PNEUMOLOGIA 2018

Milano, 14 – 16 giugno 2018 · Centro Congressi Palazzo delle Stelline

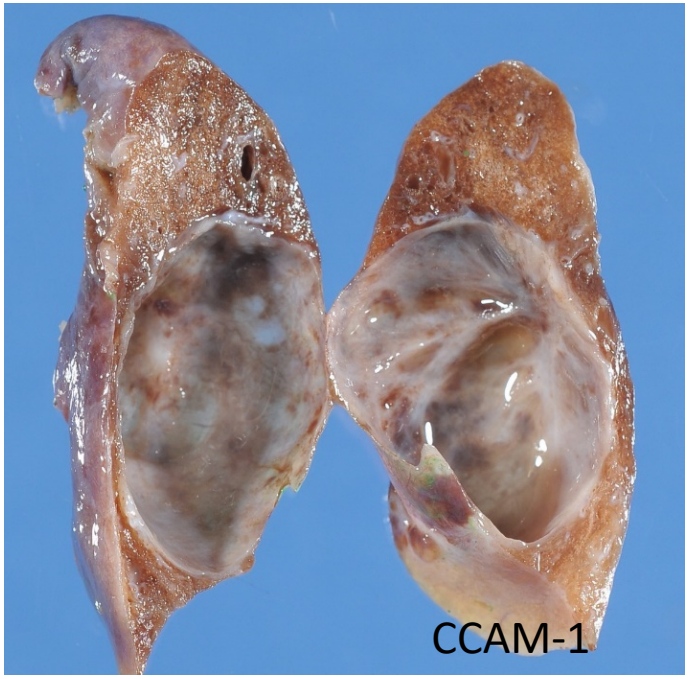
La diagnosi differenziale delle patologie cistiche

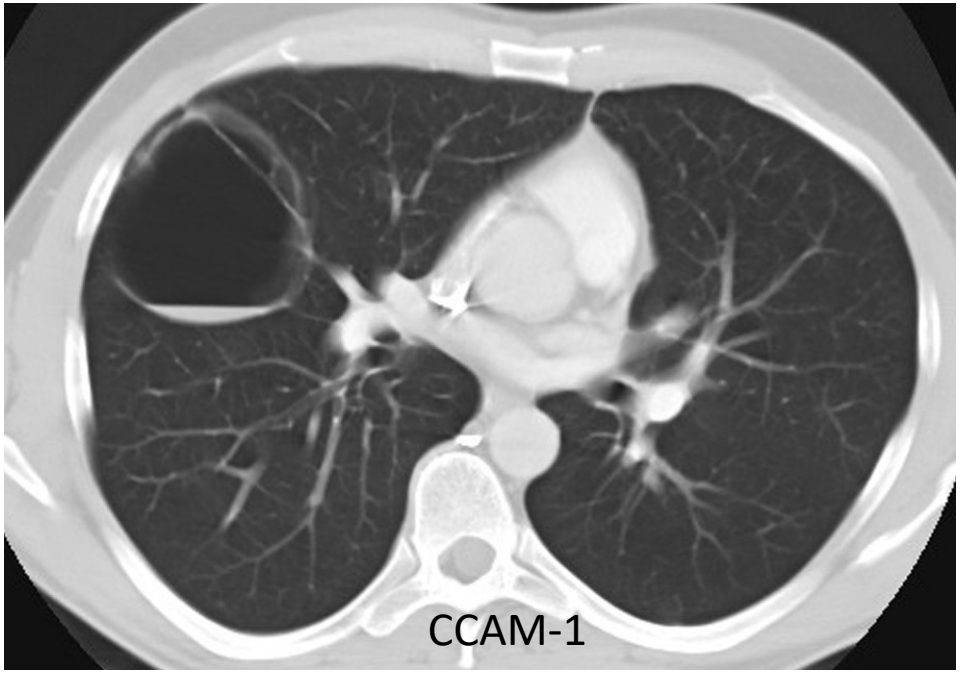
Olga Torre
U.O. di Pneumologia e Terapia Semi Intensiva
Servizio di Fisiopatologia Respiratoria ed Emodinamica Polmonare
Osp. San Giuseppe - MultiMedica, Milano

Cisti polmonari - definizione

Si definisce cisti polmonare una struttura dotata di parete sottile solitamente a contenuto aereo, ma talora liquido o solido, di forma sferica più o meno regolare

Sulla TC una cisti appare come un'area nel parenchima polmonare a basso coefficiente di attenuazione dotata di un'interfaccia ben definita con il normale polmone circostante





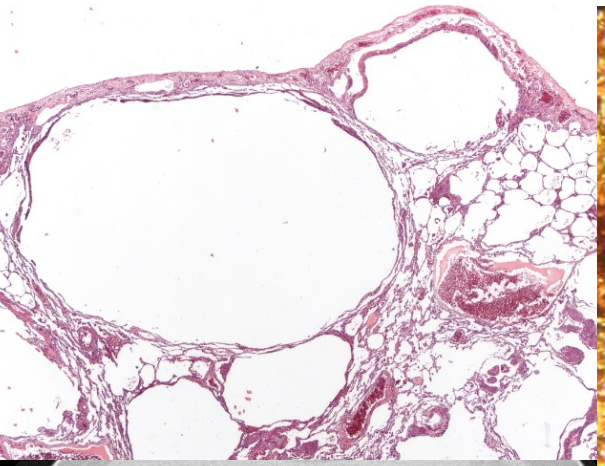
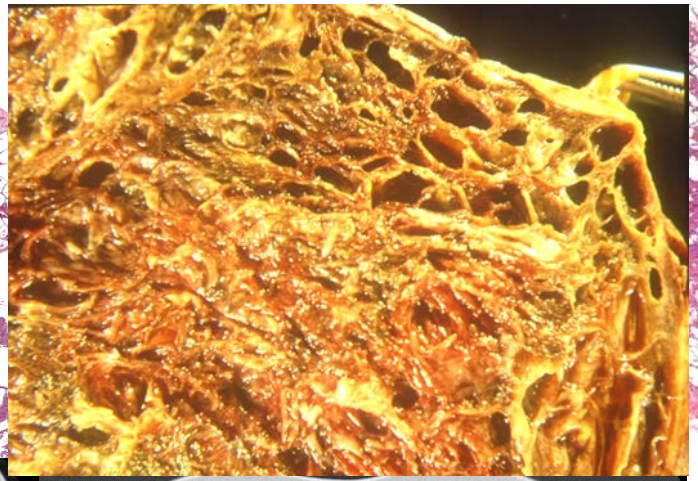
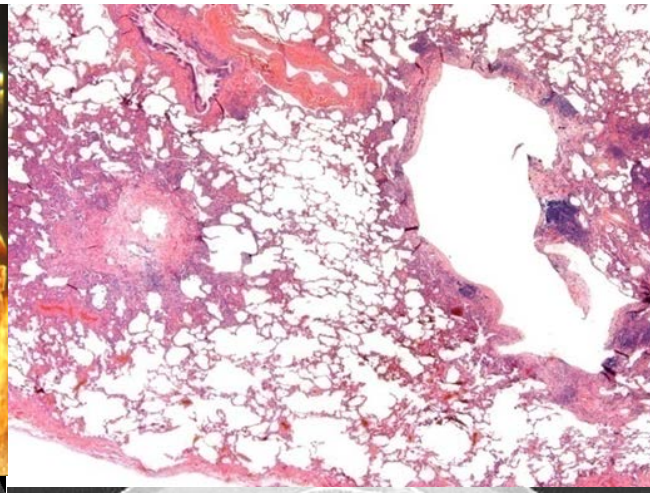
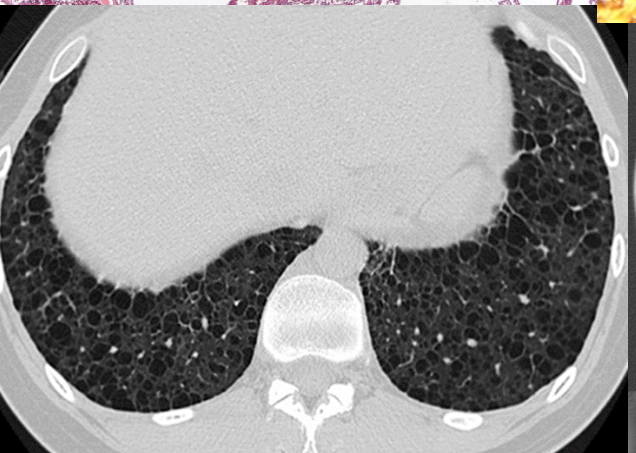
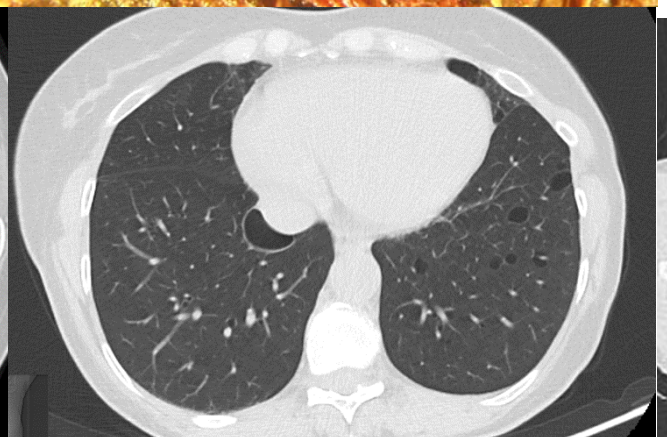
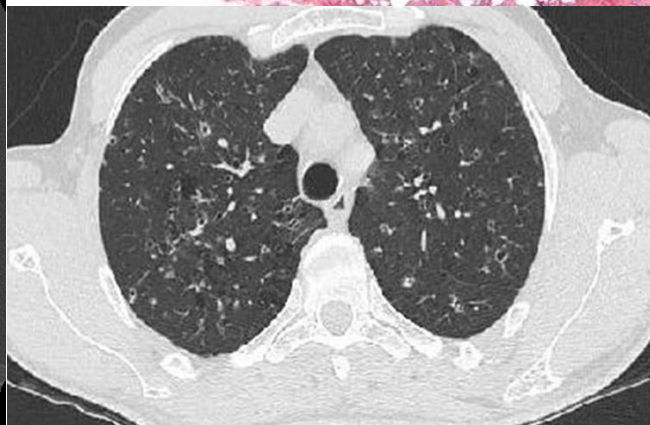
Cisti polmonari - definizione

Cyst	Thin-walled (<2 mm), spherical parenchymal lucency interfaced with normal lung.
Cavity	Gas-filled space within pulmonary consolidation, mass, or nodule, typically thick walled (>2 mm) and more irregularly shaped than cysts
Bulla	Spherical focal lucency, >1 cm in diameter, bounded by a thin wall (usually <1 mm). It is usually accompanied by emphysematous changes in the adjacent lung
Bleb	Cystic air space bounded by a thin wall adjacent to the visceral pleura, typically ,1 cm in size

Hansell DM et al. Radiology 2008

Diffuse Cystic Lung Diseases

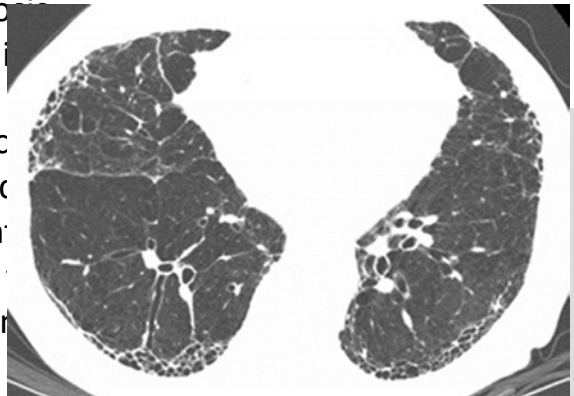
Diffuse cystic lung diseases are characterized by cysts in more than one lung lobe, the cysts usually being bilateral.

