Review and Update in Pulmonary Critical Care Medicine: Pearls in Chest Imaging

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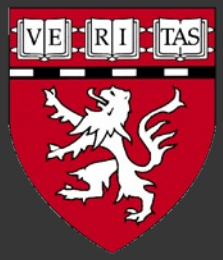


Disclosure of Conflict of Interest

I have no financial relationships with commercial entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on patients

Goals

- Describe Radiographic features of various IIP with DDx
- Discuss Cystic Lung diseases
- Present appearance of small and large airways diseases
- Review smoking related lung diseases

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

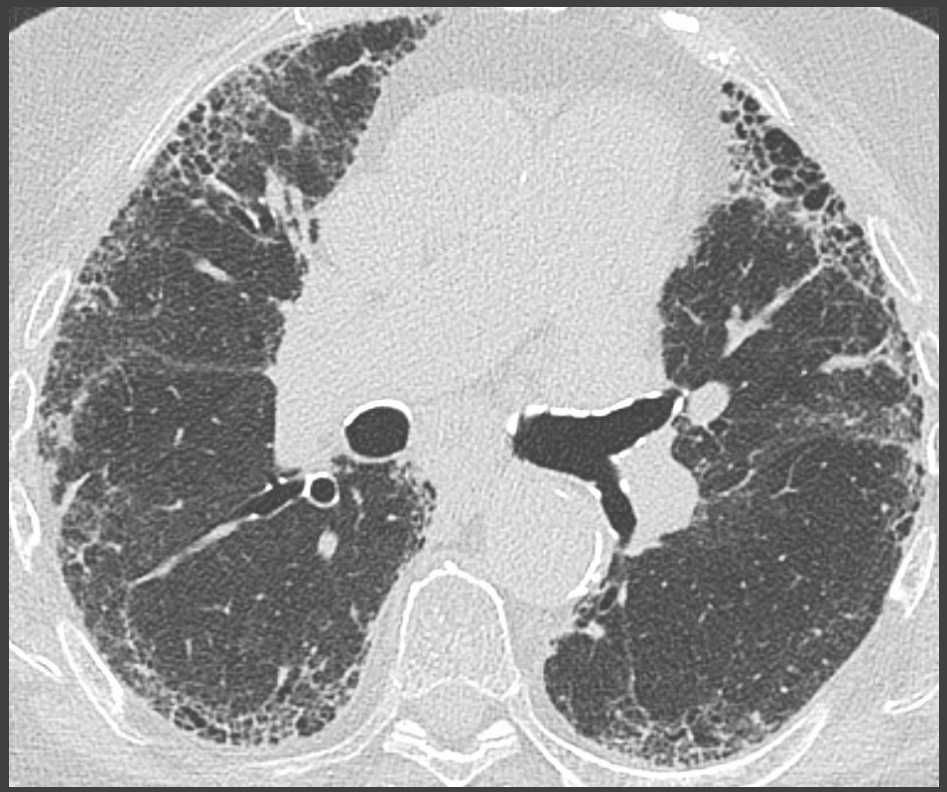
Lynch et al Lancet Respir Med 2018; 6: 138–53

Honeycombing dilemma

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

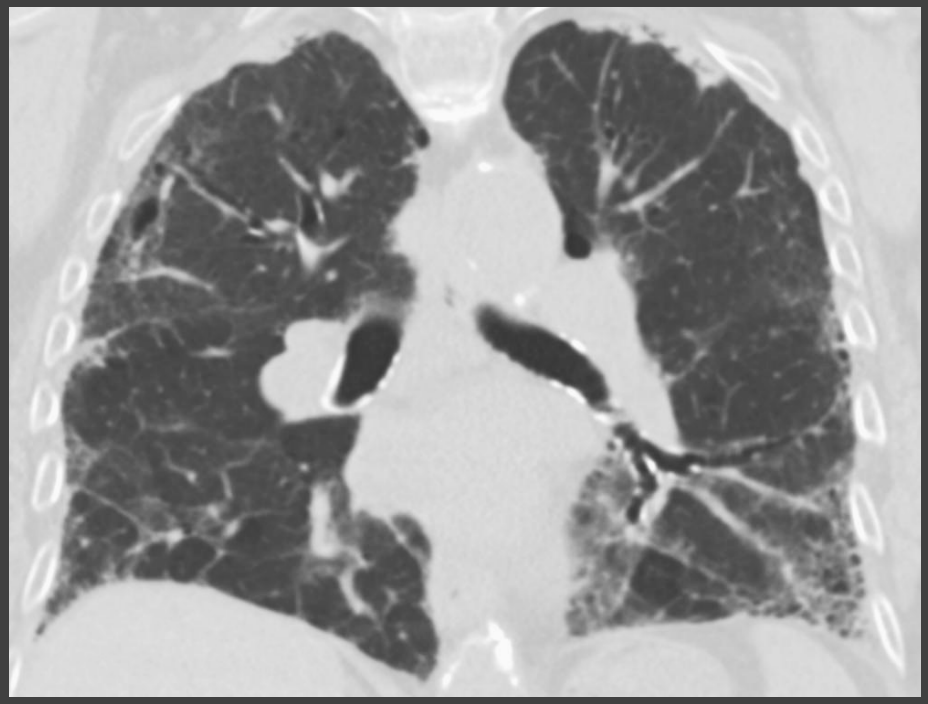
Patient History

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



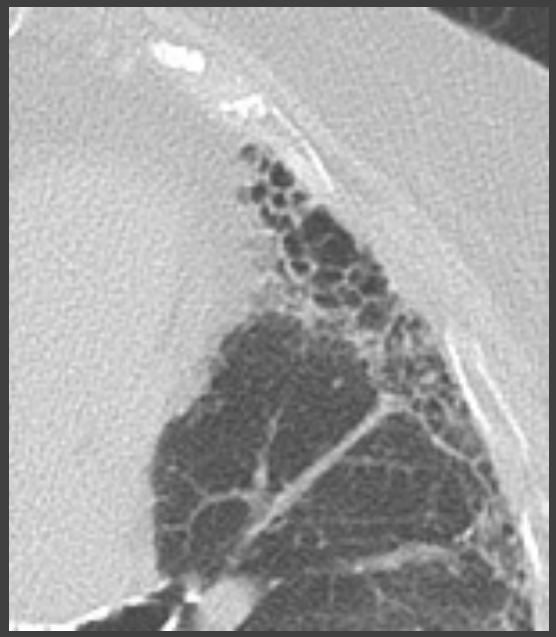
Findings

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



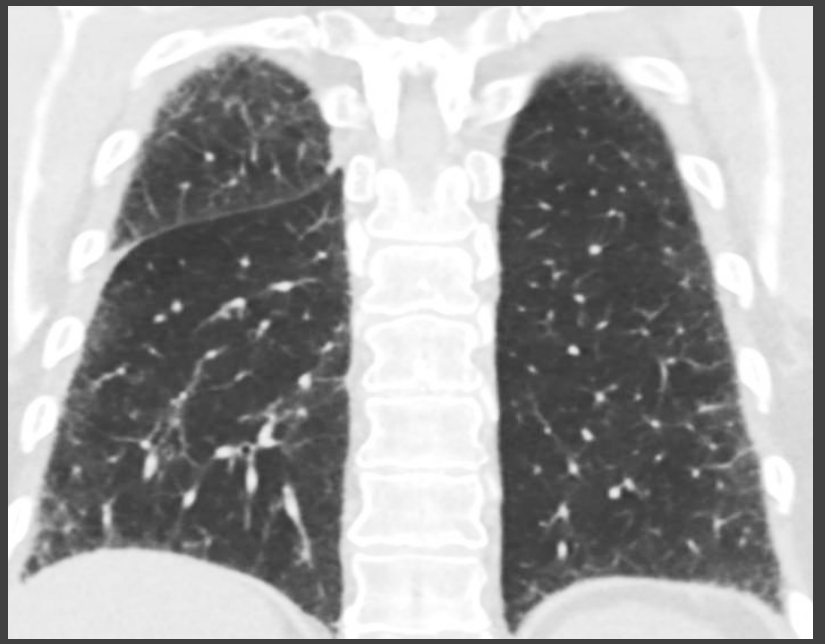
Typical UIP

- 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



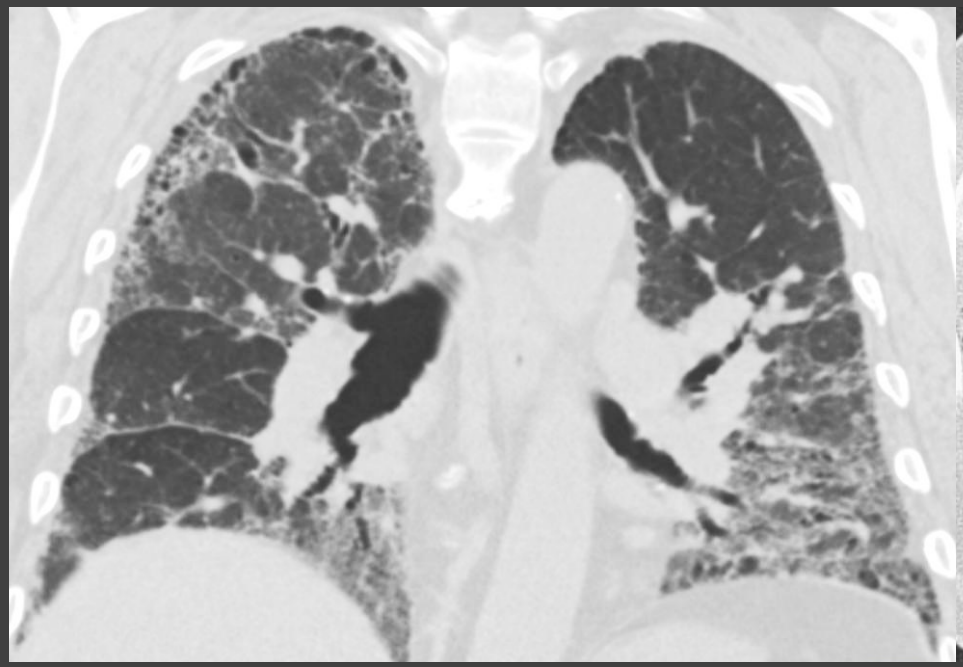
Probable UIP

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

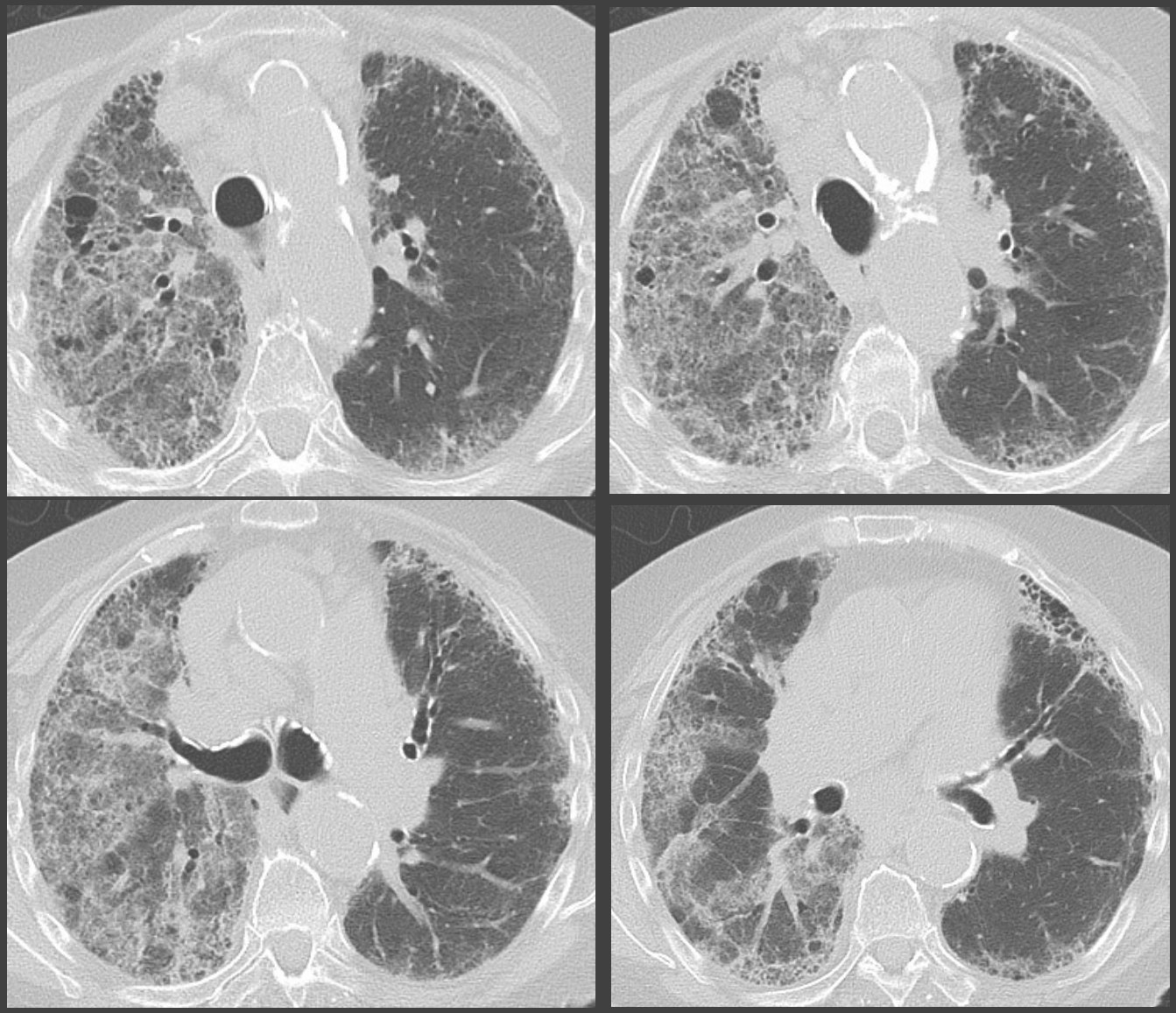


Indeterminate for UIP: But path proven UIP

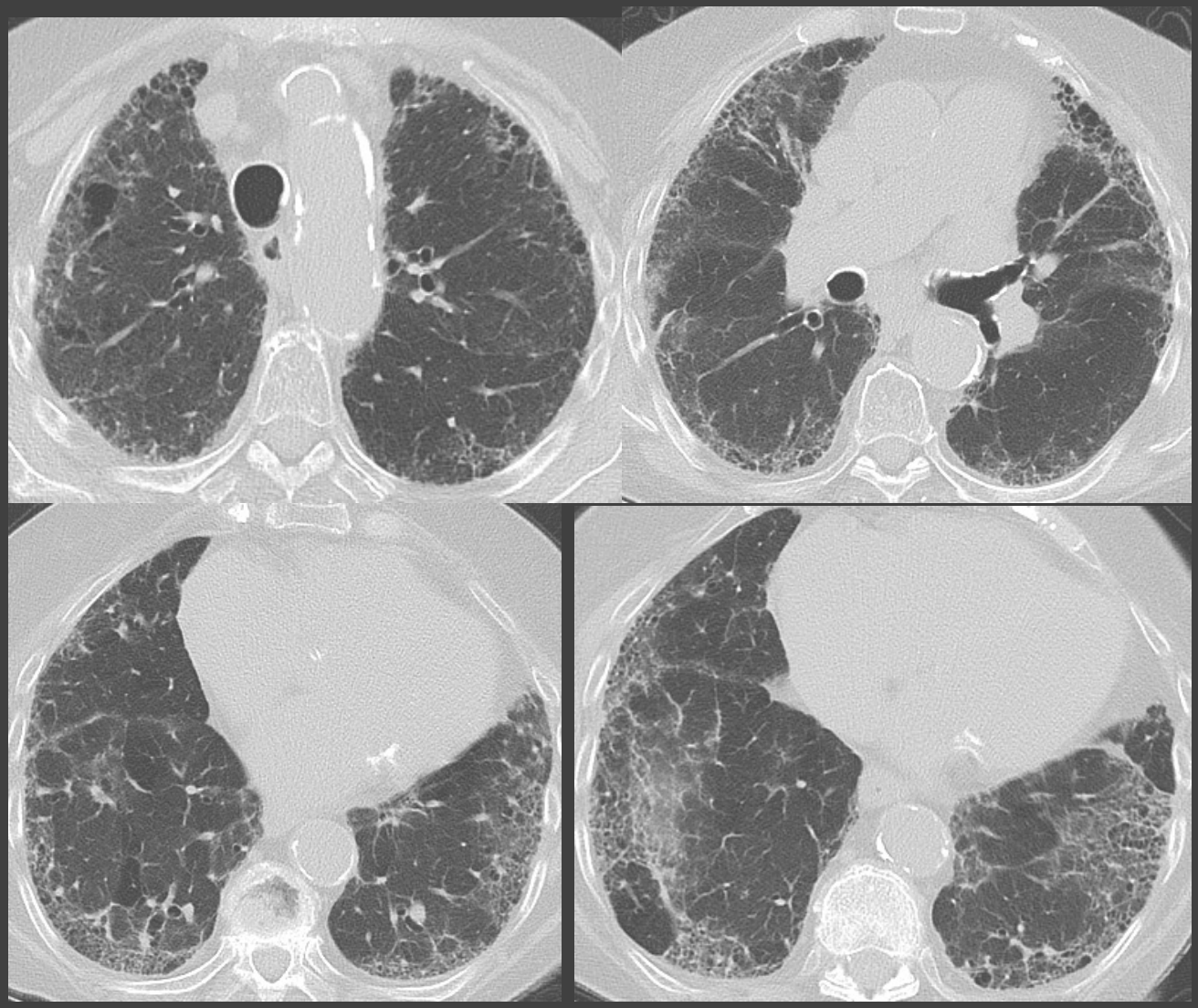
- Basal predominant traction bronchiectasis without honeycombing
- May have mosaic attenuation or patchy GGO



