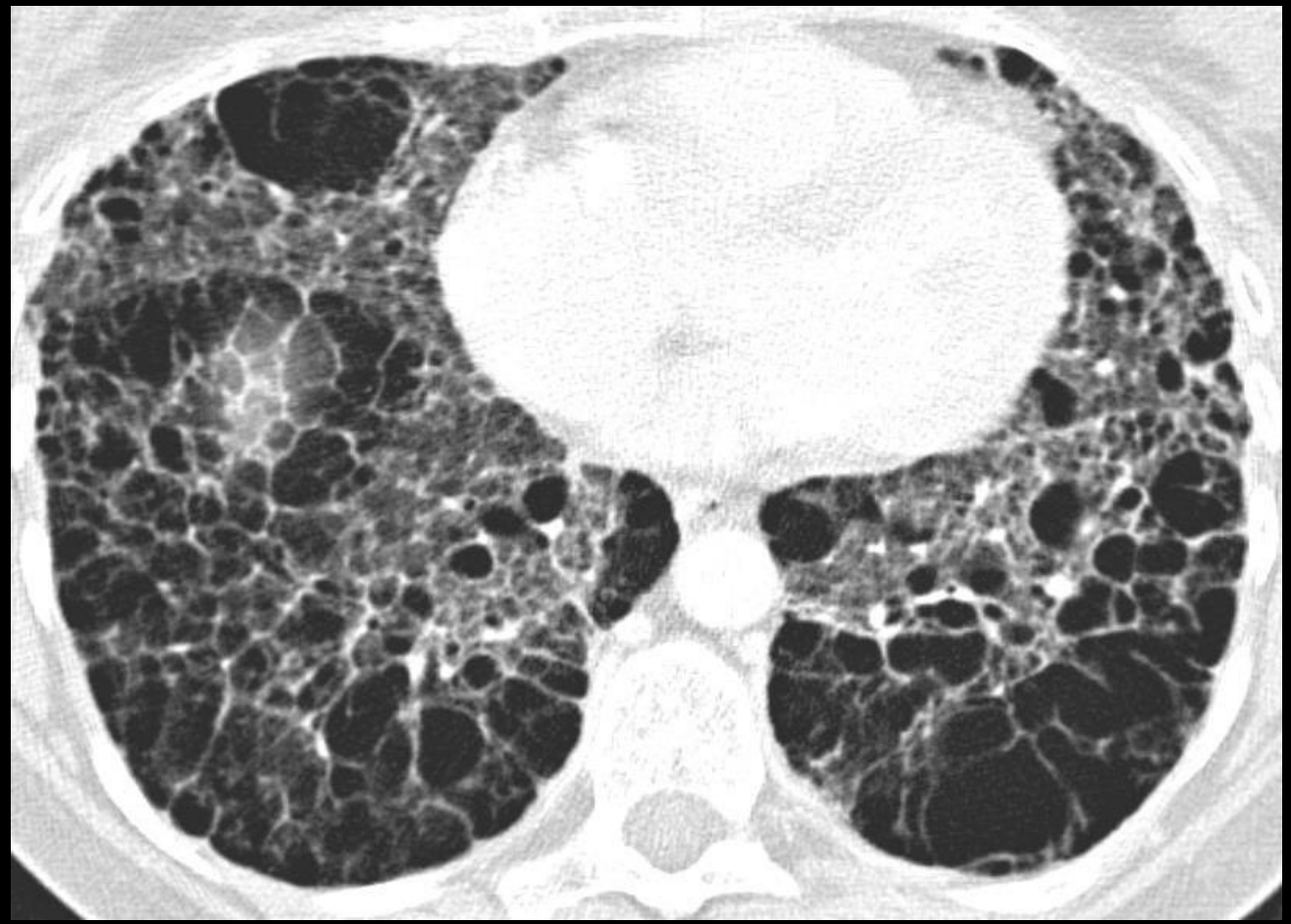
Combined pulmonary fibrosis emphysema (CPFE)

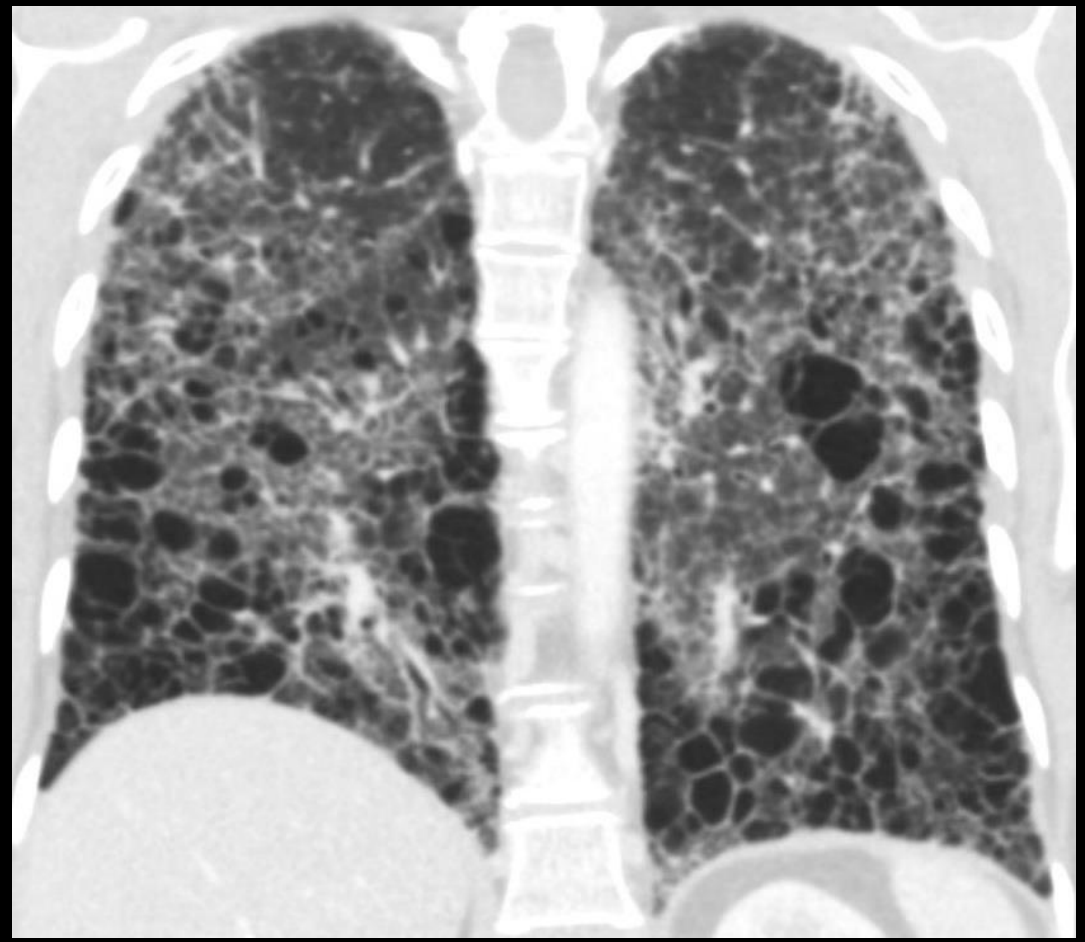
- Associated with heavy cigarette smoking
- Coexisting patterns of interstitial fibrosis and emphysema
- Any type of fibrosis including AEF, NSIP, and UIP may be included
- 47% and 55% of patients present with PHTN at diagnosis and during follow-up respectively

Imaging in CPFE

- All patients exhibited upper zone emphysema and lower zone fibrosis
- Emphysema may be that of centrilobular or paraseptal patterns
- Emphysema should involve >10% of the lung volume
- Bulky cystic lesions with thick walls predominantly in the upper lobes may be due to AEF or unclassified emphysema with fibrosis

Diagnosis: Unclassifiable IIP in smokers





Unclassifiable IIP in smokers

- The final diagnosis cannot be determined even after interdisciplinary consultation
- Overlapping histologic patterns is common in smokers
- This group exhibit slow progression and longer survival than IPF
- Airway centered cysts with fibrosis
- Many show normal FEV_1 and FVC but low DLCO

Imaging in Unclassifiable IIP in smokers

- Cystic dilatation of peripheral bronchi
- Airway centered cysts which progress
- Progression of cysts to large airspaces causing lung destruction
- Small-airways centered interstitial fibrosis

Navigating the ILD Maze

- Is this UIP pattern or not?
- If so, is it IPF?
- Diagnosis of IPF cannot be made unless other causes of fibrosing ILD are excluded
- Systemic, Exposure, Familial causes
- Suspect IPF if pt > 60 y/o, male, and hx of cigarette smoking

Lynch et al Lancet Respir Med 2018; 6: 138–153

CT Scanning tips in Idiopathic Interstitial Pneumonias

- Thin section imaging 1mm-1.25 mm
- Inspiratory phase
- Expiratory phase in end tidal volume
- Prone imaging

Revised HRCT Classification of UIP

	Typical UIP CT pattern	**Probable UIP CT pattern**	**CT pattern indeterminate for UIP**	**CT features most consistent with non-IPF** diagnosis
Distribution	Basal predominant (occasionally diffuse), and subpleural predominant; distribution is often heterogeneous	Basal and subpleural predominant; distribution is often heterogeneous	Variable or diffuse	Upper-lung or mid-lung predominant fibrosis; peribronchovascular predominance with subpleural sparing
Features	Honeycombing; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis *; absence of features to suggest an alternative diagnosis	Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis *; honeycombing is absent; absence of features to suggest an alternative diagnosis	Evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern	Any of the following: predominant consolidation, extensive pure ground glass opacity (without acute exacerbation), extensive mosaic attenuation with extensive sharply defined lobular air trapping on expiration, diffuse nodules or cysts

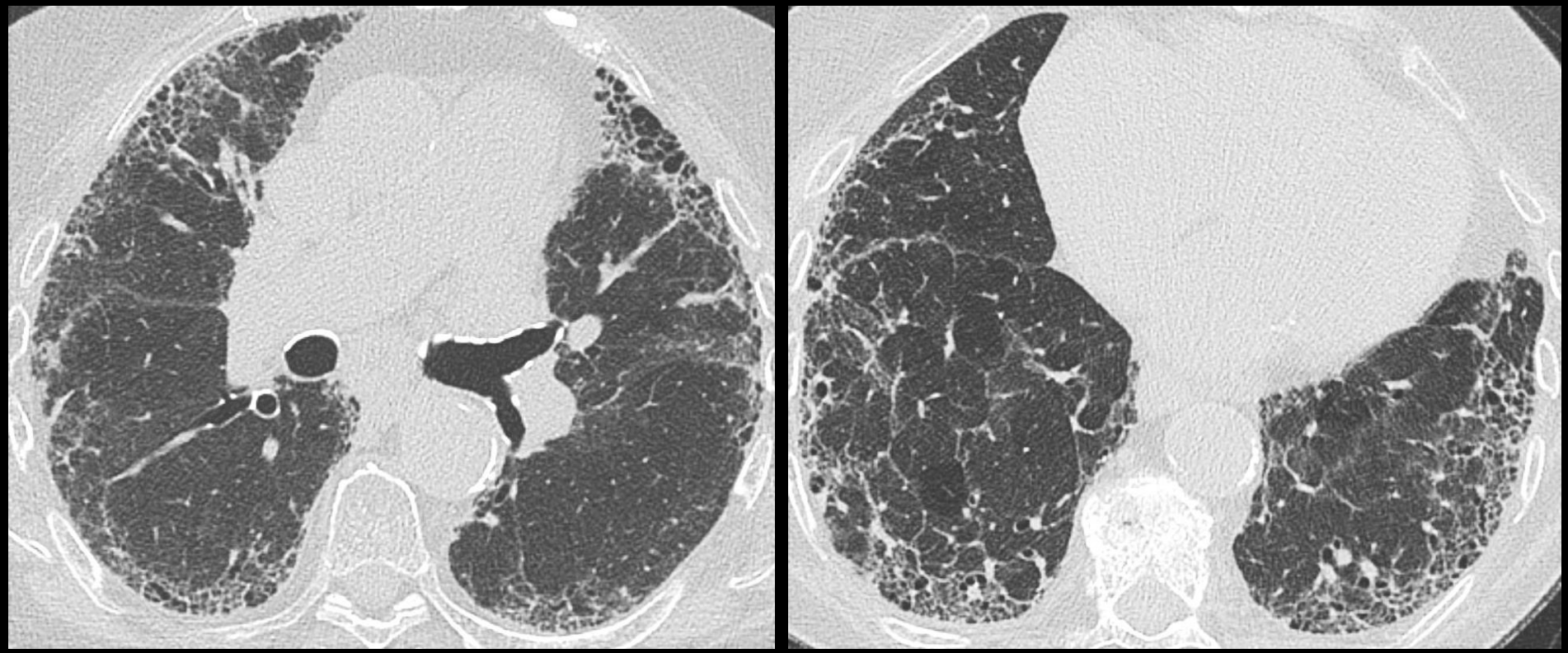
Lynch et al Lancet Respir Med 2018; 6: 138–53

Honeycombing dilemma

- Honeycombing vs traction bronchiectasis/bronchiolectasis
- Honeycombing – subpleural, well defined walls
- Traction bronchiectasis/ bronchiolectasis – separated from pleural surface and one another

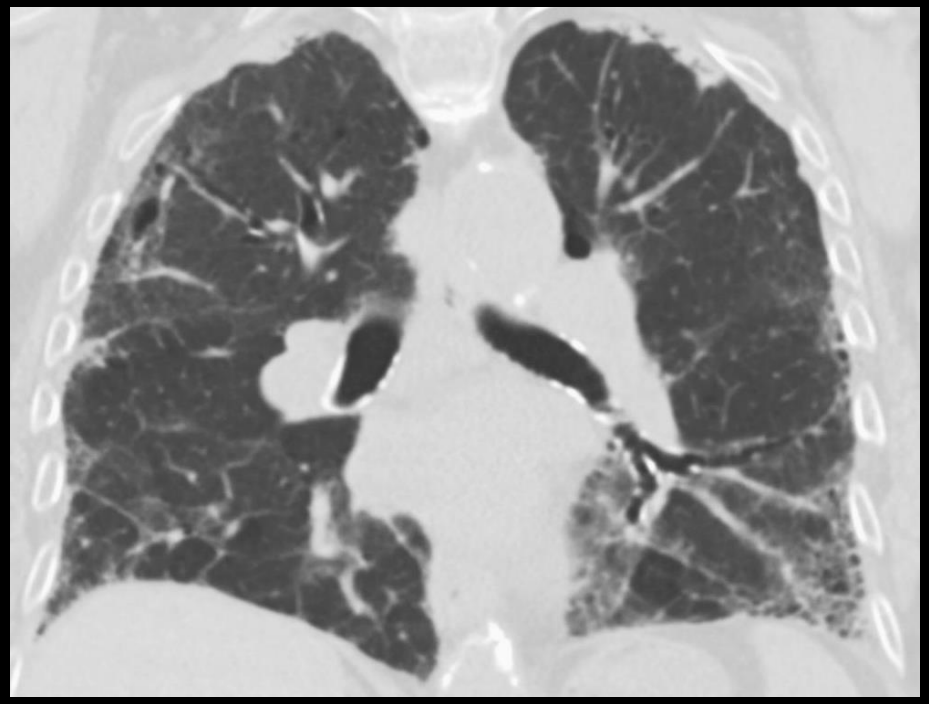
Patient History

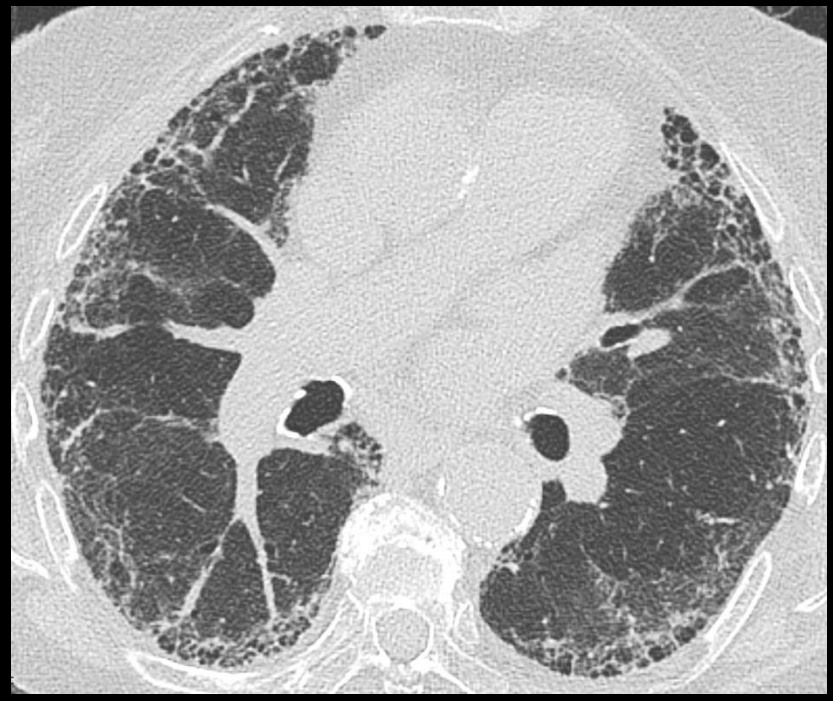
82 y/o female who presented with several month h/o dry cough and DOE



Findings

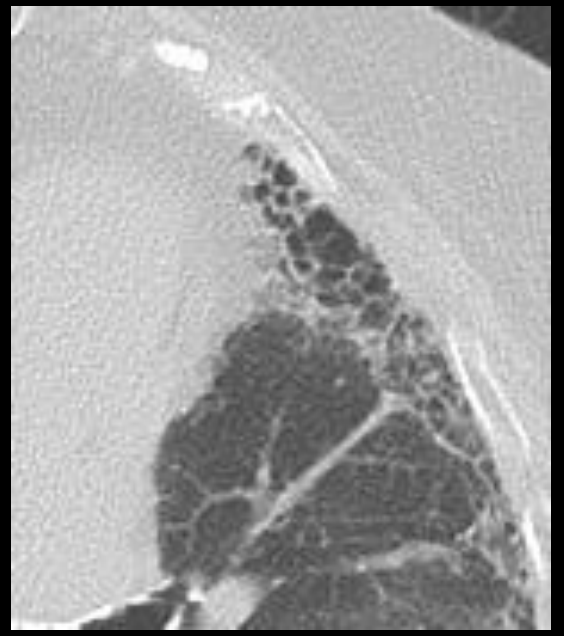
- Basal and subpleural honeycombing
  Bronchiolectasis
- Reticulation upper lobes
- Craniocaudal gradient on coronal images





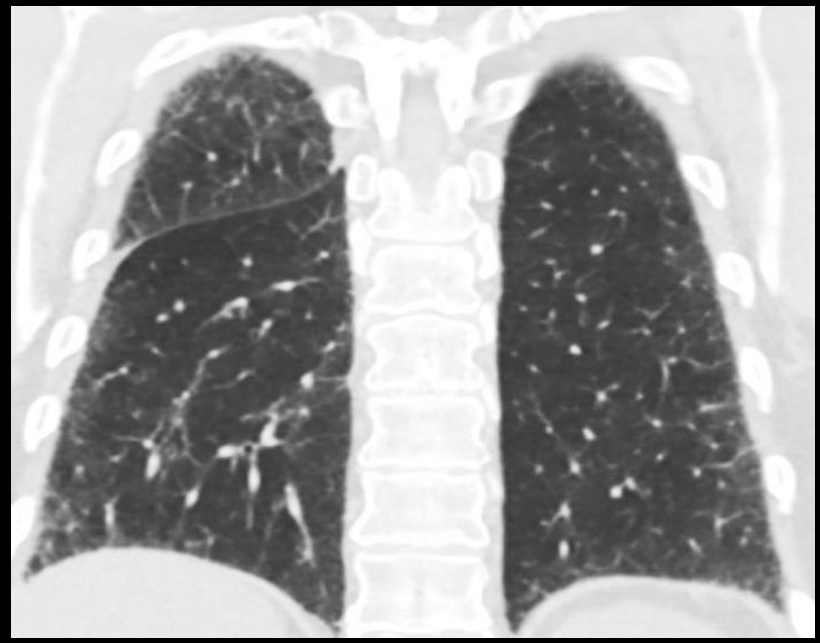
Typical UIP

- Subpleural predominant reticular abnormality
  - Honeycombing; traction bronchiectasis
  - Usually in posterobasal portion of lung
- Clear craniocaudal gradient on coronal images
- GGO is not typical
- Heterogeneous distribution



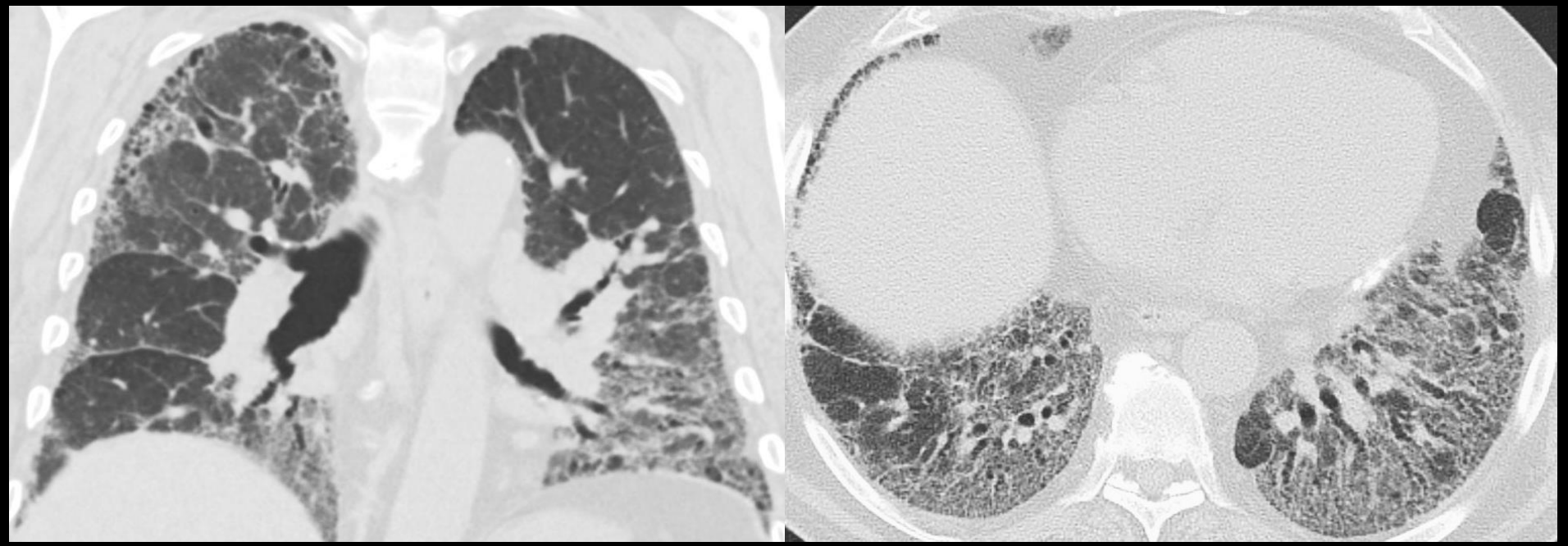
Probable UIP

- Basal predominant, subpleural reticular abnormality
- Peripheral traction bronchiectasis
- No honeycombing