Classification of DCLDs

Gupta N et al, AJRCCM 2015

1. *Neoplastic*	Lymphangioleiomyomatosis Pulmonary Langerhans cell histiocytosis, and non-Langerhans cell histiocytoses Other primary and metastatic neoplasms such as sarcomas, adenocarcinomas, pleuropulmonary blastoma, etc.	5. *Associated with interstitial lung diseases*	Hypersensitivity pneumonitis Desquamative interstitial pneumonia
2. *Genetic Developmental Congenital*	Birt-Hogg-Dubé syndrome Proteus syndrome, neurofibromatosis, Ehlers-Danlos syndrome Congenital pulmonary airway malformation, bronchopulmonary dysplasia,etc.	6. *Smoking related*	Pulmonary Langerhans cell histiocytosis Desquamative interstitial pneumonia
3. *Associated with lympho – proliferative disorders*	Lymphocytic interstitial pneumonia Follicular bronchiolitis Sjögren syndrome Amyloido Light chai	7. *Other/ Miscellaneous*	Post-traumatic pseudocysts Fire-eater's lung Hyper IgE syndrome
4. *Infectious*	Pneumoc Staphyloc Recurren Endemic Paragoni	8. *DCLD mimics*	Emphysema Alpha-one antitrypsin deficiency Bronchiectasis Honeycombing seen in late stage scarring interstitial lung diseases



Classification of DCLDs

Gupta N et al, AJRCCM 2015

1. *Neoplastic*	Lymphangioleiomyomatosis Pulmonary Langerhans cell histiocytosis, and non-Langerhans cell histiocytoses Other primary and metastatic neoplasms such as sarcomas, adenocarcinomas, pleuropulmonary blastoma, etc.
2. Genetic Developmental Congenital	Birt-Hogg-Dubé syndrome Proteus syndrome, neurofibromatosis Ehlers-Danlos syndrome Congenital pulmonary airway malformation, bronchopulmonary dysplasia,etc.
3. *Associated with lympho – proliferative disorders*	Lymphocytic interstitial pneumonia Follicular bronchiolitis Sjögren syndrome Amyloidosis Light chain deposition disease
4. *Infectious*	Pneumocystis jiroveci Staphylococcal pneumonia Recurrent respiratory papillomatosis Endemic fungal diseases Paragonimiasis
5. *Associated with interstitial lung diseases*	Hypersensitivity pneumonitis Desquamative interstitial pneumonia
6. *Smoking related*	Pulmonary Langerhans cell histiocytosis Desquamative interstitial pneumonia
7. *Other/ Miscellaneous*	Post-traumatic pseudocysts Fire-eater's lung Hyper IgE syndrome
8. *DCLD mimics*	Emphysema Alpha-one antitrypsin deficiency Bronchiectasis Honeycombing seen in late stage scarring interstitial lung diseases

Percorso diagnostico

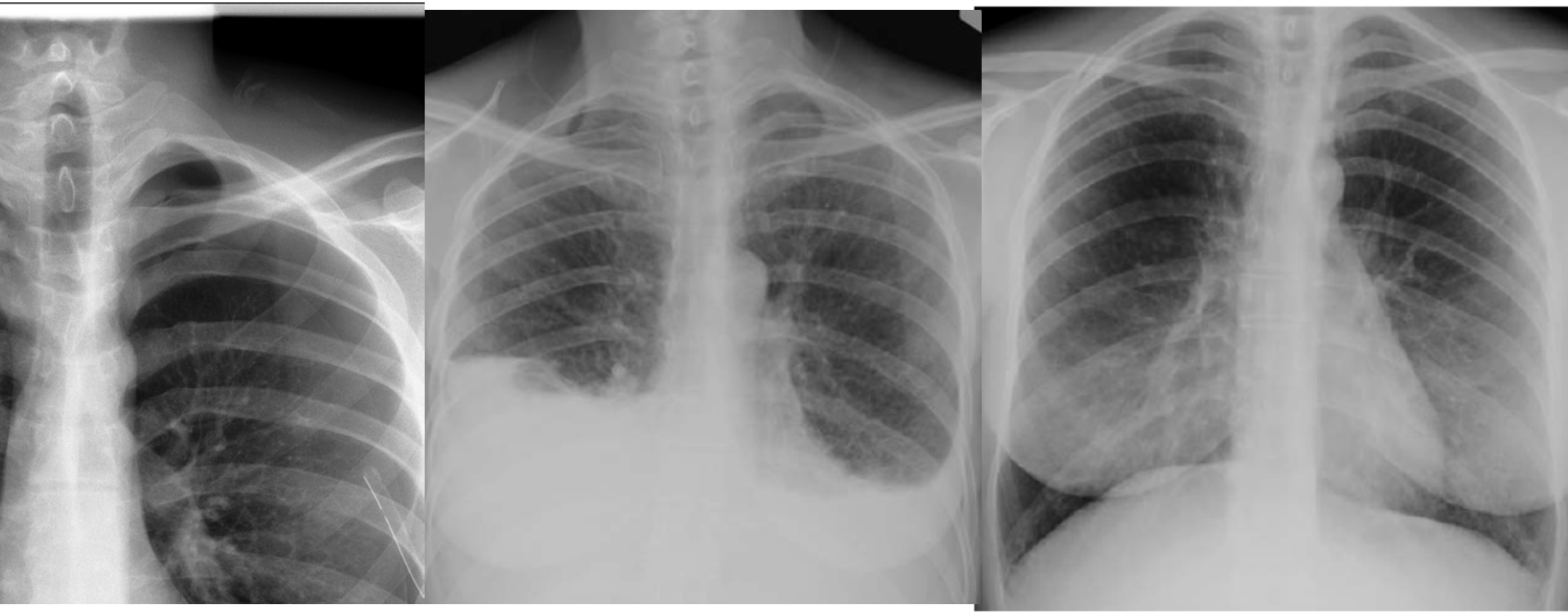
- Esordio clinico
- Imaging
- Dati clinici/anamnestici
- Indagini di laboratorio/genetica
- FBS/BAL
- Istologia

Esordio

- Acuto, subacuto/andamento cronico
- Riscontro occasionale
- Riscontro durante approfondimento diagnostico di patologia extrapolmonare

- Dispnea
- Tosse
- Pneumotorace
- Chilotorace
- Emottisi, chiloptisi
- Algie toraciche
- Sintomi sistemici (malessere, febbre…)

Rx torace

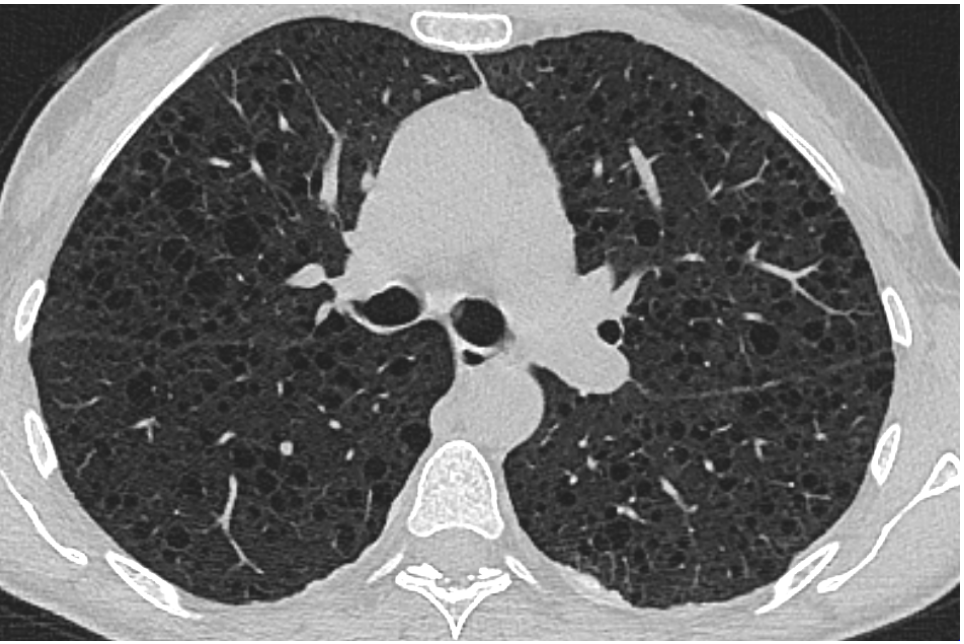


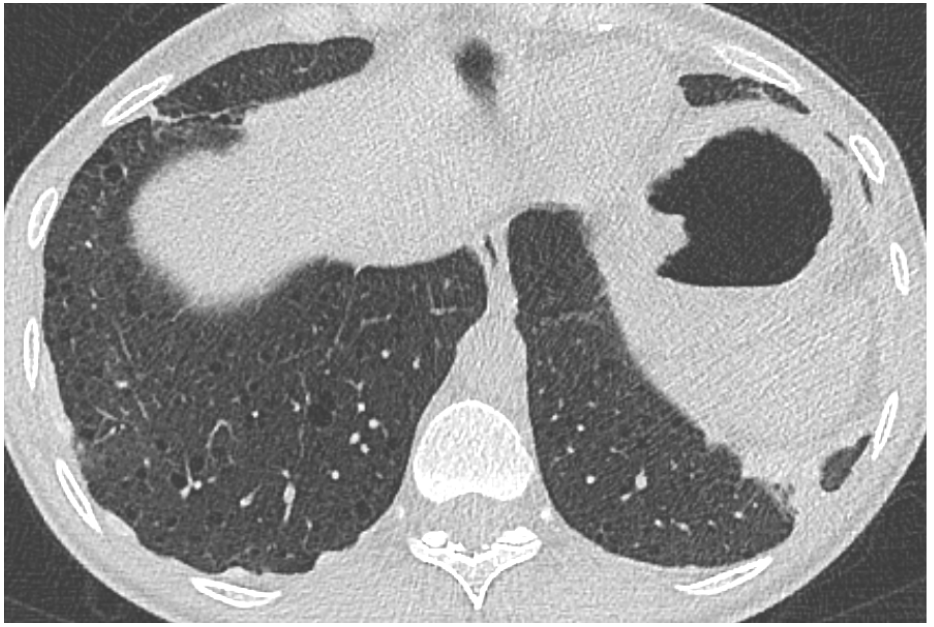
Chest HRCT is the most useful modality for the initial evaluation of a patient with DCLD

