Current Pulmonology Reports (2024) 13:215–232
https://doi.org/10.1007/s13665-024-00359-8

REVIEW

Cystic Lung Diseases: A Radiology Primer

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Accepted: 15 July 2024 / Published online: 12 August 2024
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Abstract

Purpose of Review Cystic Lung Diseases (CLD) represent a diverse group of lung diseases characterized by the presence of intraparenchymal cysts. The purpose of this review is to provide an imaging primer and a proposed systematic approach to characterizing CLDs based on CT findings.

Recent Findings Over the past decade, there have been tremendous advances in the understanding of pathophysiology and in therapeutic options for CLD. For example, Lymphangioleiomyomatosis (LAM) is now classified as low-grade metastasizing neoplasm and use of mTOR inhibitors (Sirolimus) has shown some promising results in the management. Providing an appropriate differential for CLD is pivotal for optimizing patient's treatment.

Summary Management of CLD is a multidisciplinary effort, with imaging playing a vital role. After initially excluding cyst-mimics, the differential diagnosis of CLD can be narrowed based on cyst features, distribution, and ancillary characteristics utilizing the systematic approach provided herein.

Keywords Cystic lung disease · Radiology · Computed tomography

Introduction

With the increasing use of chest CT in the modern era, pulmonary cysts are often encountered. A cyst (Fig. 1) is a round parenchymal lucency or low-attenuating area, with a thin wall (<2 mm) and well-defined interface with normal lung parenchyma [1] Cysts typically contain air, but occasionally may have fluid or solid material [1]. Several mechanisms (Fig. 2) have been proposed for the etiology of cysts, including the formation secondary to the check-valve obstruction, destruction and remodeling of the parenchyma by enzymes (for example; proteases), and ischemic dilatation of small airways/alveoli secondary to infiltration/obstruction of the small vessels [2].

Regardless of the cause, cysts are a frequently discovered finding in both asymptomatic patients, as well as in patients with non-specific clinical symptoms, including cough and shortness of breath. Cysts can be focal or diffuse. Focal cysts are often seen as an incidental finding with aging [3, 4]. In contrast, multiple cysts without bilateral distribution can be seen in congenital lesions (e.g., congenital pulmonary airway malformation) and as a sequela of prior infection, inflammation, or trauma resulting in pneumatocele formation. Cysts may also be seen as a manifestation of cystic lung disease (CLD), presenting a diagnostic challenge for the radiologist as well as the pulmonologist [5–7].

CT is the preferred modality for the detection of cysts and differentiation of cysts from other air-filled lung lesions that mimic cystic lung diseases. Radiographic characterization is often augmented by clinical evaluation and laboratory testing in making the correct diagnosis of cystic lung disease and often obviate the surgical lung biopsy. This review provides an approach to distinguish cysts from cyst mimics, and an overview of some of the common diffuse cystic lung disease.

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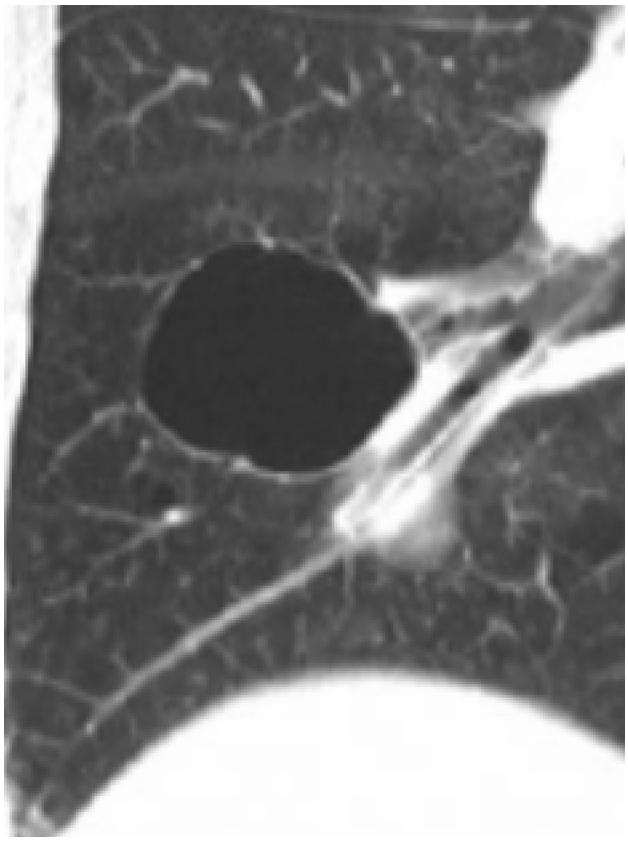