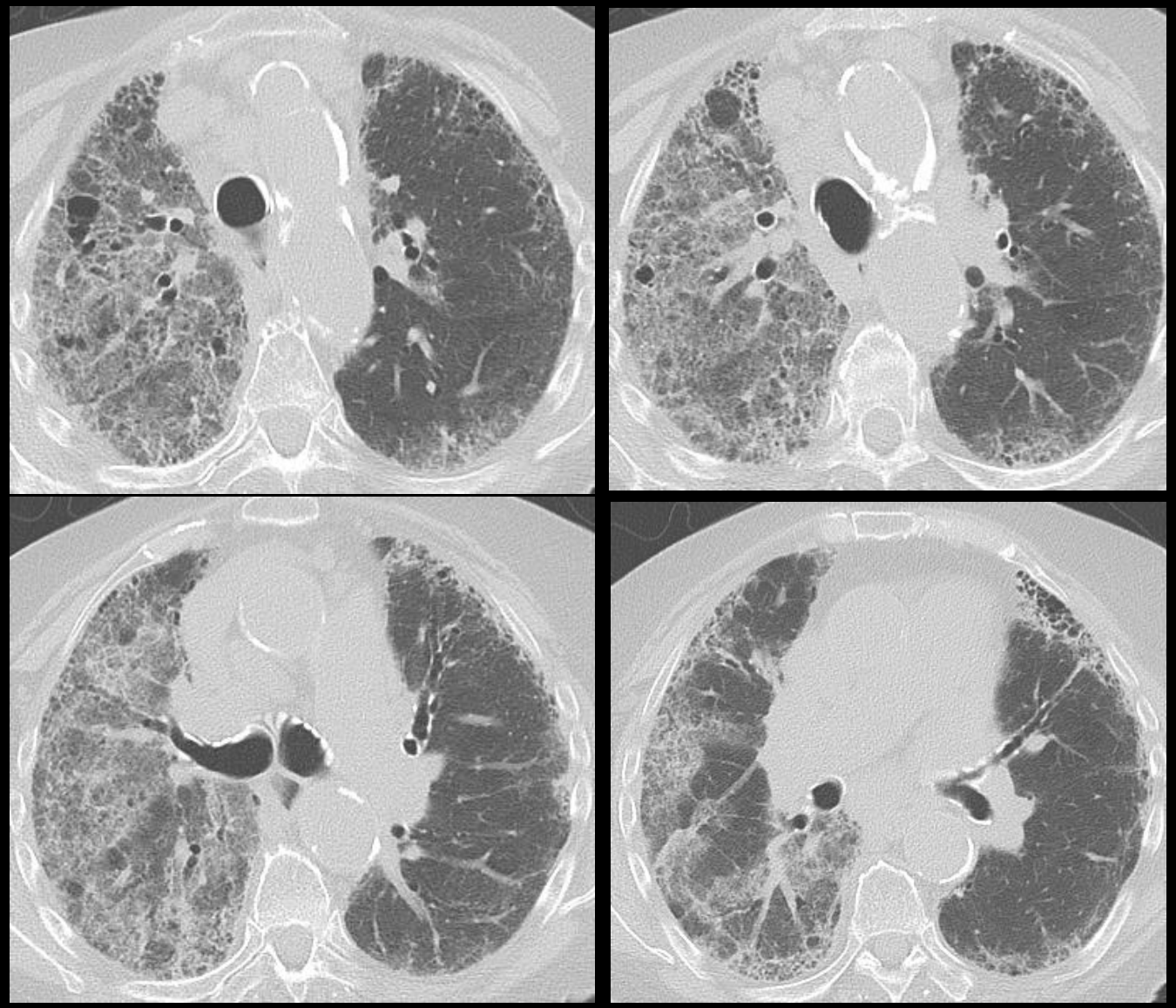


Indeterminate for UIP: But path proven UIP

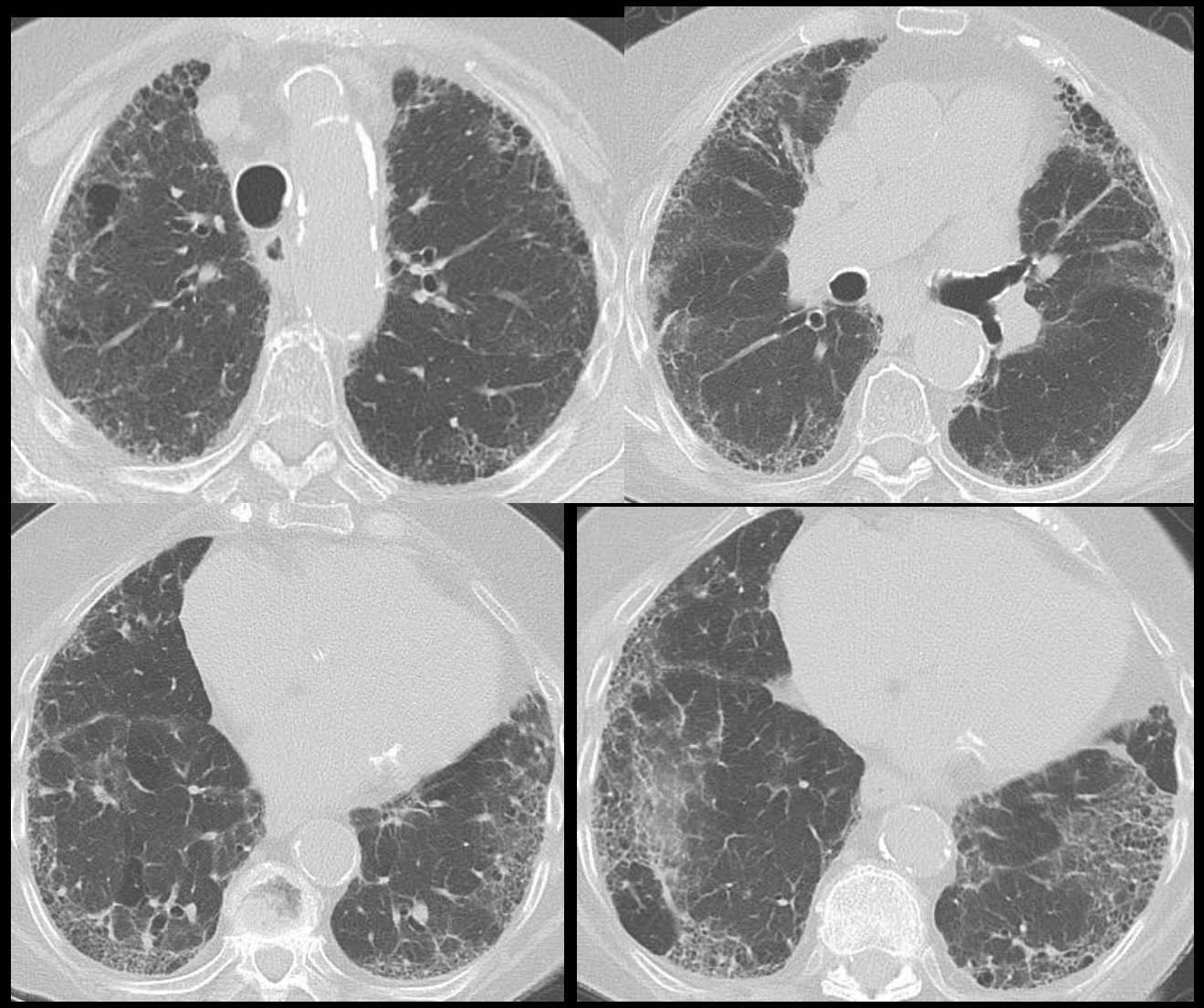
- Basal predominant traction bronchiectasis without honeycombing
- May have mosaic attenuation or patchy GGO



62-Year-old woman comes in with shortness of breath for two weeks? Diagnosis?

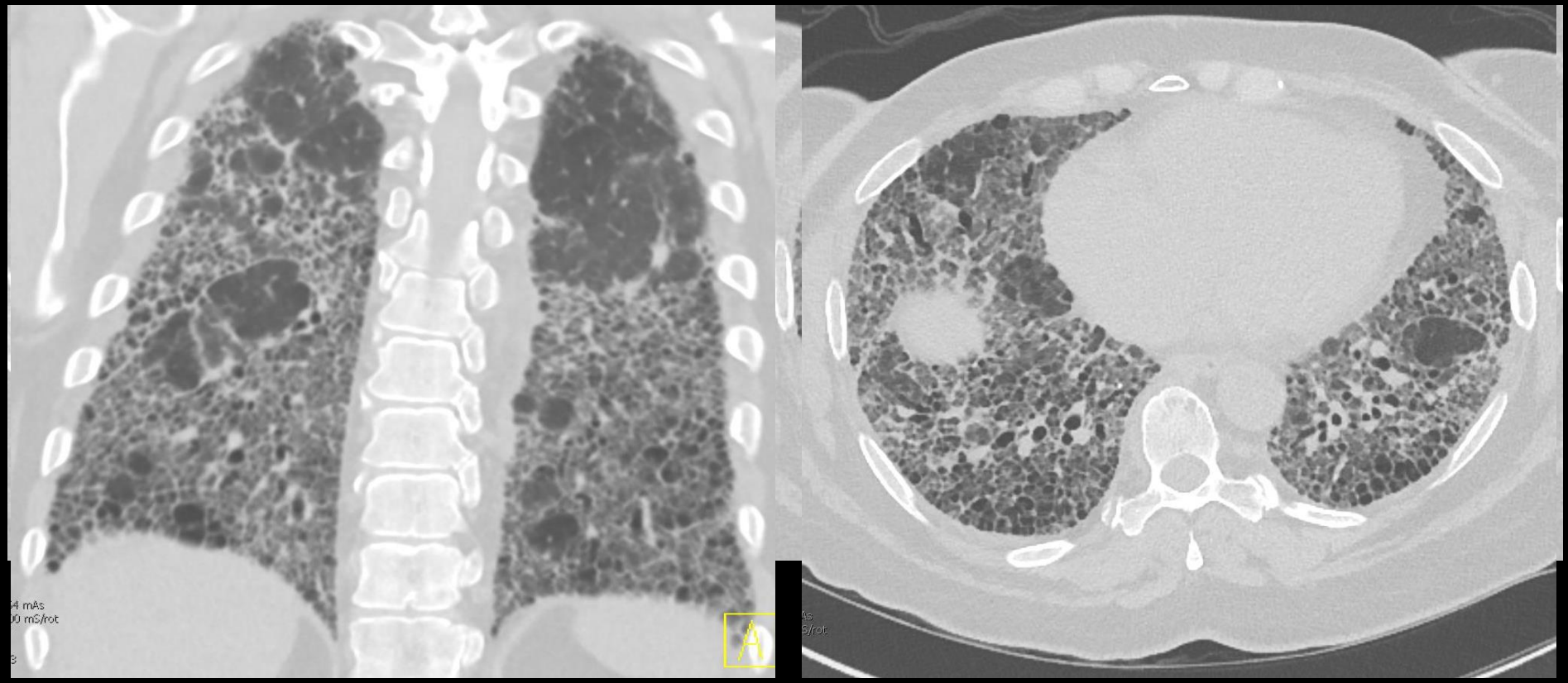


Same patient 7 weeks later after treatment



Familial IPF: Short Telomere Syndrome

- Imaging findings in familial IPF can differ from sporadic IPF with higher prevalence of diffuse or upper lobe predominant fibrosis



Lynch et al Lancet Respir Med 2018; 6: 138–153

Non-IPF diagnosis

- Upper or mid lung predominant fibrosis
- Peri-bronchovascular predominant disease
- Spares lung periphery
- Consolidation
- Extensive pure GGO
- Extensive mosaic attenuation
- Sharply defined lobular air trapping
- Diffuse nodules or cysts

Teaching points

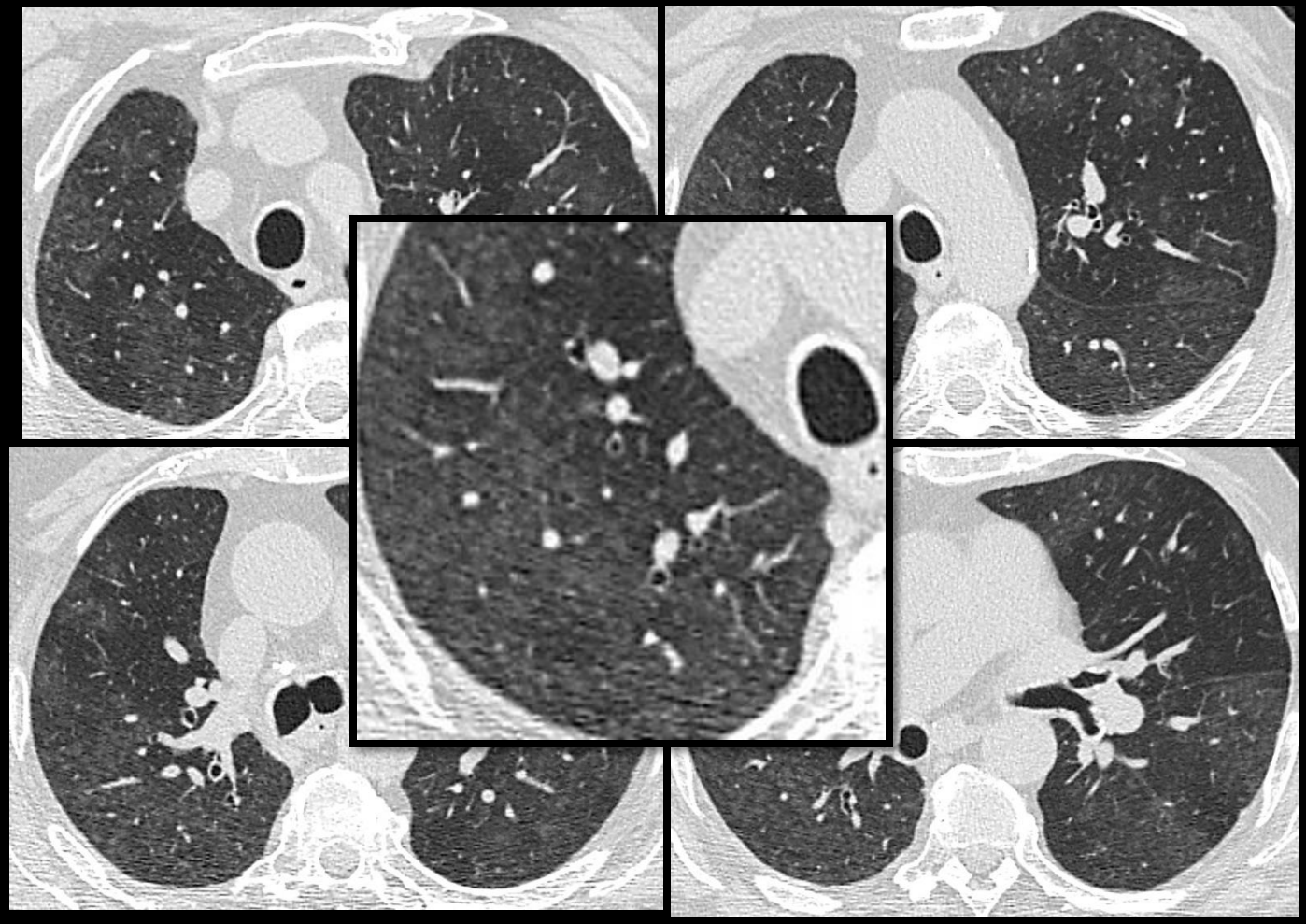
IPF versus other causes for fibrosing ILD

- Assess for systemic diseases - CTD or other autoimmune disease, granulomatous disease
- Presence of pericardial or pleural effusion can suggest CTD
- Exposure to antigens
- Genetic syndromes
- Obtain expiratory imaging to exclude air trapping
- No bx needed in typical and probable UIP

Case: 86 y/o man with 65 pack year smoking history presents with SOB and cough

Diagnosis: RB-ILD

DDx: Acute hypersensitivity Pneumonitis



Respiratory bronchiolitis-interstitial lung disease (RB-ILD)

- Clinical diagnosis made in heavy smokers
- Patients complain of dyspnea and cough over weeks to months
- See abnl pulmonary function tests in RB-ILD
- On histology peribronchiolar fibrosis and peribronchiolar macrophages
- On a spectrum with DIP pathologically
- Some patients show widespread macrophage distribution much like DIP

Radiologic findings in RB-ILD

- Central bronchial wall thickening
- Centrilobular nodules
- Areas of GGO
- Some reports indicate upper lung zone predominance
- HP is in the differential

Conclusions

- History Matters
- Patterns are also important
- Look for associated findings
- Distribution is helpful

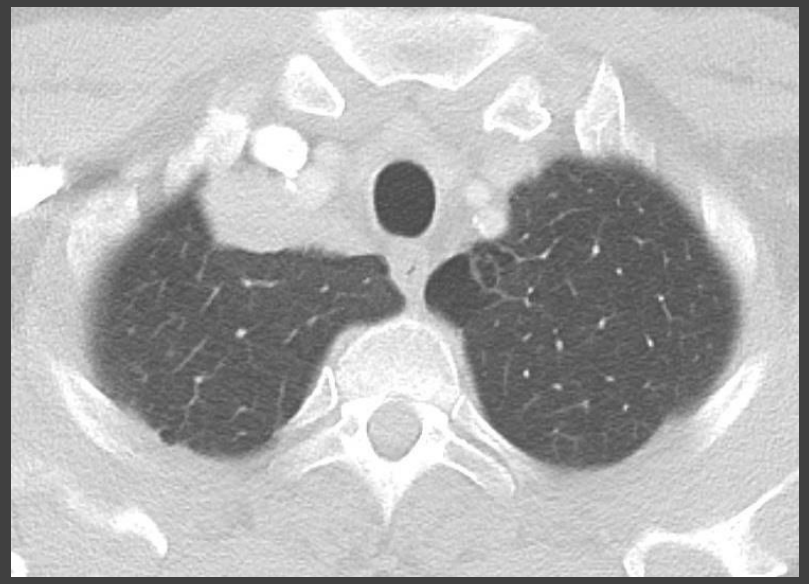
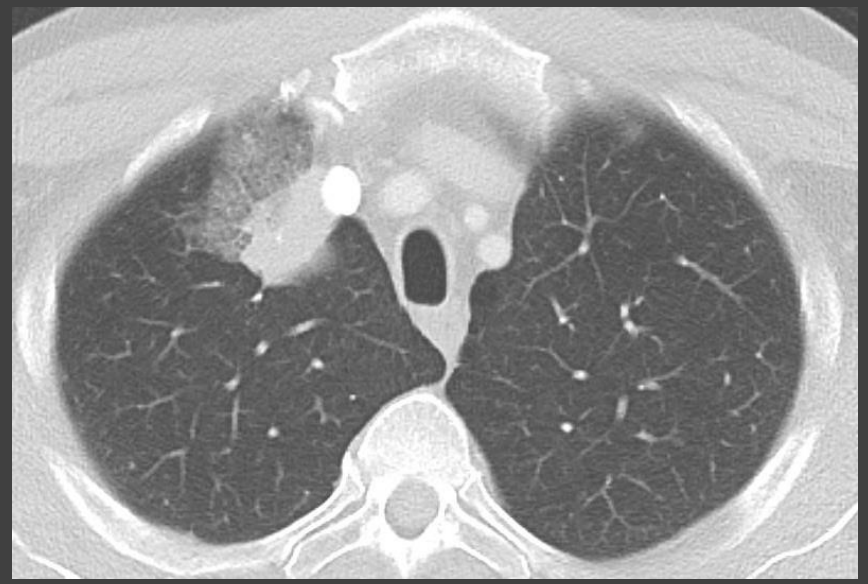
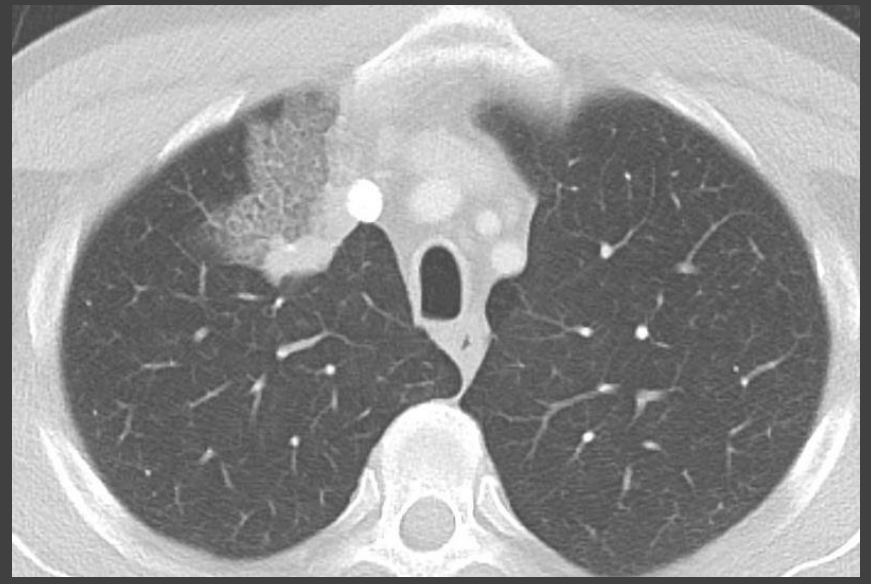
Missed Lung Cancer on Plain Film

Missed Lung Cancer

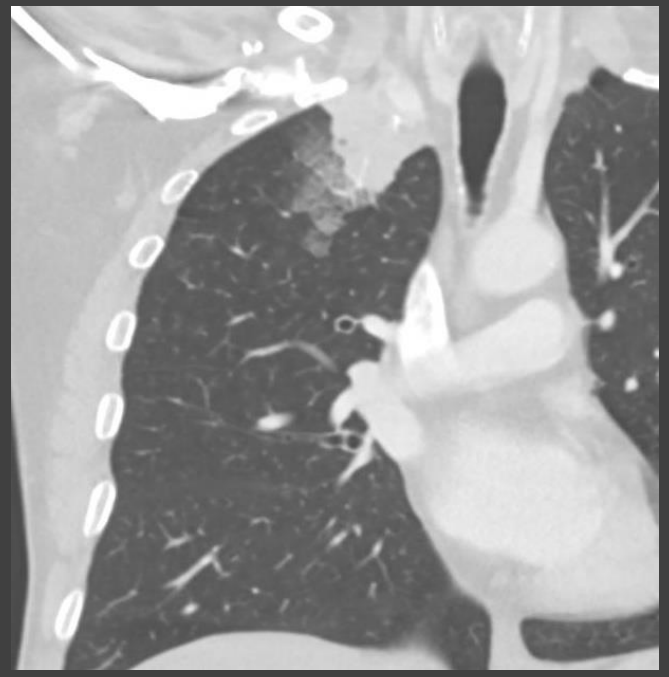
- Lung cancer is the leading cause of cancer-related death in the US
- Radiologists play an important role in the diagnosis of lung cancer
- Nearly 40% of lung cancers are asymptomatic at the time of diagnosis
- Many of these are diagnosed with chest radiographs performed for unrelated clinical indications
- Missed lung cancer is a leading cause of medical malpractice among radiologists
- 90% of missed cancers involve CXR

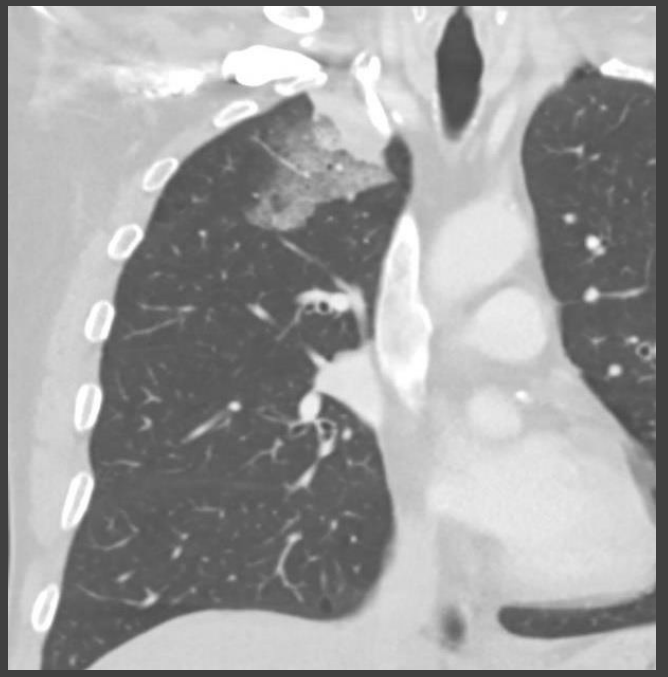
Case 1: 59 y/o male presented with right chest wall pain. CXR performed and read as normal