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

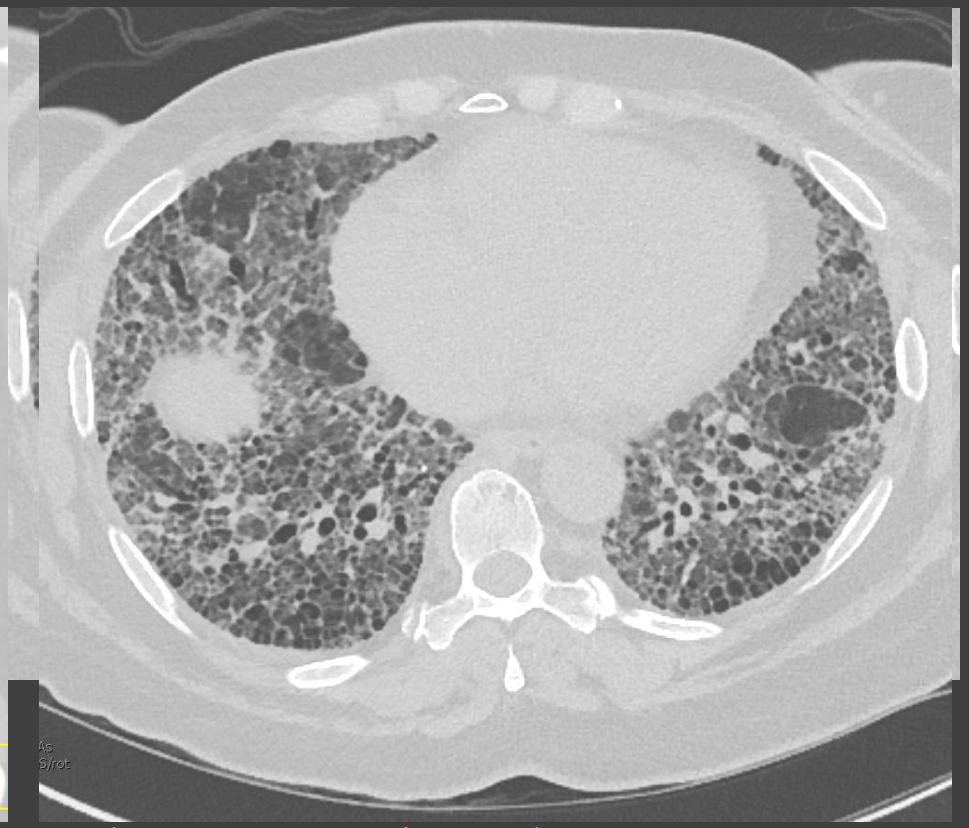


Same patient 7 weeks later after treatment



Familial IPF: Short Telomere Syndrome

- Imaging findings in familial IPF can differ from sporadic IPF with higher prevalence of diffuse or UL 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

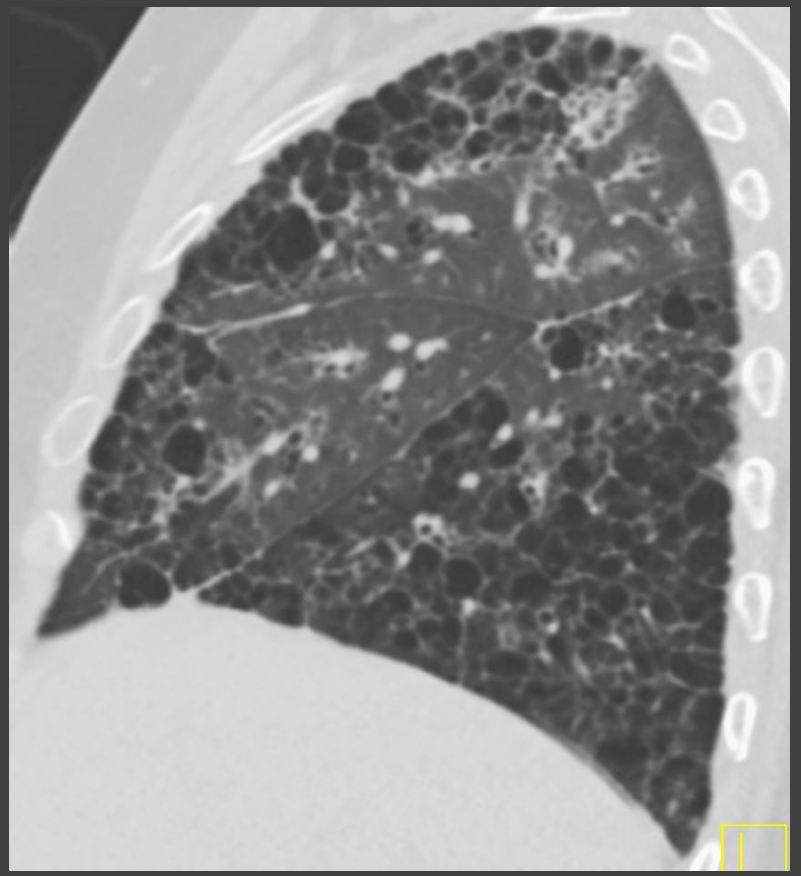
Teaching points

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

Patient History

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

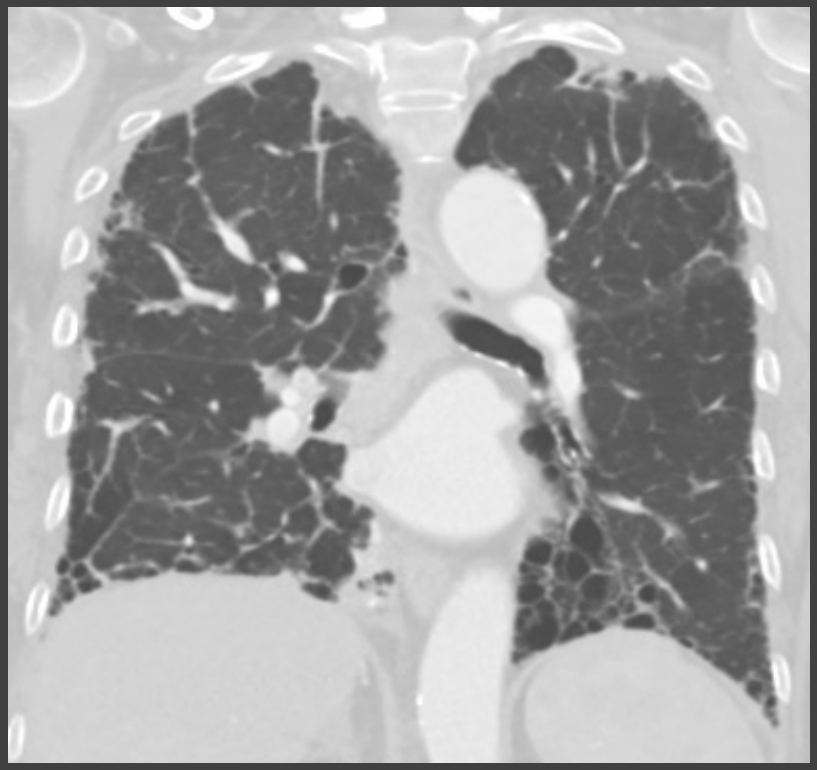


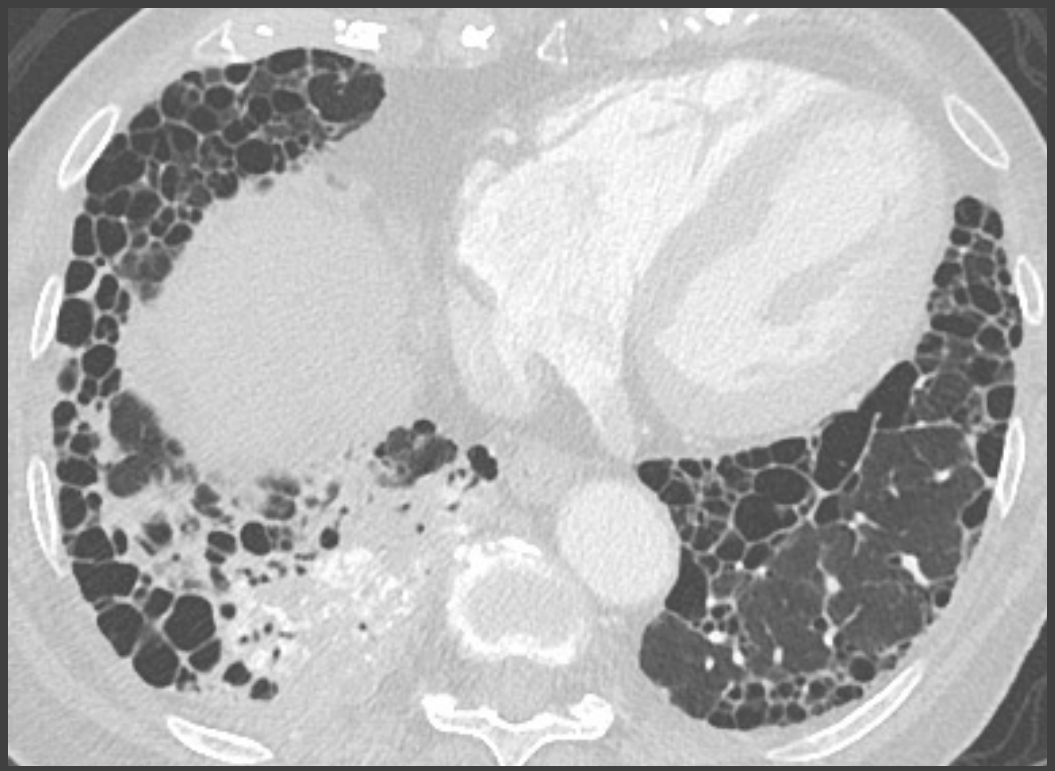
Findings

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

DDx CTD UIP

- Exuberant honeycombing has been found to be a key finding in UIP related to CTD





Chung et al AJR 2018;210:307-313

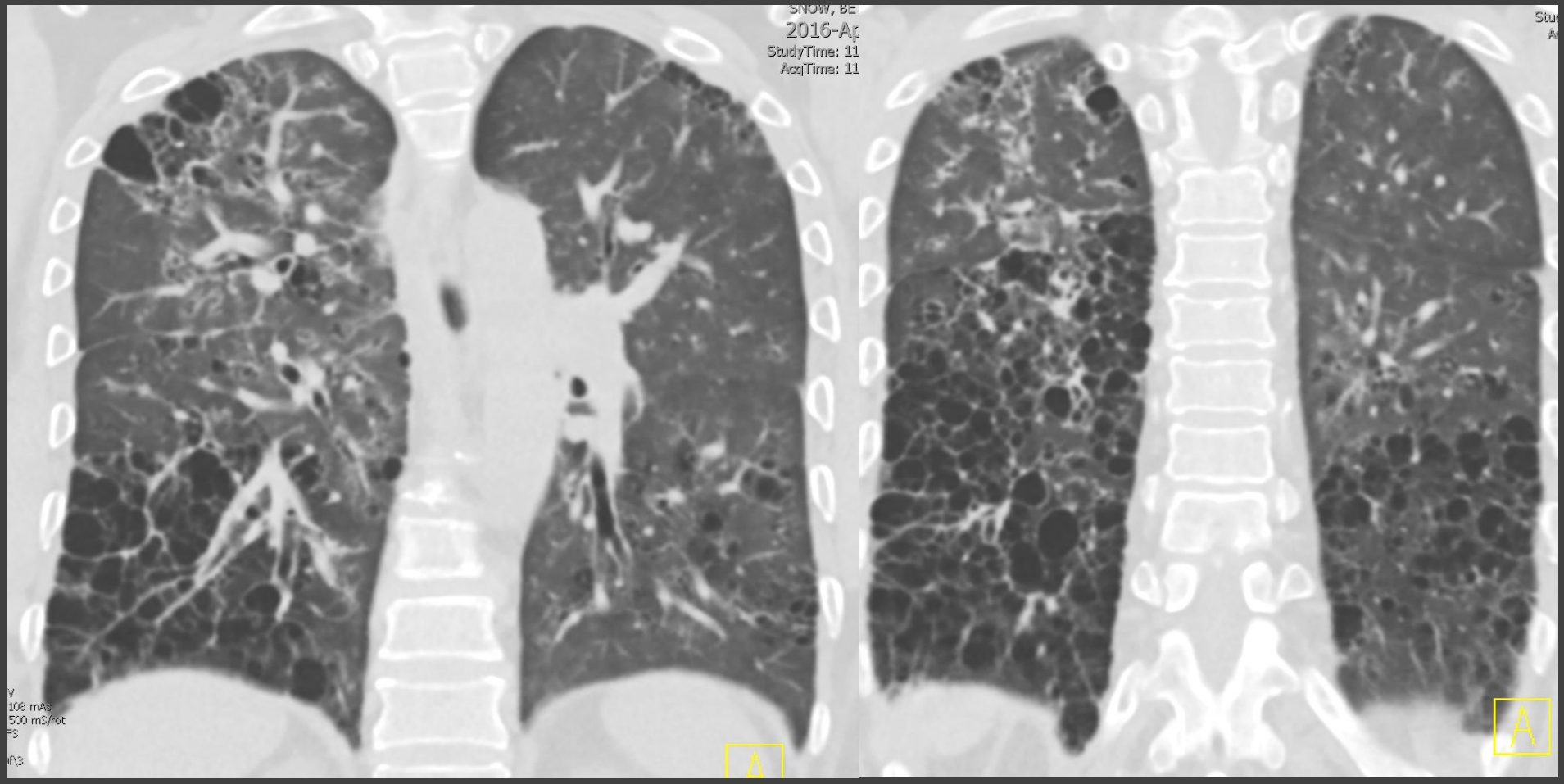
DDx CTD UIP

- 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

DDx CTD UIP

Straight edge sign



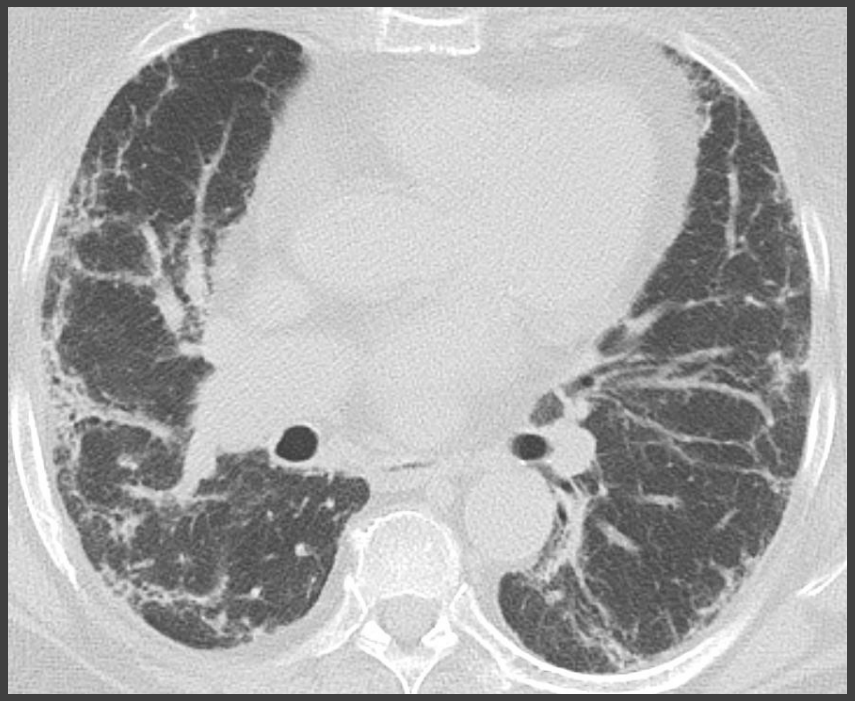
Teaching Points

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

Chung et al AJR 2018;210:307-313

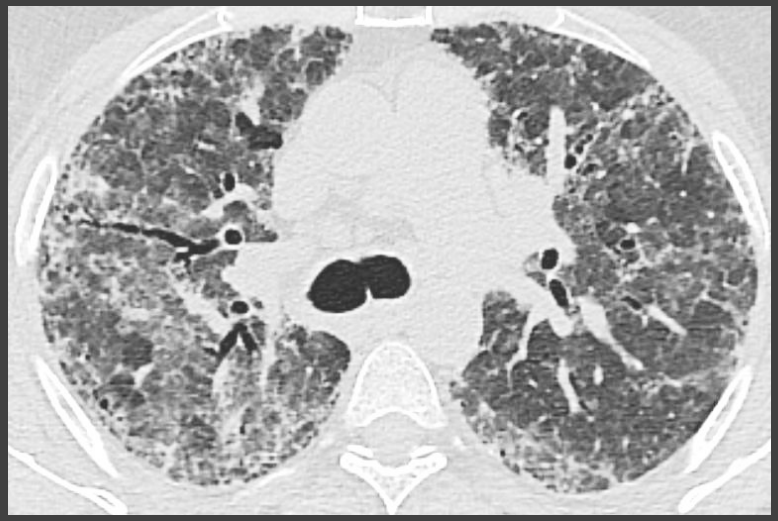
Patient History

63 y/o female with h/o RA who presents with several month history of SOB and dry cough. VATS biopsy was performed