DCLDs

LAM	- A low-grade neoplasm that most commonly affects women of reproductive age, characterized by the proliferation of atypical smooth muscle cells (LAM cells) expressing myogenic and melanocytic proteins (gp100->HMB45 monoclonal antibody). - LAM can be sporadic (S-LAM) or associated to TSC (TSC-LAM) - Mutations in TSC genes (somatic, SLAM; germline, TSC-LAM)
PLCH	- A diffuse lung disease characterized by peribronchiolar infiltration by Langerhans cells and other immune cells and formation of granulomas - Smoking related - Somatic mutations in BRAF, MAP2K1
Birt-Hogge-Dubè (BHD)	- An autosomal-dominant syndrome caused by mutations in FLCN gene encoding the tumor suppressor protein folliculin.

TC torace - LAM





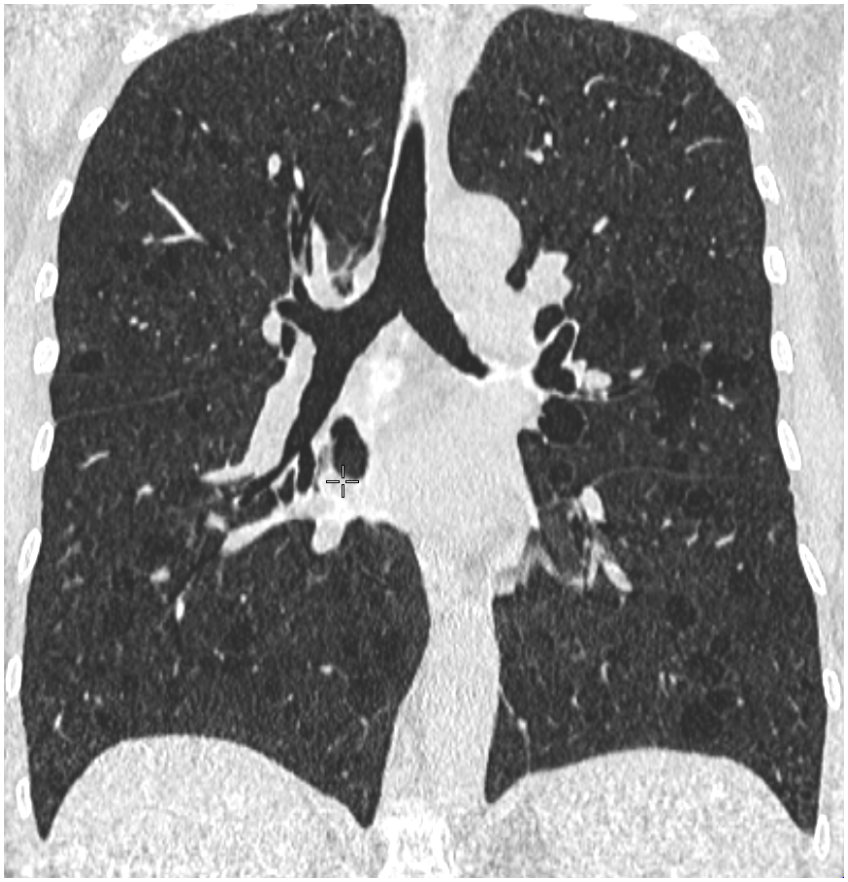
Distribution	Diffuse	Associated findings	Pnx, pleural effusion
Size	2mm-2cm		
Shape	Round, regular, uniform		

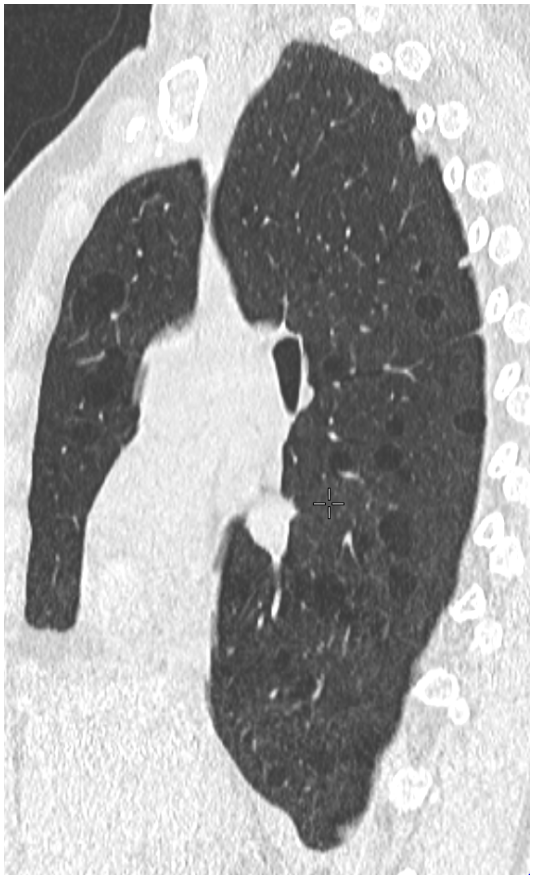
Characteristic HRCT: multiple (more than 10) thin-walled round well-defined air-filled cysts with no other significant pulmonary involvement (with the exception of MMPH in TSC)

Compatible HRTC: few (more than two and fewer than 10) typical cysts

Johnson SR et al, ERJ 2010

TC torace - LAM



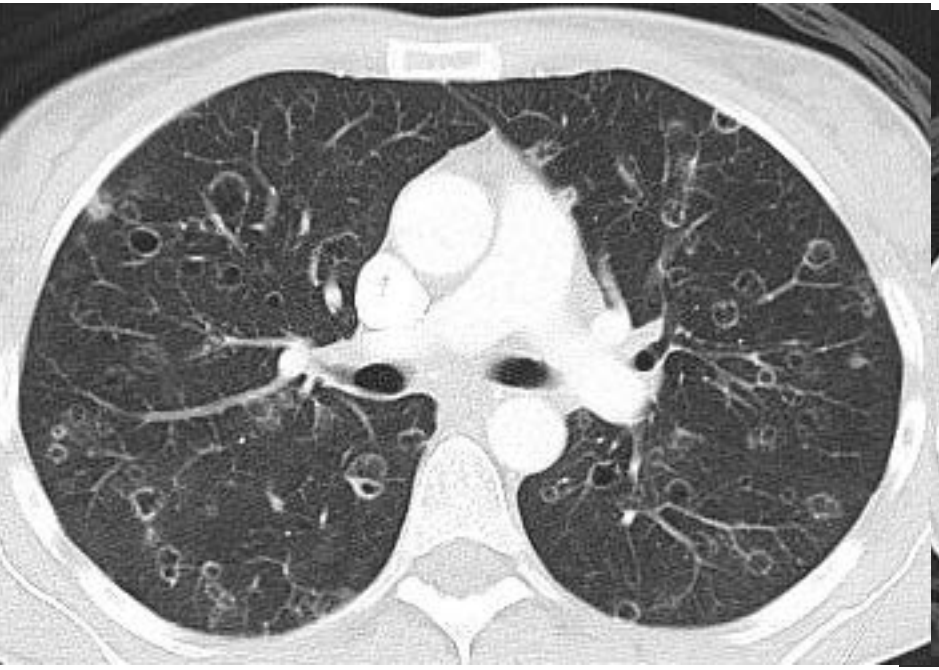


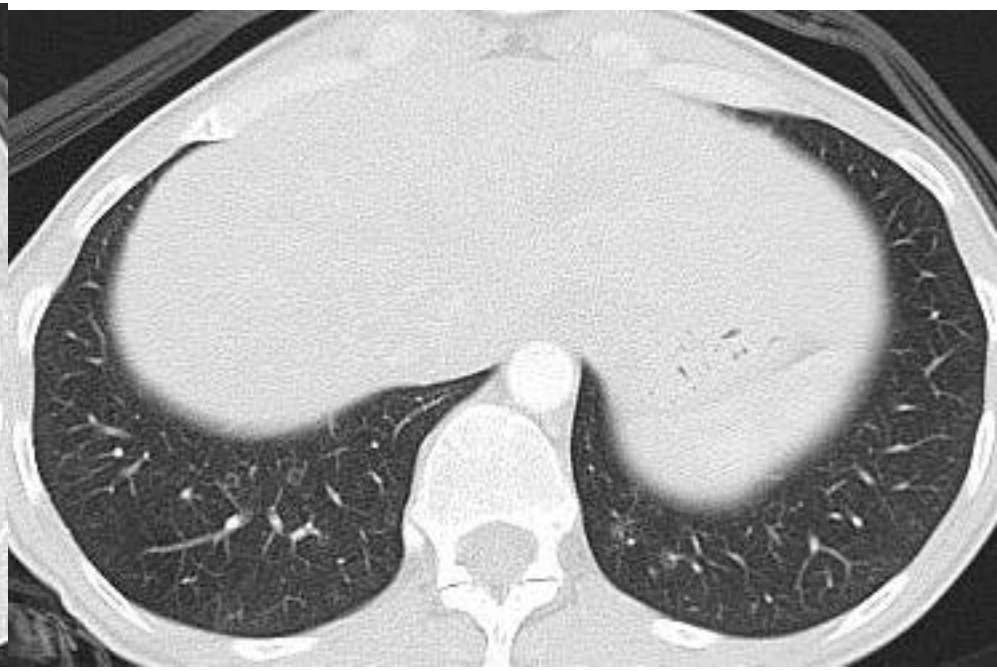
Characteristic HRCT: multiple (more than 10) thin-walled round well-defined air-filled cysts with no other significant pulmonary involvement (with the exception of MMPH in TSC)