Case 1: The patient returned two weeks later complaining of worsening right chest wall pain. CT was performed

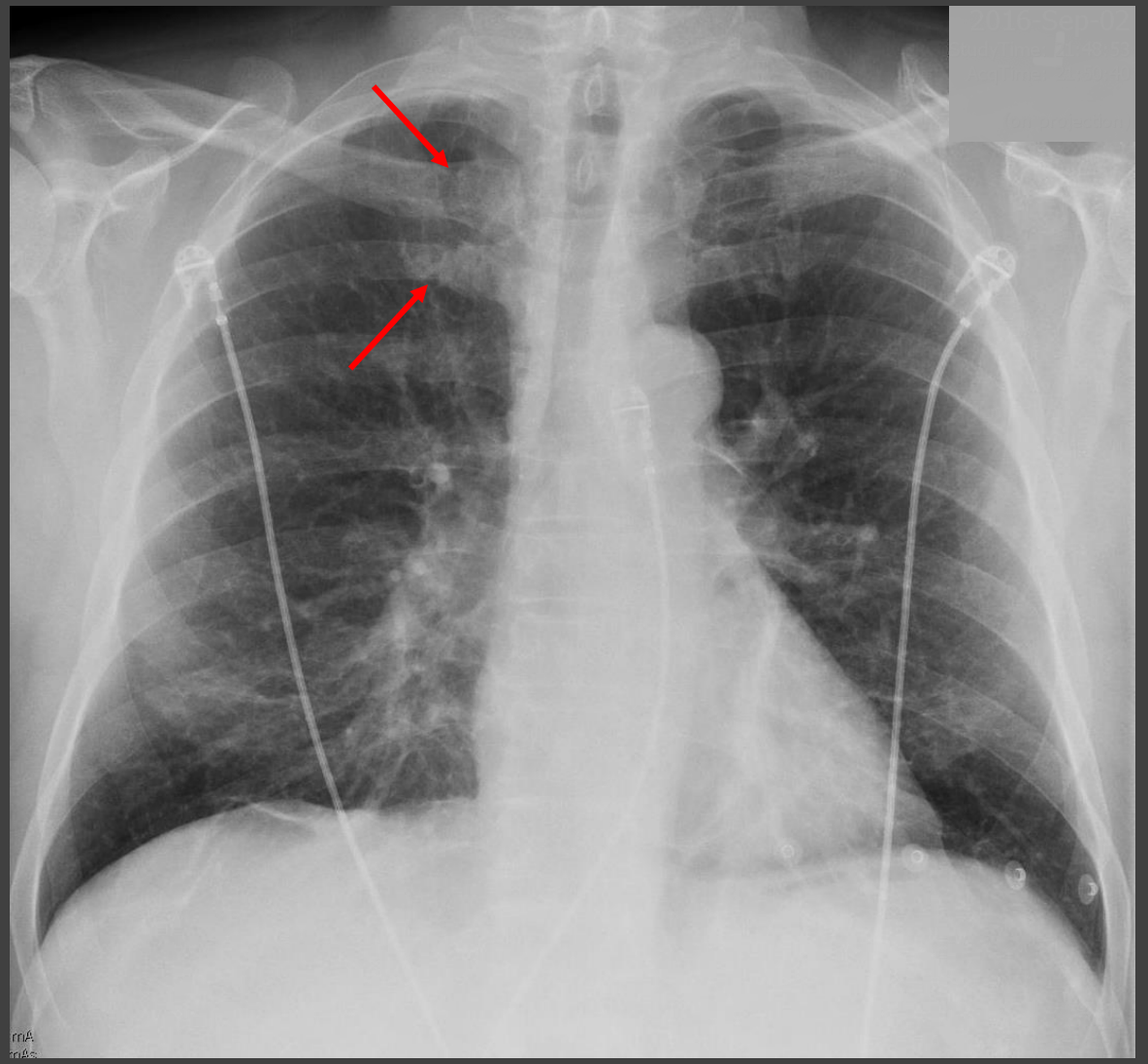
Case 1: Coronal images of the same patient



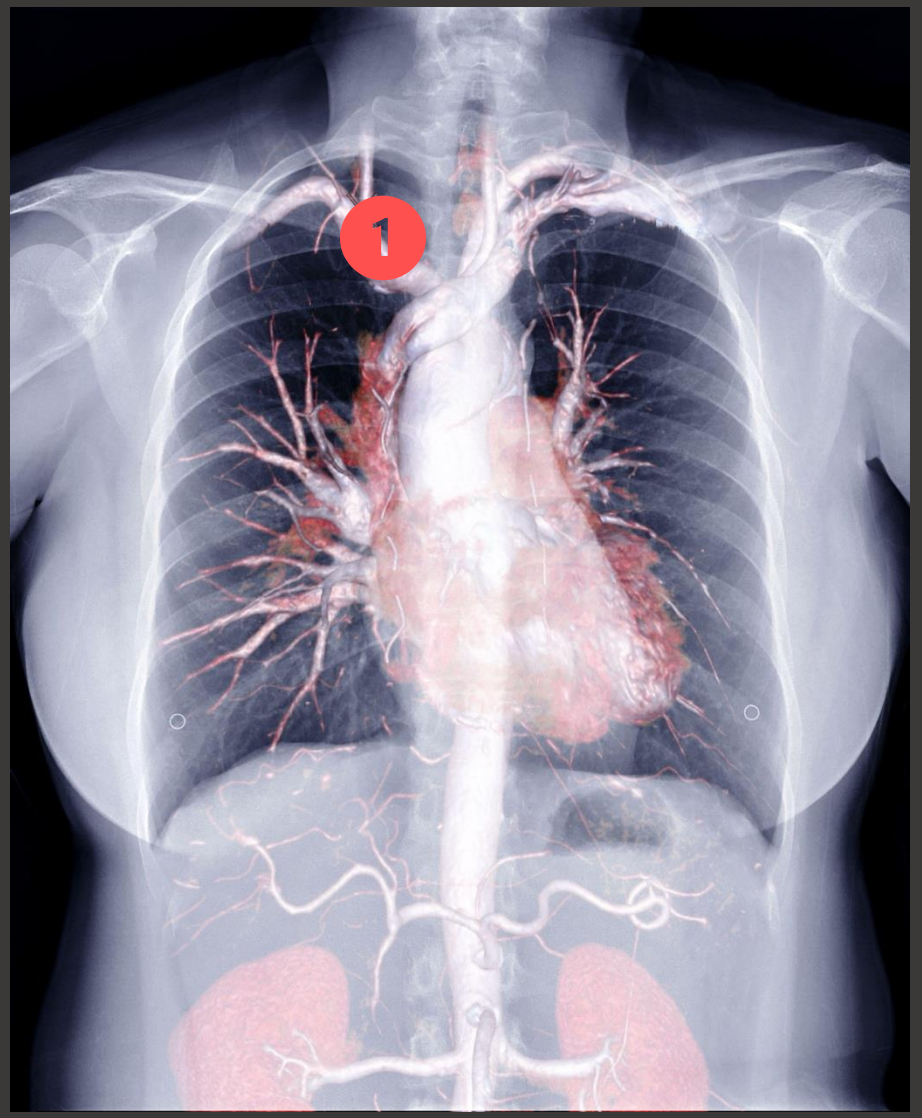


Case 1: Recap of salient points

- Always compare side to side
- Remember the lung apices
- In this case right apex more opaque
- Beware of areas of overlapping structures



Schematic of locations of most missed lesions



Missed lung cancer: causes

- Observer error – most significant cause
  - Scanning error 30% of errors
  - Recognition error 25% of errors
  - Decision-making error 45% of errors
  - Satisfaction of search
- Tumor characteristics
  - Size
  - Conspicuity
  - Tumor histology
  - Location most are in the upper lobes 81% * with 56% in RUL
- Technical considerations

Del Ciello et al Diagn Interv Radiol 2017; 23:118-126

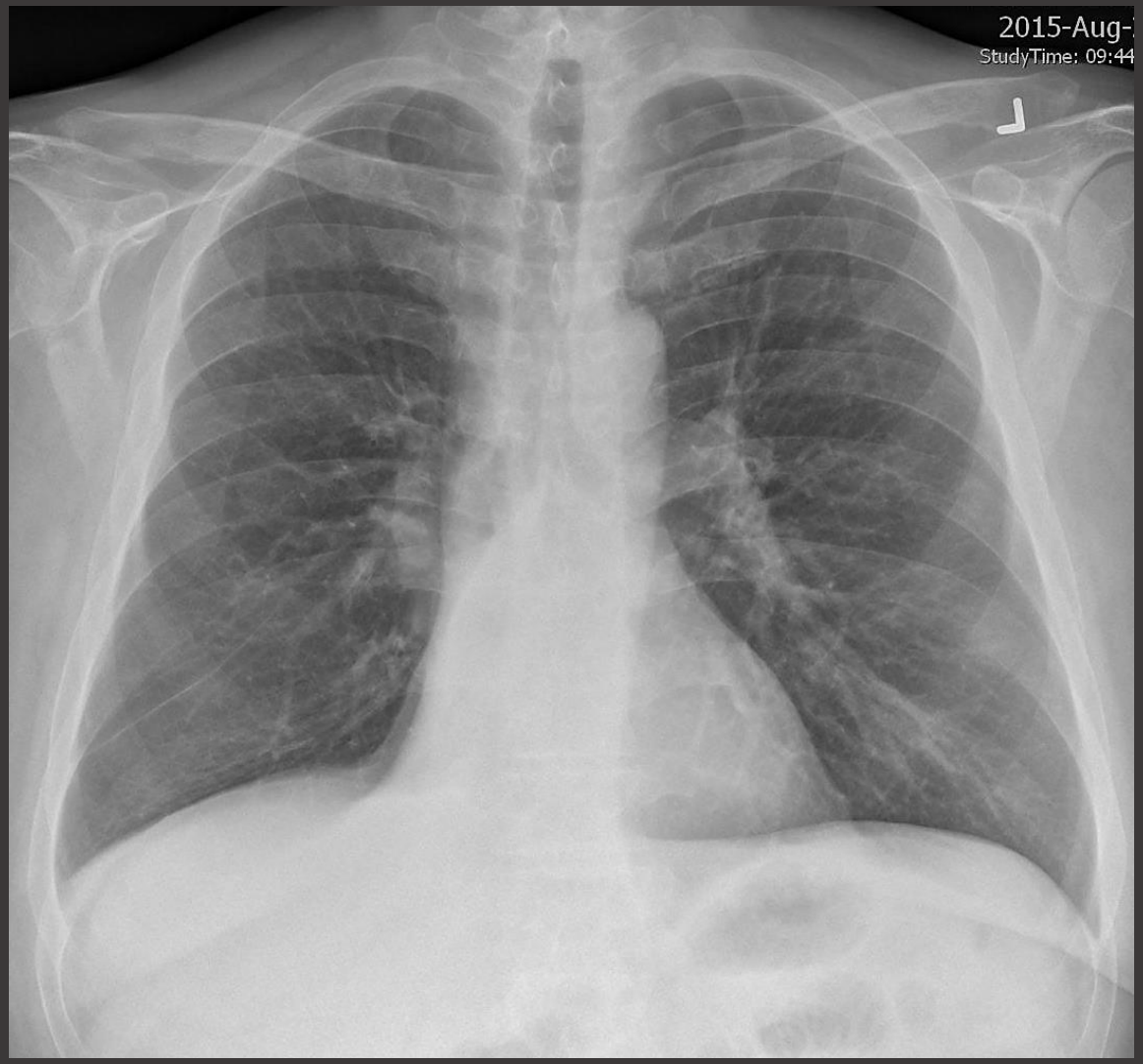
** Austin JH et al Radiology 1992;182:115-122*

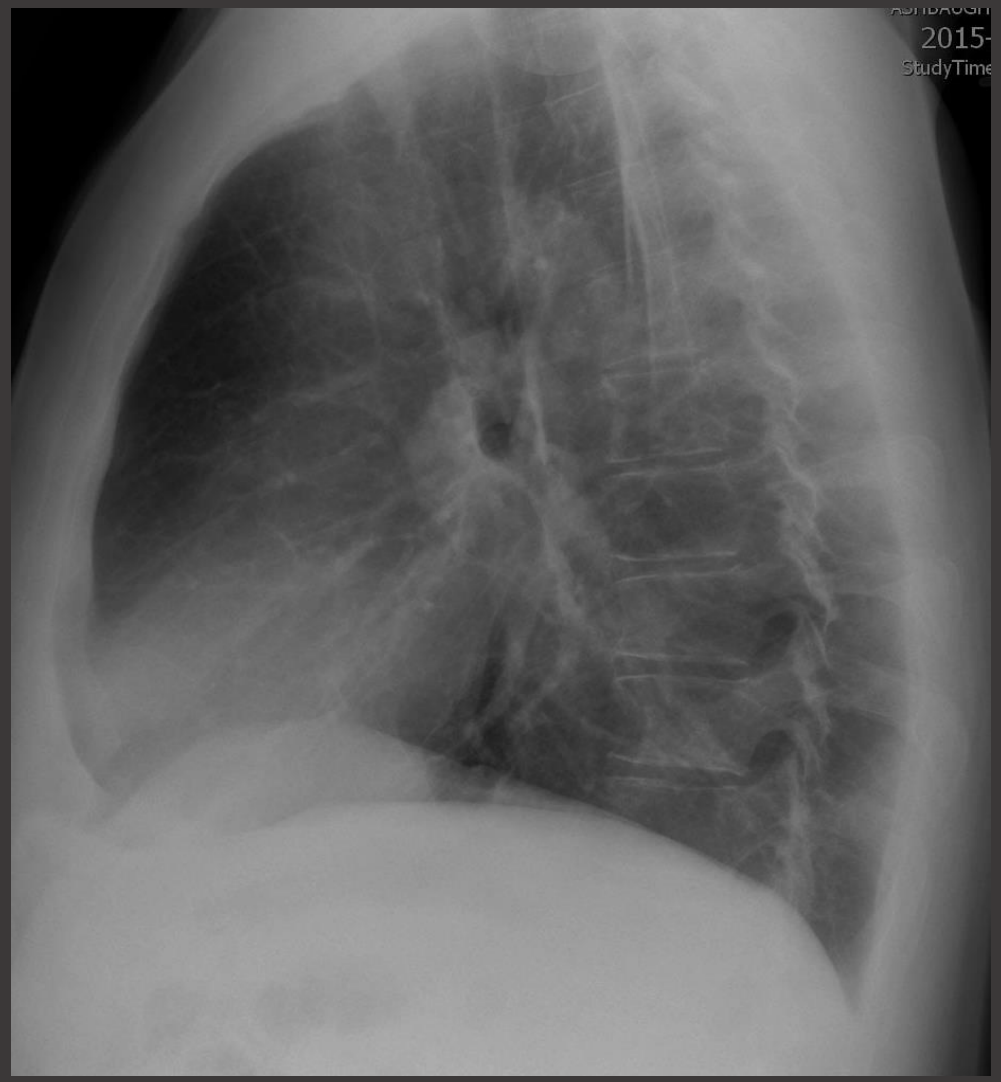
Missed lung Cancer on CXR: Other Contributors

- Poor imaging quality
- Poor viewing conditions (important with reading from home)
- Poor nodule conspicuity due to
  - small size – mean diameter of missed lung cancer is 1.3 to 1.6 cm
  - GGN
  - Ill-defined margins
  - Overlying structures

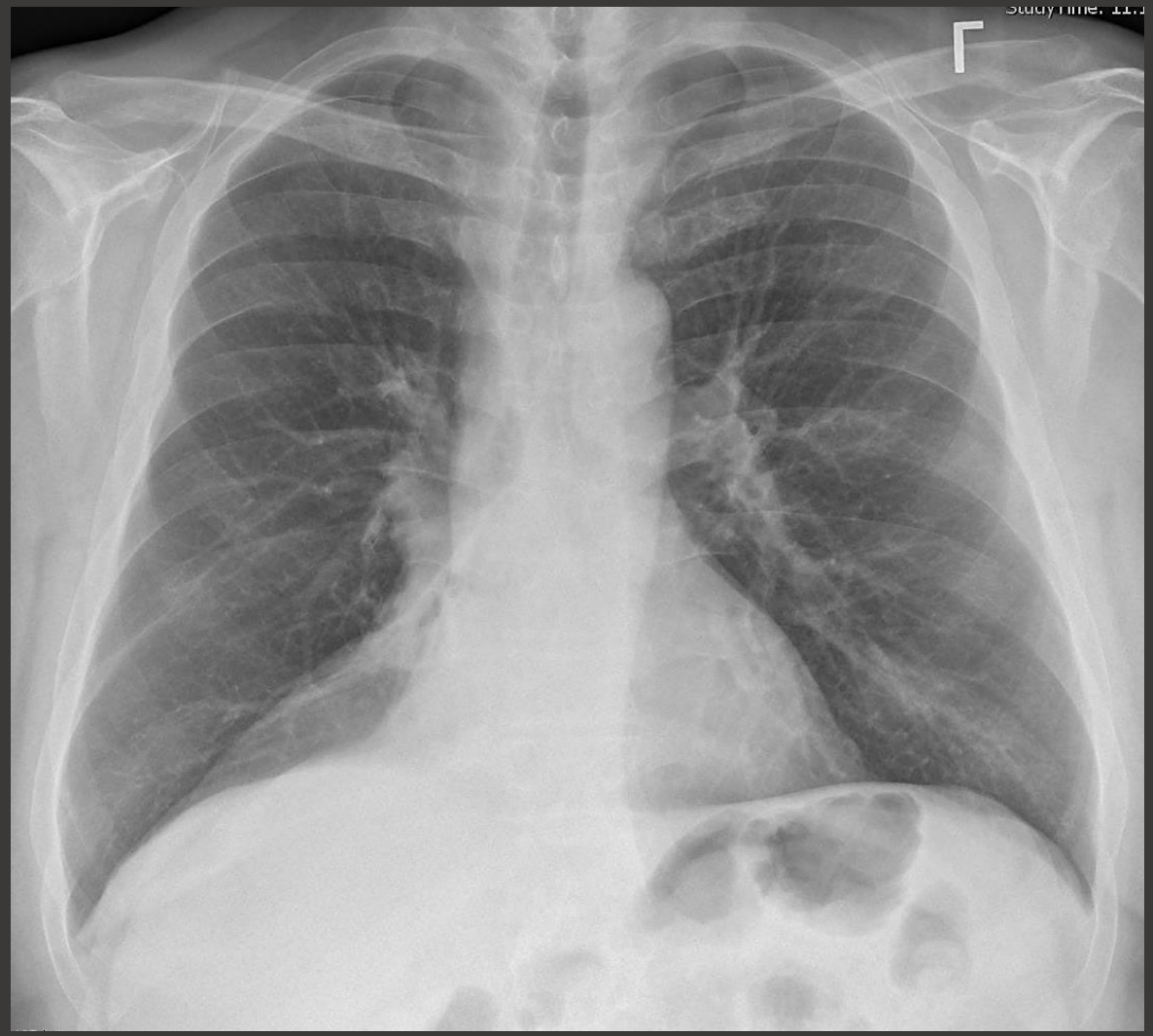
Hossain et al Radiol Clin N Am 56 (2018) 365-375

Case 2: 59 y/o male presented with shortness of breath with exercise for two months. CXR was performed





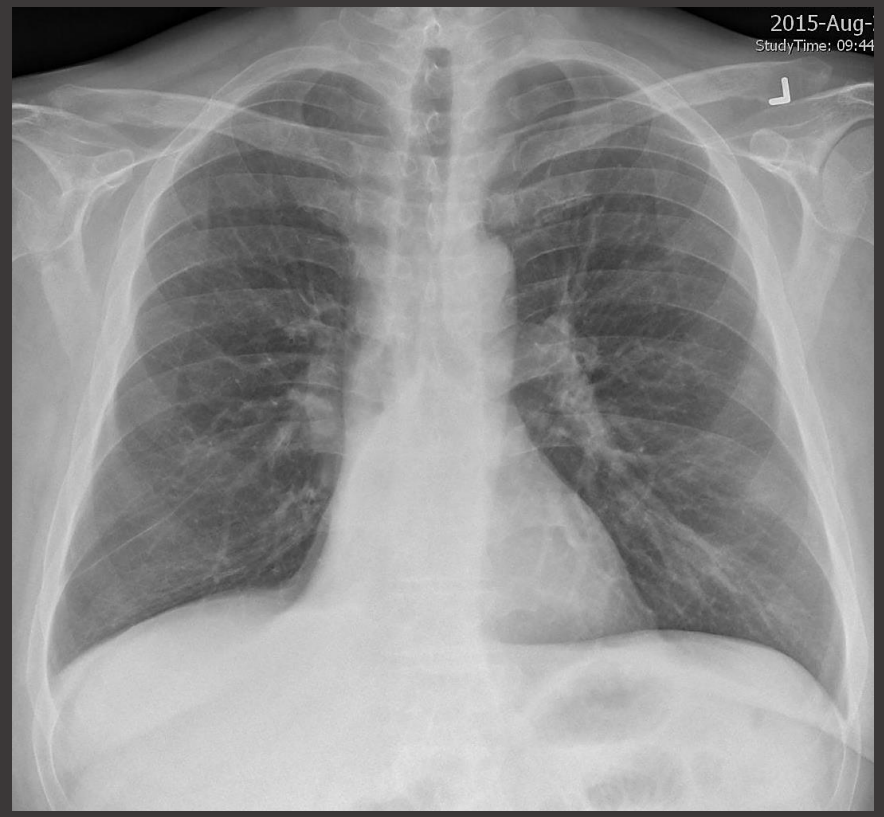
Case 2: He then presented seven months later with worsening symptoms and this CXR was performed followed by a CT scan

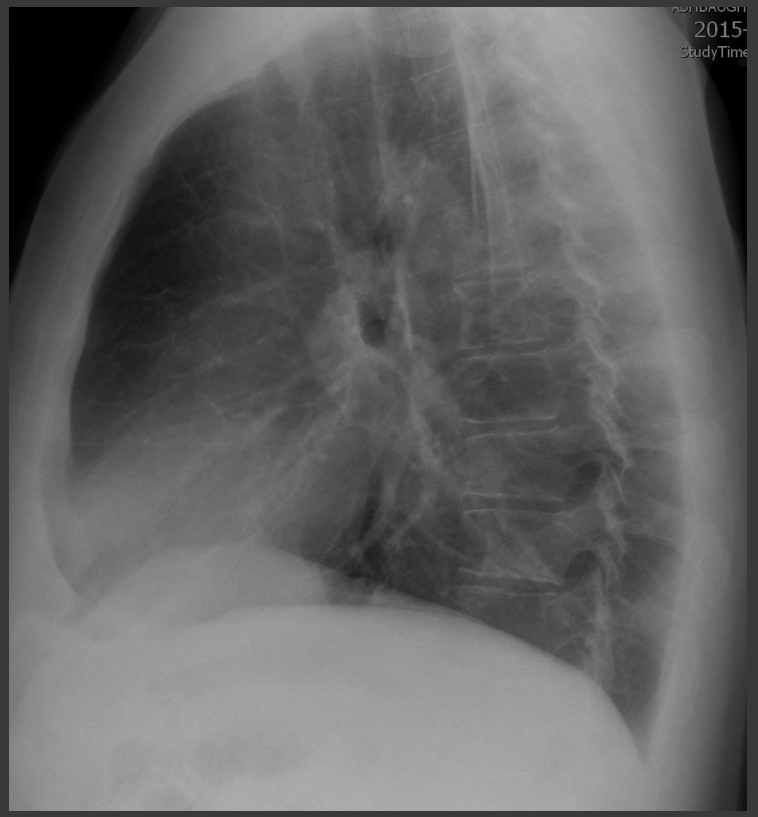


Case 2: same patient returned 7 months later with worsening symptoms. What was missed?