Fig. 1 CT image of a lucency in the lung parenchyma with thin wall compatible with a pulmonary cyst

Cyst Mimics

In approaching the radiologic evaluation of cystic lung disease, it is important to first distinguish between true cystic lung disease and other air-filled lesions within the lungs. This distinction is made by identifying key imaging characteristics, including cyst size, wall thickness, location, distribution, as well as ancillary findings, helping to differentiate the various types of cystic lesions. Common mimics of cysts that should be considered include pneumatoceles, cavitary lesions, bullae, emphysema, honeycombing and bronchiectasis (Table 1).

Pneumatocele and Cavitary Lesions

A pneumatocele (Fig. 3), like a cyst, is a thin-walled air-filled space, but is commonly a transient finding resolving in weeks, versus a cyst which is permanent. Pneumatoceles can be either the sequalae of infection or following traumatic injury. Notably, cysts have a well-defined interface with normal lung parenchyma, whereas pneumatoceles (especially in the acute setting) may be found adjacent to consolidation and/or ground glass opacities [1, 7].

Cavitary lesions can mimic cystic lung disease. In contrast to a cyst, a cavity is thick-walled (>4mm), with variable attenuation on CT, due to fluid, debris, or soft tissue (Fig. 4). Cavitary lesions can be the sequelae of infection, including bacterial, mycobacterial, and fungal pneumoniae, as well as systemic inflammatory disorders, such granulomatosis with polyangiitis and rheumatoid arthritis. Cavitary malignancies (especially with squamous cell cancers) are often irregular in shape with eccentrically thickened walls (> 10 mm) [8].

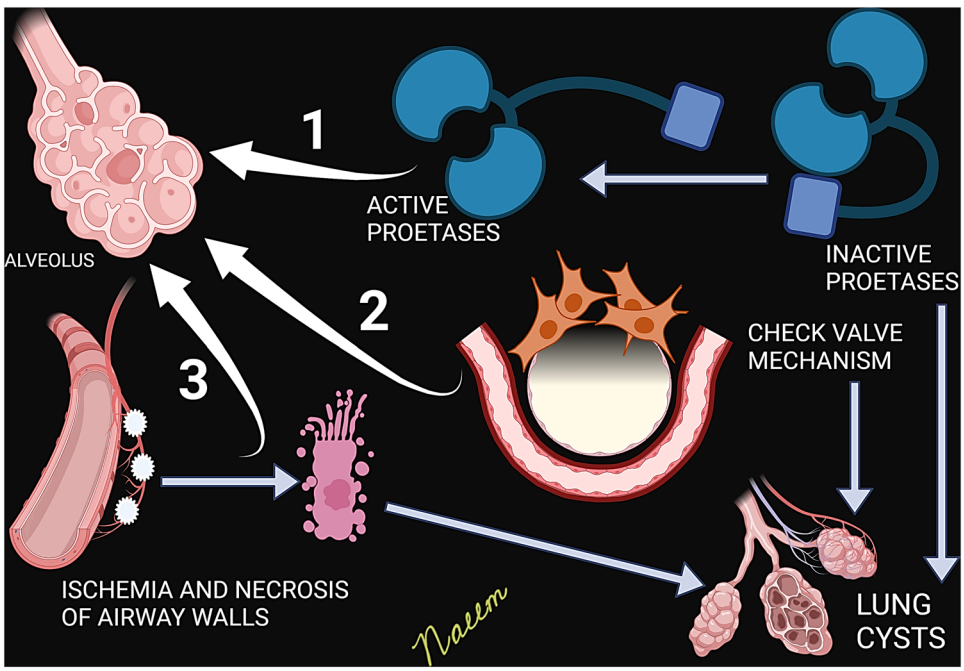

Fig. 2 The illustration explains three proposed mechanisms that may lead to a cyst formation. Remodeling induced by matrix-degrading enzymes (for example: proteases, label 1). Check-valve obstruction due to infiltrative diseases (such as LAM) with distal overinflation (label 2). Ischemia leading to necrosis resulting in ischemic dilation of small airways and alveoli (label 3)