Compatible HRTC: few (more than two and fewer than 10) typical cysts

Johnson SR et al, ERJ 2010

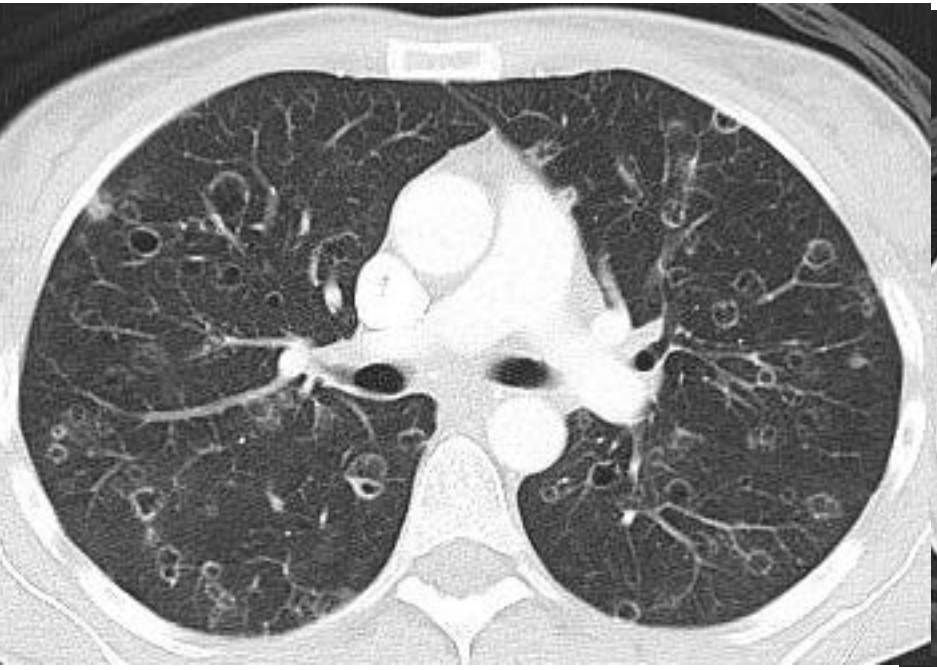
TC torace - PLCH

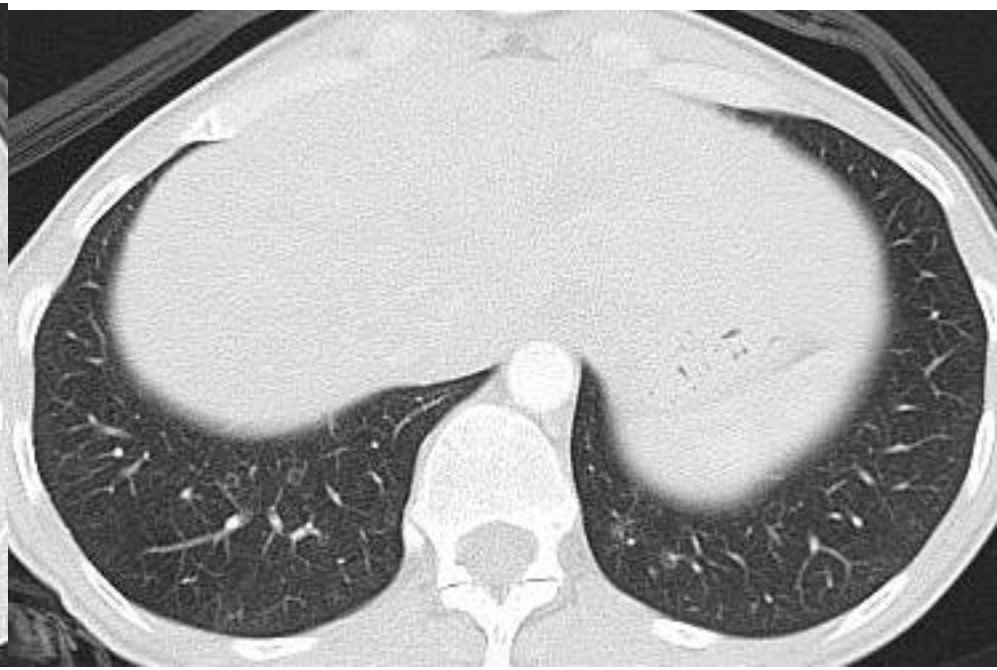




Distribution	Upper/middle lung zones Sparing of costophrenic angles	Associated findings	Nodules, micronodules Cavities Ground glass opacities
Size	Variable		
Shape	Irregular, bizarre		

TC torace - PLCH



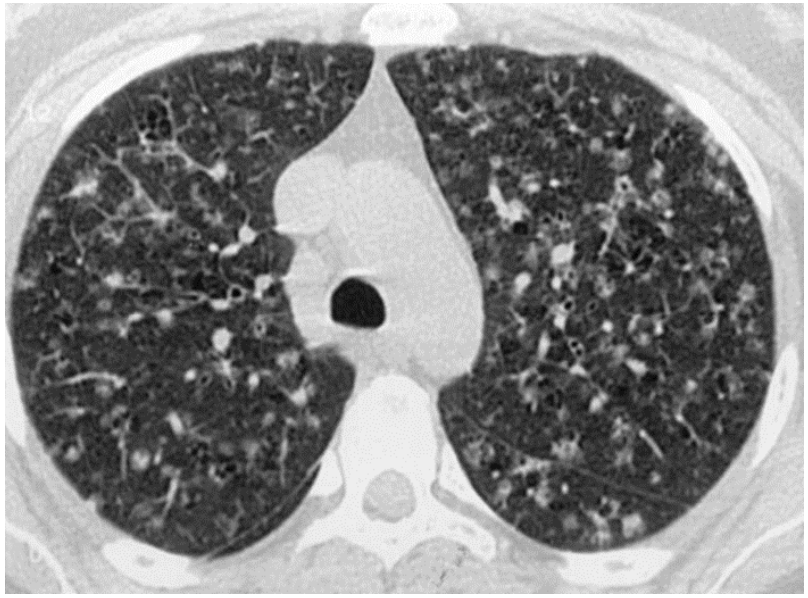


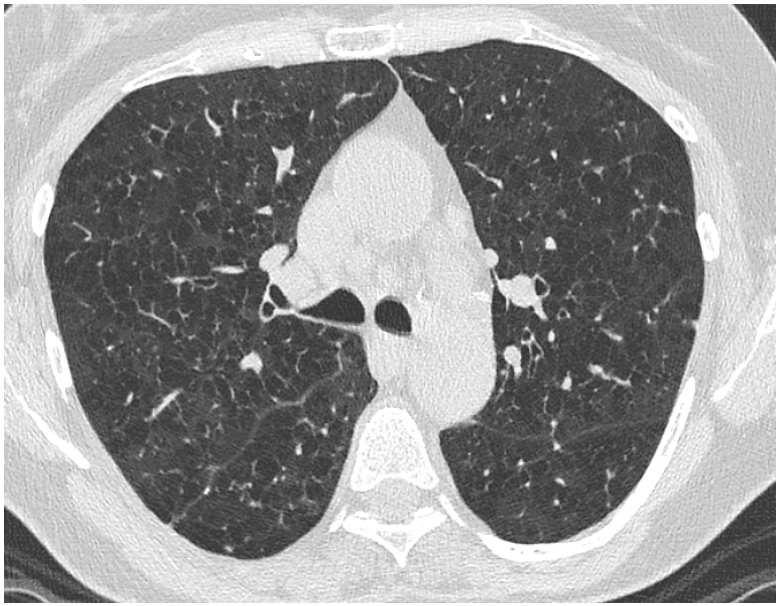
Longitudinal observation of CT features suggests the following evolutionary sequence for pulmonary lesions:

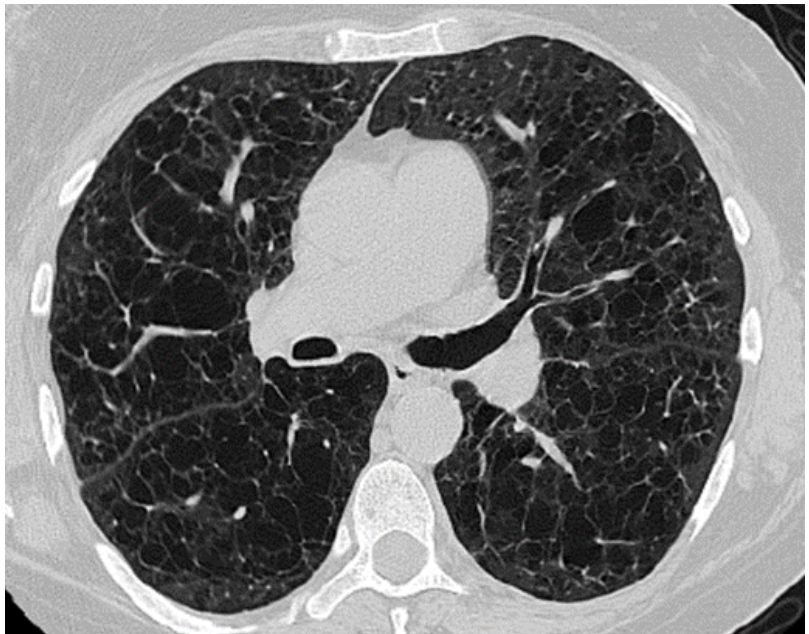
Nodule → Cavitated nodule → Thick walled cysts → Thin walled cysts