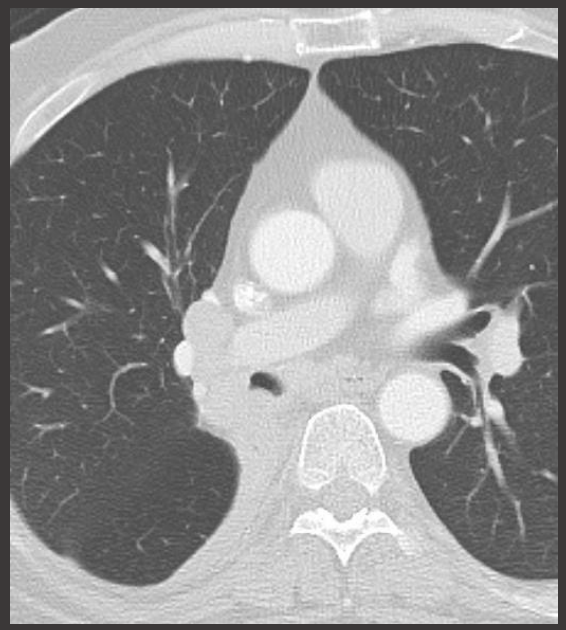
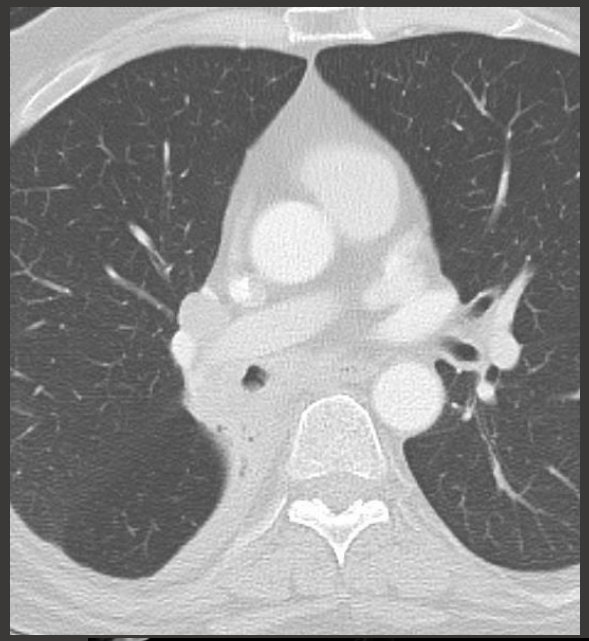
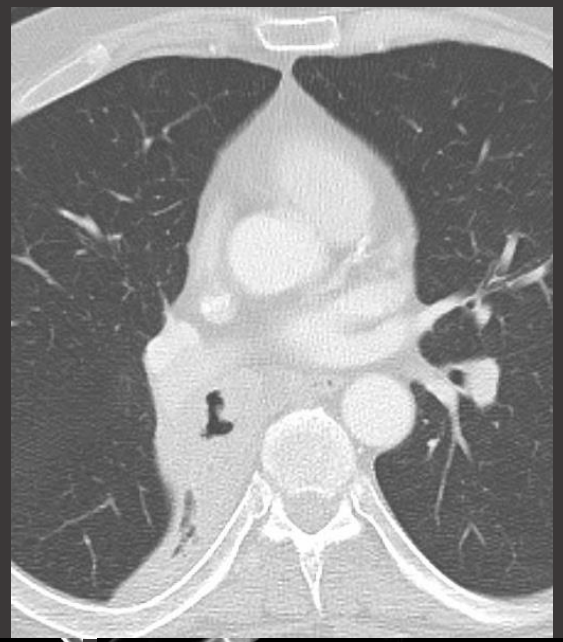
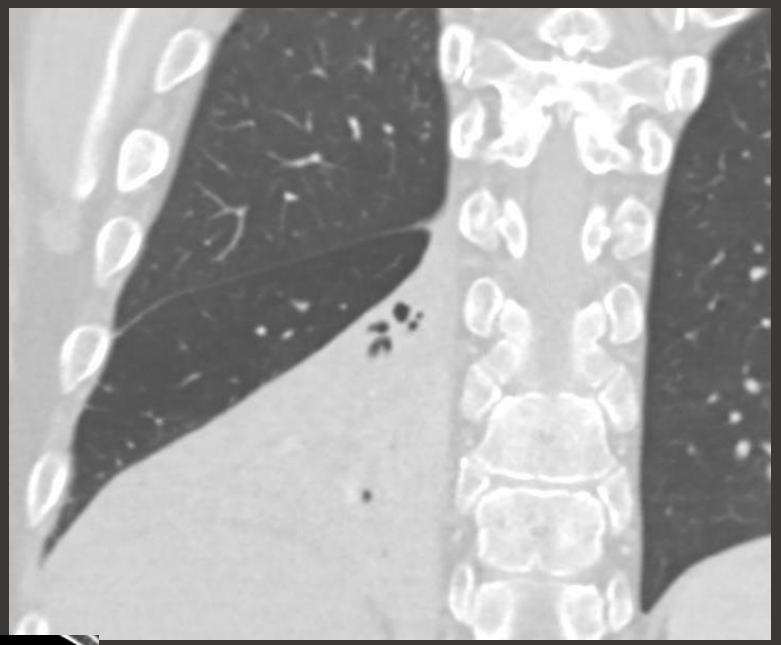
Answer ?

A. Right paratracheal mass
B. Right upper lobe atelectasis
C. Left hilar lymph node enlargement
D. Right lower lobe atelectasis



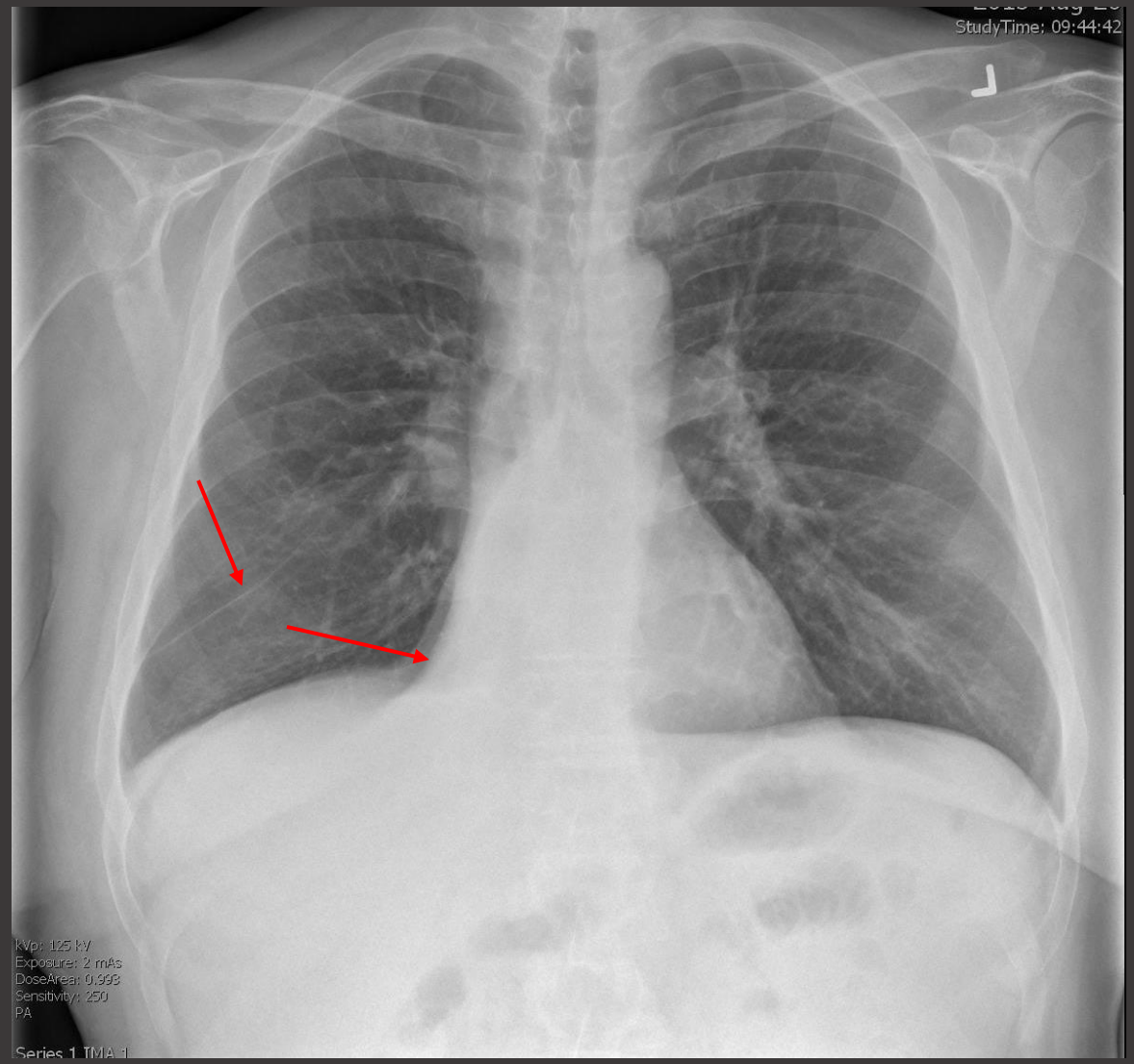


Case 2: CT scan of the chest was performed

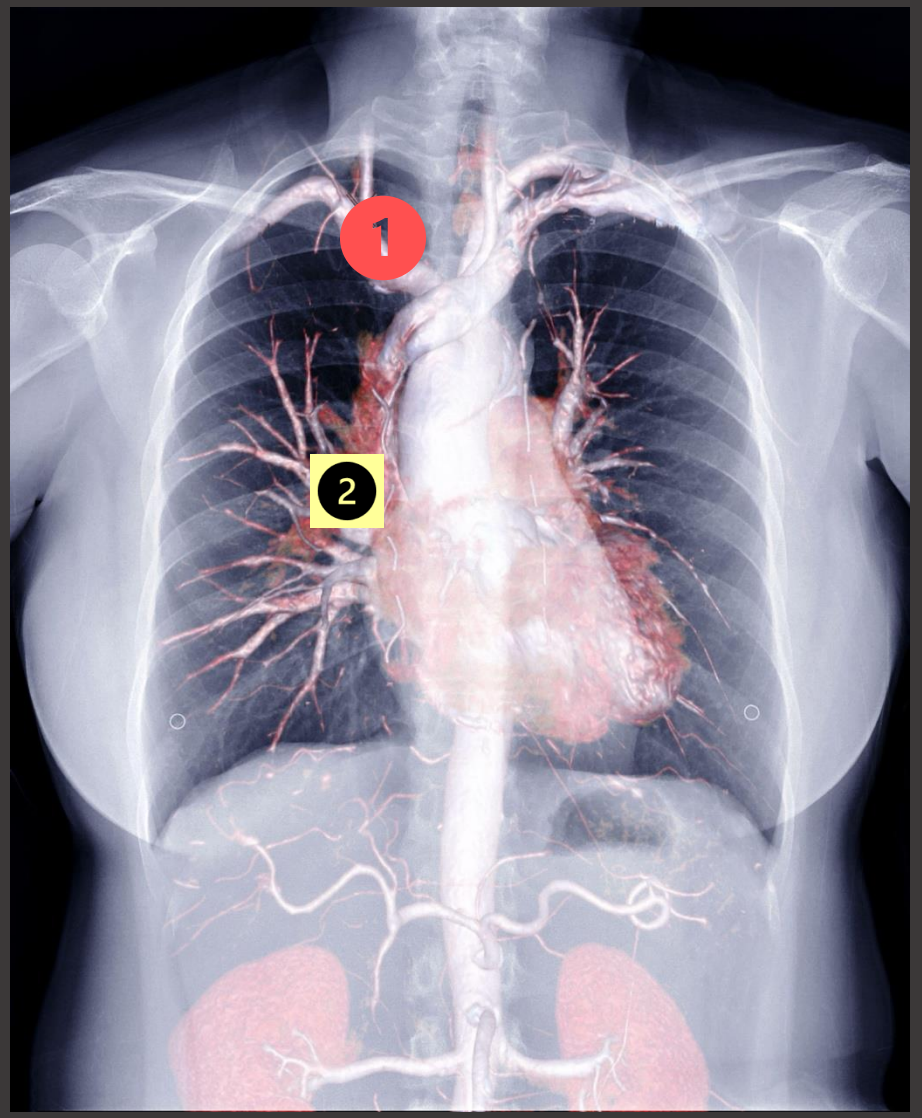





Case 2: Recap original CXR…salient points

- The right lung should be larger than the left
- The Minor fissure moved inferiorly
- Second well demarcated line posterior to the heart is the major fissure
- Missed RLL atelectasis
- If you miss atelectasis you may miss lung cancer

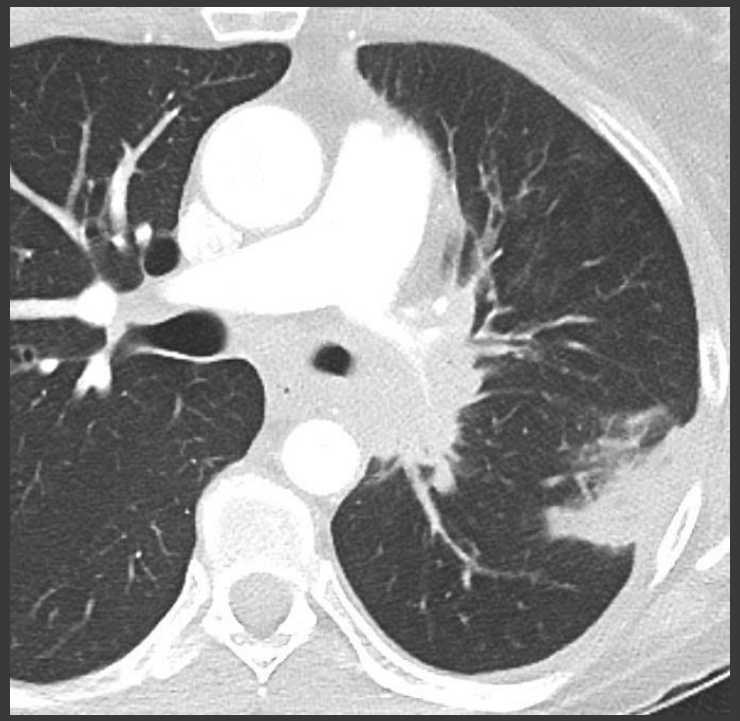


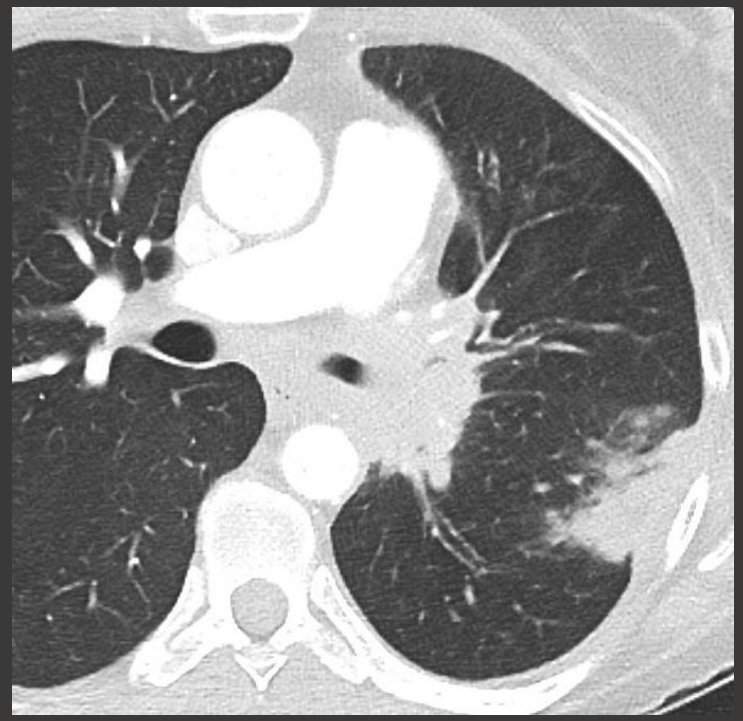
Schematic of locations of most missed lesions

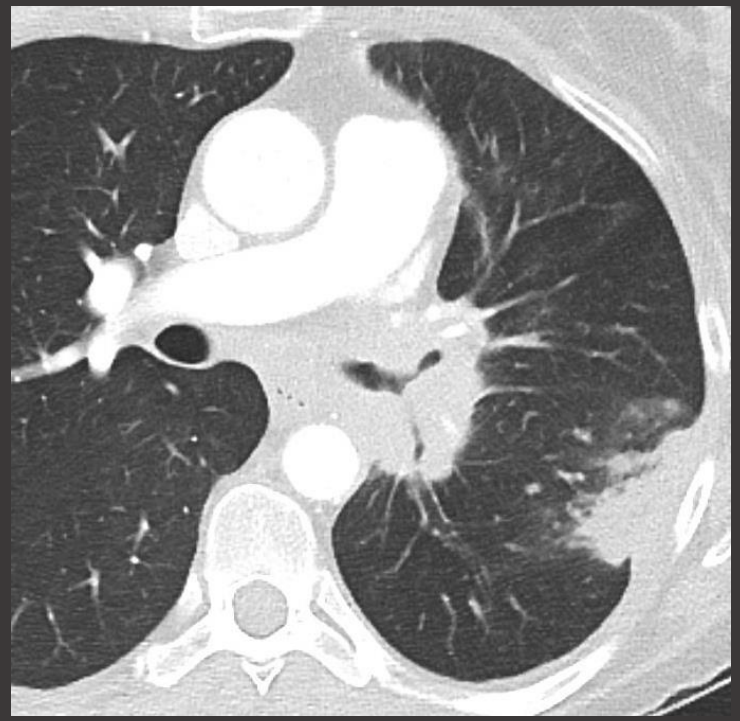


Case 3: 45 y/o female with 46.5 pack year smoking history, presents to ED with DOE, chest pain while lying on left side. Patient treated and released

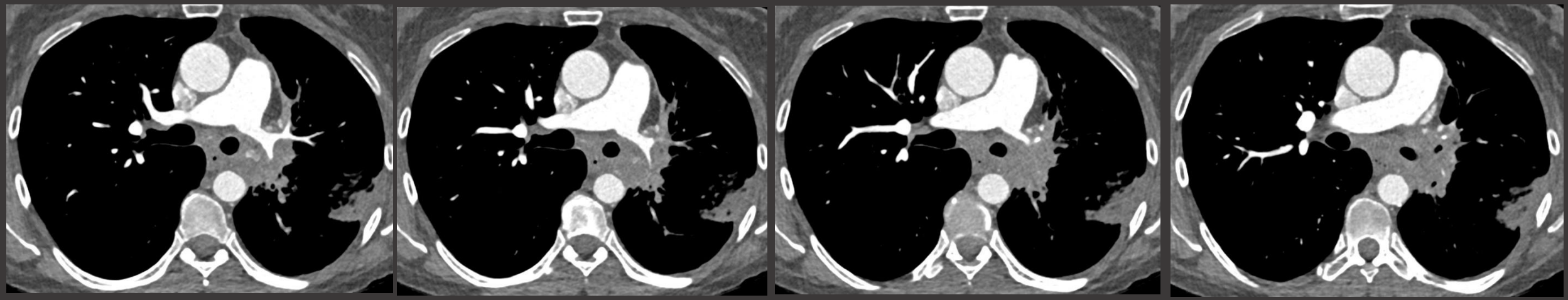
Case 3: Same patient returned to the ED a few days later stating that her symptoms were no better, and, in fact, chest pain was worse. CT was obtained for evaluation for PE





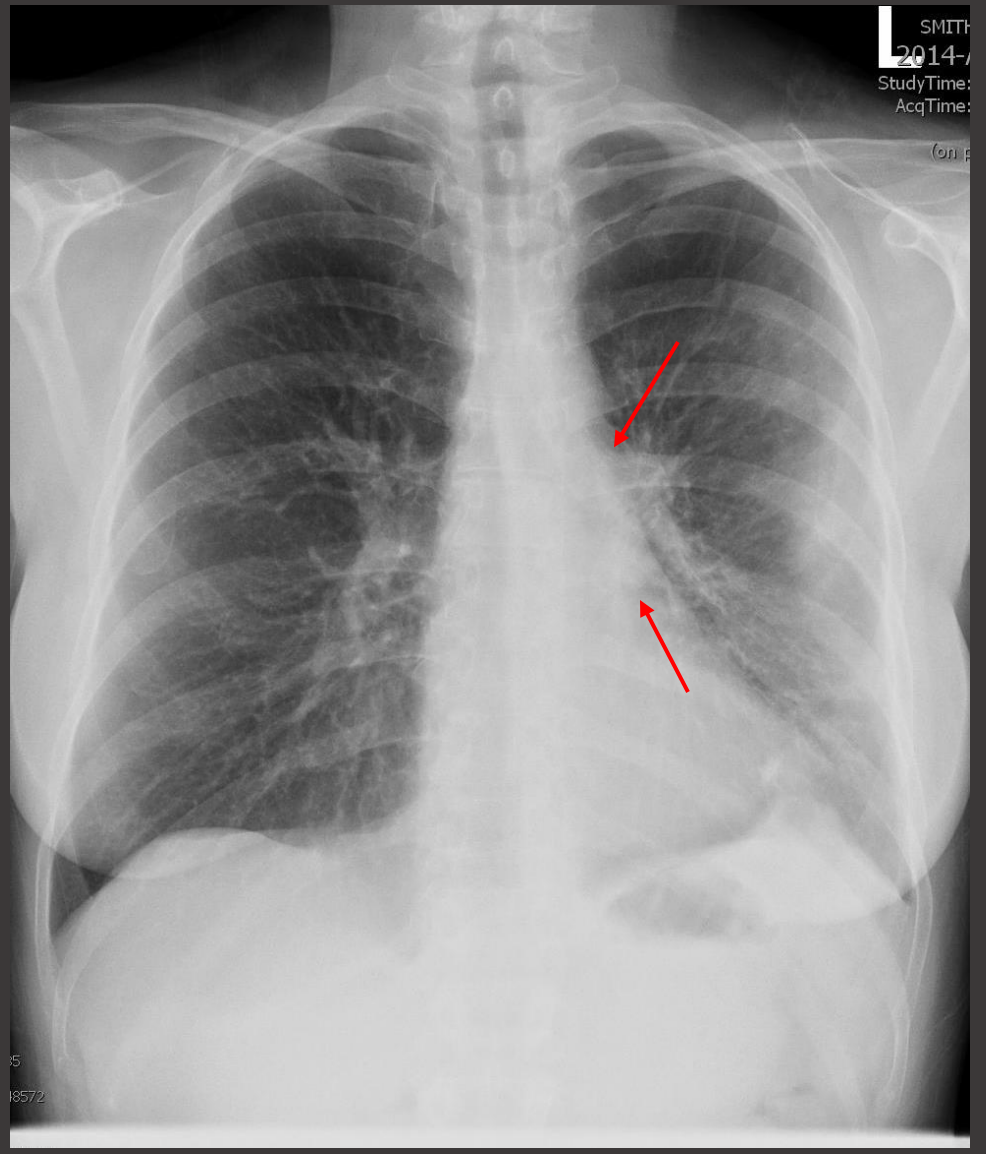


Case 3: Same patient; returned to the ED a few days later stating that her symptoms were no better, and, in fact, chest pain was worse. CT was obtained for evaluation for PE