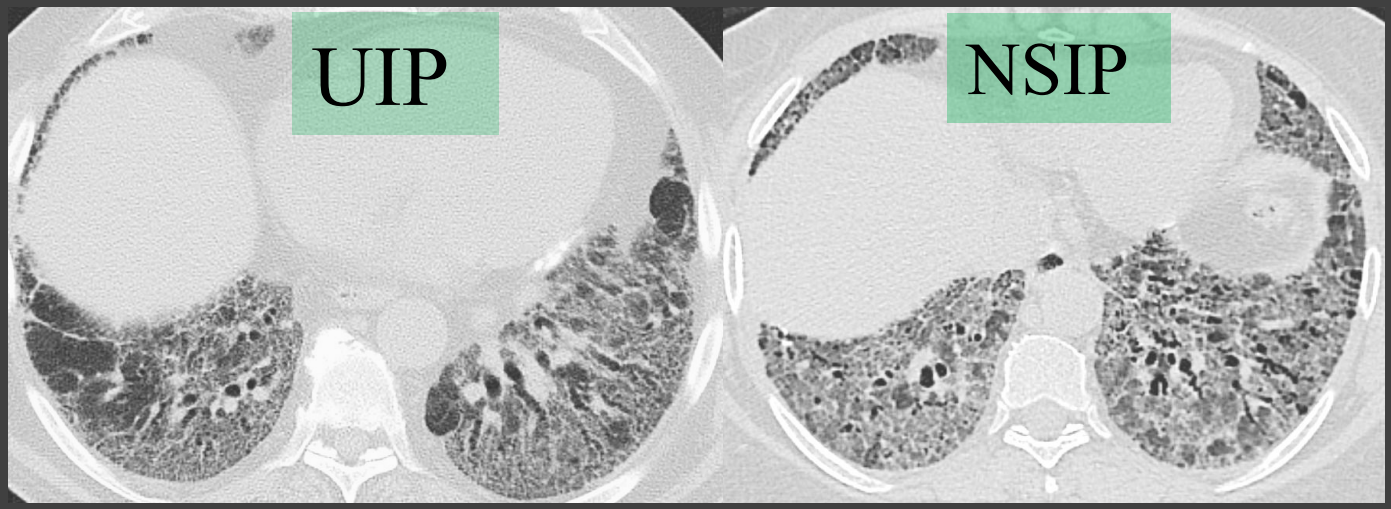
DDx Fibrotic NSIP

- Ground glass attenuation is usually seen
- Traction bronchiectasis
- Typically, no honeycombing
- Early stage spares the periphery



Teaching Points

- Considerable overlap between NSIP and Indeterminate UIP
- Histopathologic differences between NSIP and UIP are not well defined
- Possible that bx proven fibrotic NSIP includes cases of UIP and vice versa



MacDonald et al Radiology 2001; 221:600-605

Diagnostic Approach to Diffuse Cystic Lung Disease

- Intraparenchymal w/o other findings
  - LAM, PLCH, Birt-Hogg-Dubé, LIP, malignancy
  - Infection, tracheobronchial papillomatosis
- Intraparenchymal with nodules
  - LIP, PLCH, Amyloid, Light chain deposition
- Intraparenchymal with GGO
  - Pneumocystis
  - DIP
- Subpleural
  - Bullae, paraseptal emphysema, Honeycombing

Intraparenchymal Cysts

Cysts only

- LAM
- PLCH
- Birt Hogg Dube
- LIP
- Malignancy/Mets
- Tracheobronchial Papillomatosis
- Infection

Cysts with Nodules

- LIP
- PLCH
- LCDD
- Amyloid
- Metastasis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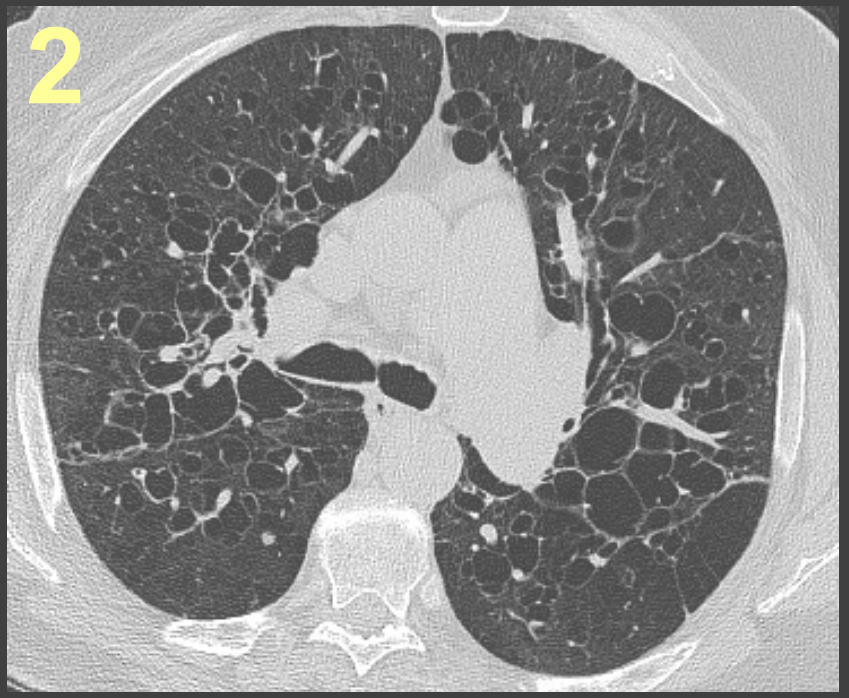
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Cysts

- A round parenchymal space with a well defined wall
- Usually air containing
- Commonly used to describe enlarged airspaces in LAM, PLCH, Endstage pulmonary fibrosis
- Emphysema: focal region/regions of low attenuation usually without visible walls

Lymphangioleiomyomatosis: Sporadic

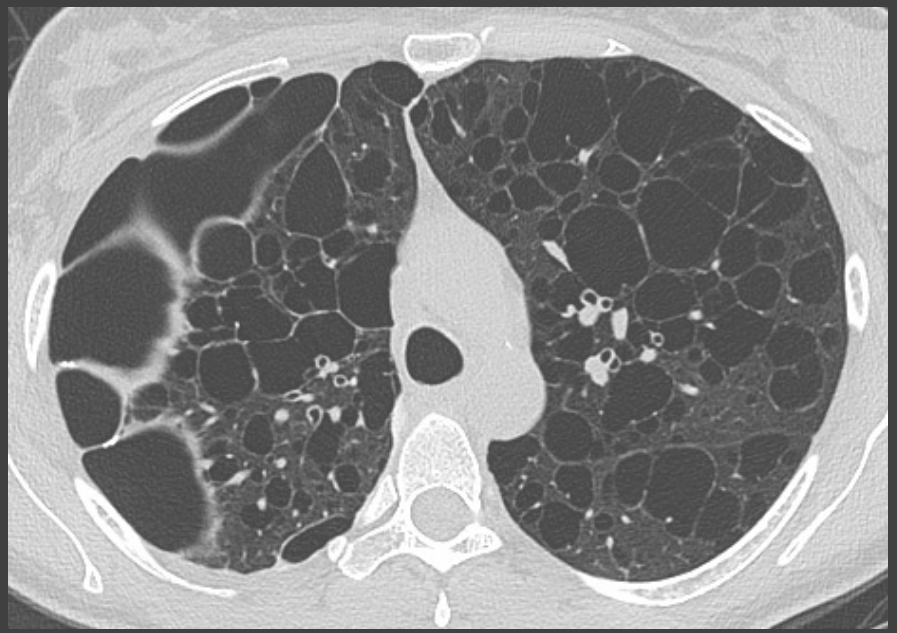
- Sporadic LAM
  - Hamartomatous cystic lung disease
  - Mean age at dx 30-35 (but age increasing)
  - Age distribution may extend beyond reproductive years
  - Onset and exacerbation may coincide with pregnancy and parturition
  - Abnl smooth muscle may have ER/PR
  - Elevated VEGF-D levels >800 $pg.ml^{-1}$

Cysts in LAM

- Nodules or small clusters of SM cells (LAM cells) near cysts and around airways and vessels (arteries and lymphatics)
- Cysts are diffuse involving whole lung
- Uniform cysts

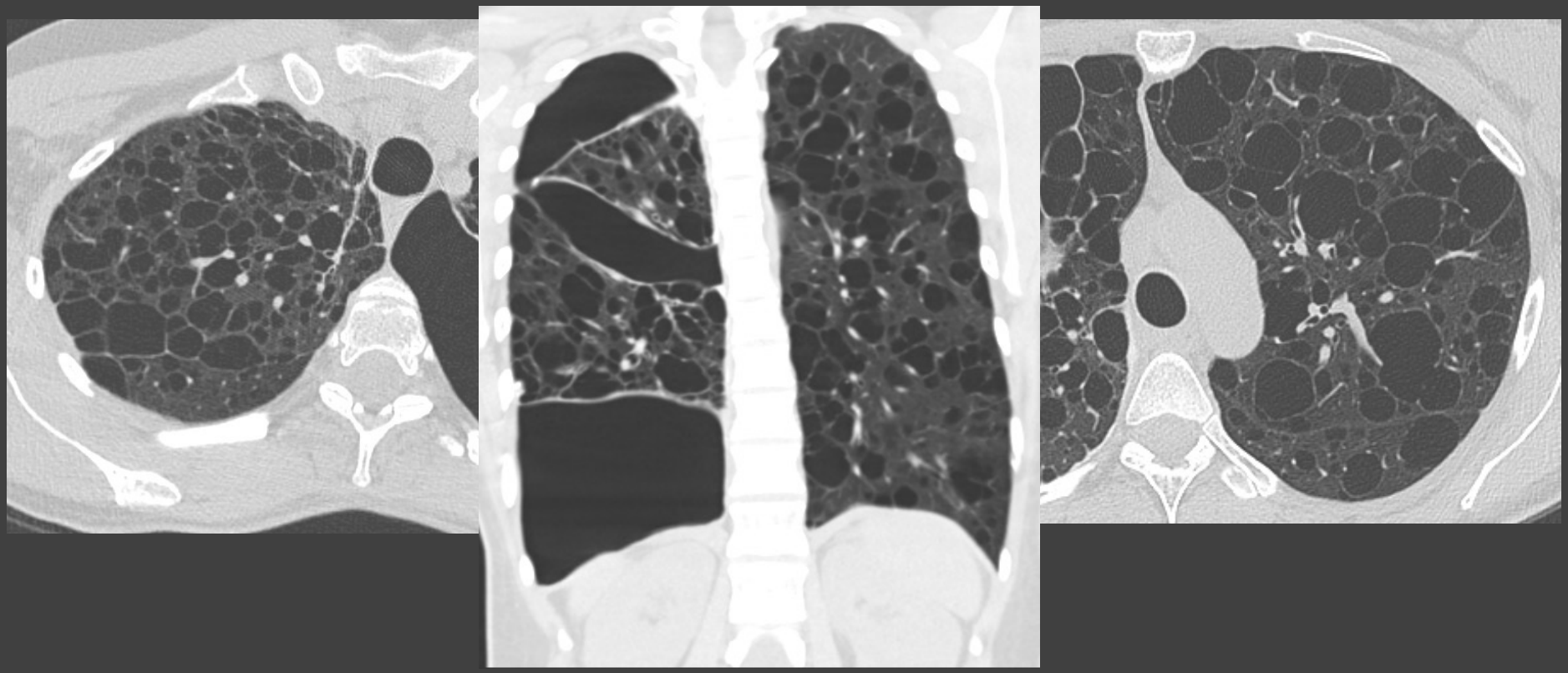
Cysts in LAM

- Cysts may also arise due to degradation of the interstitium by metalloproteinases produced by LAM cells
- Larger cysts may coalesce-mimic emphysema



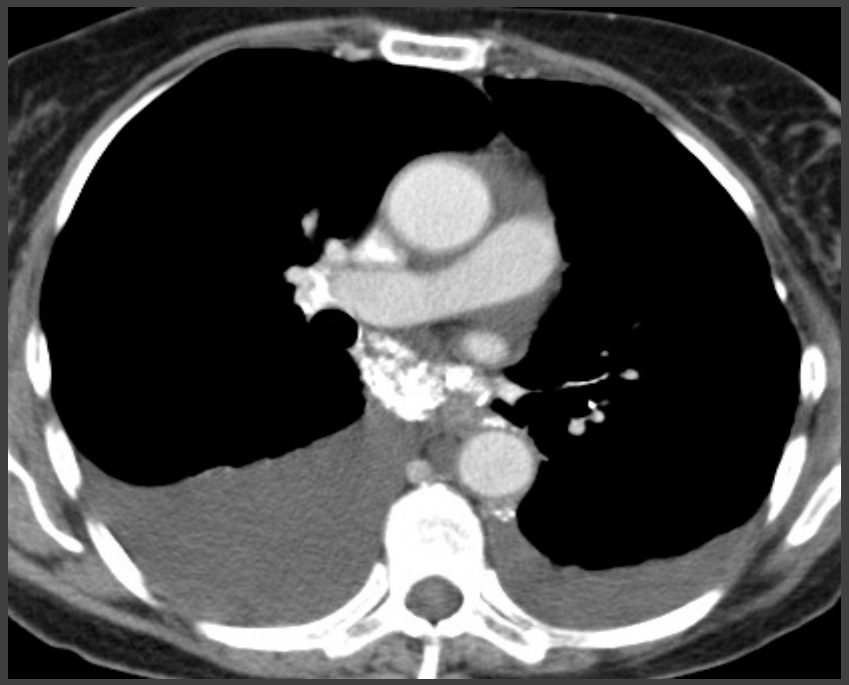
Pleural disease in LAM

- PTX; presenting manifestation in 40-50% of pts; 60-80% develop PTX at some time