Table 1 Common cyst mimics and their characteristics

Cyst Mimic	Common causes	Wall thickness	Shape	Location	Size
Pneumatocele	Infection, trauma, aspiration of chemical or barotrauma	Thin	Variable	Variable	Variable, transient
Cavitation	Infection, Malignancy	Thick, > = 4mm	Irregular	Variable	Variable
Bleb	Smoking, Young thin person (subpleural alveolar rupture)	Thin, < 1 mm	Regular, well defined	Under visceral pleura, mostly apices	< 1–2 cm
Bullae	Smoking	Thin, < 1mm	Regular, well defined	Under visceral pleura, mostly apices	> 2 cm
Honeycombing	Fibrosing interstitial lung disease (UIP-IPF, CTD-ILD)	Variable, 1-3mm	Well-defined, multi-layered or clustered appearance	Subpleural region, basal predominance	3 to 10 mm
Cystic bronchiectasis	Congenital (for example: Mounier-Kuhn syndrome), impaired host defenses (for example: Cystic fibrosis)	Thick	Saccular dilation	Depending on the cause (for example: Cystic fibrosis is upper lung predominant)	Variable

Emphysema

Emphysema occurs following the destruction of the secondary pulmonary lobule, which can be either congenital (α1-antitrypsin deficiency) or secondary to smoking. Emphysema is categorized as centrilobular, paraseptal, or panacinar whether disease primarily involves the central acinus, distal acinus, or entire secondary pulmonary lobule respectively (Fig. 5). On CT, emphysema is seen as multiple, small lucencies, usually with an imperceptible wall. A central dot can be seen within the dilated air space, representing a dilated terminal bronchial artery referred to as the dot sign, which is a hallmark finding of centrilobular emphysema [9, 10]. The distribution of emphysema is dependent on the etiology, with smoking related emphysema most pronounced within upper lungs and congenital form of emphysema most pronounced with the lower lungs.

Bulla/Bullae

Bulla, which are air spaces > 10 mm, can also be seen within the lung adjacent to emphysema. Bulla(e) can be single or multiple, and primarily have a subpleural distribution and measure less than 10 mm (Fig. 6). This is contrast to cysts, which are typically not clustered in a subpleural location [1].

Bronchiectasis

Bronchiectasis is the irreversible dilatation of the bronchial tree, which is secondary to infections and conditions that predispose to infection. Bronchiectasis may also be seen from inherent disorders of the bronchial wall or from traction from adjacent fibrosis. On CT, bronchiectasis appears as dilated airways, with associated bronchial wall thickening. The airways may have a cylindrical, varicoid, or cystic configuration. Lack of bronchial tapering within the lung periphery and/or relatively increased size of distal bronchi to the adjacent pulmonary artery, can be additional clues of bronchiectasis. In contrast to cysts, bronchiectasis will show continuity with the airways. Other findings including tree in bud appearance of the distal airways, mucus impaction, and mosaic attenuation can be seen, helping to differentiate bronchiectasis from cystic lung disease [6, 11, 12]. Cystic bronchiectasis will often have air/fluid levels which can also be used to distinguish it from true cystic lung disease (Fig. 7).

Honeycombing

Honeycombing cysts, associated with lung fibrosis and is a characteristic finding of usual interstitial pneumonia (Fig. 8). On CT, honeycombing radiographically appears as multiple small lucencies, with thin walls, 3–10 mm in size usually stacked in 2 or more rows. The distribution of honeycombing is subpleural. Fibrotic changes, including subpleural reticulation/scaring and traction bronchiectasis, are other findings associated with findings of honeycombing [13].