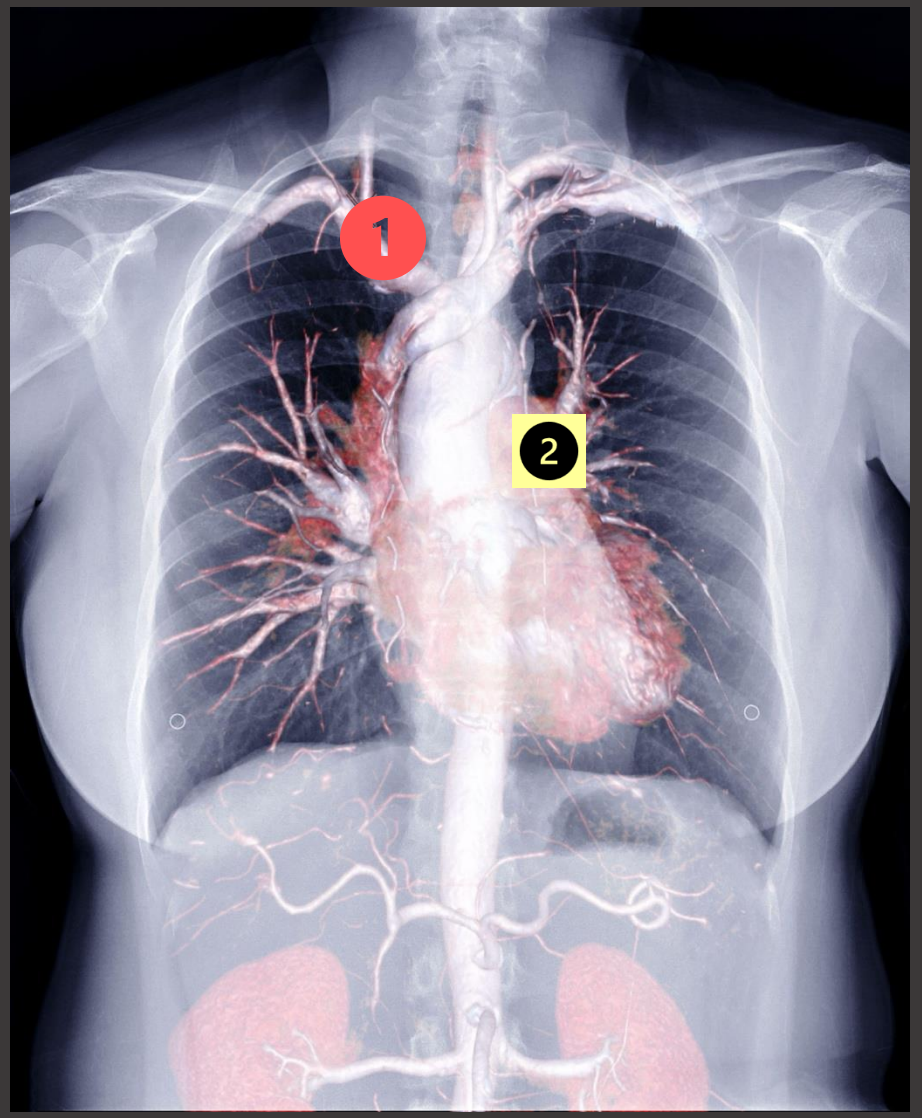


Case 3: Recap of original case. Salient points

- Don’t forget to keep looking when an abnormality is found
- Finish the search pattern
- Be sure the hila are normal

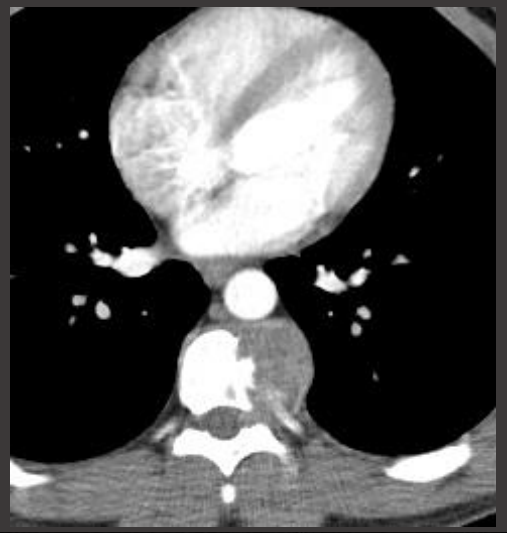
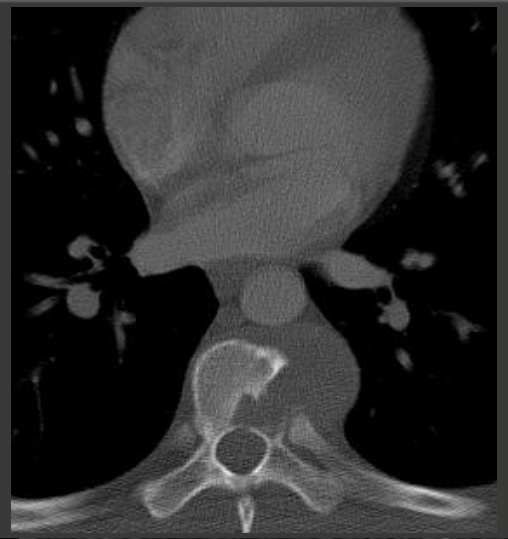
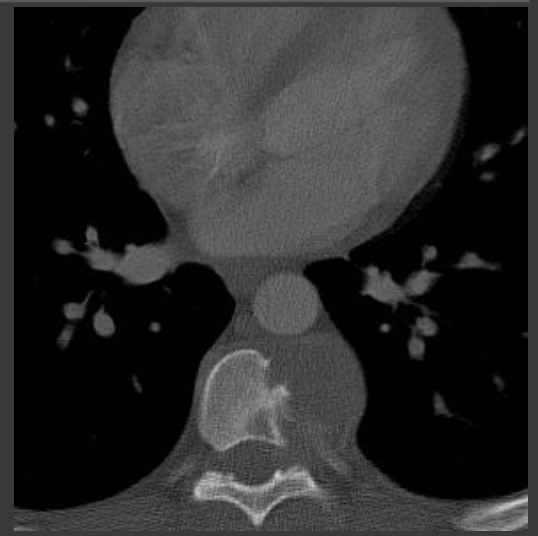


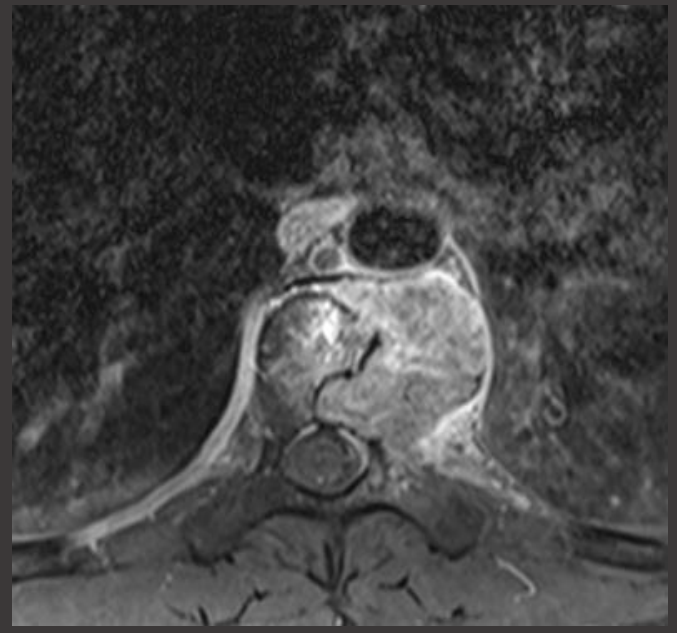
Schematic of locations of most missed lesions



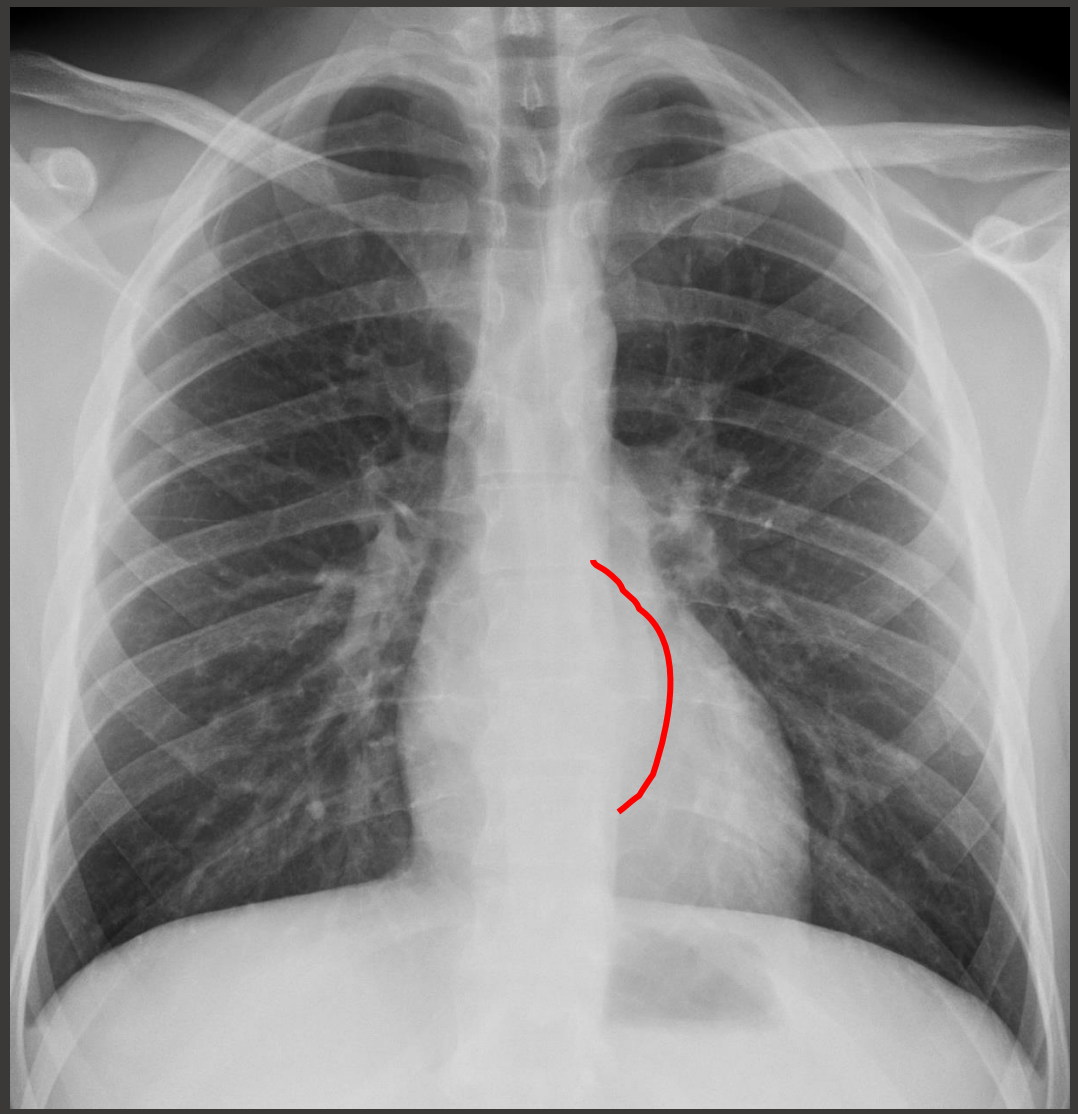
Case 5: 36 y/o male presented with persistent back pain. CXR was read as normal

Case 5: Same patient returned a few days later with numbness and worsening back pain.

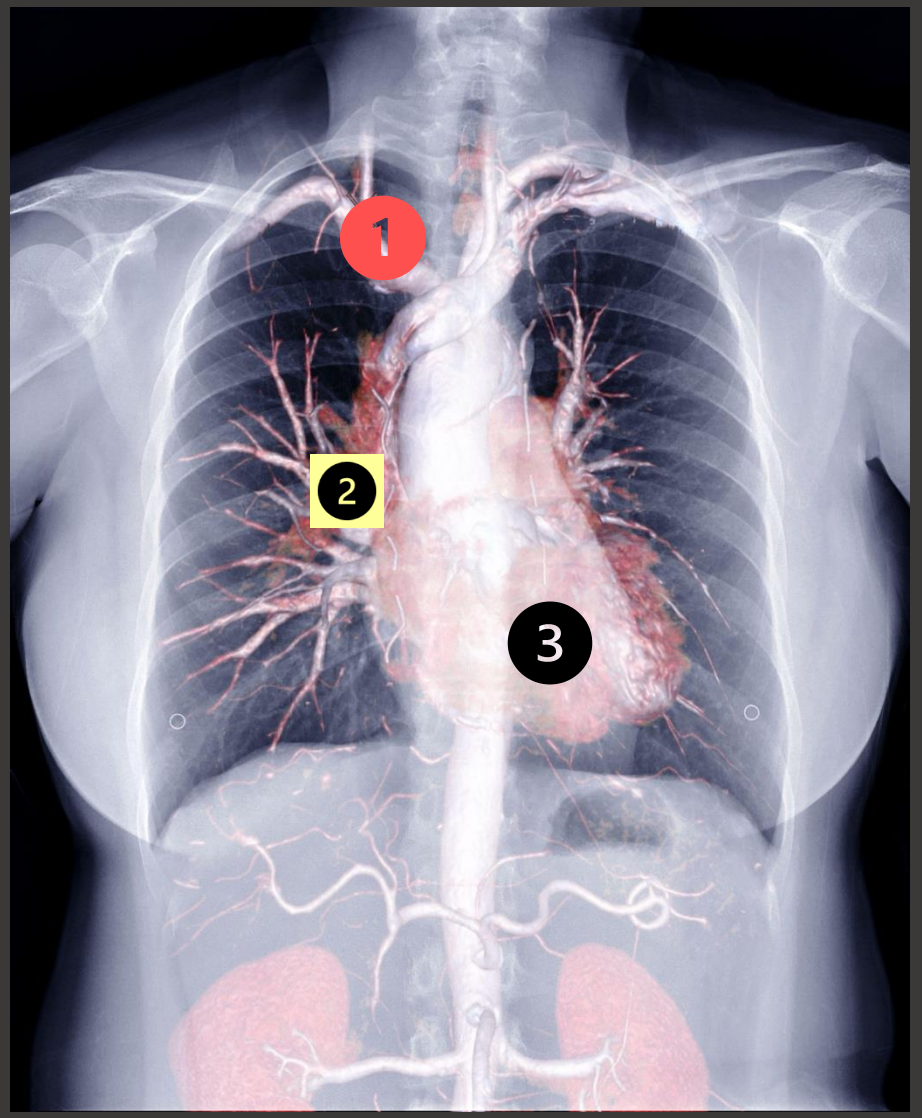







Case 5: Hiding in plain sight? What was missed?

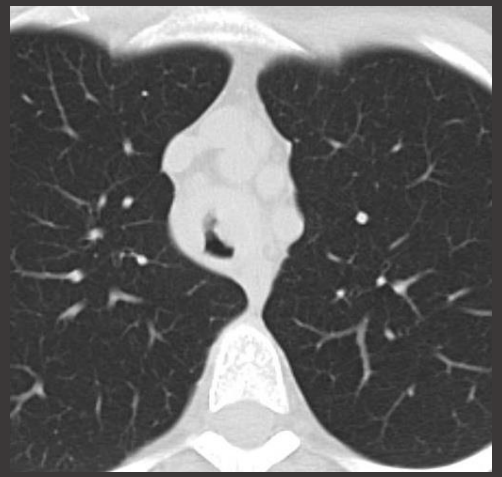


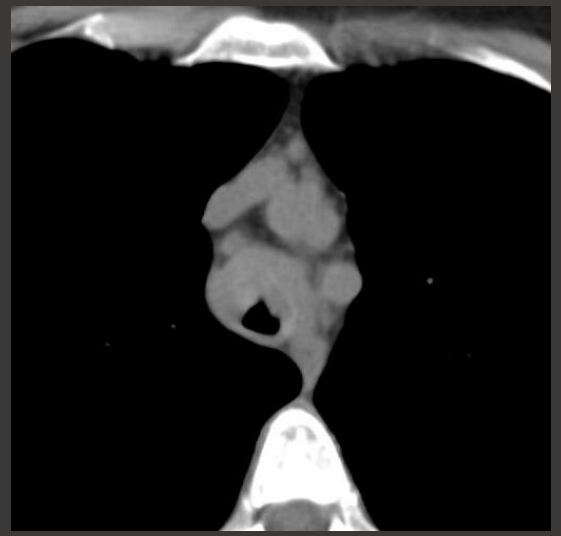
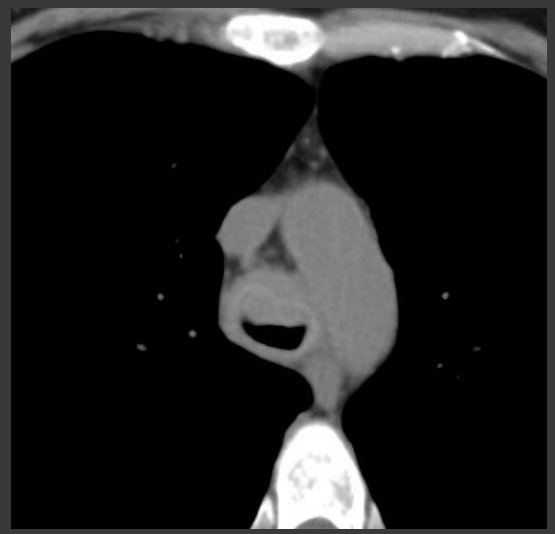
Schematic of locations of most missed lesions



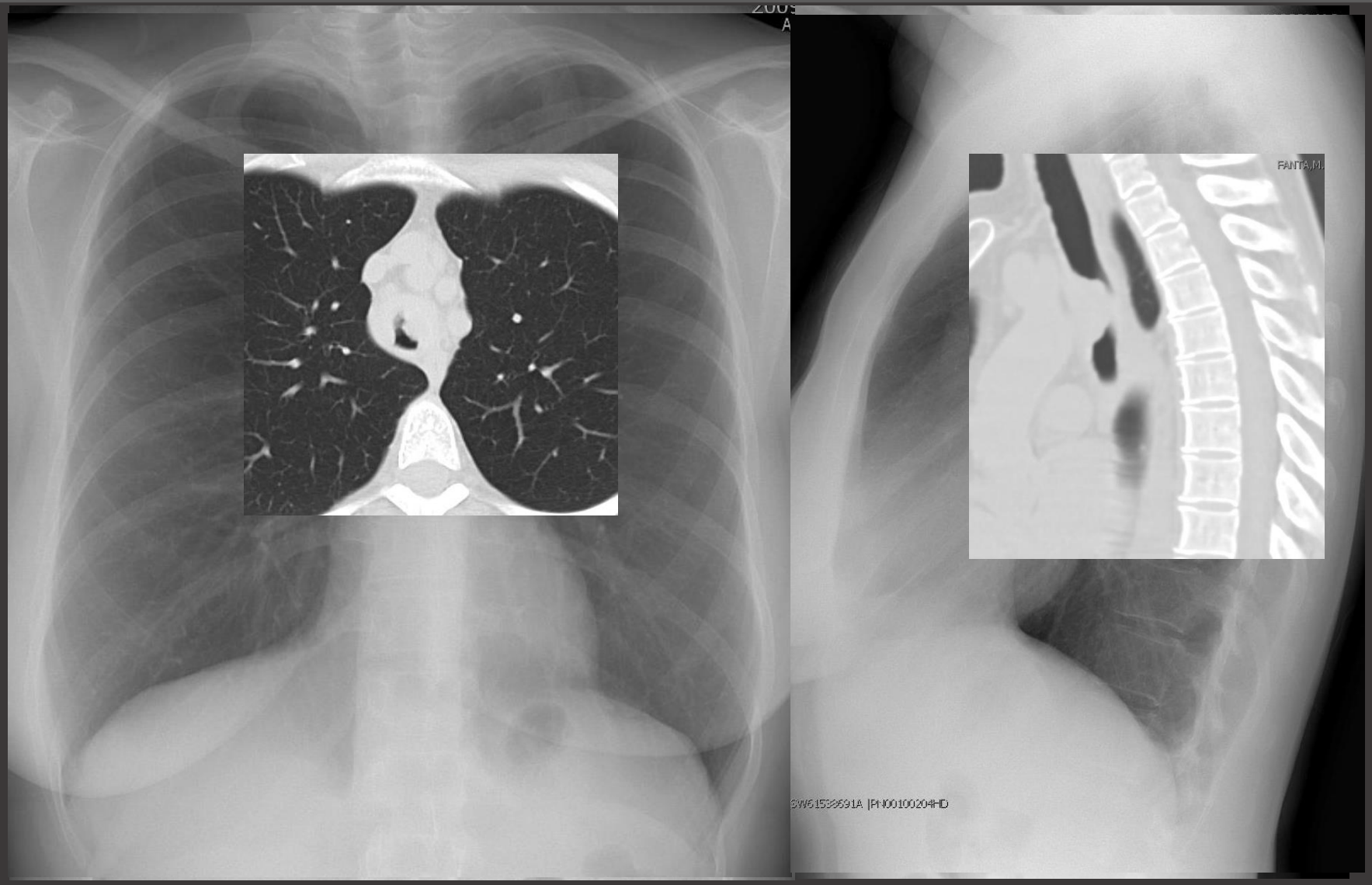
Case 6: 49 y/o female presented with midline pain in the upper anterior chest for several weeks' duration.