Pleural Disease in LAM

- Chylous pleural effusions



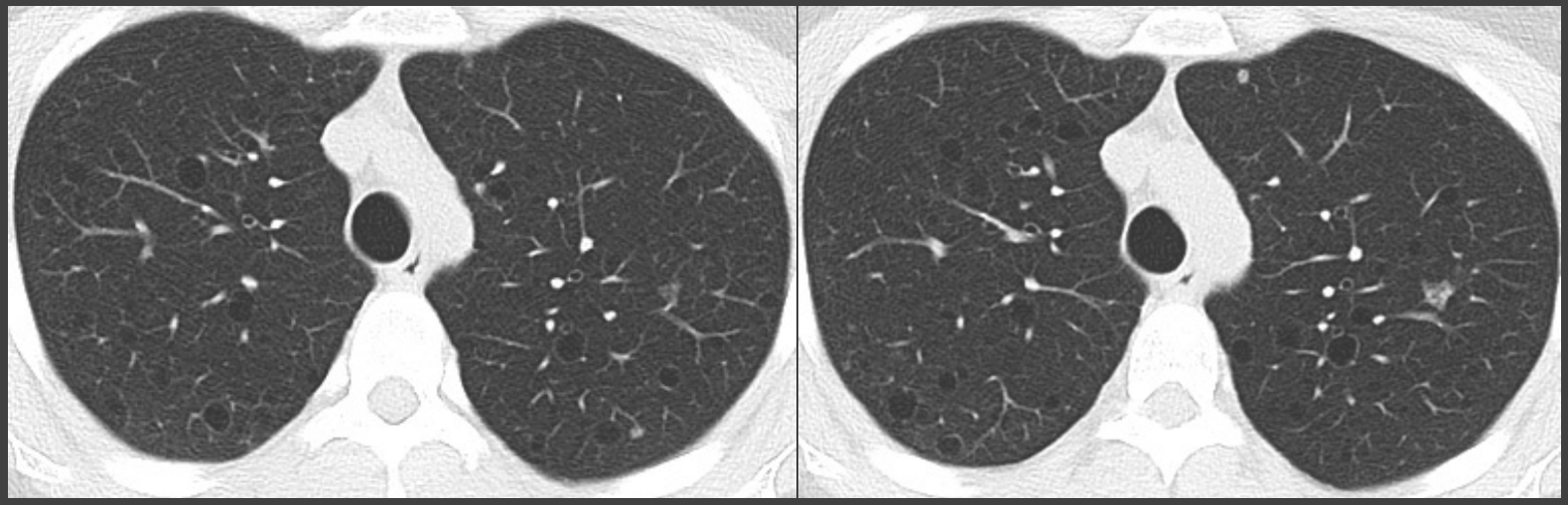
Lymphangioleiomyomatosis: TSC-LAM

- TSC-LAM
  - Autosomal dominant neurocutaneous syndrome
  - 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

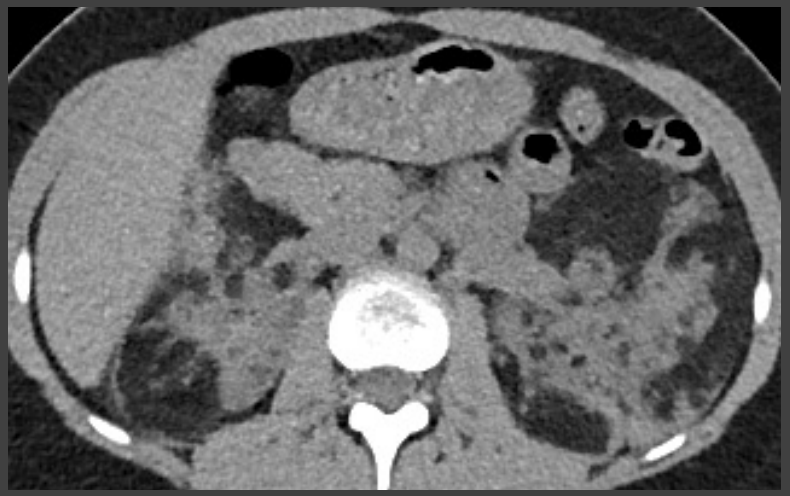
Lymphangioleiomyomatosis: TSC-LAM

- TSC-LAM
  - 5-10 X more common than S-LAM
  - Less severe than sporadic form
  - 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)

Tuberous Sclerosis Complex

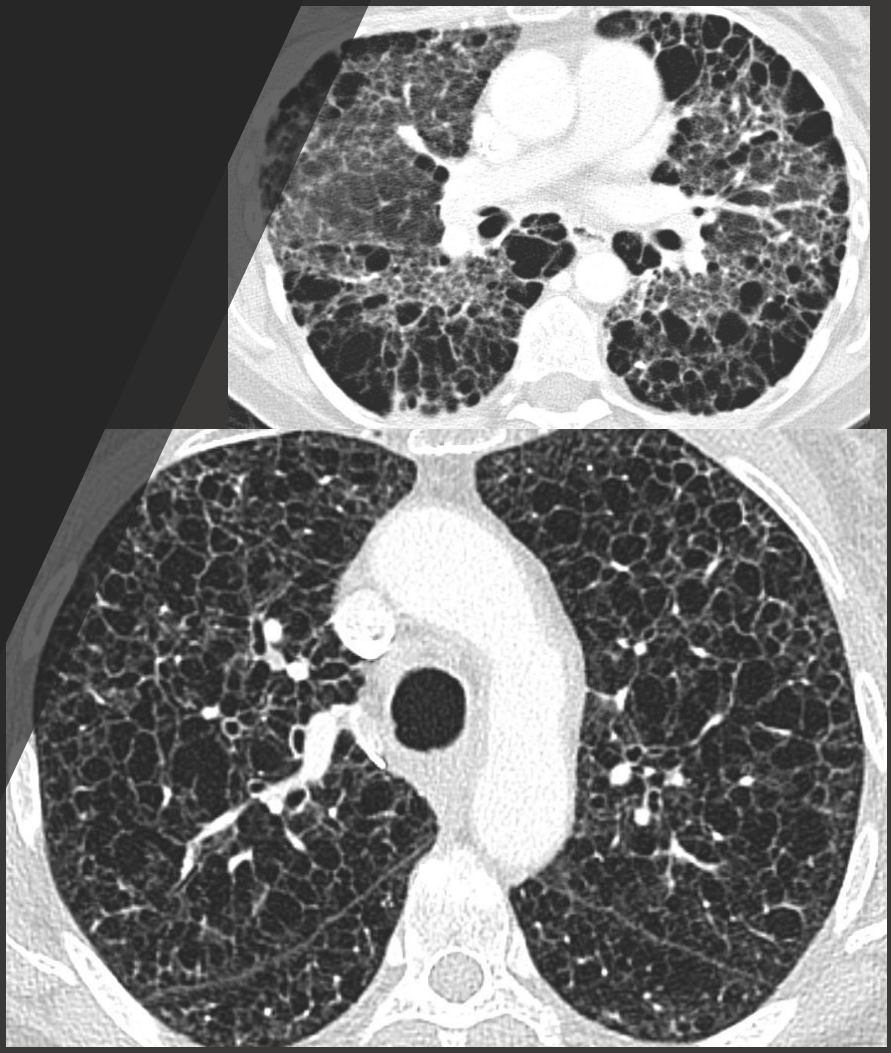


Tuberous Sclerosis Complex with sclerotic bone lesions and angiomyolipomas



Smoking-related Interstitial lung Diseases

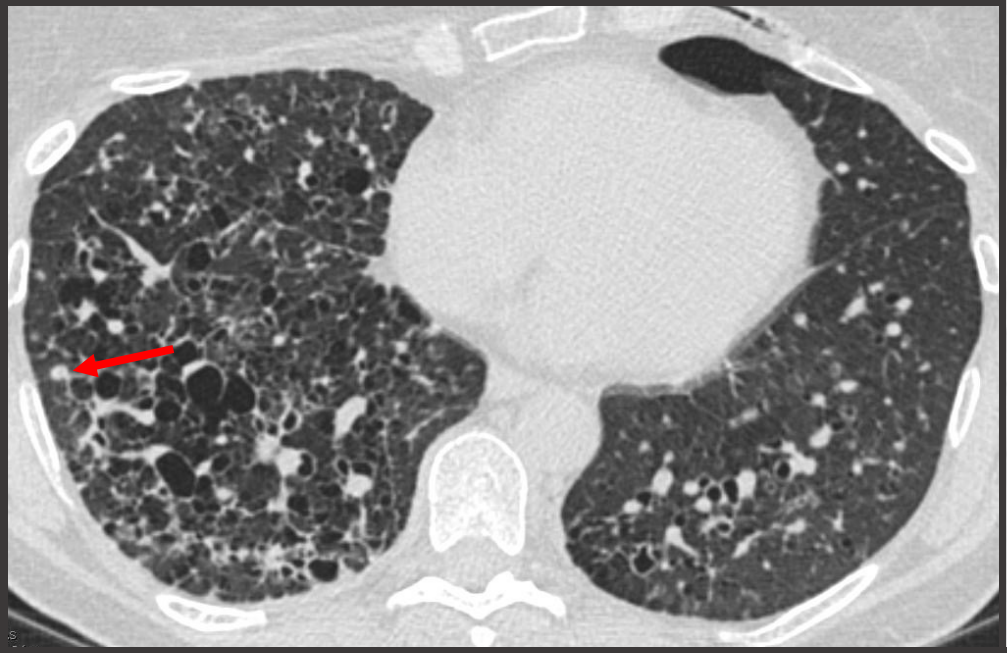
- Pulmonary Langerhans Cell histiocytosis (PLCH)
- Respiratory bronchiolitis-interstitial lung disease (RB-ILD)
- Desquamative interstitial pneumonitis (DIP)
- Airspace enlargement with fibrosis (AEF) (SRIF)
- Combined pulmonary fibrosis emphysema (CPFE)
- Unclassifiable IIP in smokers

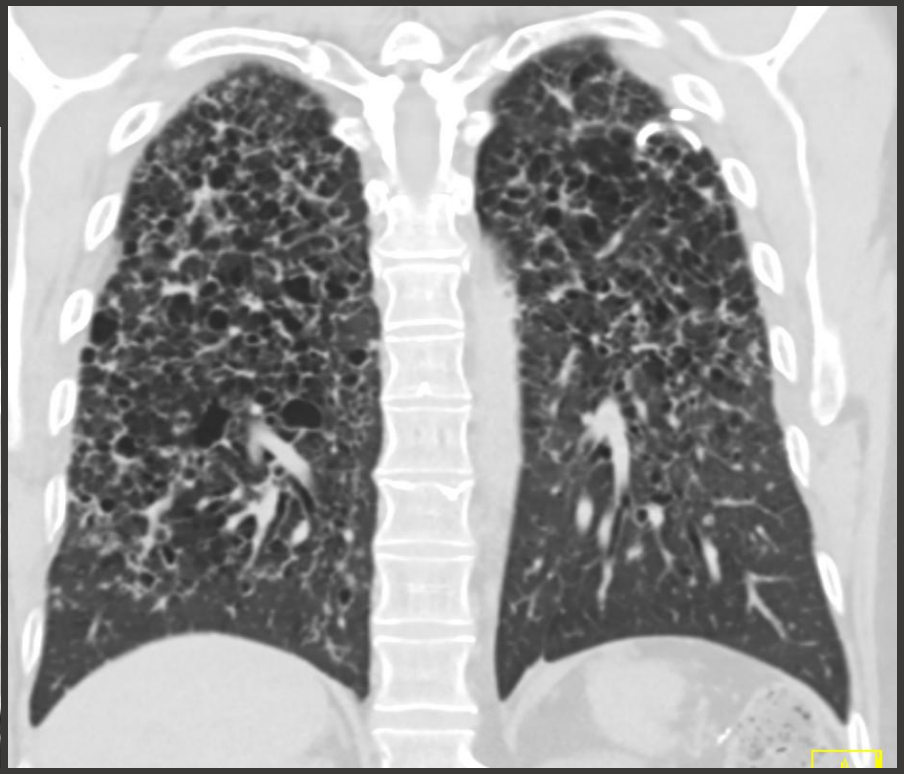


Fibrosis in smokers

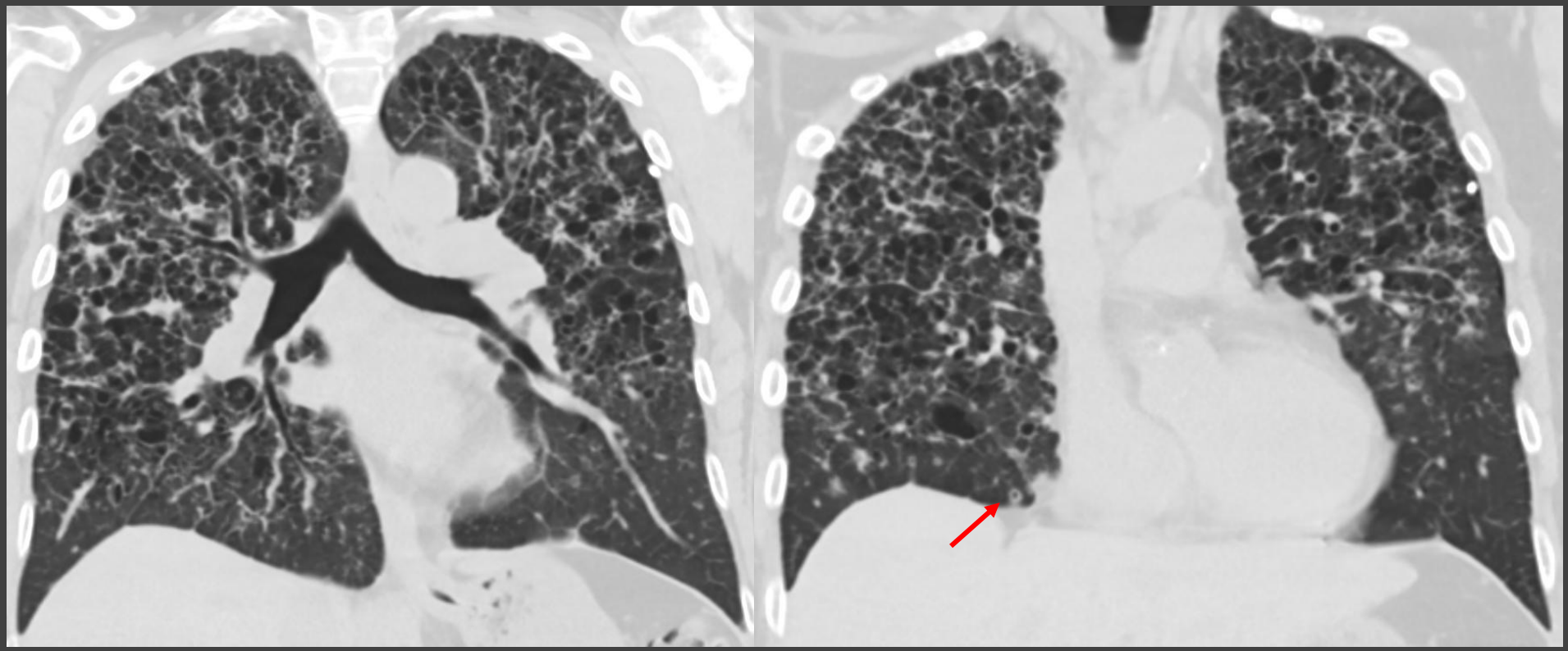
- Smoking strongly associated with IPF
- Cysts with small dots are frequently seen on HRCT images of smokers
- These cysts are likely due to destruction of lung by emphysema
- In smokers, fibrosis of all types can be present including UIP pattern and collagenous type
- Both emphysema and fibrosis can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

Case One: 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



Pulmonary Langerhans cell histiocytosis

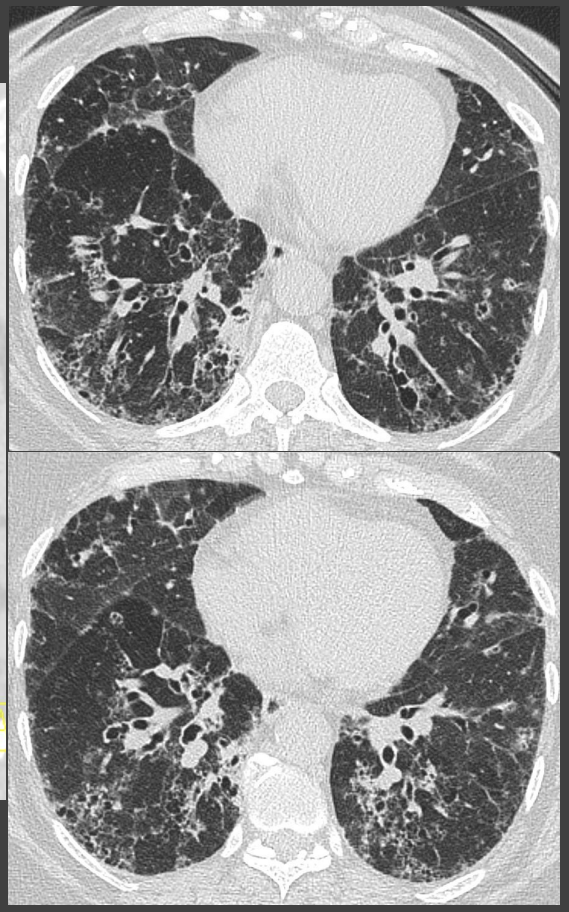
- Patients are 3rd to 4th decades of life; affects men and women equally
- >90% pts have smoking history
- Only a small percentage develop PLCH
- Mechanism of pathogenesis is unclear but appears to be that proliferation of Langerhans cells represents abnl immune reaction directed at components of cigarette 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