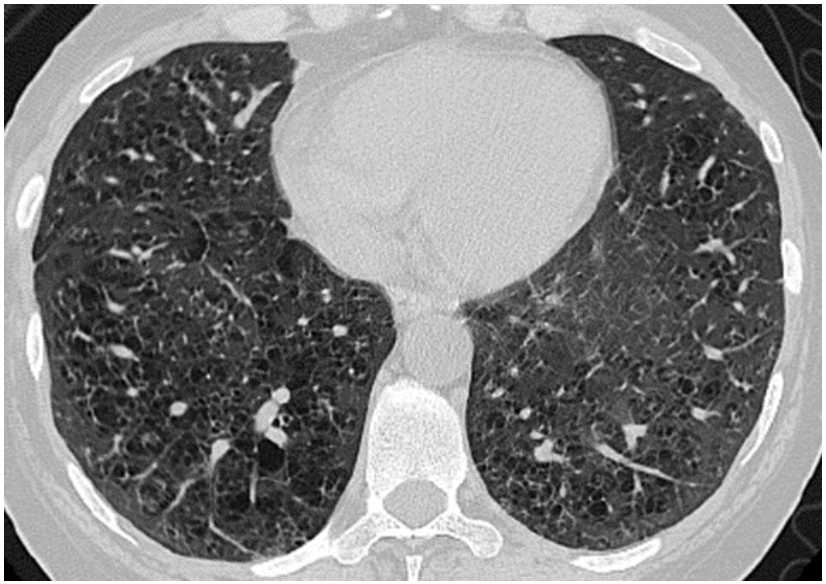
Brauner et al. Radiology 1997

TC torace - PLCH

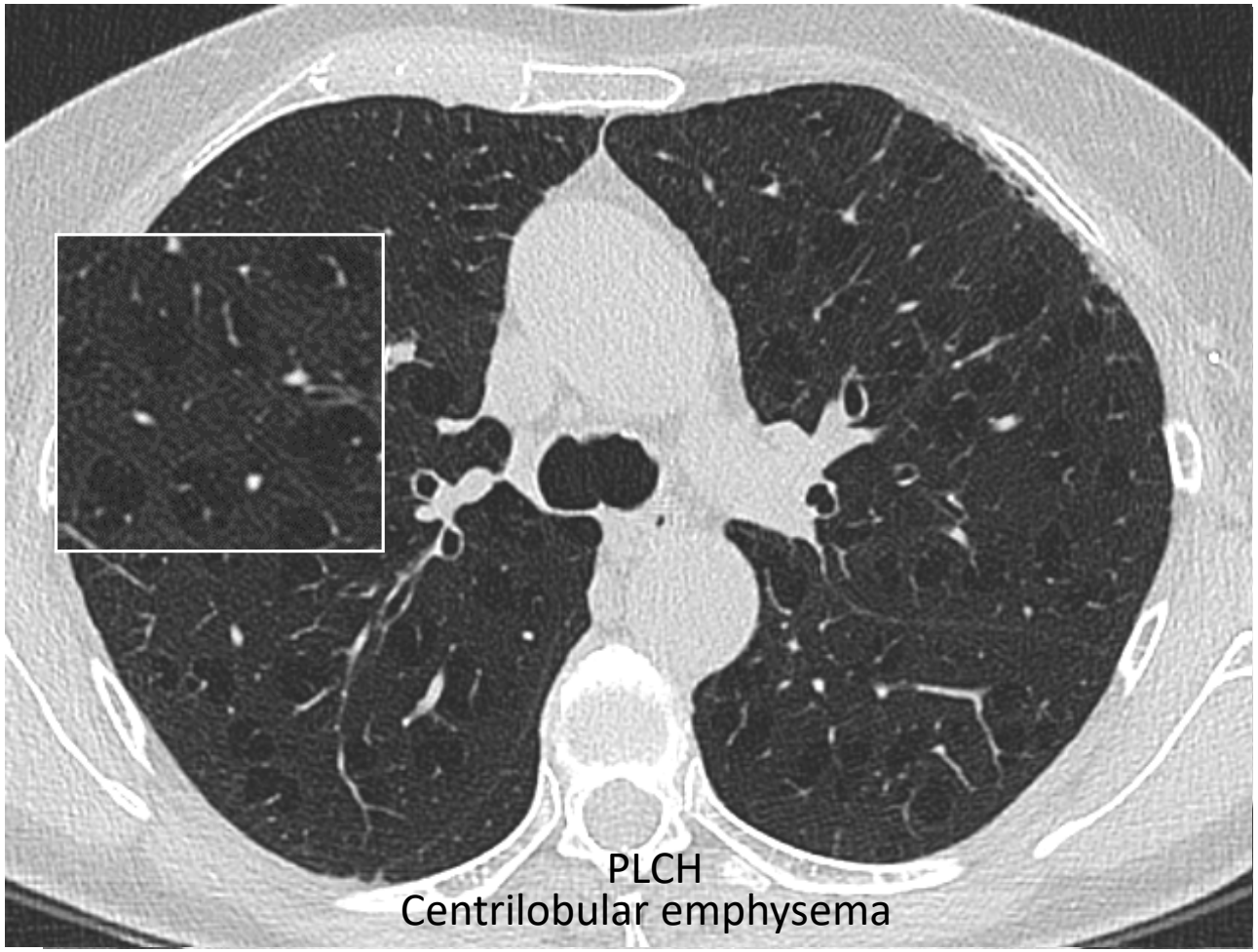






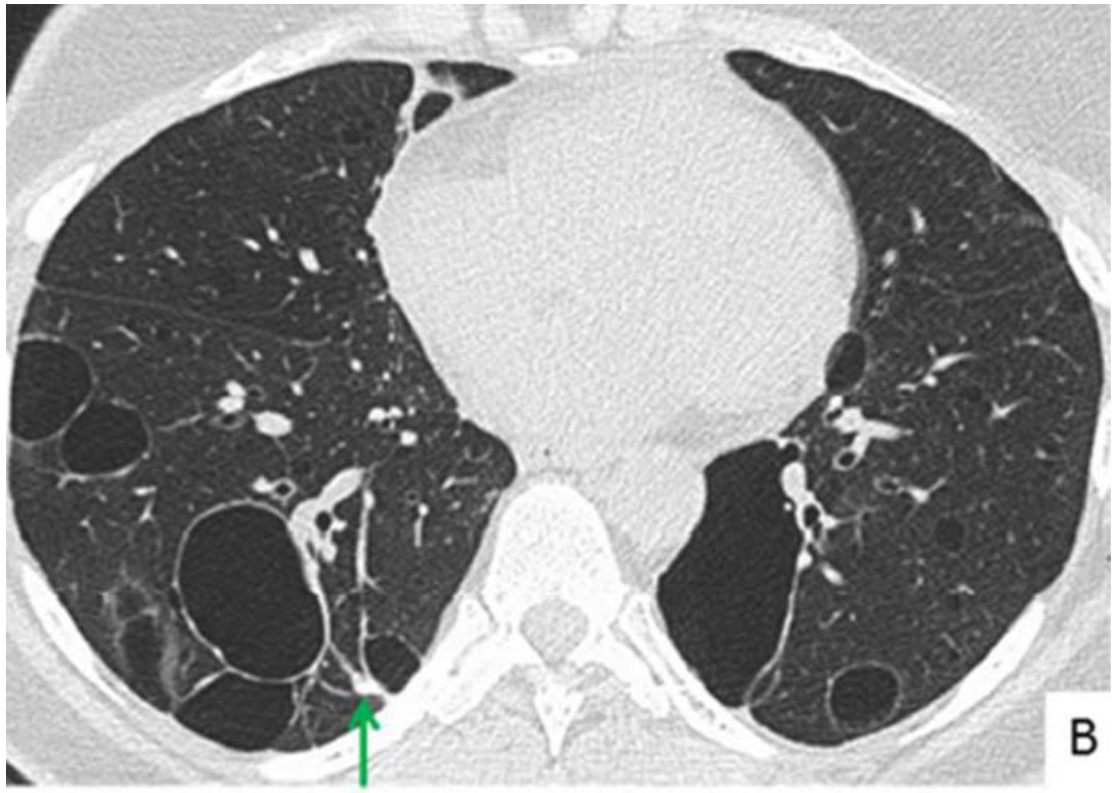


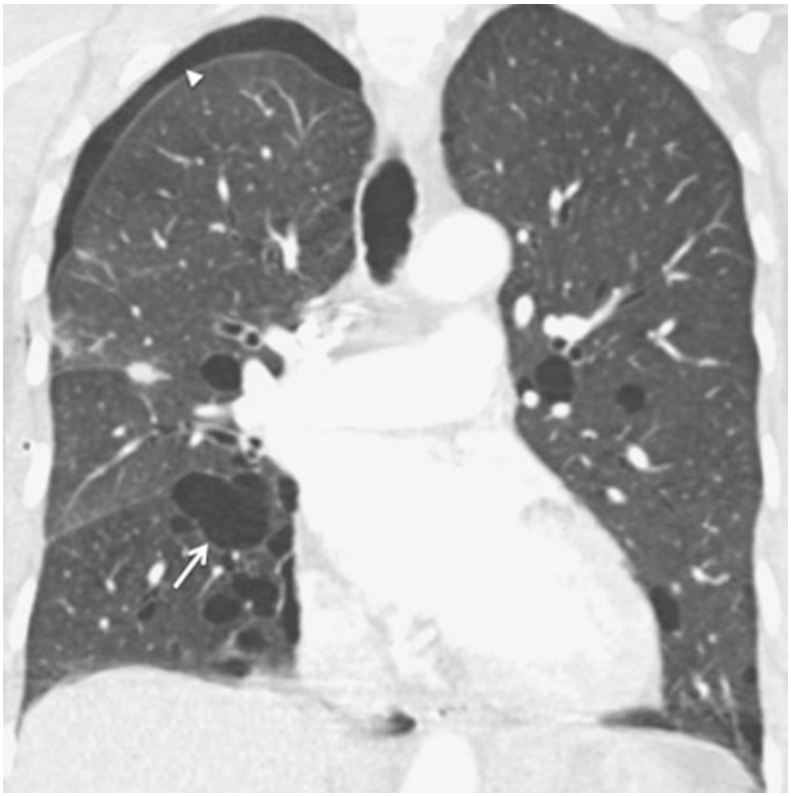
TC torace - DCLDs



PLCH
Centrilobular emphysema

TC torace - BHD





Distribution	Basilar/subpleural and near vessels	Associated findings	Cysts abut pleura and vessels
Size	Variable, average < 1cm		
Shape	Elliptical, lentiform		

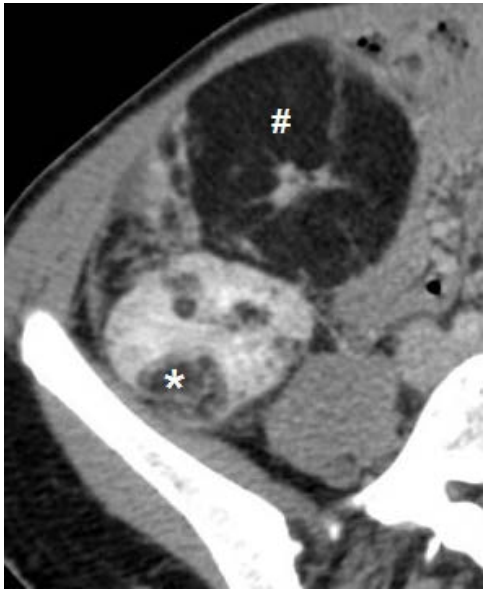
Extrapulmonary manifestations

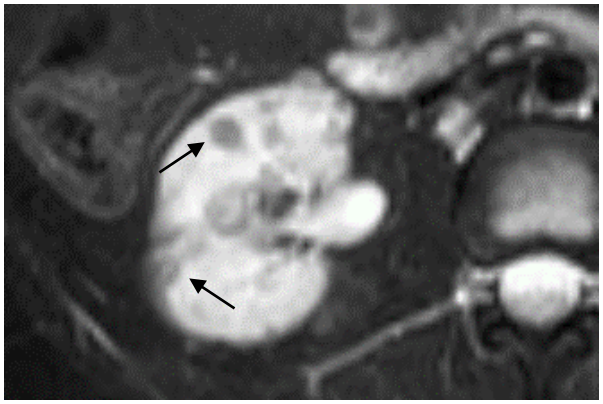
LAM	- Renal angiomiolypomas - Lymphangioleiomiomas - Linfoadenopathy - TSC lesions (skin angiofibromas, periungeal fibromas, hypopigmented macule, tuber corticali , SEGA)
PLCH	- Diabete insipidus - Skin lesions - Osteolytic bone lesions
Birt-Hogge-Dubè (BHD)	- Renal tumors - Skin lesions (fibrofolliculomas)