Case 6: Same patient returned to PCP a few days later with unrelenting midline anterior chest pain

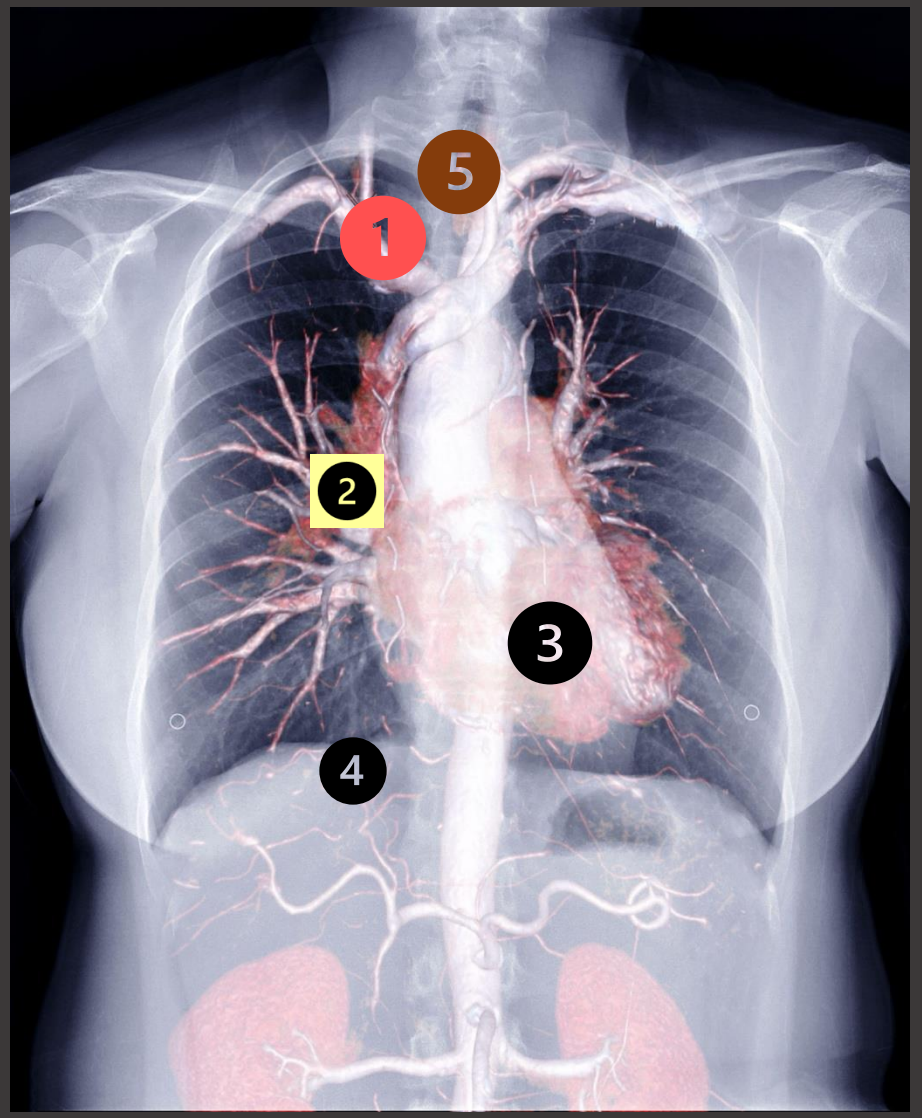




Case 6: In retrospect CXR performed one year prior is shown



Schematic of locations of most missed lesions

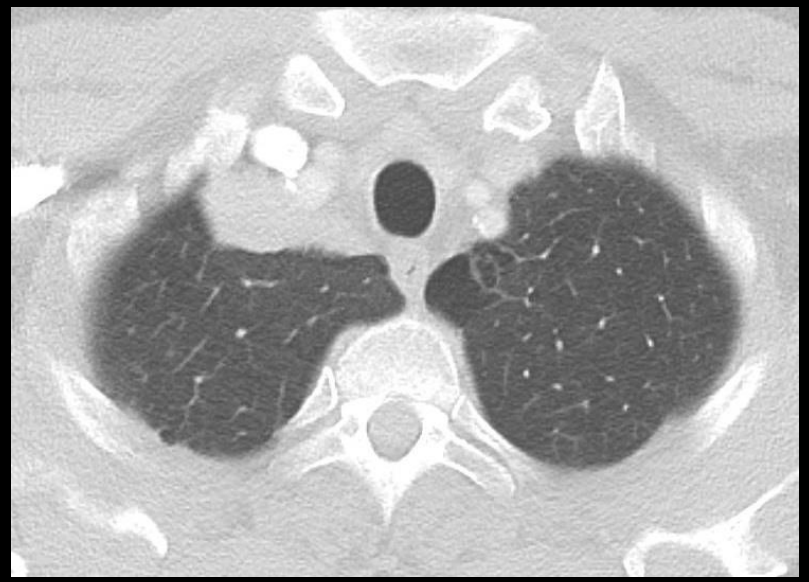
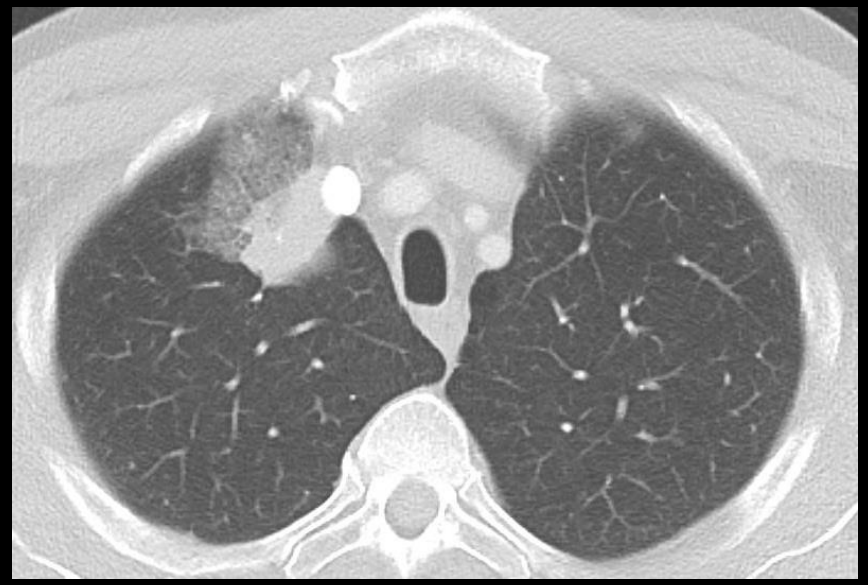
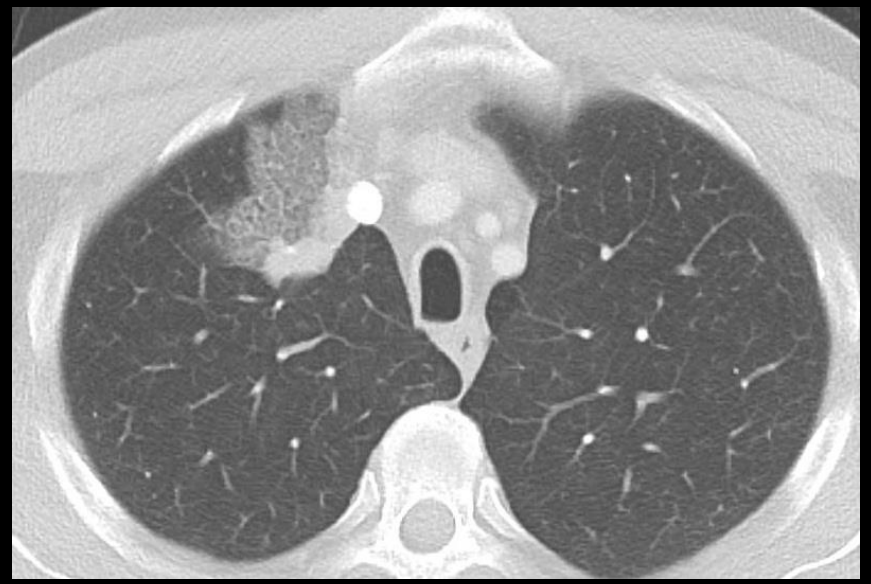


Missed Lung Cancer

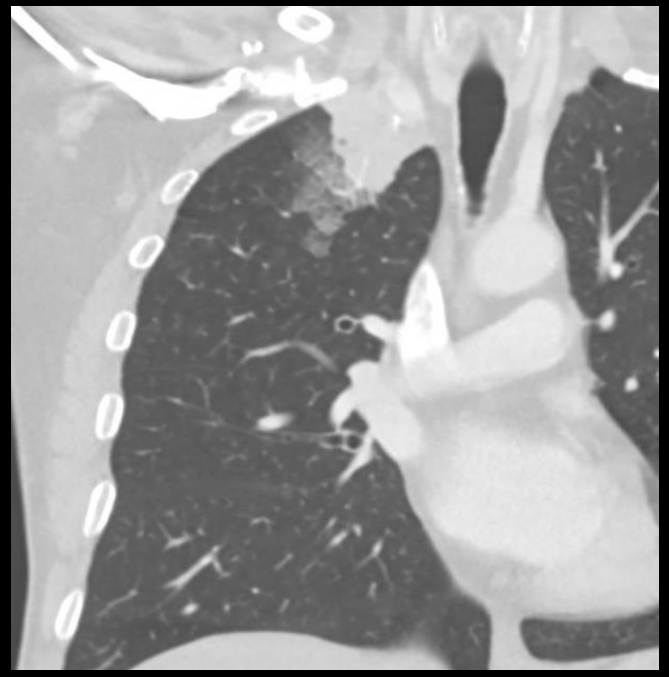
- Lung cancer is the leading cause of cancer-related death in the US
- Radiologists play an important role in the diagnosis of lung cancer
- Nearly 40% of lung cancers are asymptomatic at the time of diagnosis
- Many of these are diagnosed with chest radiographs performed for unrelated clinical indications
- Missed lung cancer is a leading cause of medical malpractice among radiologists
- 90% of missed cancers involve CXR

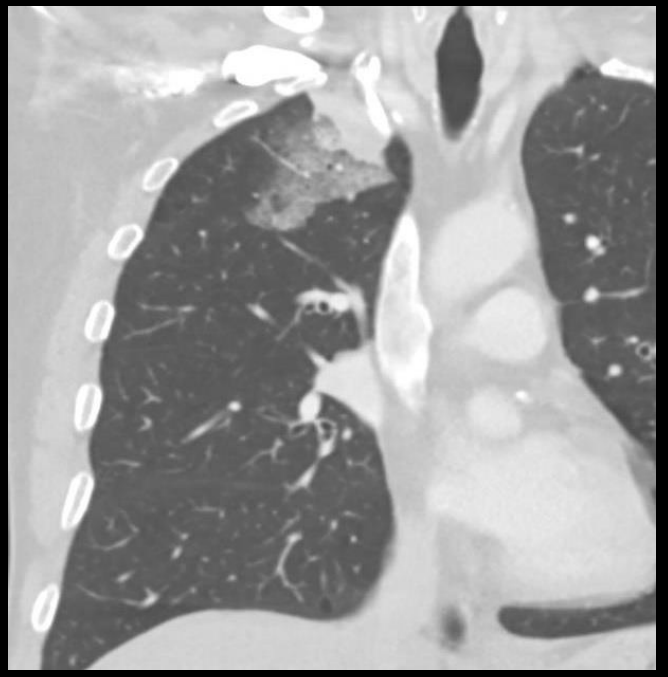
Case 1: 59 y/o male presented with right chest wall pain. CXR performed and read as normal

Case 1: The patient returned two weeks later complaining of worsening right chest wall pain. CT was performed

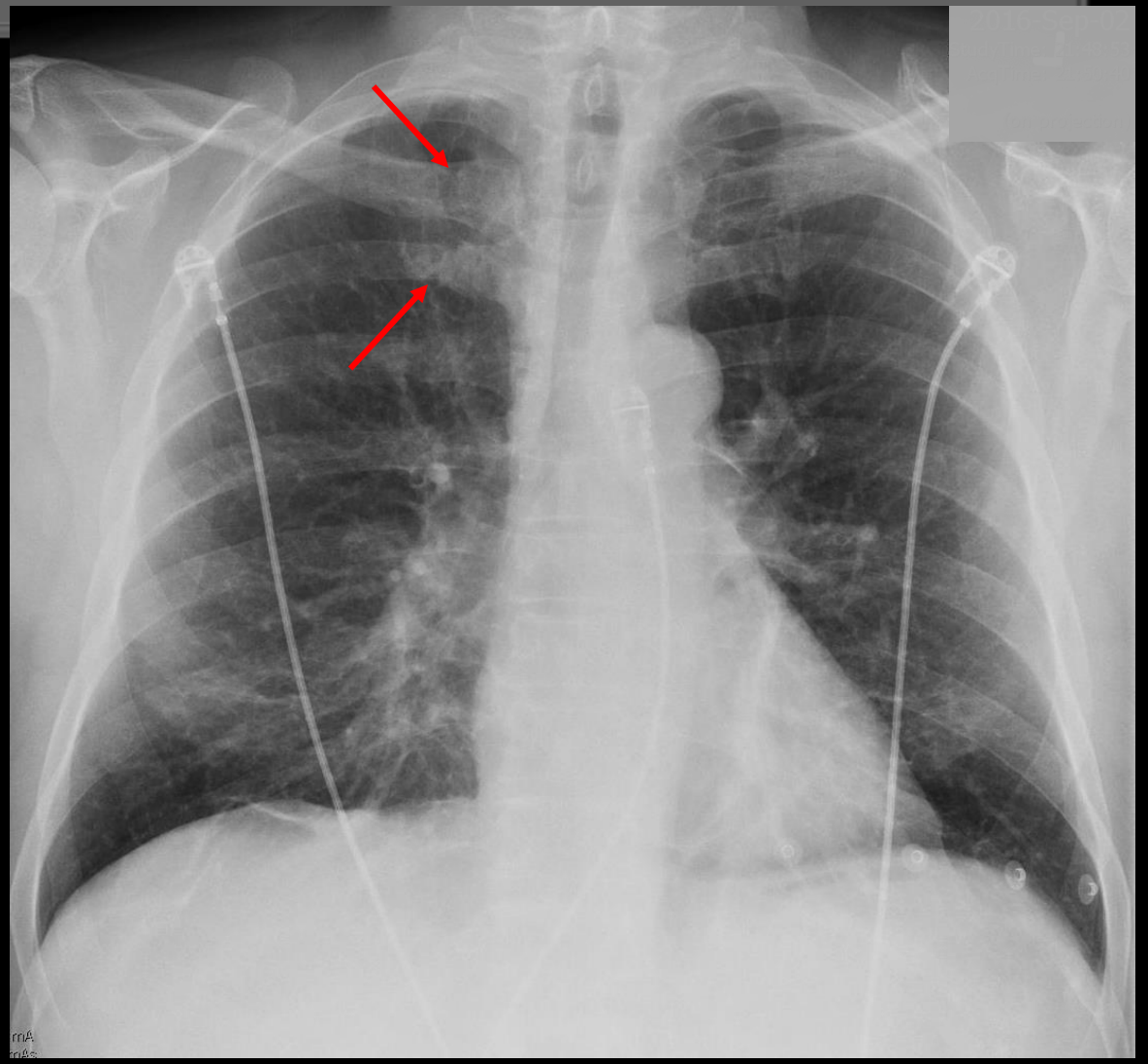
Case 1: Coronal images of the same patient



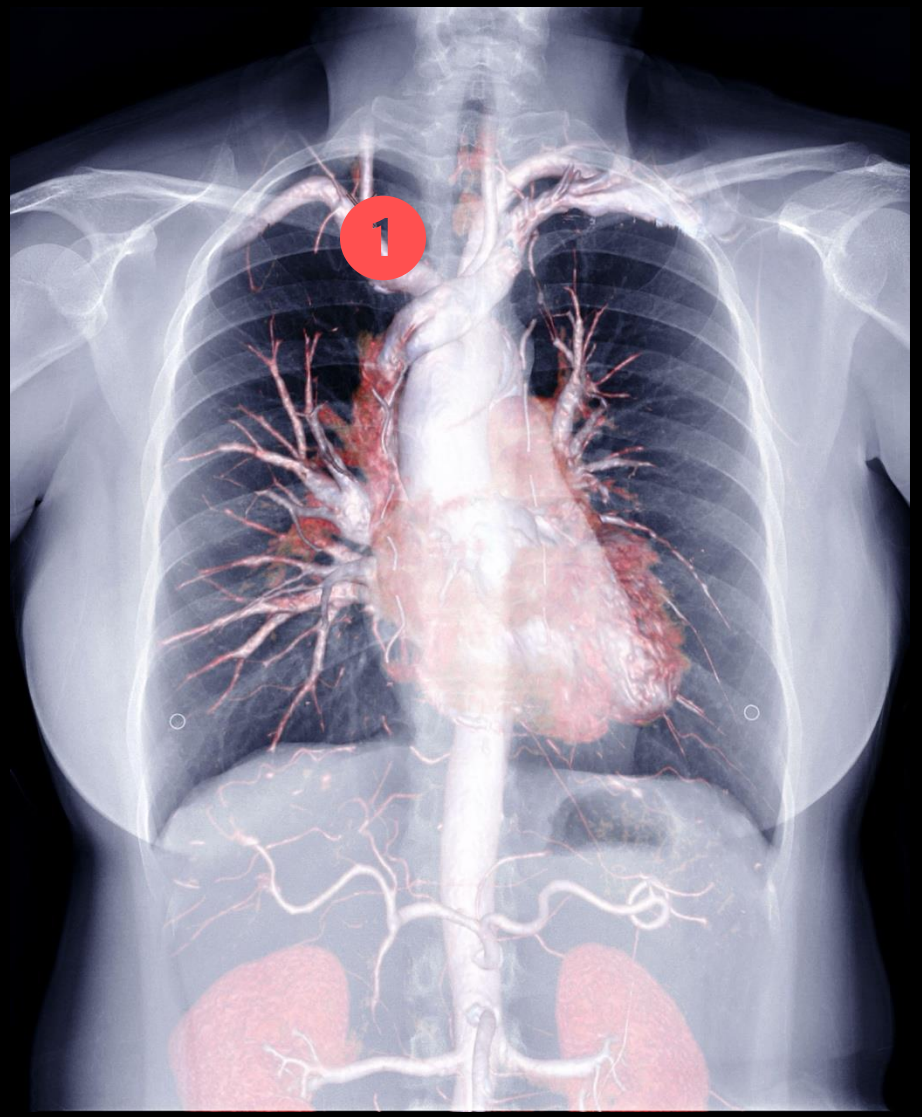


Case 1: Recap of salient points

- Always compare side to side
- Remember the lung apices
- In this case right apex more opaque
- Beware of areas of overlapping structures



Schematic of locations of most missed lesions



Missed lung cancer: causes

- Observer error – most significant cause
  - Scanning error 30% of errors
  - Recognition error 25% of errors
  - Decision-making error 45% of errors
  - Satisfaction of search
- Tumor characteristics
  - Size
  - Conspicuity
  - Tumor histology
  - Location most are in the upper lobes 81% * with 56% in RUL
- Technical considerations

Del Ciello et al Diagn Interv Radiol 2017; 23:118-126

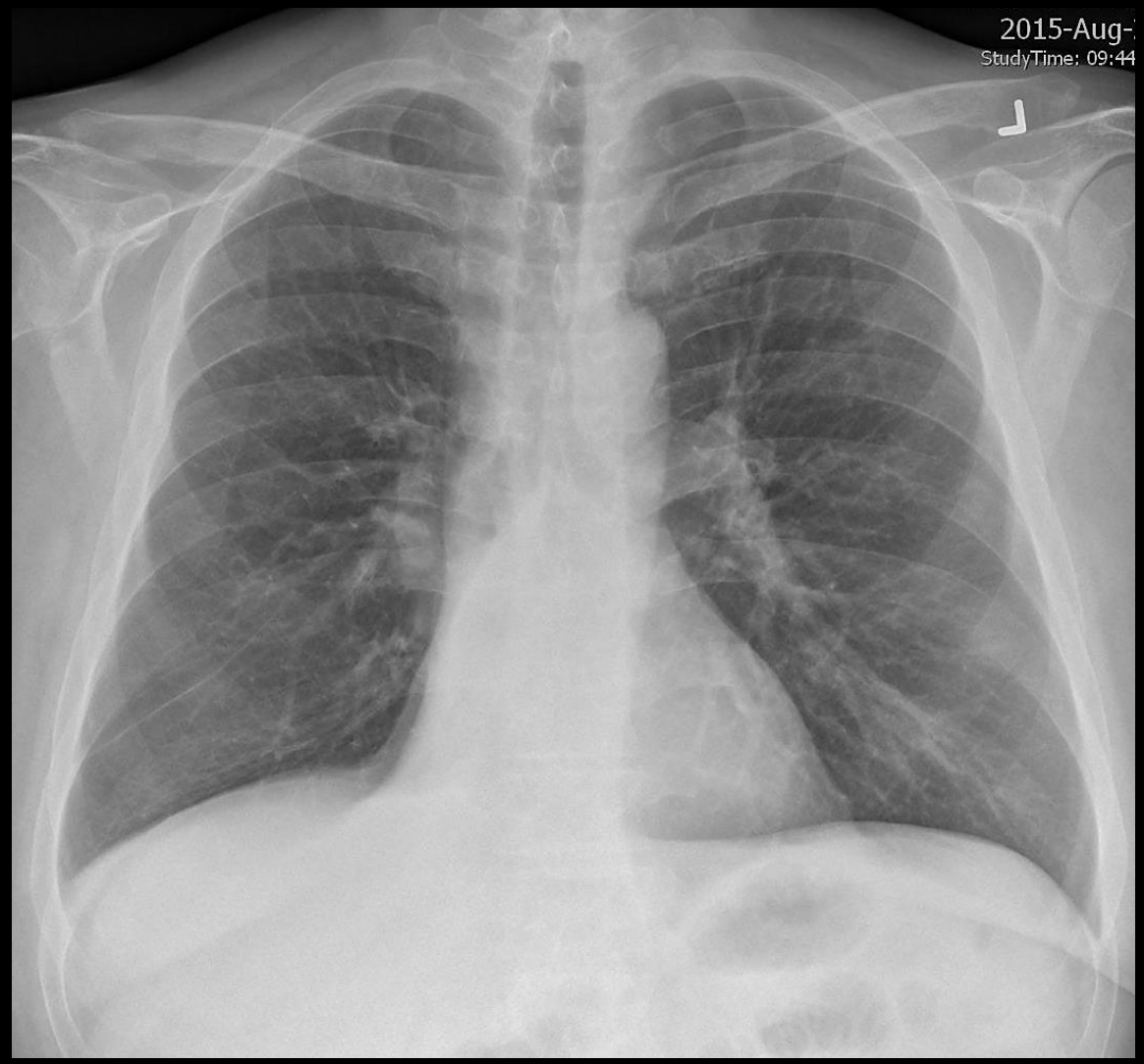
** Austin JH et al Radiology 1992;182:115-122*

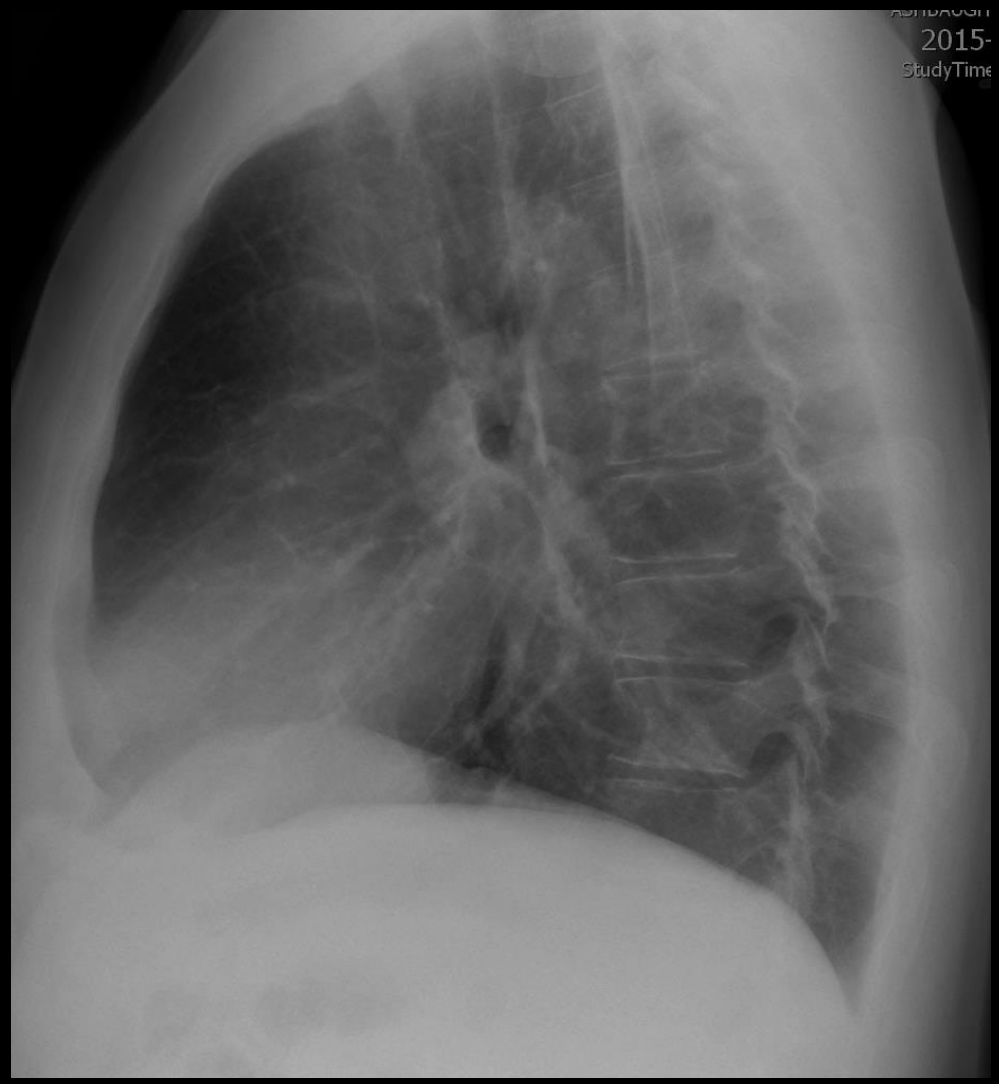
Missed lung Cancer on CXR: Other Contributors