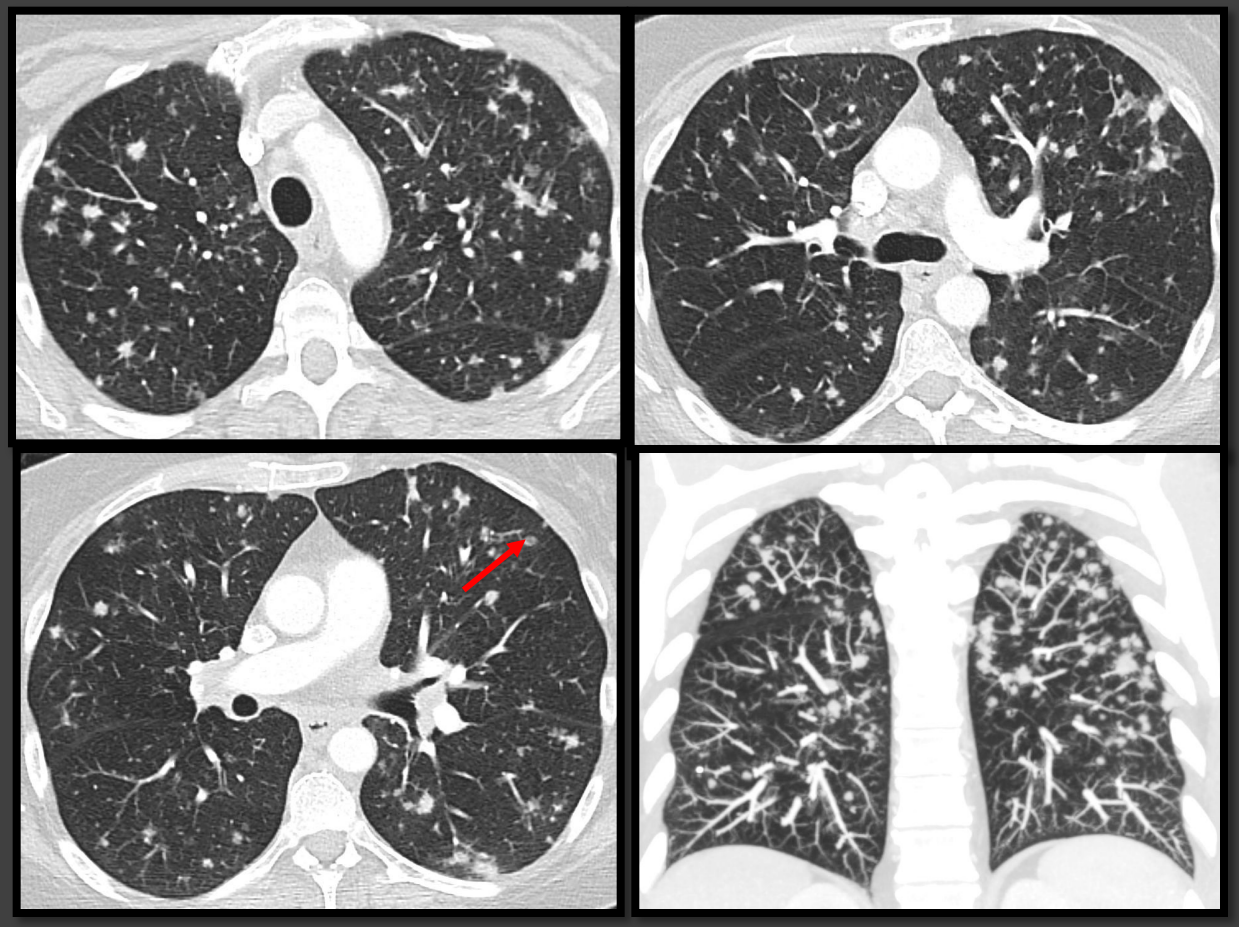
Histologic features

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



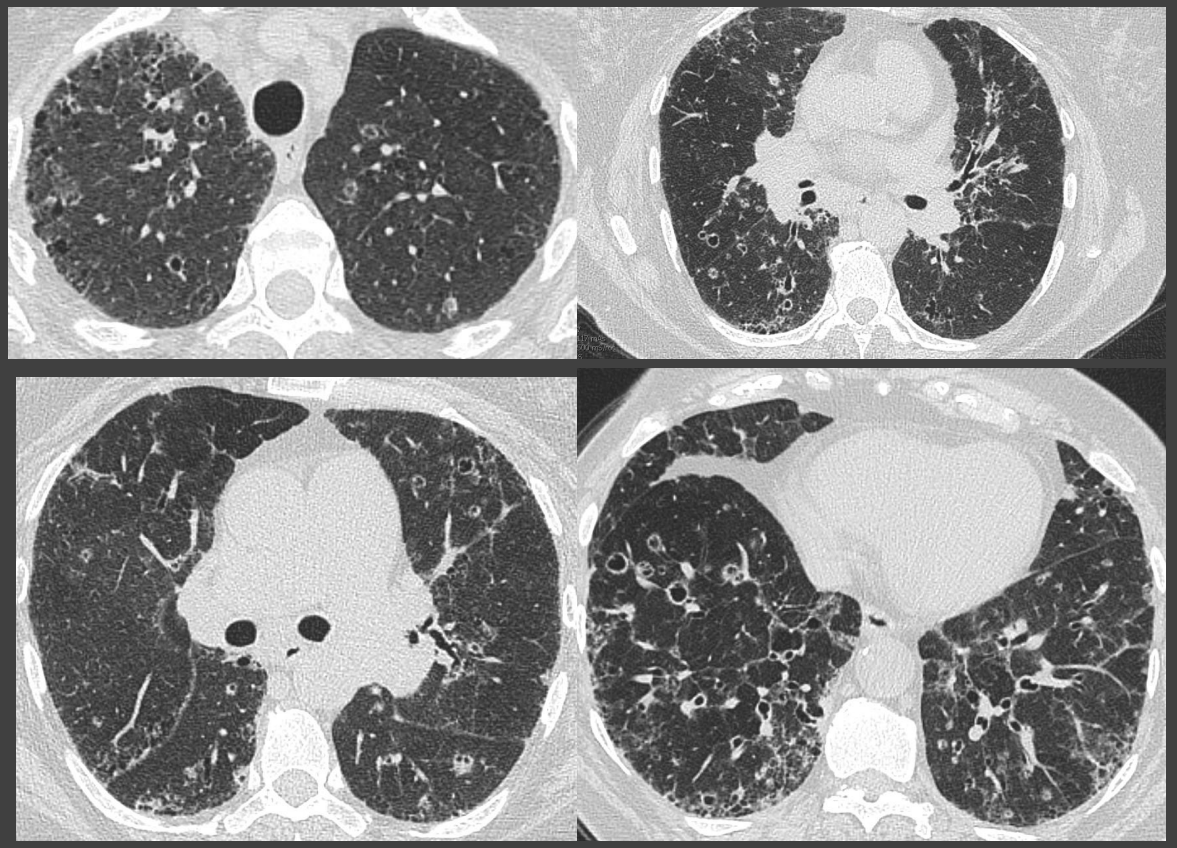
Radiologic Findings

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



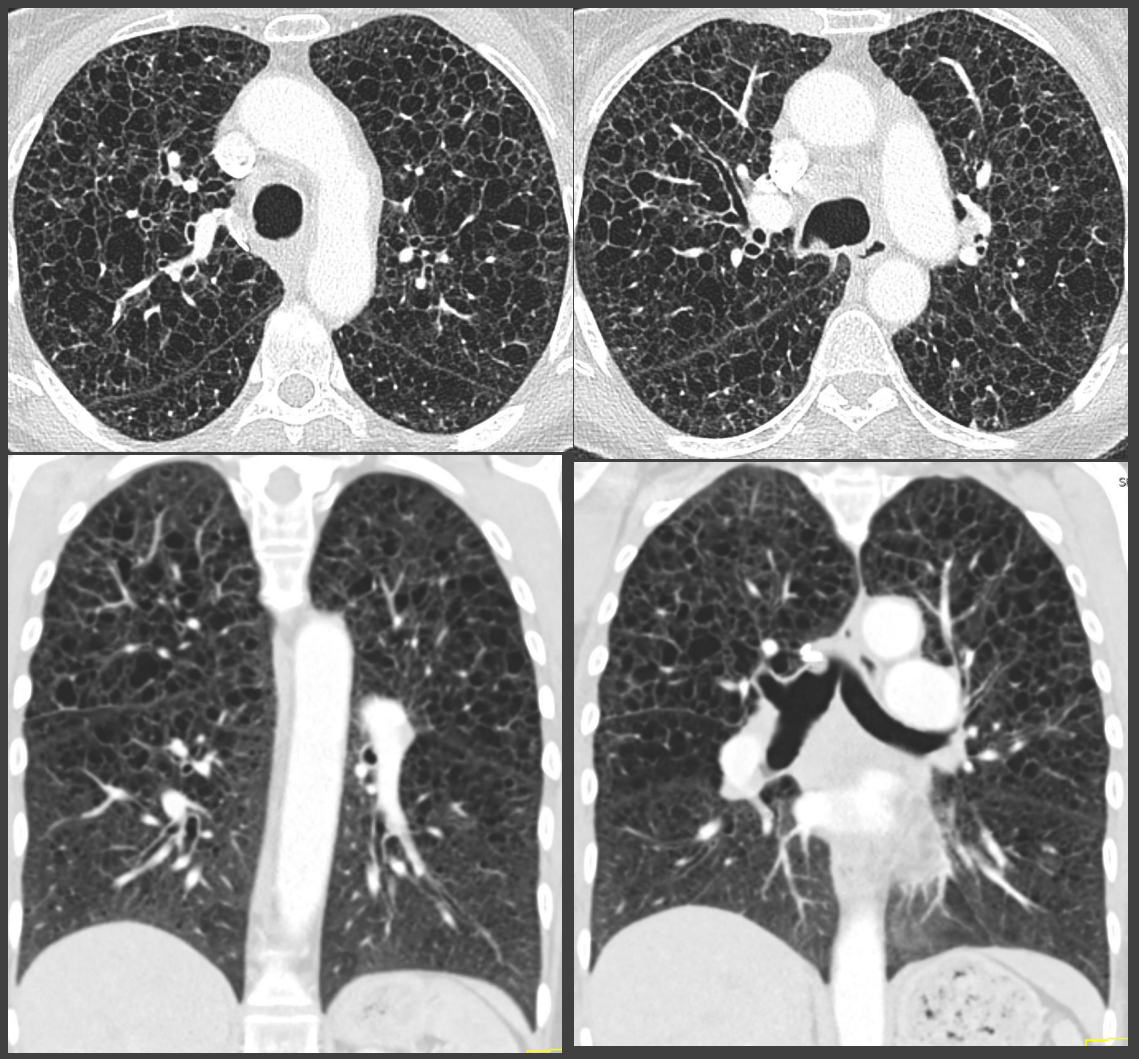
Radiologic Findings

- 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



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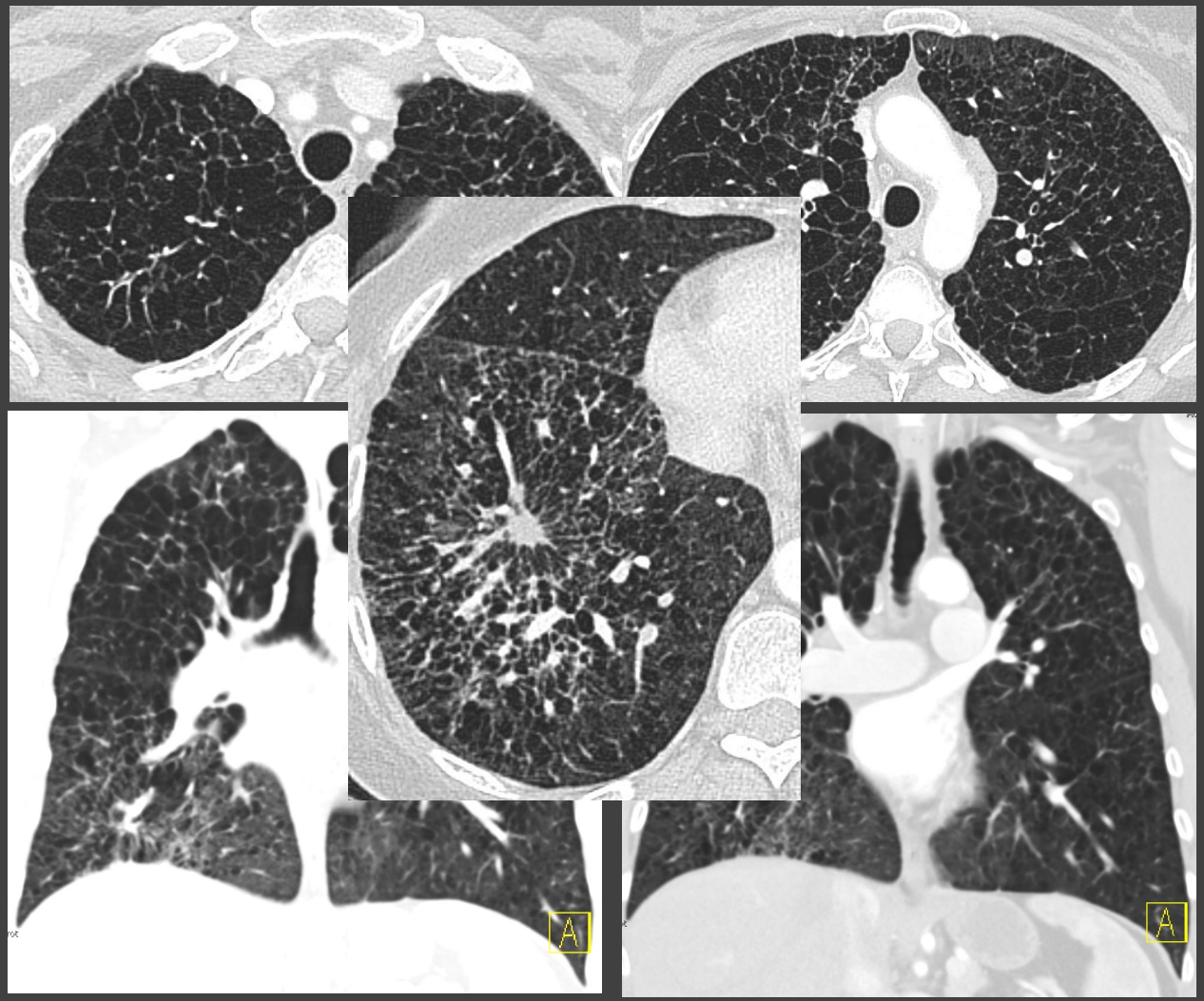
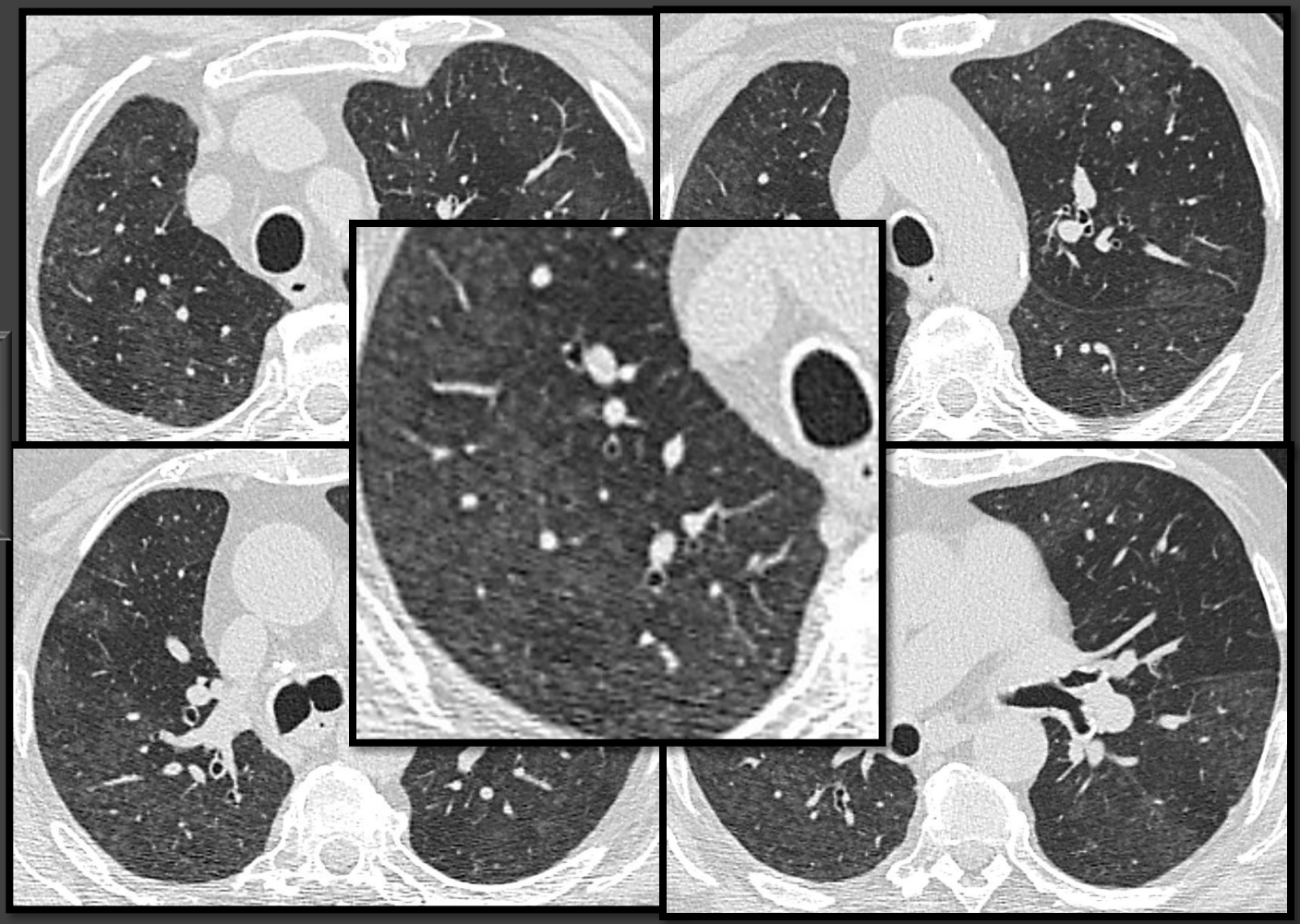