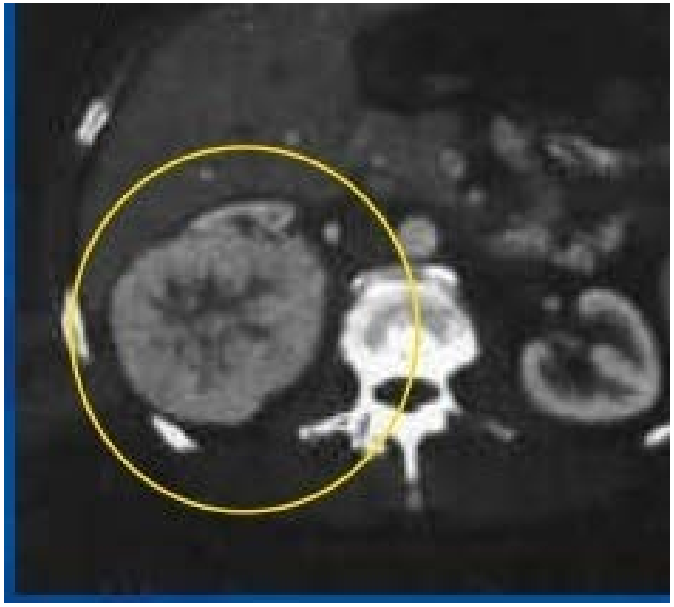
Extrapulmonary manifestations

LAM

BHD





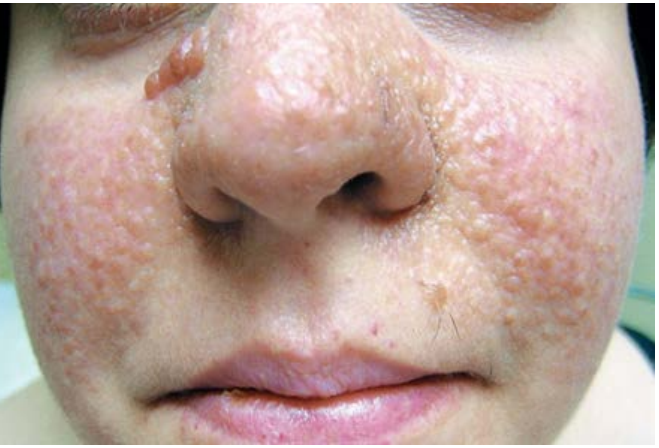


Angiomiolipoma

Oncocitoma

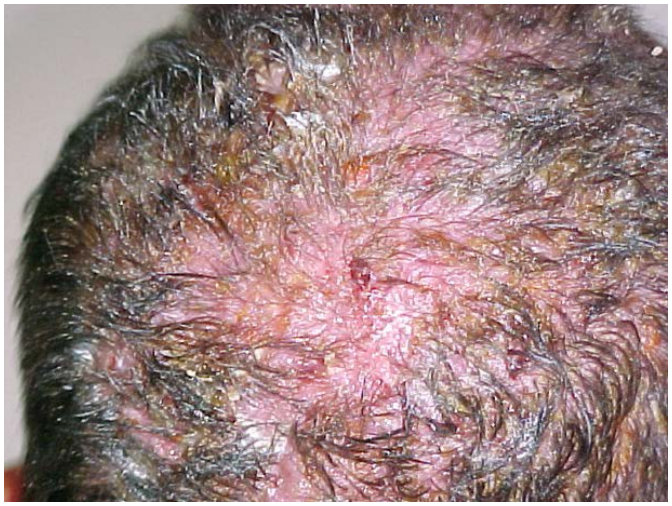
Extrapulmonary manifestations

TSC-LAM



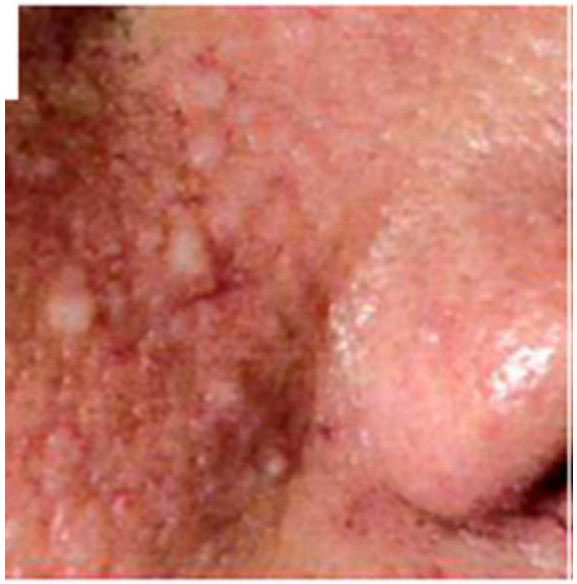
Angiofibromas

LCH



Scalp rush

BHD

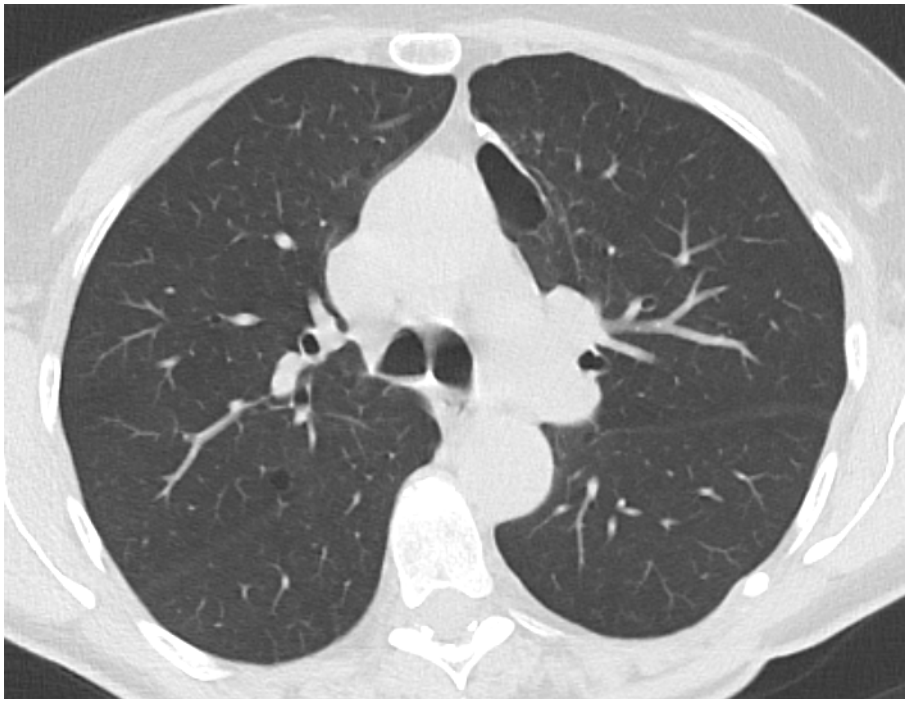


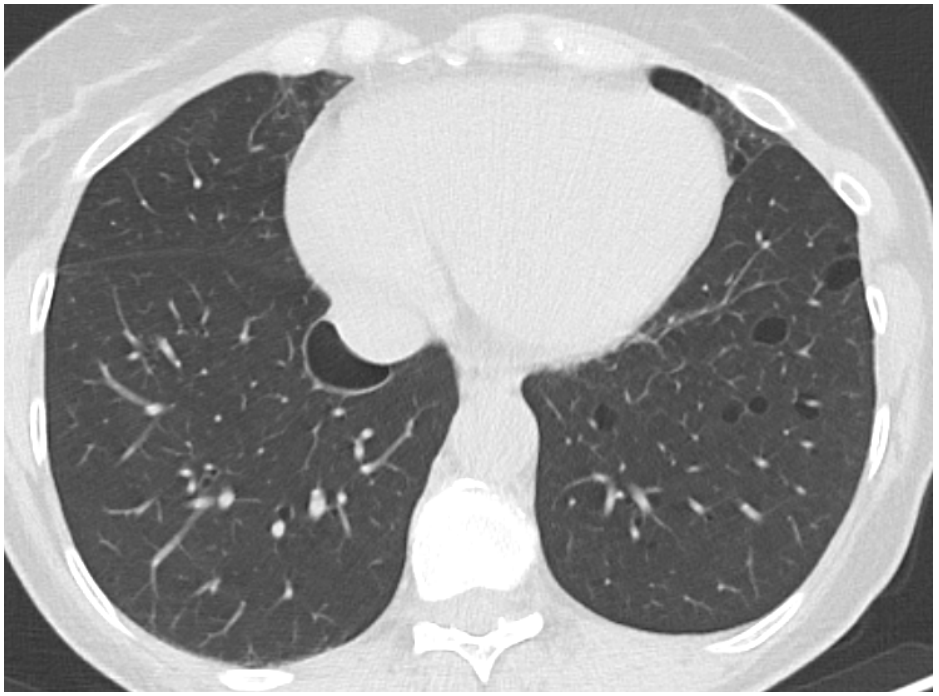
Fibrofolliculomas

DCLDs

LIP/follicular bronchiolitis	- LIP: a diffuse involvement of lung parenchyma by reactive pulmonary lymphoid tissue - FB: a pattern of lymphoid follicular hyperplasia centered on airways, vessels, and interlobular septa They can be idiopathic or associated with a variety of underlying conditions, most commonly autoimmune disorders like (Sjögren syndrome, etc…) or immunodeficiency states
Amyloidosis	- A heterogenous group of disorders characterized by extracellular deposition of proteins in an abnormal fibrillary fashion. - Systemic or localized - Primary or secondary - Usually pulmonary nodules, rarely as DCLD
Light-chain deposition disease (LCDD)	- A monotypic kappa light chain deposition in the alveolar walls, small airways, and vessels - Usually associated to linfoproliferative disorders