- Poor imaging quality
- Poor viewing conditions (important with reading from home)
- Poor nodule conspicuity due to
  - small size – mean diameter of missed lung cancer is 1.3 to 1.6 cm
  - GGN
  - Ill-defined margins
  - Overlying structures

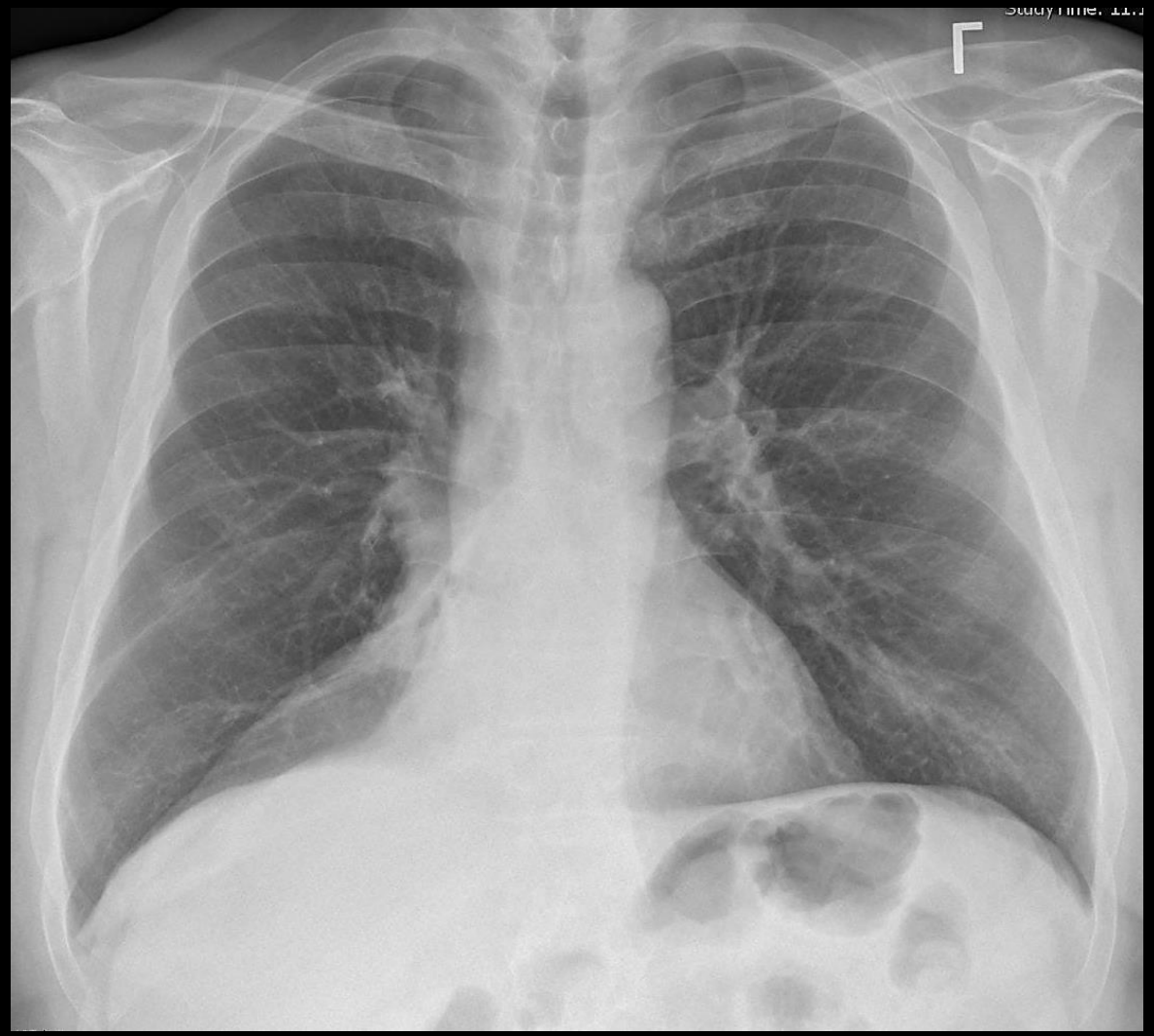
Hossain et al Radiol Clin N Am 56 (2018) 365-375

Case 2: 59 y/o male presented with shortness of breath with exercise for two months. CXR was performed





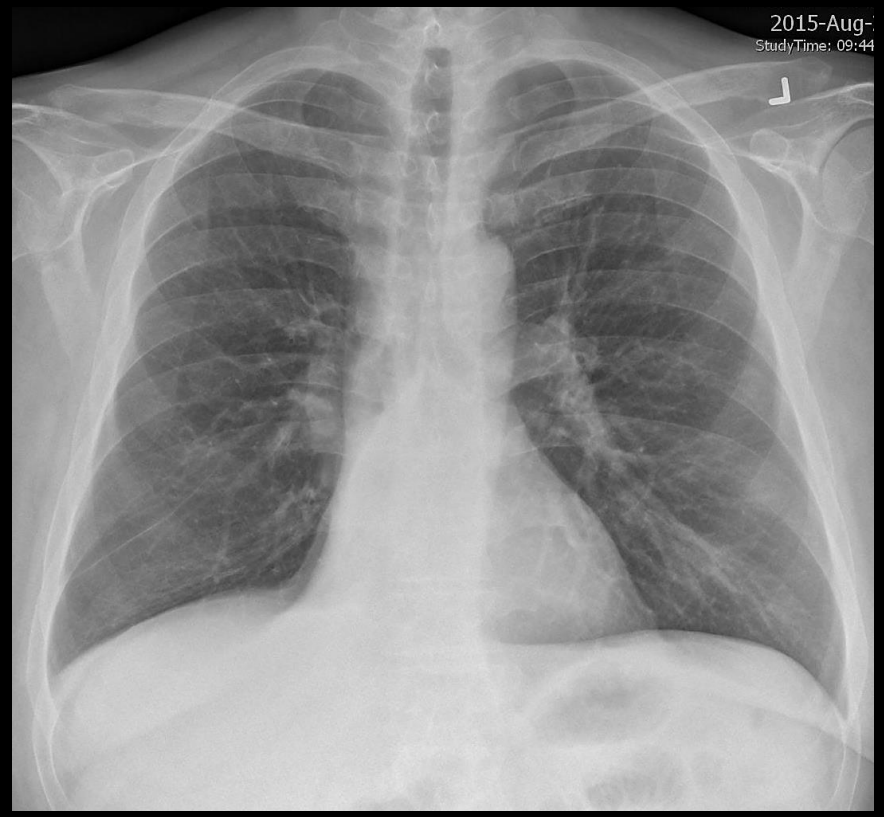
Case 2: He then presented seven months later with worsening symptoms and this CXR was performed followed by a CT scan

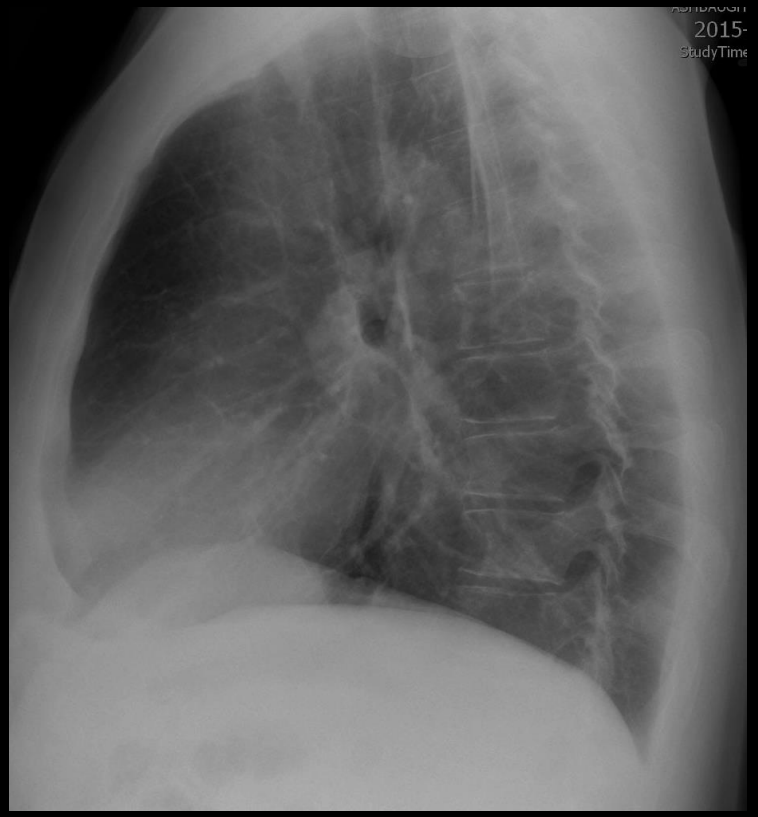


Case 2: same patient returned 7 months later with worsening symptoms. What was missed?

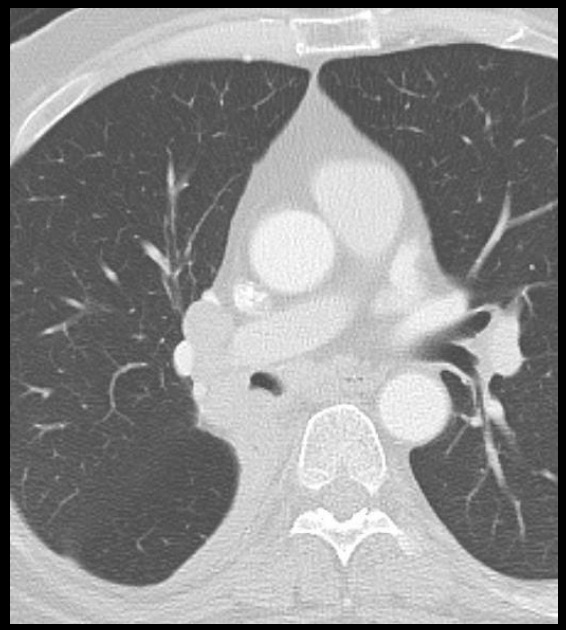
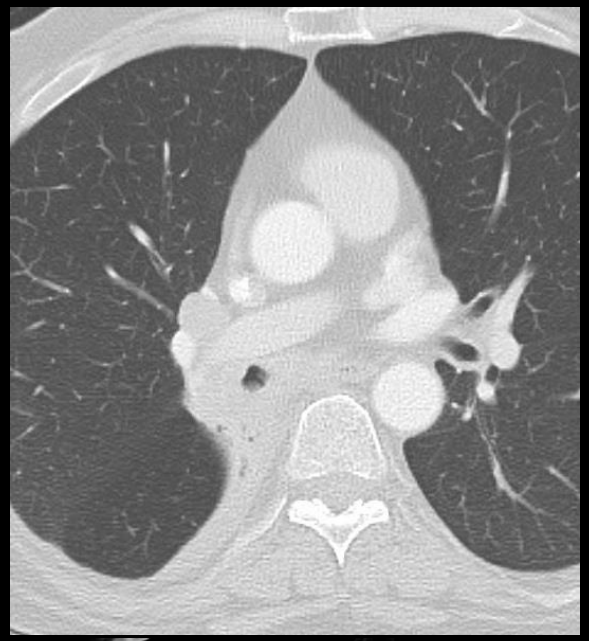
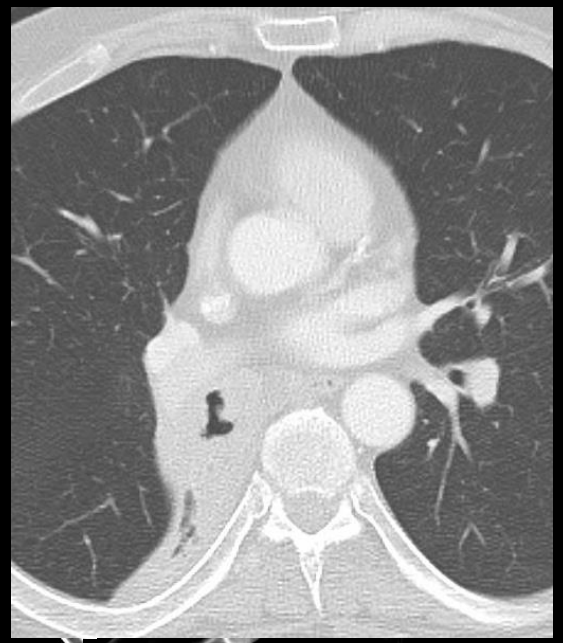
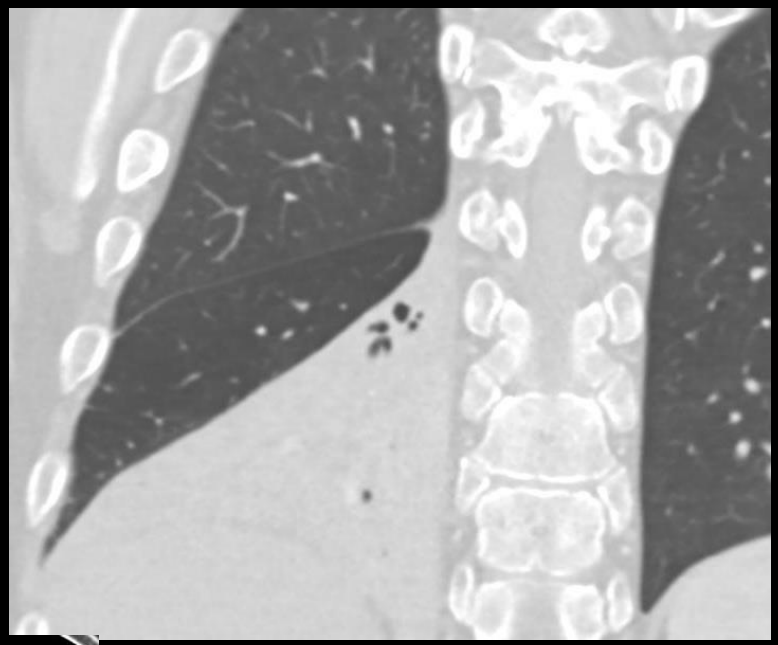
Answer ?

A. Right paratracheal mass
B. Right upper lobe atelectasis
C. Left hilar lymph node enlargement
D. Right lower lobe atelectasis



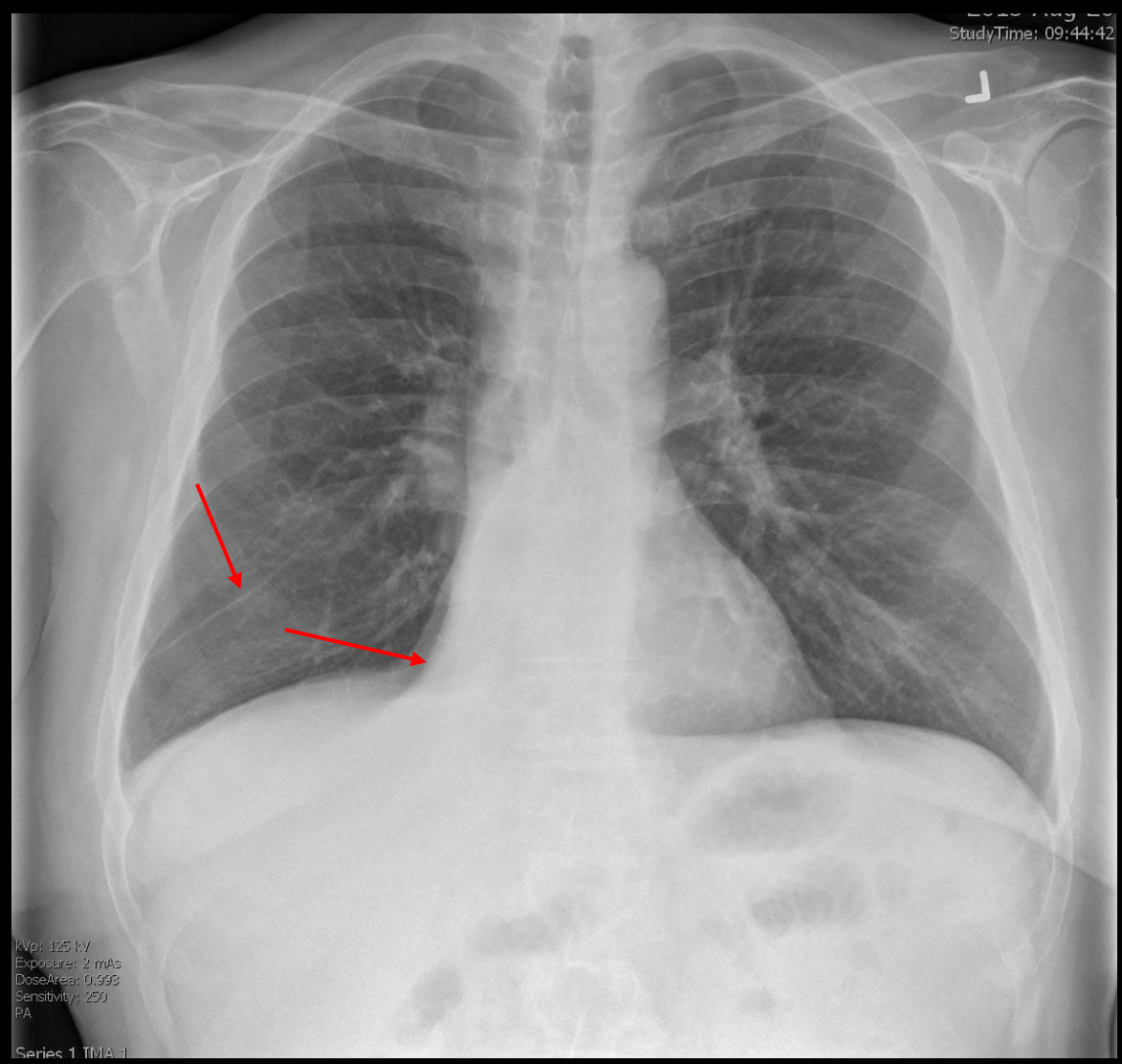


Case 2: CT scan of the chest was performed

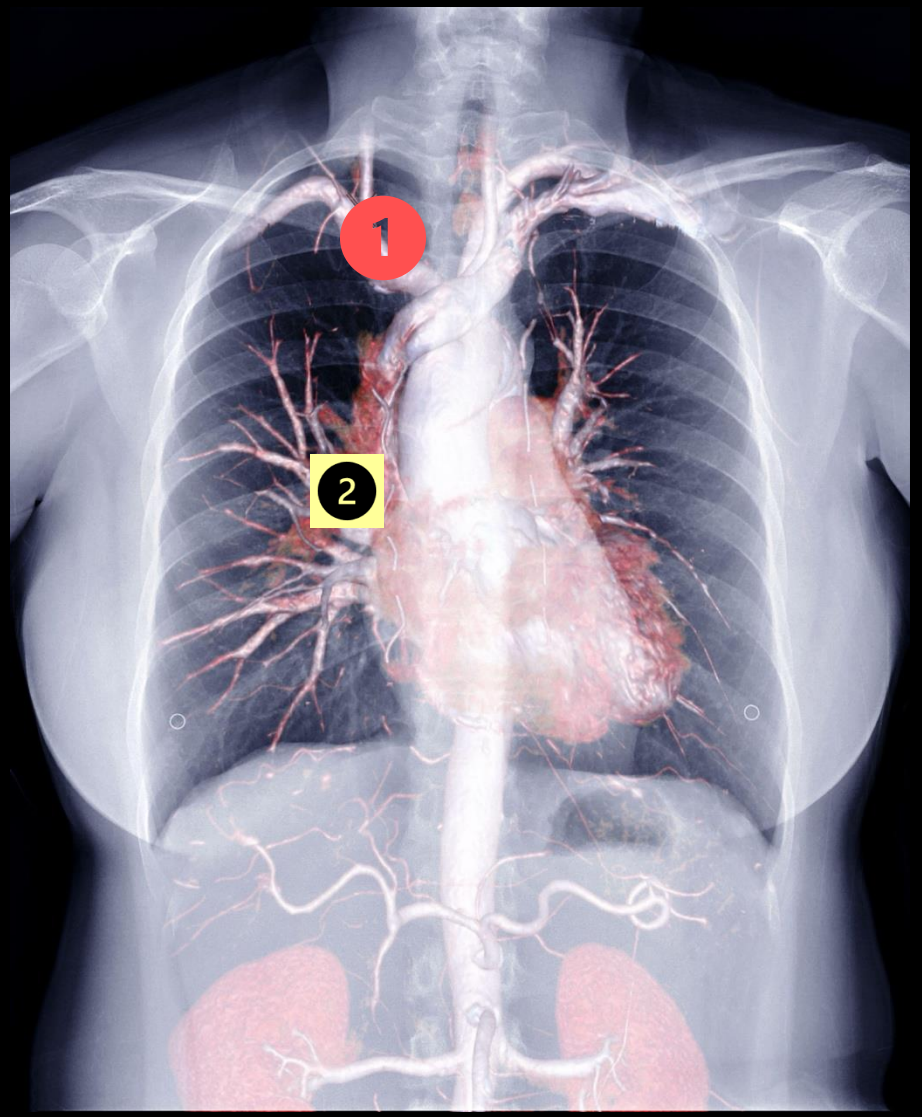





Case 2: Recap original CXR…salient points

- The right lung should be larger than the left
- The Minor fissure moved inferiorly
- Second well demarcated line posterior to the heart is the major fissure
- Missed RLL atelectasis
- If you miss atelectasis you may miss lung cancer

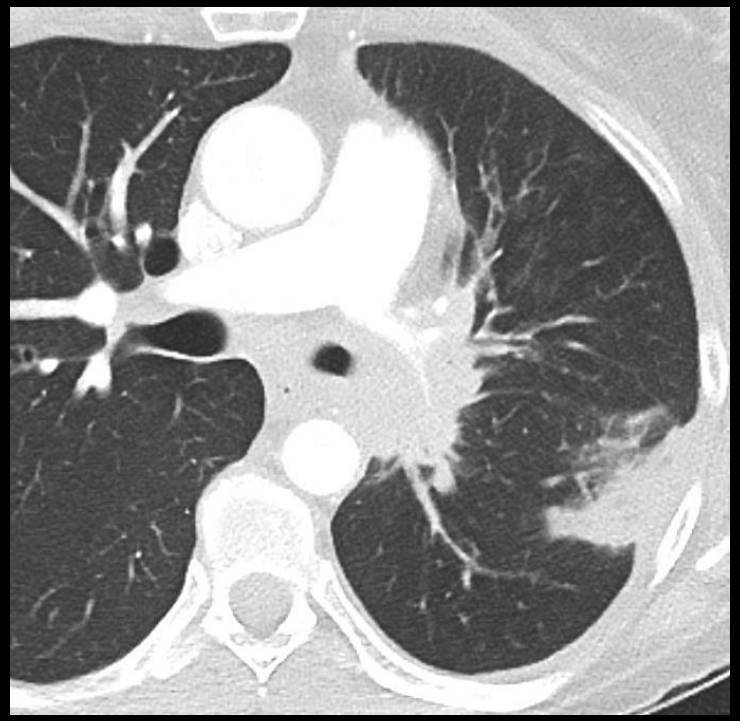


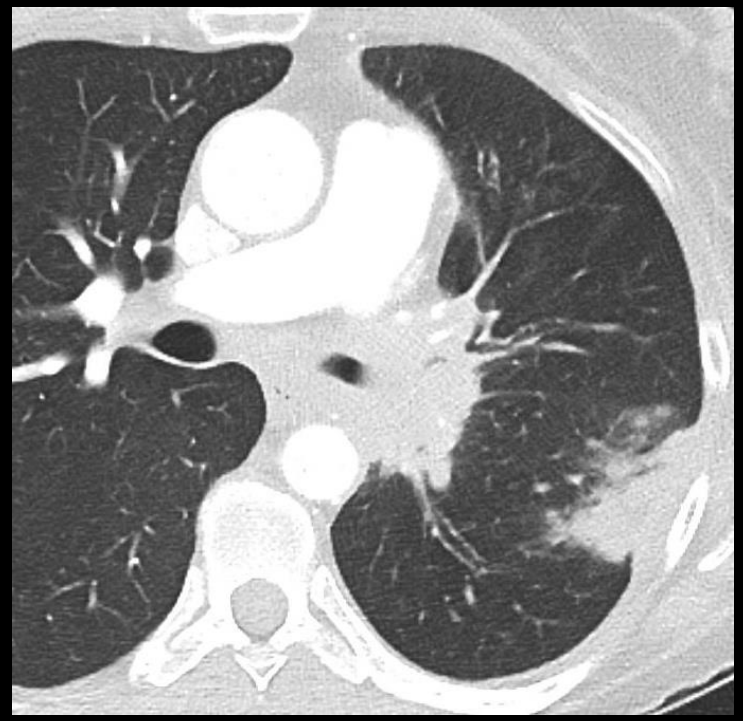
Schematic of locations of most missed lesions