Case two: 86 y/o man with 65 pack year smoking history presents with SOB and cough

Diagnosis: RB-ILD

DDx: Acute hypersensitivity Pneumonitis



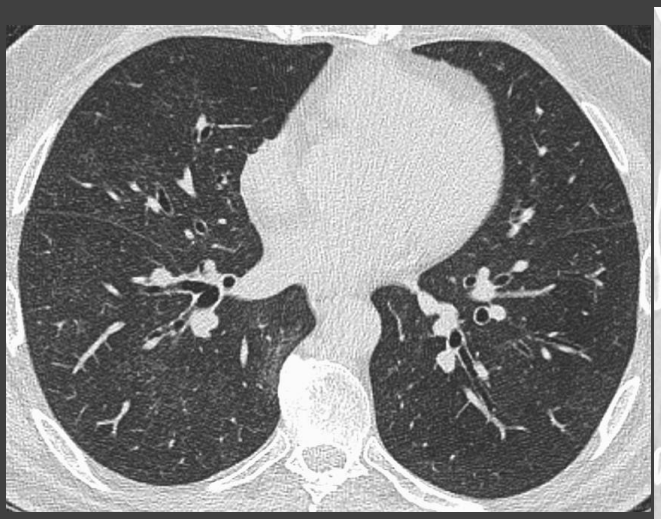
Respiratory bronchiolitis-interstitial lung disease (RB-ILD): Overview

- 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

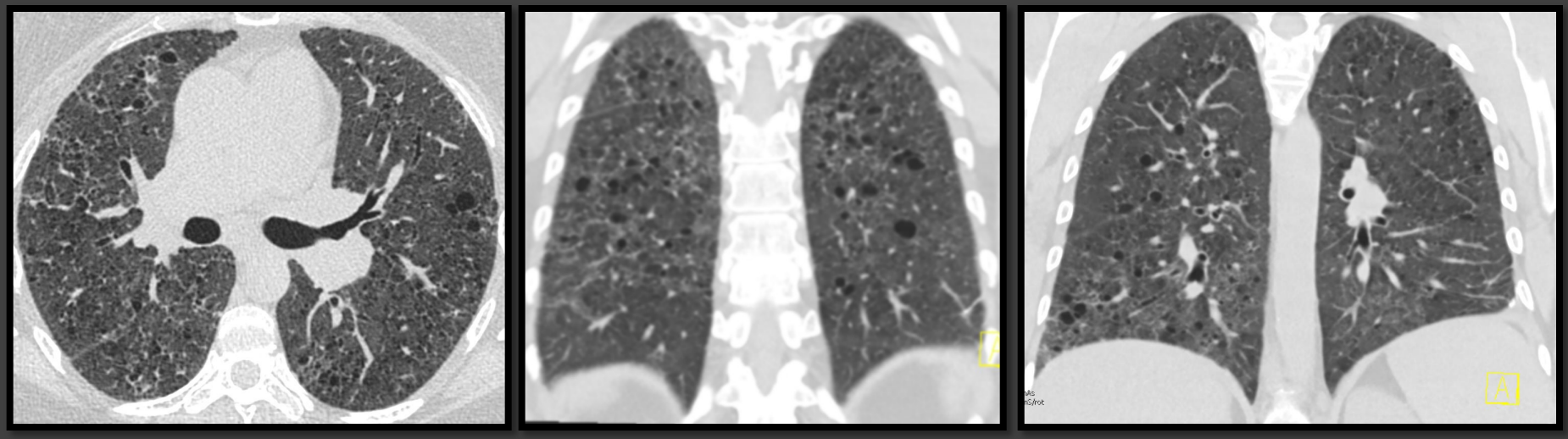
- Central bronchial wall thickening
- Centrilobular nodules
- Areas of GGO
- Some reports indicate upper lung zone predominance
- HP is in the differential

Respiratory Bronchiolitis- Interstitial Lung disease RB-ILD



Case Three: 49 y/o woman with 38 pack year smoking hx, presents with dyspnea for several months

Diagnosis: Desquamative Interstitial Pneumonia (DIP)

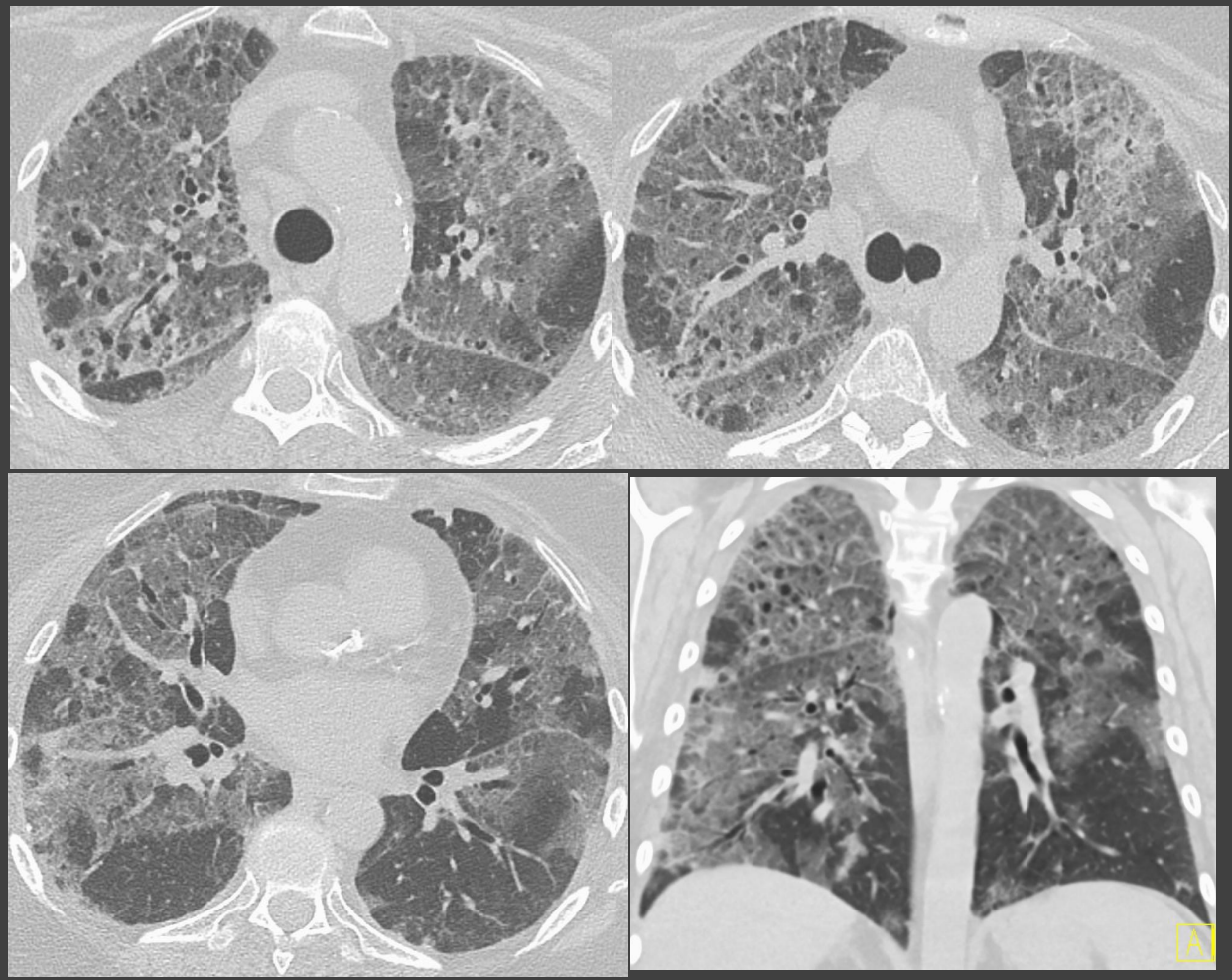


Desquamative interstitial pneumonia (DIP)

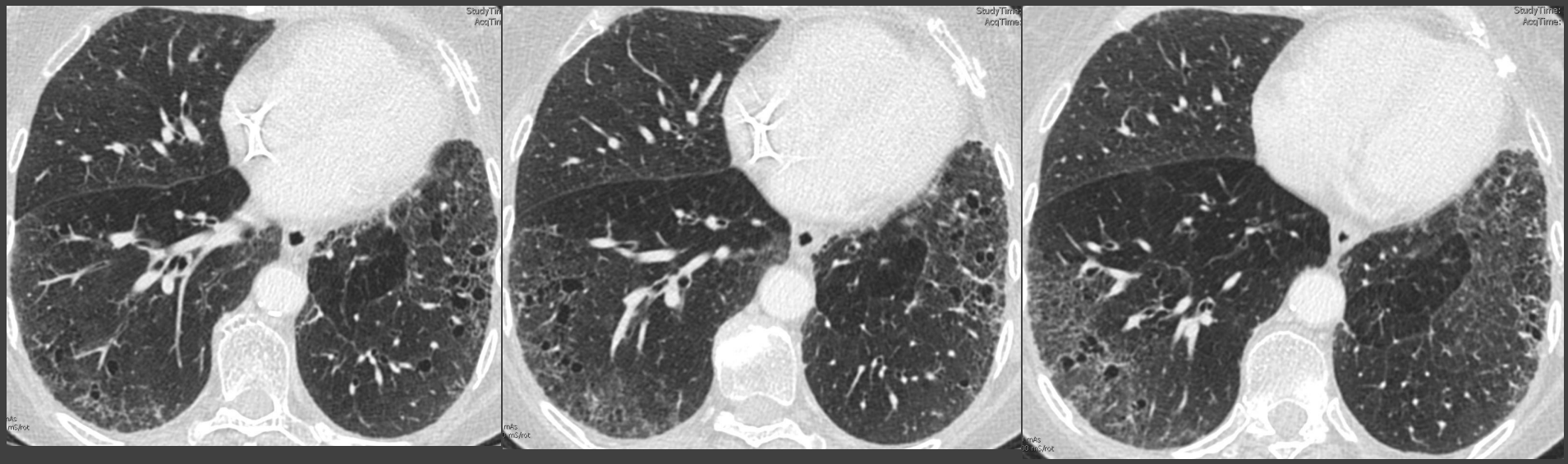
- On a spectrum with RB-ID
- Compared with RB-ILD, the diffusing capacity for carbon monoxide (DLCO) may be severely reduced
- Pigmented macrophages fill alveoli diffusely due to immune-mediated response to smoking
- Diffuse alveolar septal thickening

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



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

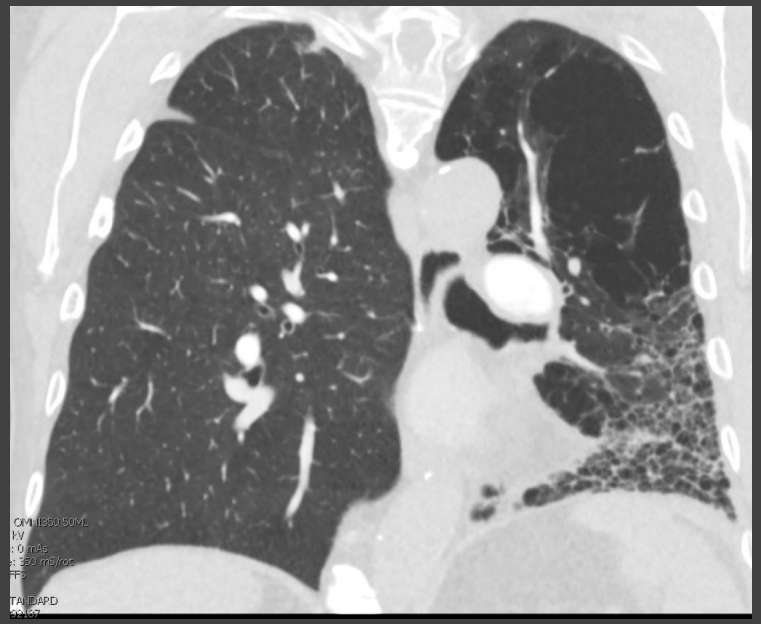
- Emphysematous change
- Absence of fibroblastic foci
- Fibrosis is confined to the subpleural and peribronchovascular interstitium
- Clinical course is stable in most cases so must be distinguished from UIP and other IIPs if symptoms worsen over time

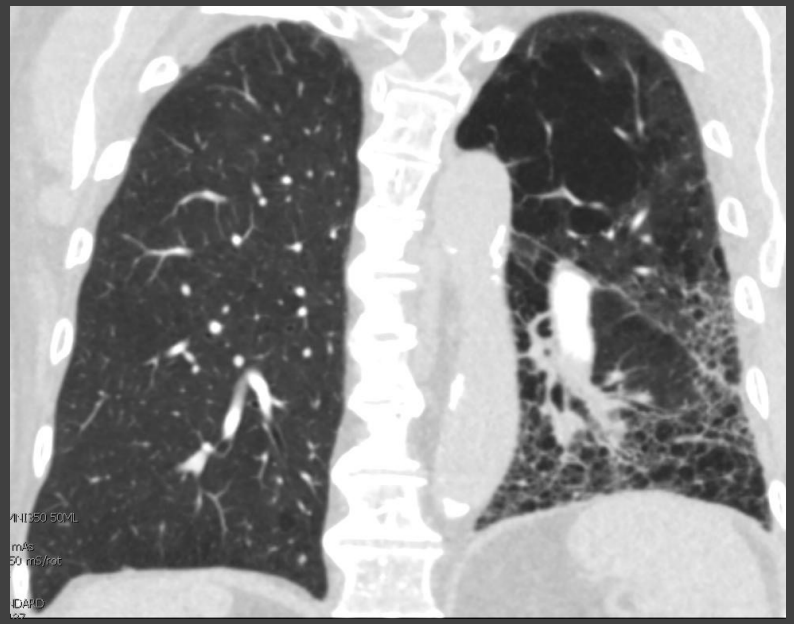
Case Five: 53 y/o man with 45 pack yr smoking history presents with severe SOB



Diagnosis: Combined Pulmonary Fibrosis Emphysema (CPFE)