TC torace – LIP/FB

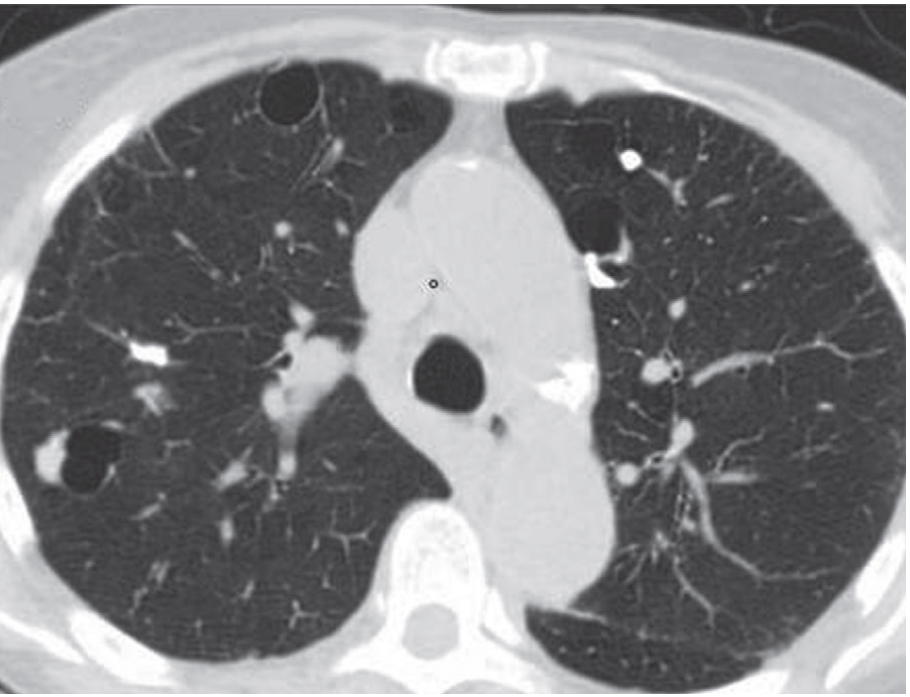




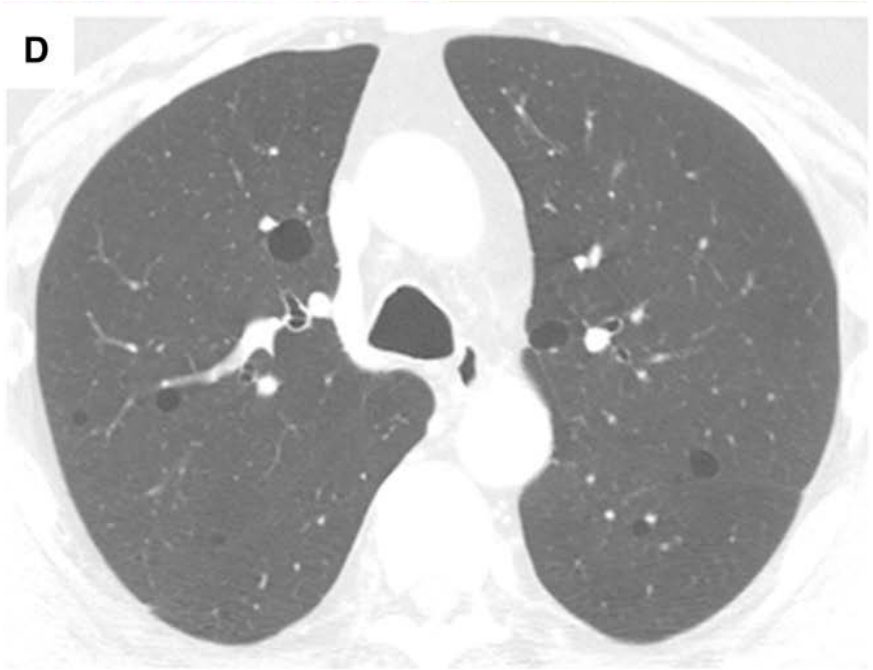
Distribution	Diffuse, random, prevalent in lower lobes often near vessels
Size	Average size 3 mm to 1 cm
Shape	Round, variable

Associated findings	Ground-glass opacities Centrilobular nodules Interlobular septal thickening Internal structures Mediastinal and hilar lymph node enlargement (LIP)

TC torace



Amyloidosis



LCDD

Distribution	Diffuse, random
Size	> 1 cm
Shape	Round, variable

Associated findings	Multiple nodules of varying attenuation, random. Nodules abut cyst walls Masses (Amyloidosis) Lymph node enlargement

Extrapulmonary manifestations

LIP/FB	- Sjögren syndrome - Other CTDs - HIV - Common variable immunodeficiency
Amyloidosis	- Systemic amyloidosis - Sjögren syndrome - Other CTDs - MALT lymphoma
LCDD	- Lymphoproliferative disorders (75% of cases in multiple myeloma or macroglobulinemia) - Renal failure

BAL/TBB

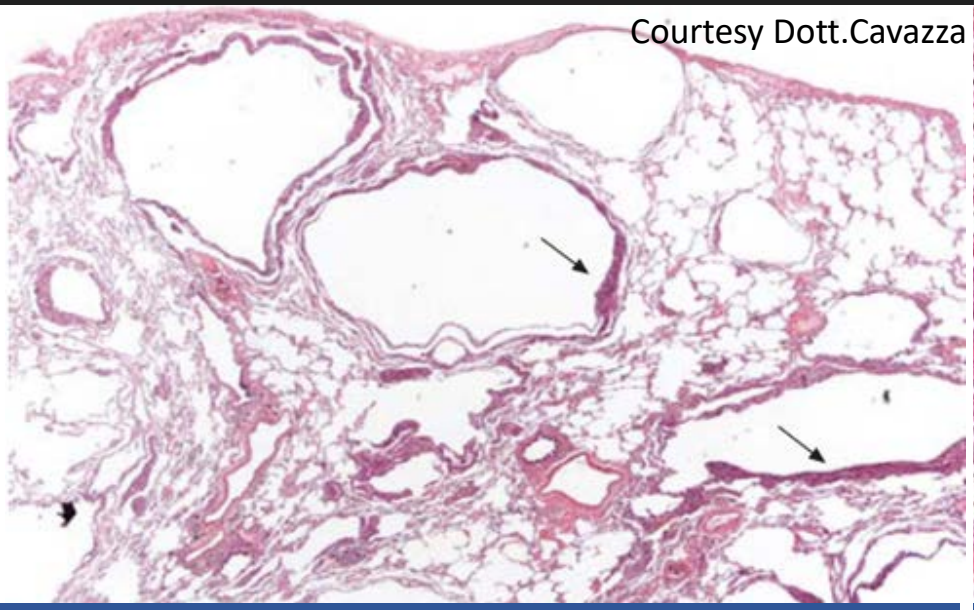
LAM	- BAL: not-significant - TBB: diagnostic yield around 50-60%, relatively safe with pneumothorax rate of 0 to 6% (based on case series) McCormack FX et al, AJRCCM 2016
PLCH	- BAL: High specificity (CD1a>5%) but low sensitivity In patients with atypical clinical and/or radiological presentation it can be used to role out interstitial lung diseases with more typical lavage findings and pulmonary infections - TBB: may have low diagnostic yield (10-50%) because of the small amount of tissue obtained and the patchy nature of the disease Harari et al, Resp Med 2012 Baqir M et al, J Bronchology Interv Pulmonol 2013
Birt-Hogge-Dubè (BHD)	- BAL: not-significant - TBB: no diagnostic yield

Definite LAM

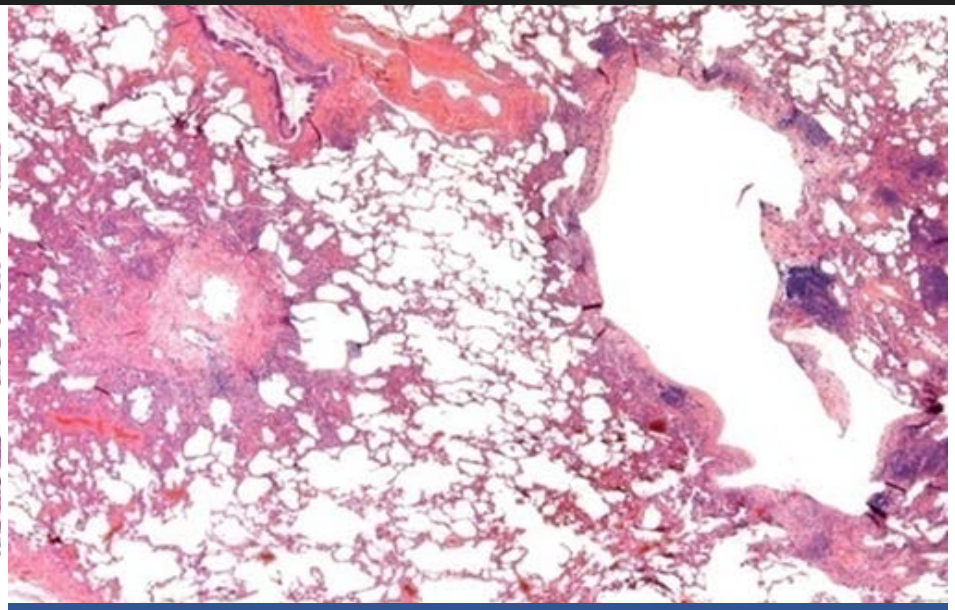
ERS guidelines 2010	ATS/JRS guidelines 2016	ATS/JRS guidelines 2016
characteristic lung HRCT + any of the followings	characteristic lung HRCT + any of the followings	Characteristic HRCT alone
✓Tuberous Sclerosis Complex ✓Chylous effusions ✓Angiomyolipomas ✓Lymphatic involvement	✓ Tuberous Sclerosis Complex ✓Chylous effusions ✓Angiomyolipomas ✓Lymphatic involvement ✓ Serum VEGFD levels ≥ 800 pg/mL	Lung biopsy