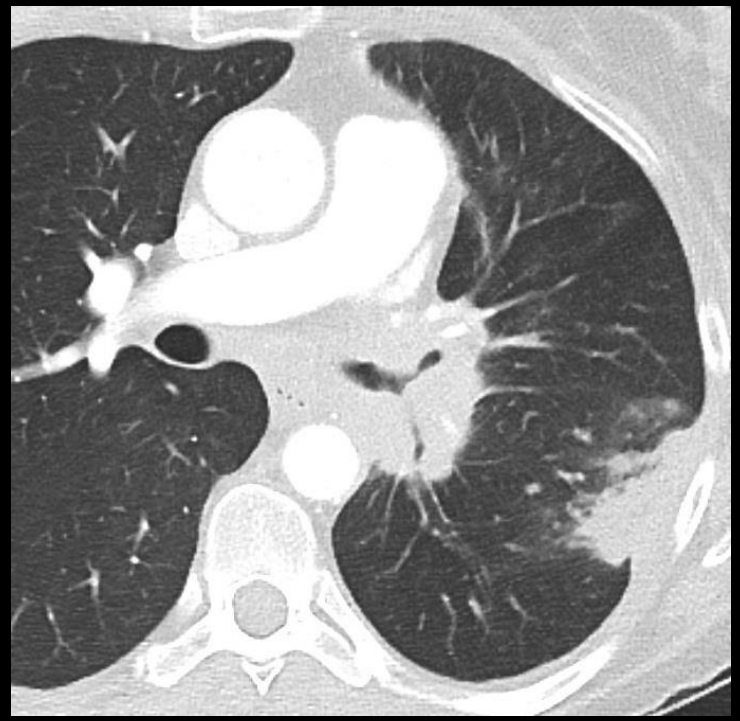


Case 3: 45 y/o female with 46.5 pack year smoking history, presents to ED with DOE, chest pain while lying on left side. Patient treated and released

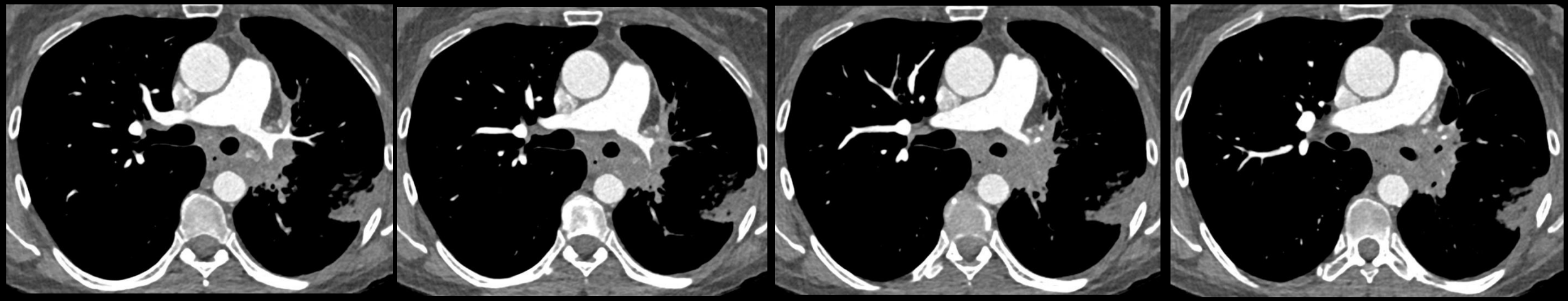
Case 3: Same patient returned to the ED a few days later stating that her symptoms were no better, and, in fact, chest pain was worse. CT was obtained for evaluation for PE





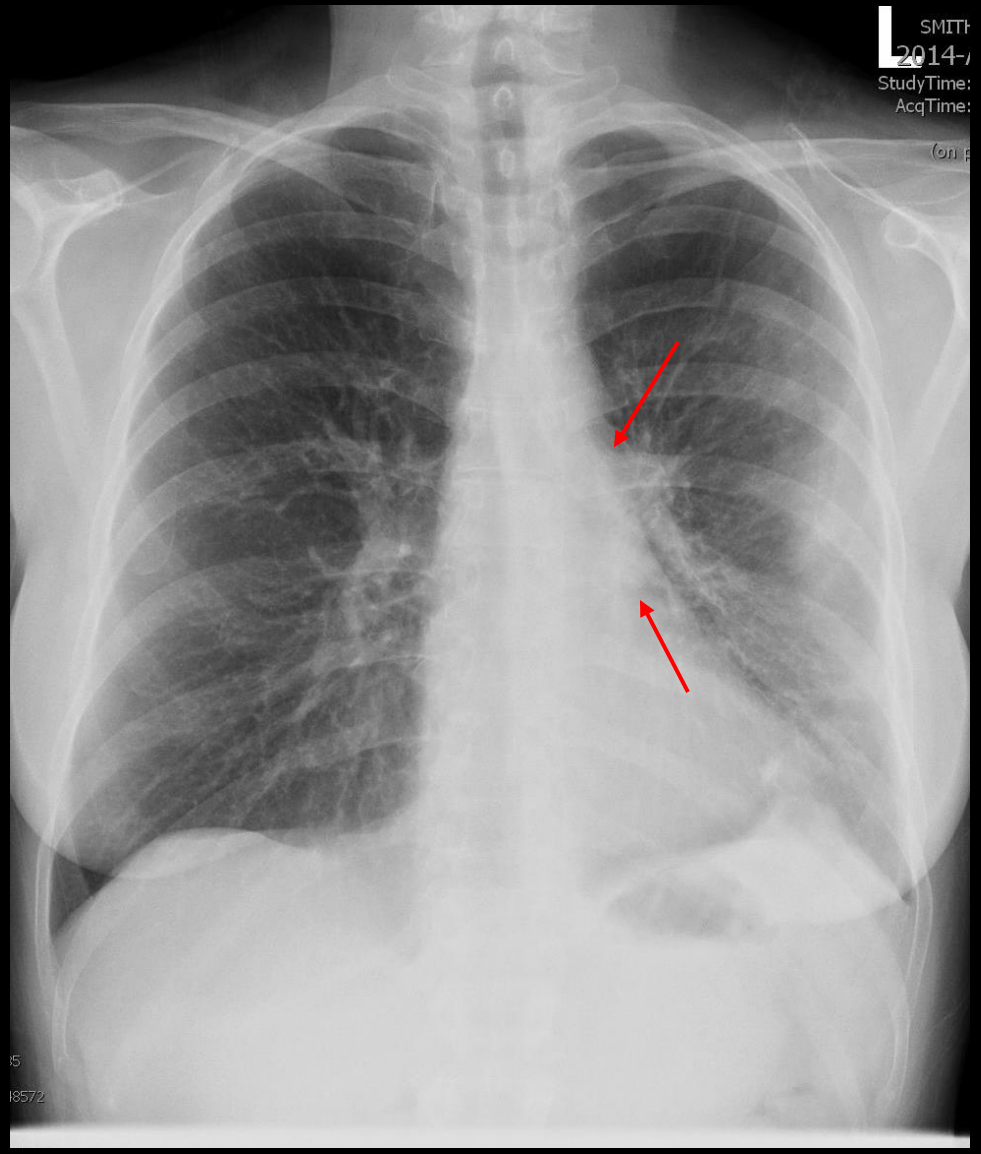


Case 3: Same patient; returned to the ED a few days later stating that her symptoms were no better, and, in fact, chest pain was worse. CT was obtained for evaluation for PE

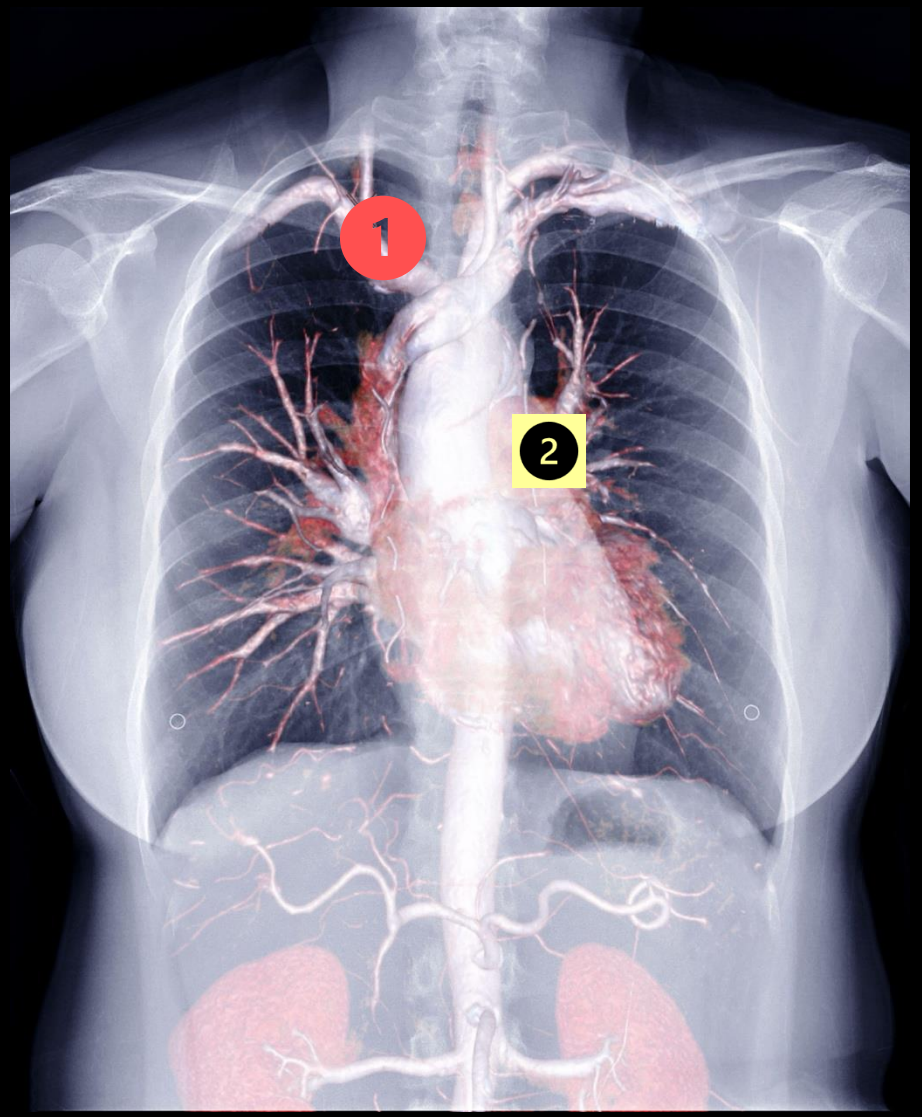


Case 3: Recap of original case. Salient points

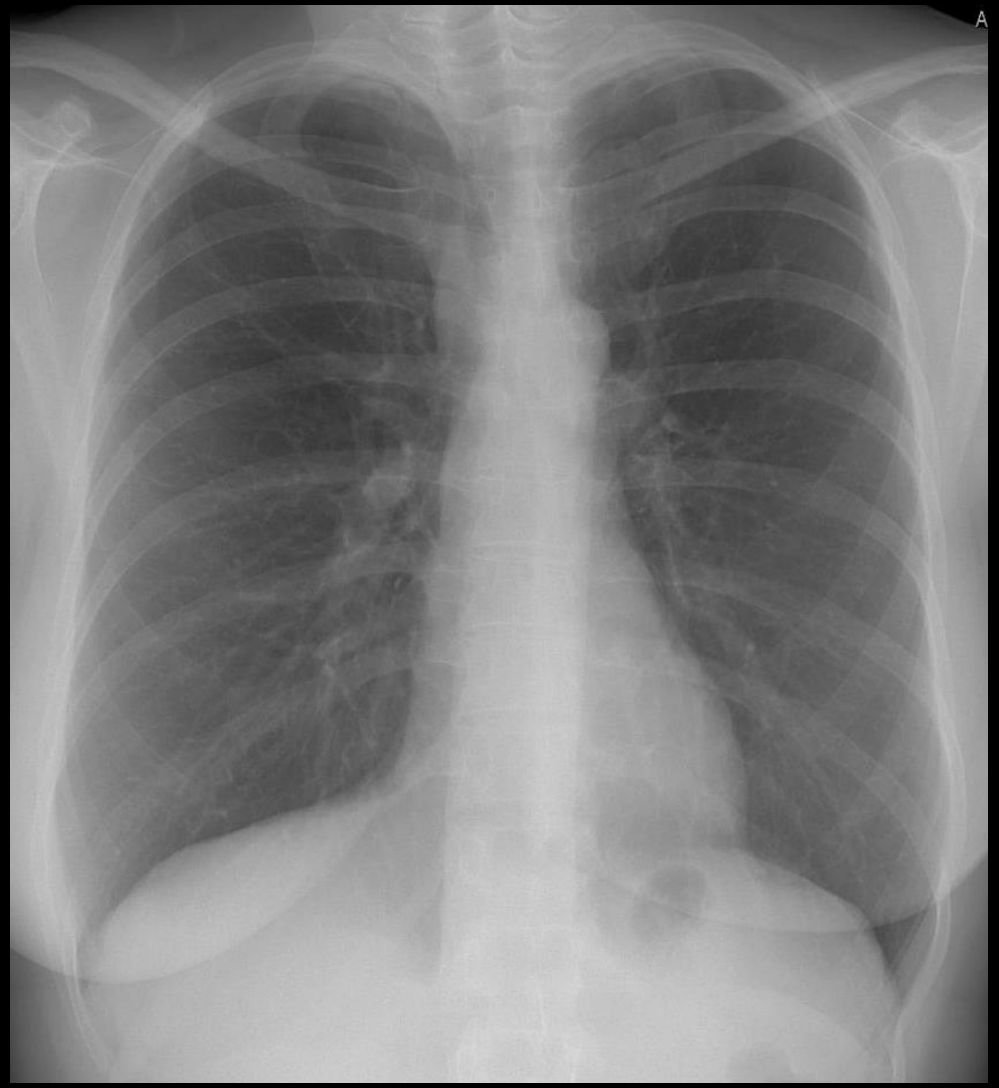
- Don’t forget to keep looking when an abnormality is found
- Finish the search pattern
- Be sure the hila are normal

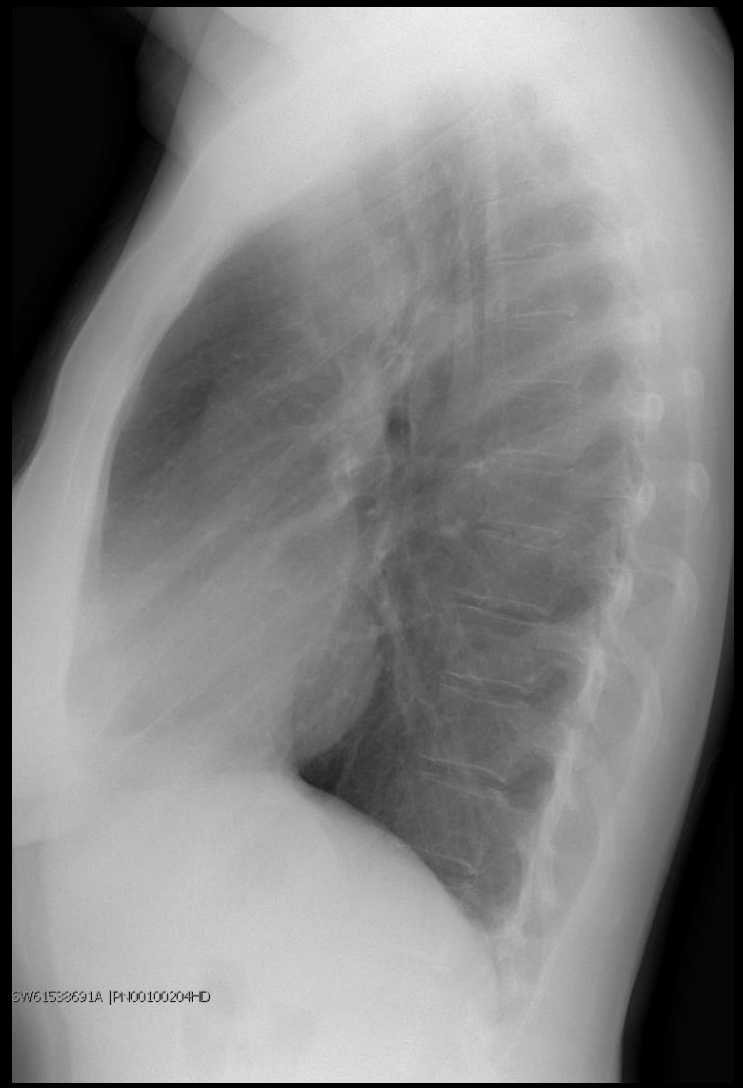


Schematic of locations of most missed lesions

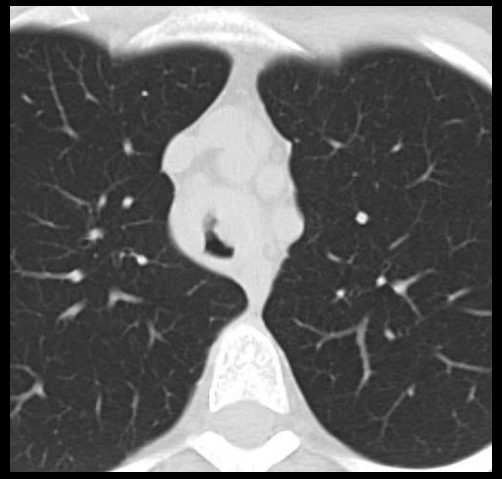


Case 6: 49 y/o female presented with midline pain in the upper anterior chest for several weeks' duration.

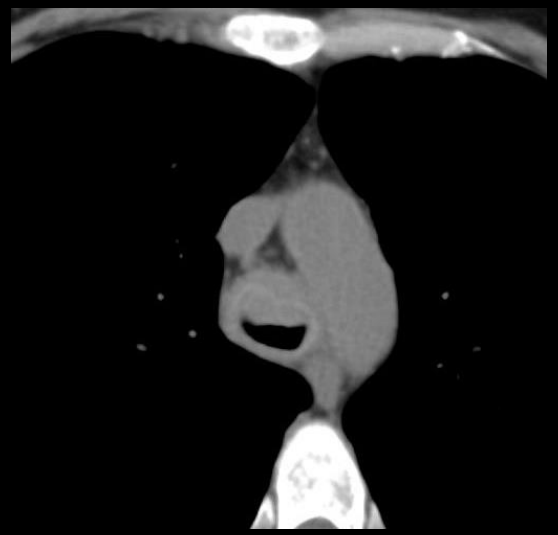




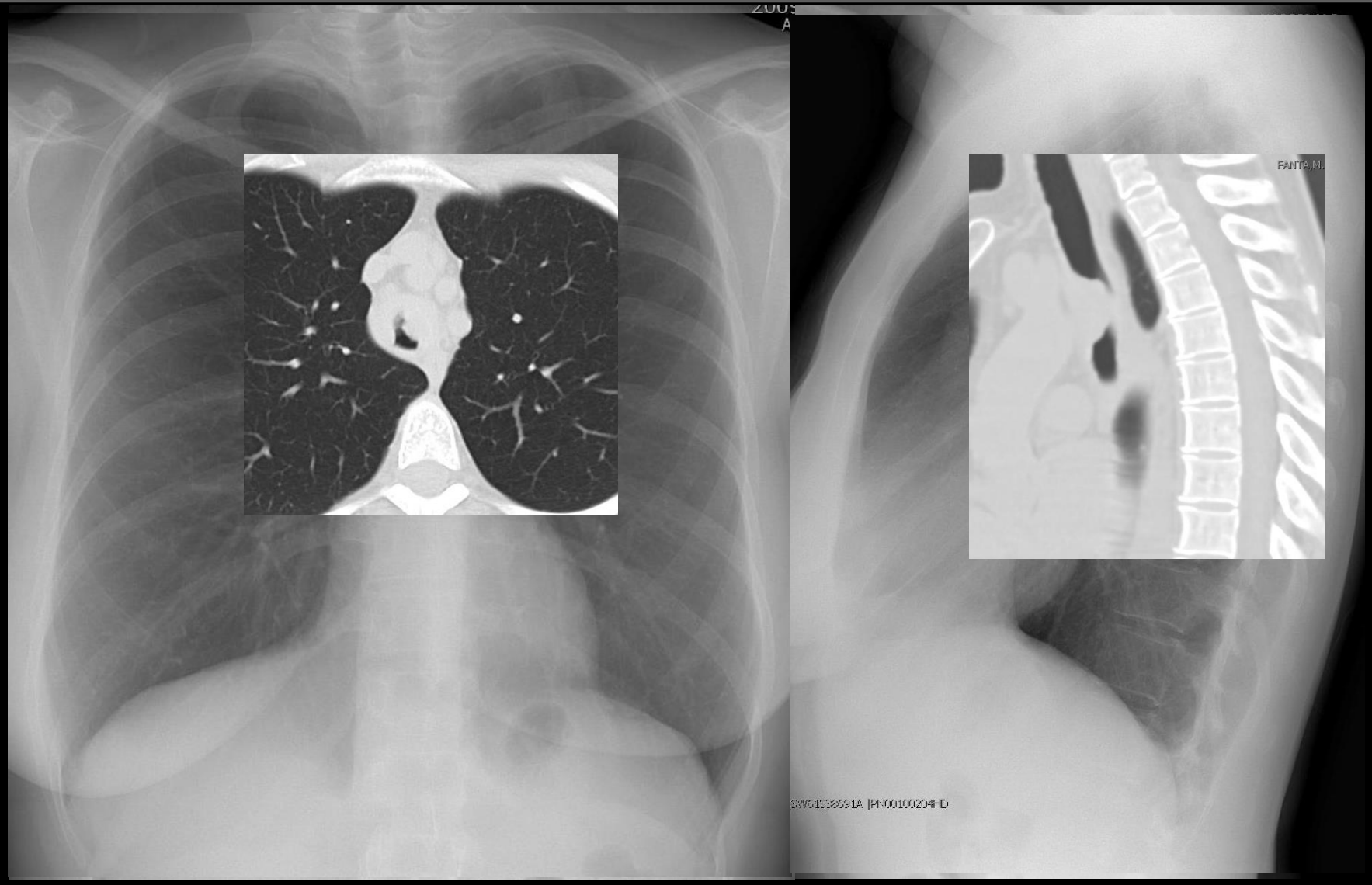
Case 6: Same patient returned to PCP a few days later with unrelenting midline anterior chest pain






Case 6: In retrospect CXR performed one year prior is shown



Schematic of locations of most missed lesions