Same patient S/P single lung transplant





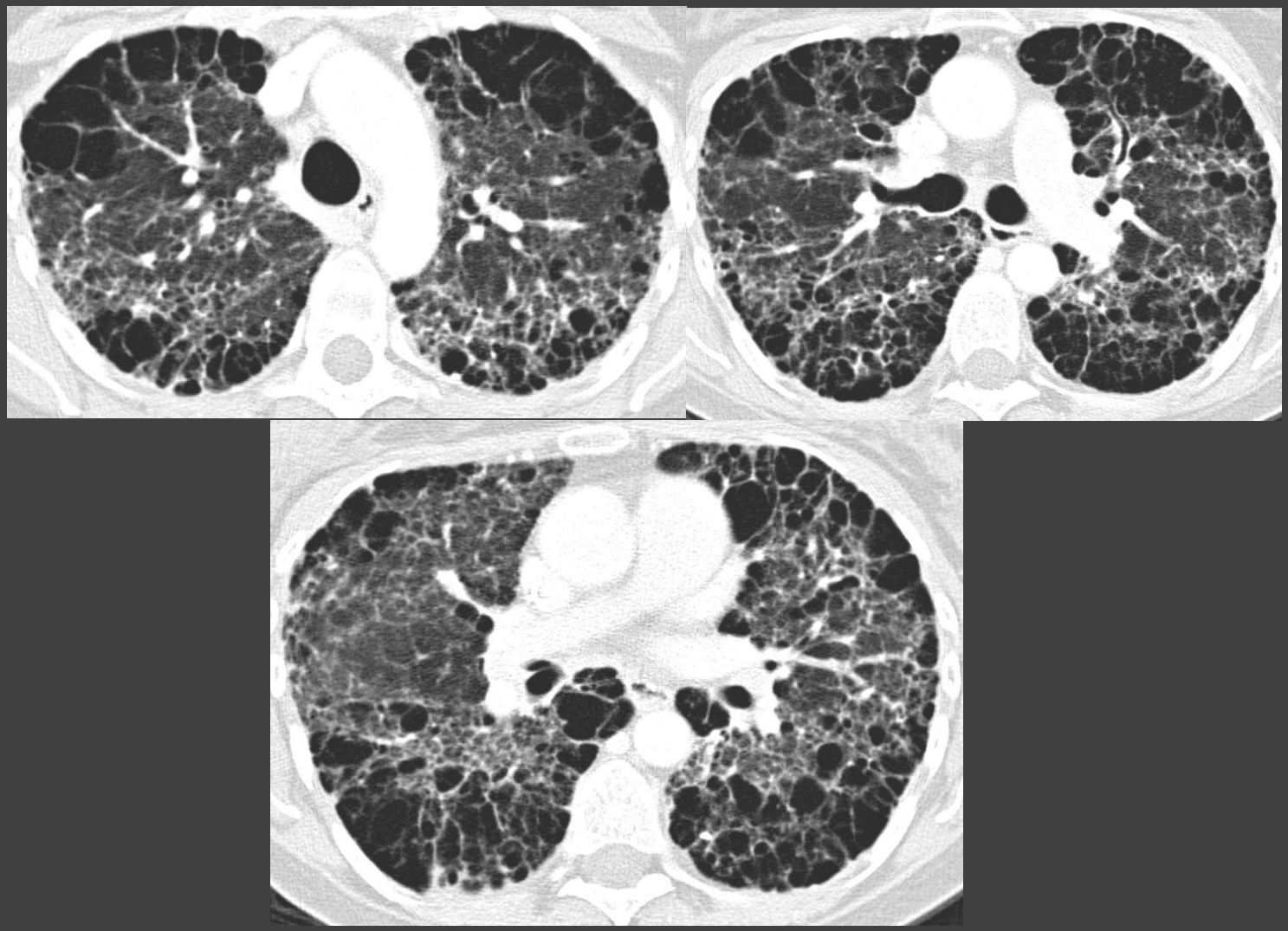
Combined pulmonary fibrosis emphysema (CPFE)

- 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

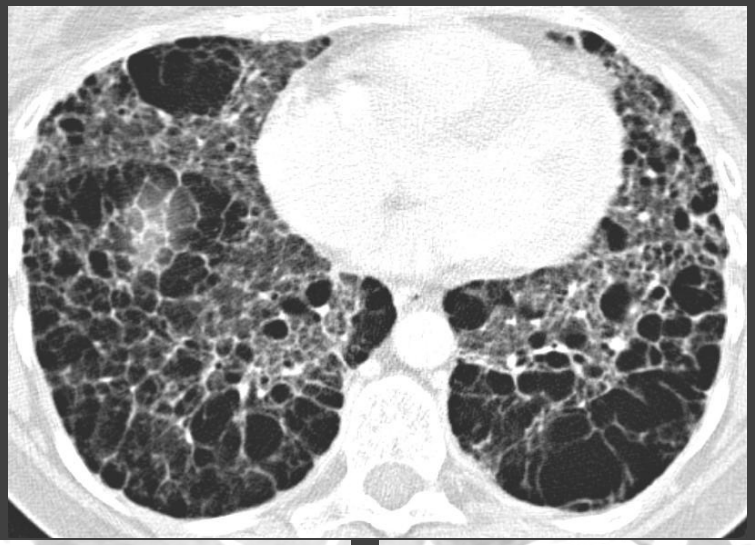
Imaging in CPFE

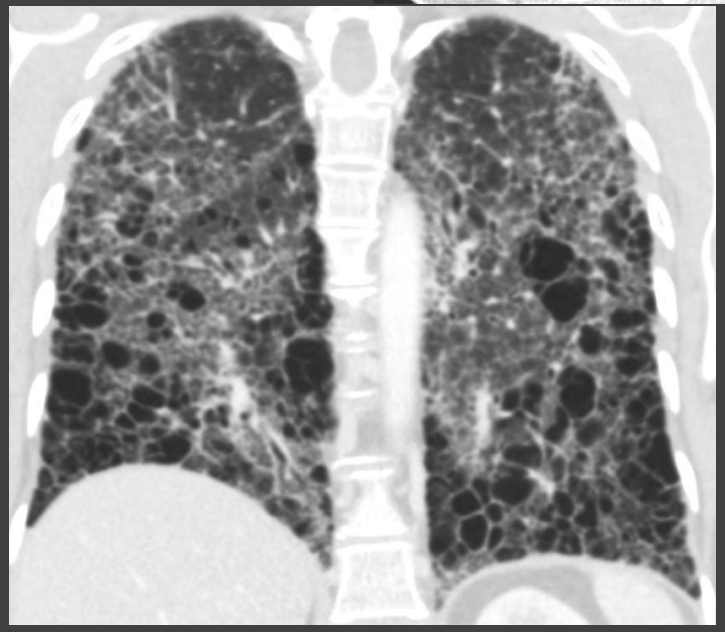
- All patients exhibited upper zone emphysema and lower zone fibrosis
- Emphysema may be that of centrilobular or paraseptal patterns
- Emphysema should involve >10% of the lung volume
- Bulky cystic lesions with thick walls predominantly in the upper lobes may be due to AEF or unclassified emphysema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

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



Diagnosis: Unclassifiable IIP in smokers



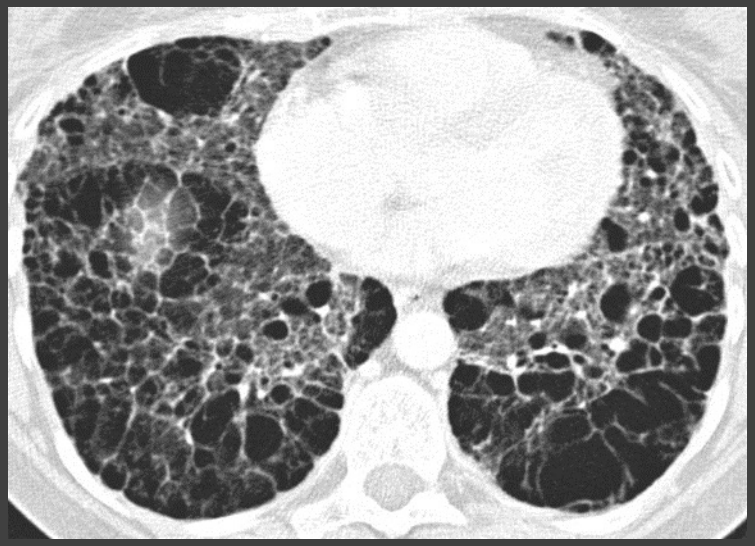


Unclassifiable IIP in smokers

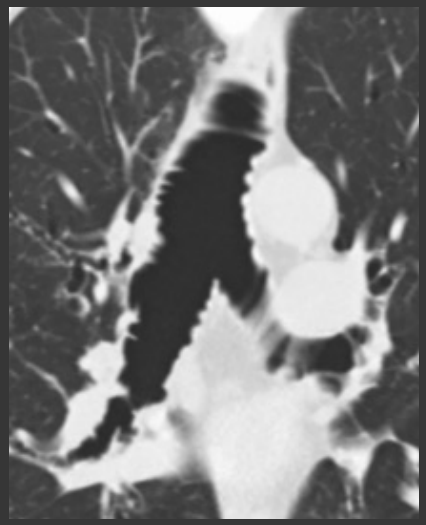
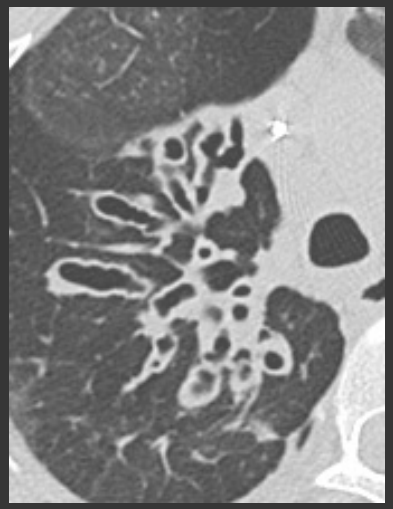
- The final diagnosis cannot be determined even after interdisciplinary consultation
- Overlapping histologic patterns is common in smokers
- This group exhibit slow progression and longer survival than IPF
- Airway centered cysts with fibrosis
- Many show normal FEV_1 and FVC but low DLCO

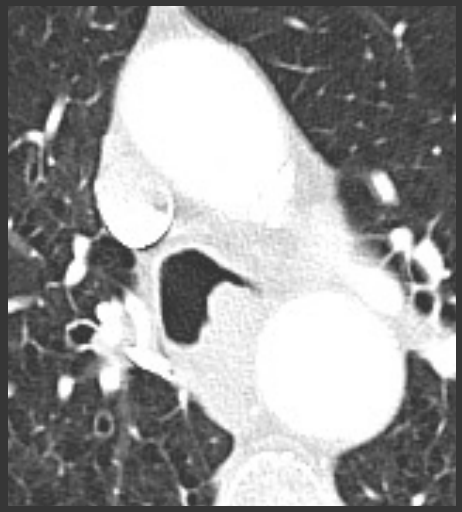
Imaging in Unclassifiable IIP in smokers

- Cystic dilatation of peripheral bronchi
- Airway centered cysts
- Cysts become large airspaces causing lung destruction
- Small-airways centered interstitial fibrosis



Airways Diseases




Imaging tips

- Dynamic expiratory CT
- End-expiratory CT
- Minimum intensity projection
- Central airways many window settings
- Small airways
  - Window center -250 to -700 HU
  - Window level 1000 to 1400 HU respectively
  - No contrast needed

Trachea and mainstem bronchi

- Diseases
  - Congenital
  - Infiltrative disease
  - Infection
  - Neoplasm
  - Airway wall abnormalities
- Symptoms
  - 75% lumen occlusion
  - hemoptysis

Tracheal and Mainstem Bronchial Neoplasms

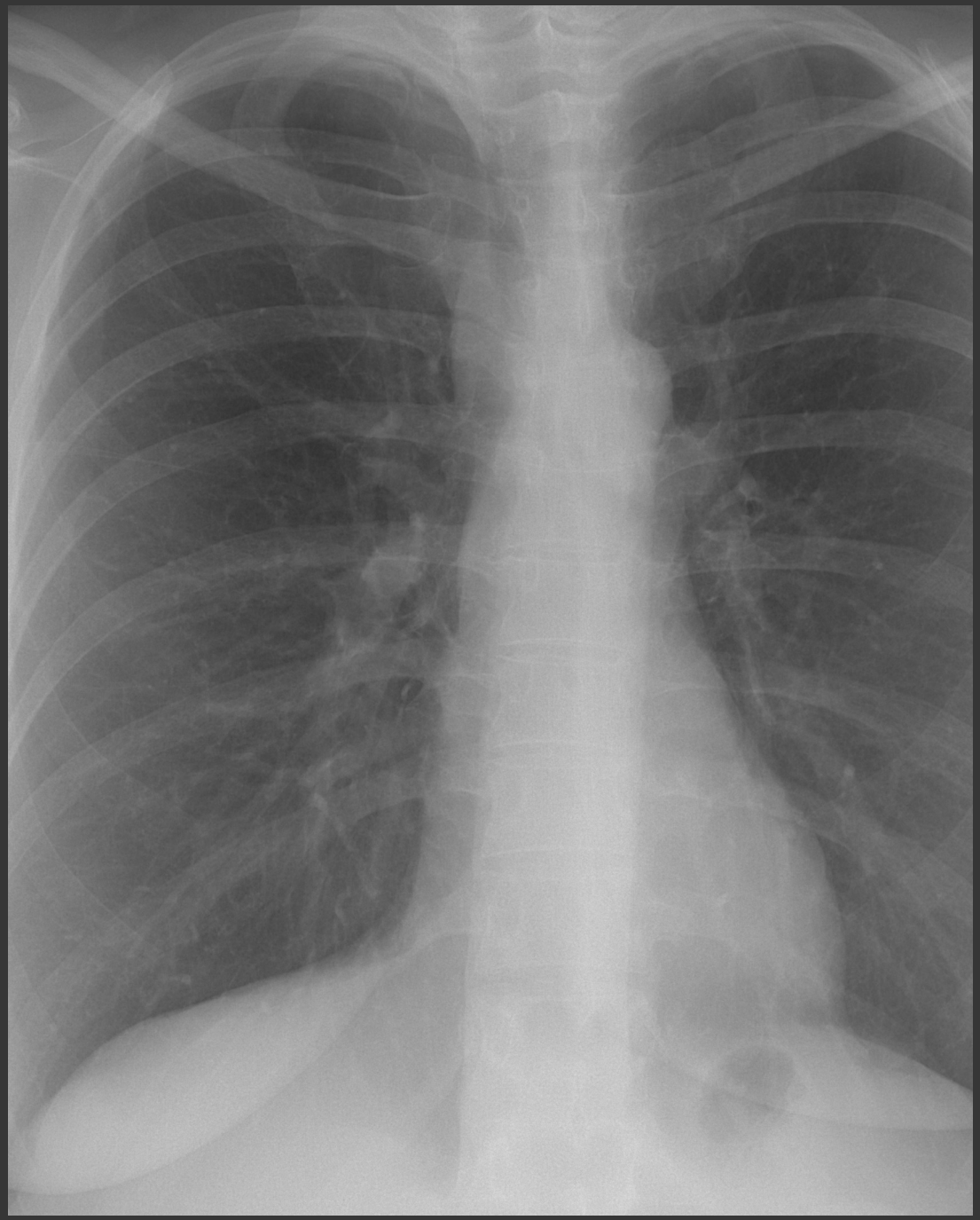
- Squamous cell carcinoma
- Sialadenoid tumors
  - Above 2 account for 86% mlg
- Metastasis
- Carcinoid
- Mucoepidermoid tumors
- Hamartomas
- Bronchial papillomas
  - Last 2 most common benign tumors

Tracheal and Mainstem Bronchial Neoplasms

- Malignant more common than benign
- Most due to direct invasion
- Benign tumors
  - Hamartomas
  - Tracheobronchial papillomatosis
  - Leiomyomas
  - Lipomas
  - Chondromas

Squamous cell carcinoma

- Most common malignancy in trachea
- Smokers
- 10% multifocal
- May extend into bronchi or esophagus