Johnson SR et al, ERJ 2010
McCormack FX et al, AJRCCM 2016

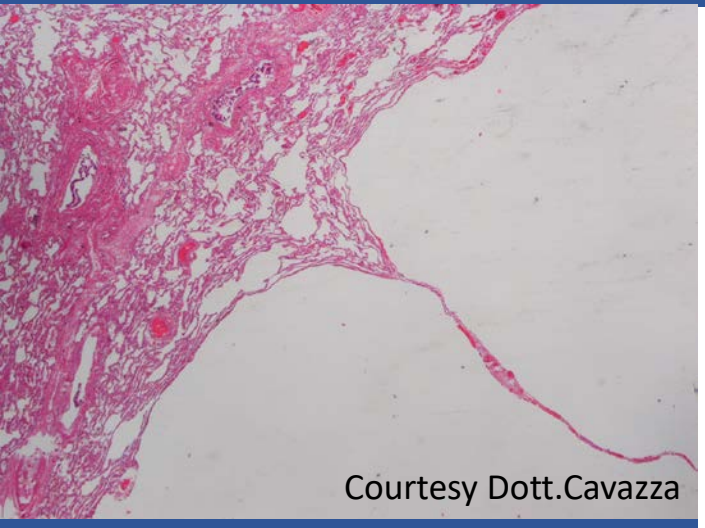
Pathologic findings



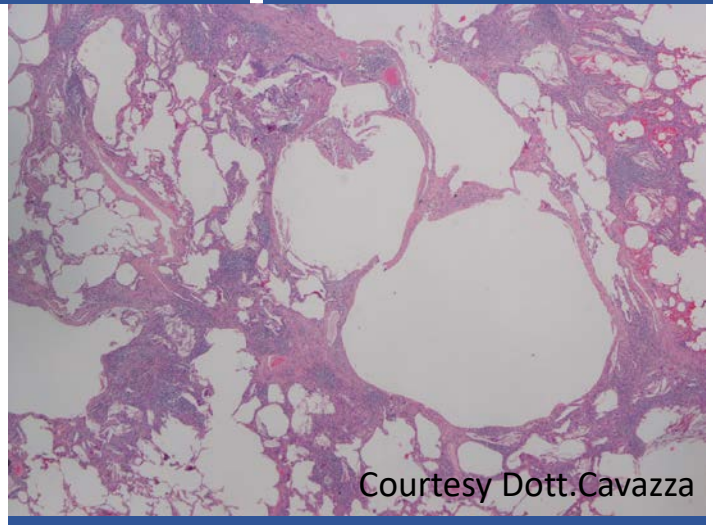
LAM



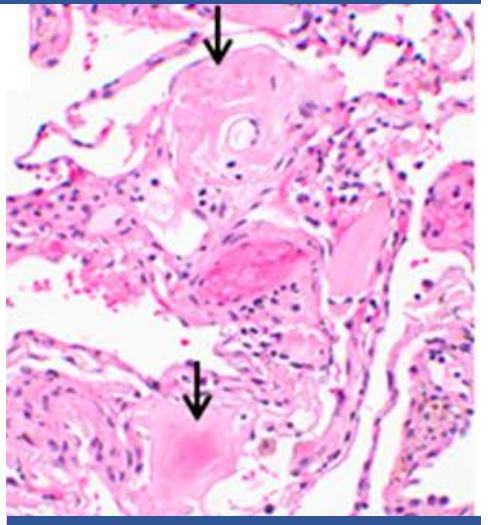
PLCH



BHD

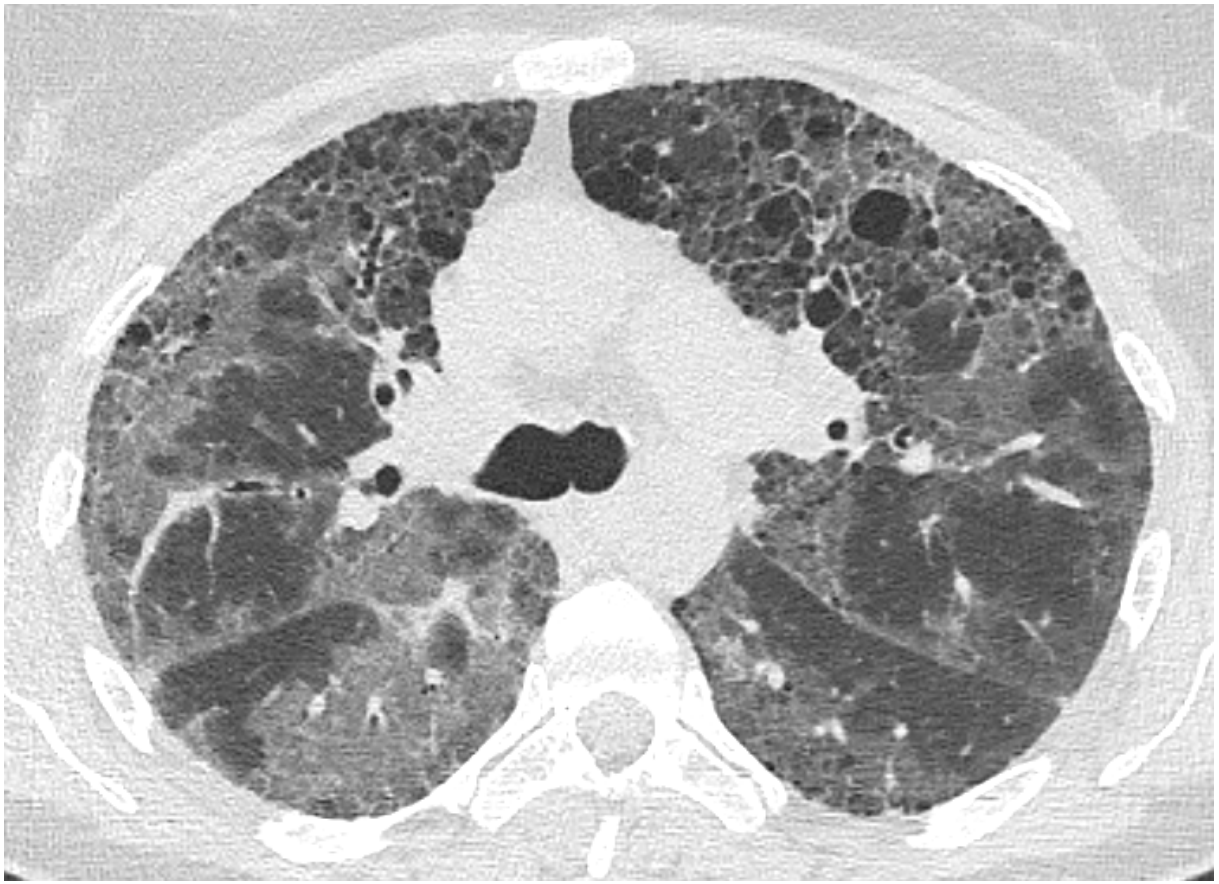


LIP



Amyloid

Cisti in altre patologie polmonari



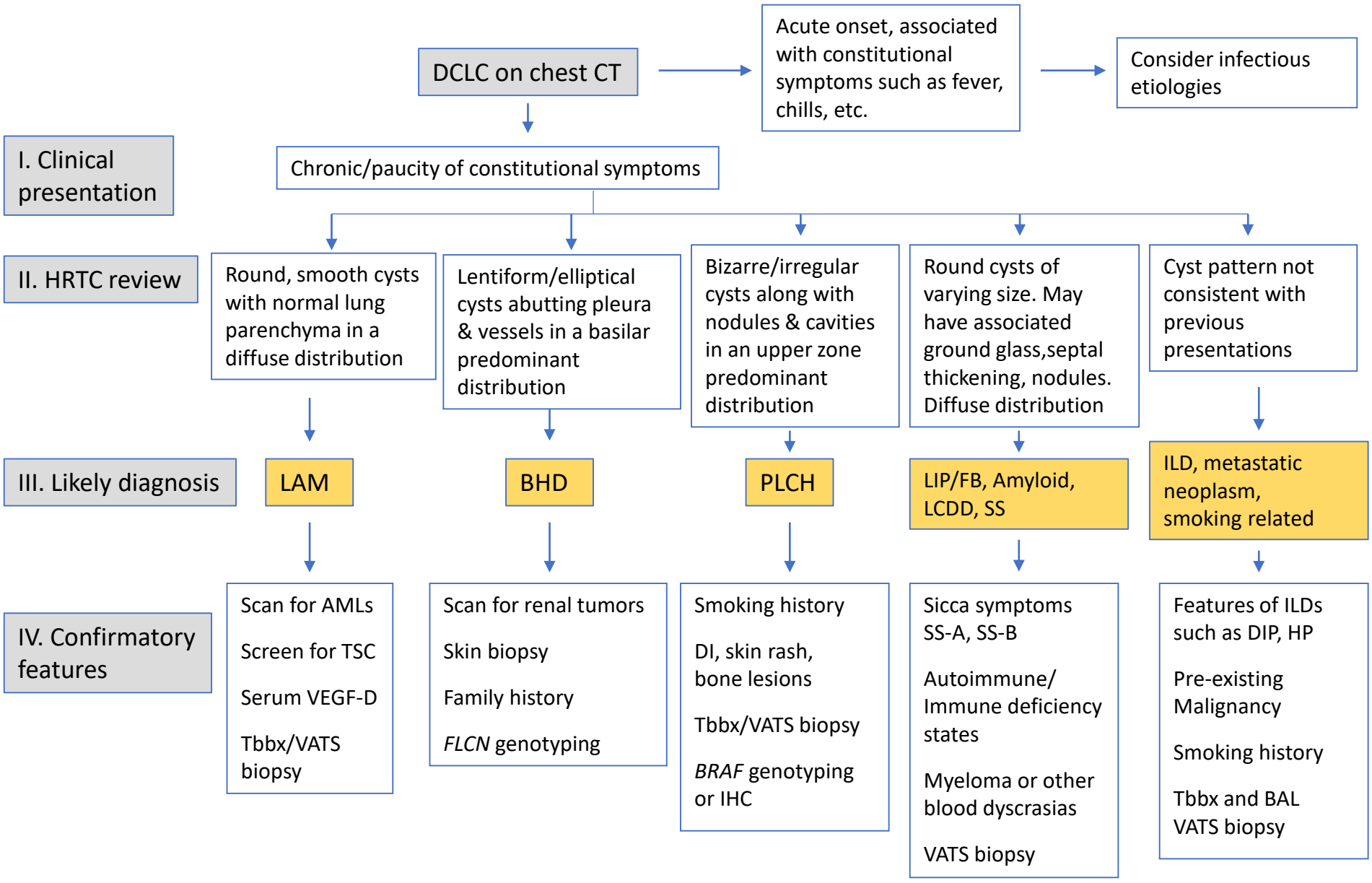
Patologia polmonare diffusa, con aspetto patchy, caratterizzata da presenza di opacità ground-glass, minimi aspetti di distorsione fibrotica e multiple cisti aeree, presenti nelle zone di ground-glass, con diametro variabile da pochi mm a circa 1 cm.

Dati demografici/clinici/laboratorio

	LAM	PLCH	BHD	LIP/FB	Amiloidosi	LCDD
Fumo		SI				
Genere	Femmine					
Laboratorio	*VEGFD sierico*	Diabete insipido	*Genetica per FLCN*	Autoimmunità Immunodeficit	Autoimmunità Amiloidosi sist.	M.linfoprolif. Insuff.renale
Storia familiare	*Possibile TSC*		*Possibile BHDS*			
Prevalenza di pnx	Fino al 70%	10-20%	24%	Non nota	Non nota	Non nota
Prevalenza PNX	XX	X	X			
PNX ricorrente	XX	X	XX			
Versamento chiloso	X					

Diagnostic algorytm

Gupta N et al, AJRCCM 2015




Grazie