Squamous cell Carcinoma of trachea

Tracheal narrowing: Tracheobronchomalacia

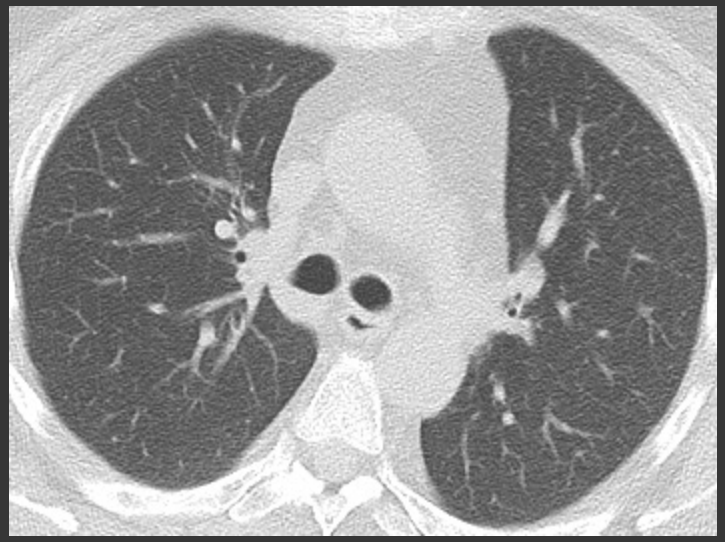
- Excessive airway collapse during expiration
- Weakening of airway cartilage
- Impaired post longitudinal elastic fibers (EDAC)
- May be congenital—self limiting
- Acquired
- Dynamic CT; Collapse of > 70%

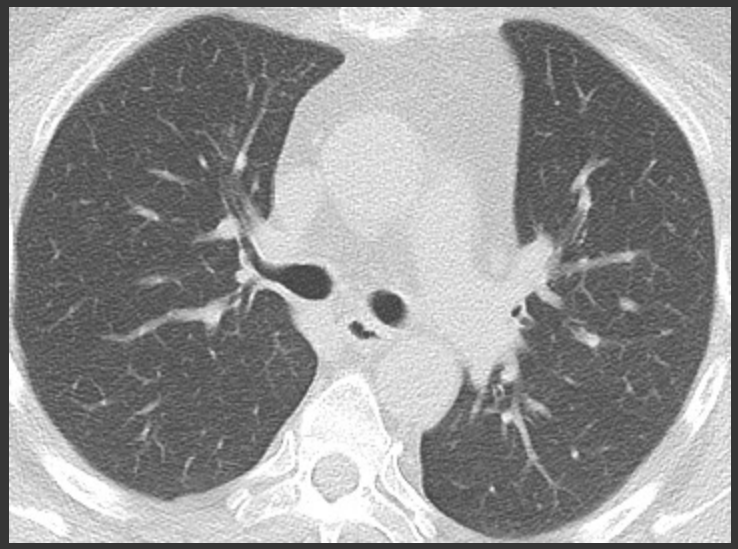
Tracheobronchomalacia

Inspiratory Images

Expiratory Images

Same patient: Tracheobronchomalacia





Small Airways Diseases

- Idiopathic syndrome of chronic airway obstruction without emphysema or chronic bronchitis
- Abnormalities involving airways 2-3 mm
- Synonym for bronchiolar disease
- Inflammation in bronchiolar wall

CT signs of Small airways diseases

- Direct
  - Centrilobular nodules, V or Y shaped branching nodules due to bronchiolar wall thickening by inflammatory cells
  - Poorly defined centrilobular nodules (GG nodules) due to inflammatory cellular infiltration of peribronchiolar alveoli
  - Bronchiolectasis

CT signs of Small airways diseases

- Indirect
  - Air trapping
  - Mosaic attenuation on insp CT
  - End expiratory CT needed
  - Caution- significant air trapping in healthy individuals

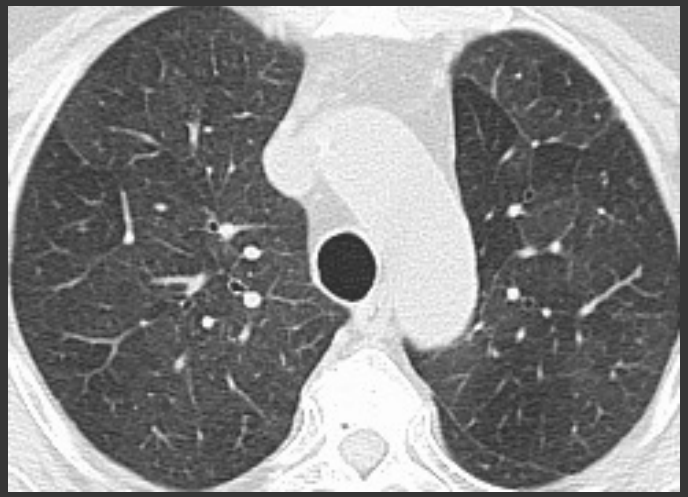
Constrictive Bronchiolitis (Bronchiolitis Obliterans)

- Concentric luminal narrowing of terminal and respiratory bronchioles
- Etiology: peribronchiolar inflammation and fibrosis w/o intraluminal granulation tissue
- Results in bronchial narrowing/obliteration
- Air trapping and mosaic attenuation
- Imaging to include end-expiratory CT

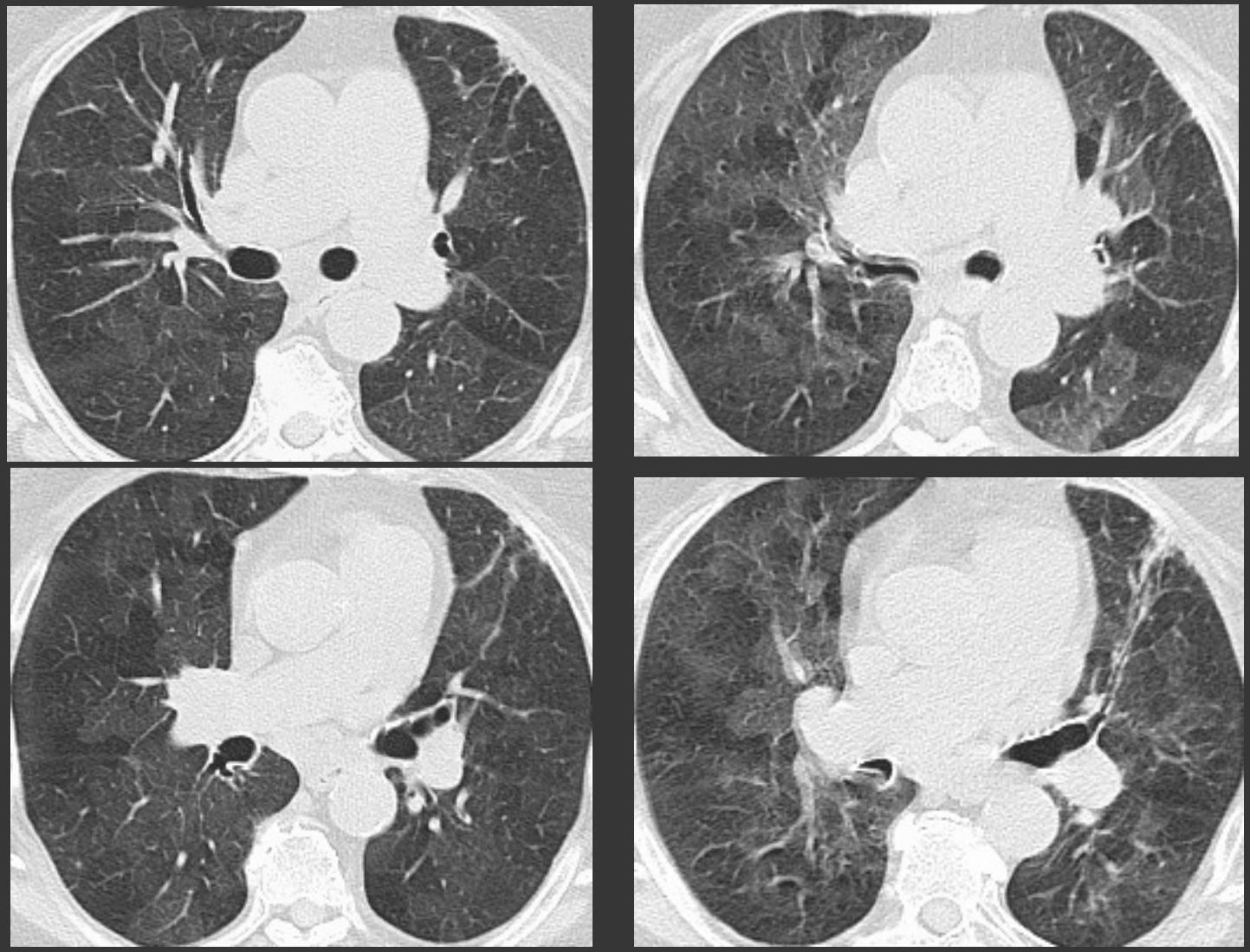
Etiology of Constrictive Bronchiolitis

- Post lung transplantation = rejection
- GVHD
- Rheumatoid arthritis
- Post infectious

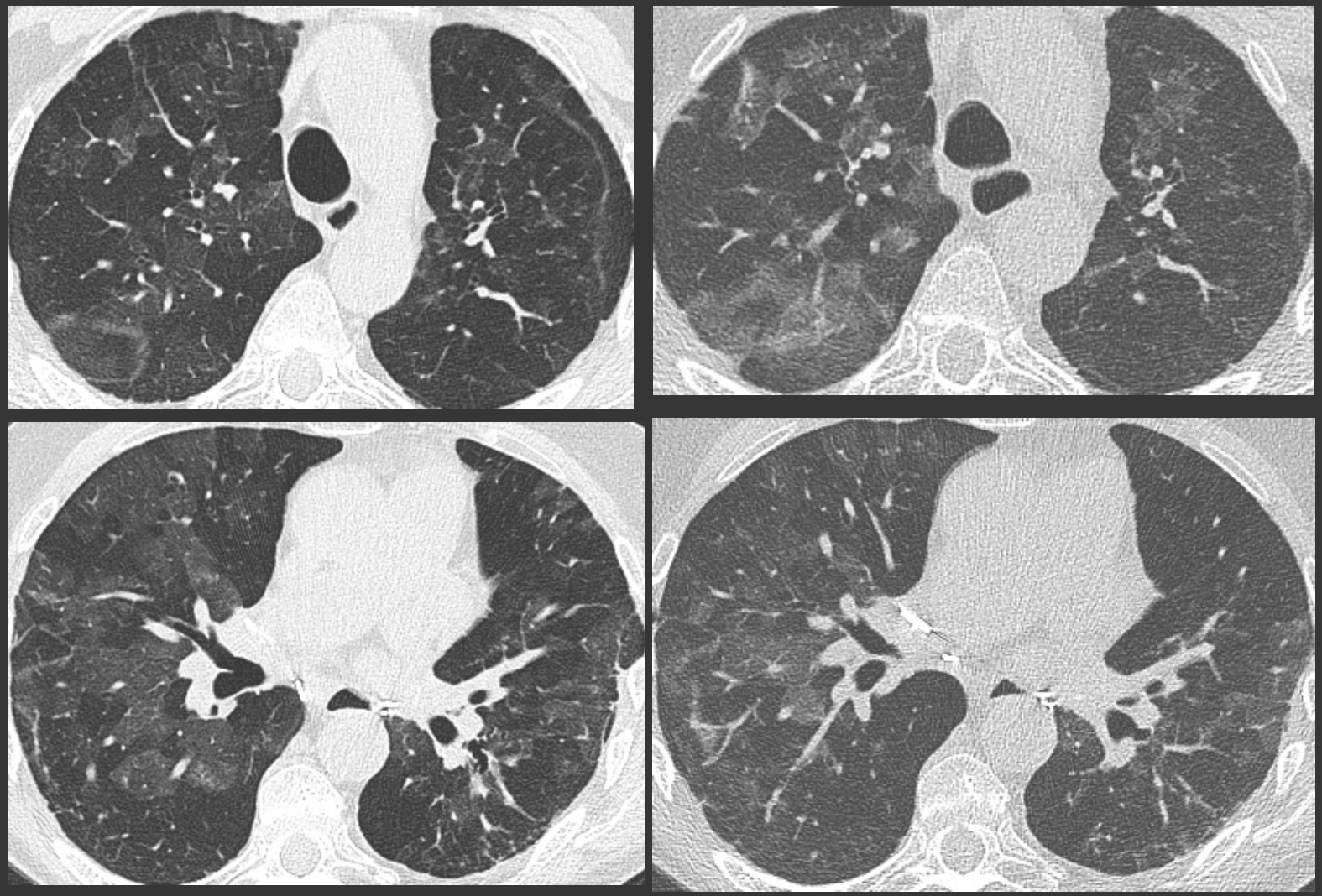
Small airways disease constrictive bronchiolitis: RA




Small airways disease constrictive bronchiolitis: RA



Bonchiolitis Obliterans syndrome post bilat lung TX



Bonchiolitis Obliterans syndrome post bilat lung TX

Conclusions

- We have seen the radiographic features of various IIP with DDx
- We have looked at pertinent cases of cystic Lung diseases
- Briefly seen a few cases of small and large airways diseases
- We have reviewed smoking related lung diseases

Question One:

What is the most helpful portion of the CT scanning protocol in working up tracheobronchomalacia?

A. Minimum intensity projection imaging

B. End-expiratory imaging

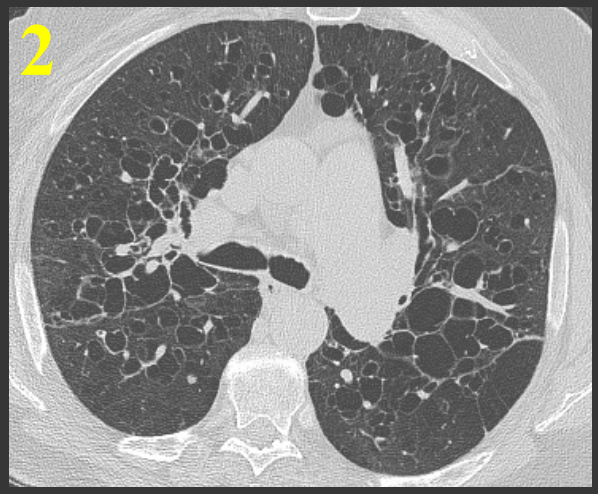
C. Dynamic expiratory imaging

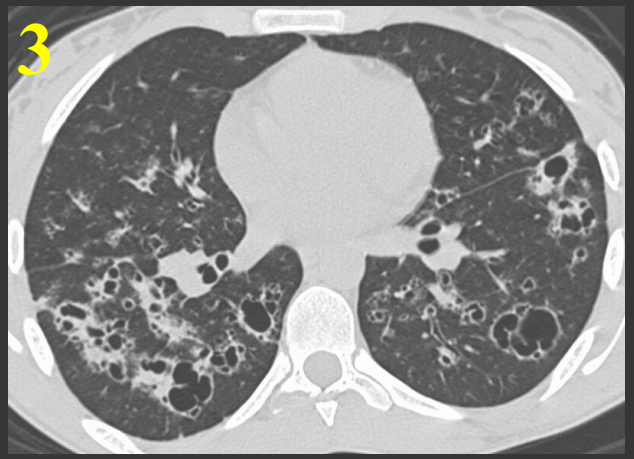
D. 3-D volumetric imaging

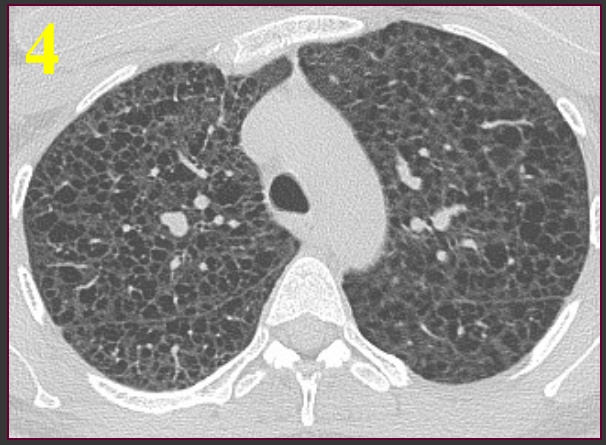
Question 3:

Which of the following is NOT associated with cigarette smoking?

A. Option 1
B. Option 2
C. Option 3
D. Option 4







References

MacMahon, H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology 2017; 284:(1): 228-243.

Pipavath Sudhakar J, et al. Radiologic Pathologic Features of Bronchiolitis. AJR 2005;185:354-363

Hartman TE, et al. Nonspecific interstitial pneumonia: variable appearance at high-resolution chest CT. Radiology 2000; 217:701-705.

Heidinger, Benedikt H, et al Imaging of Large Airways Disorders. AJR 2015; 205:41-56