Cystic Lung Disease (CLD)

An approach to CLD increases the likelihood of achieving a definitive diagnosis [14, 15]. After excluding the mimics described above, CLD may be divided into four categories based on whether the cysts are associated with lung nodules

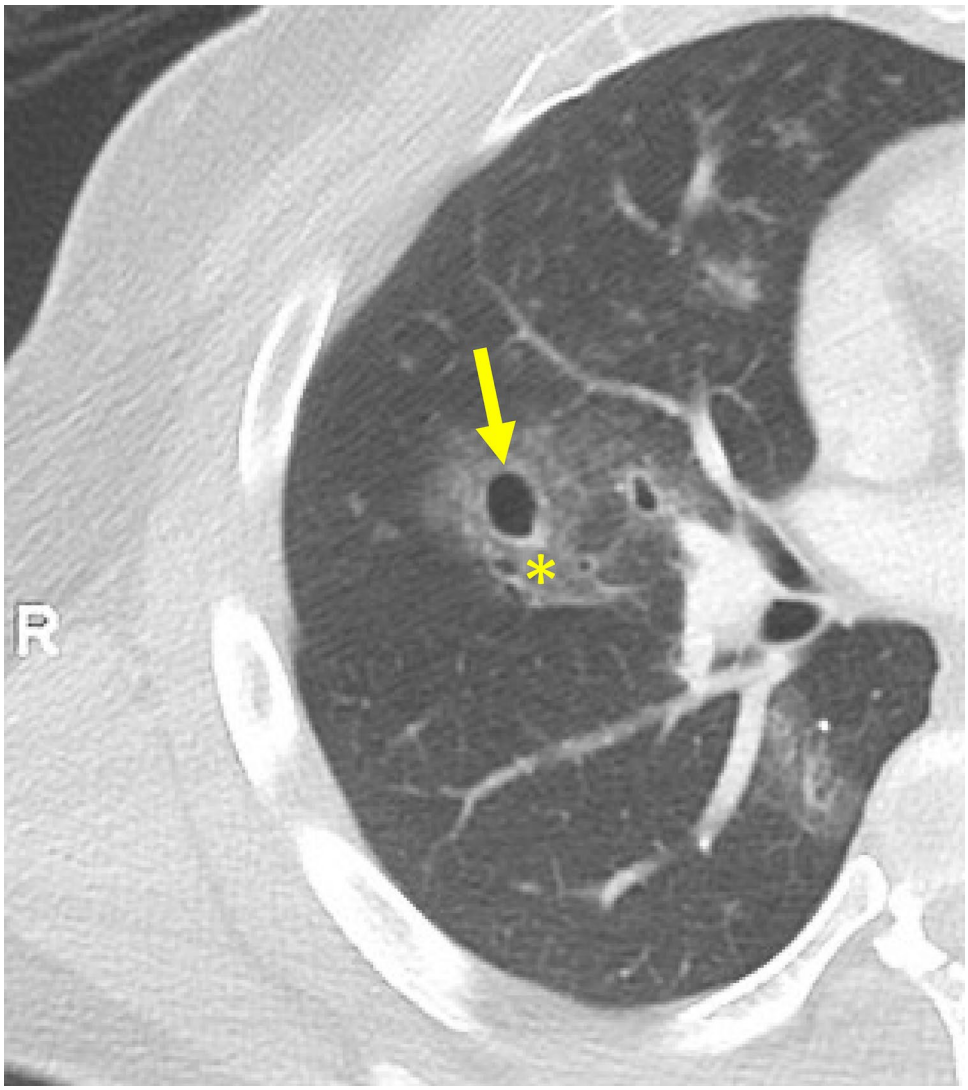

Fig. 3 CT image of a lucency (arrow) surrounded by ground glass (asterisk) in a patient with traumatic contusion

or ground glass opacifications: 1. CLD with mostly or only cysts (no other associated CT findings), 2. CLD with nodules, 3. CLD with ground glass, and 4. CLD with ground glass and nodules (Fig. 9).

(A) CLD with mostly or only cysts

(i) Lymphangioleiomyomatosis (LAM)

LAM is a rare and progressive low-grade, metastasizing neoplasm primarily affecting women, characterized by the abnormal proliferation of smooth muscle cells in the lungs, leading to the formation of cysts and progressive decline in pulmonary function [16]. LAM can be associated with tuberous sclerosis which can be seen in men and women. In TS a mutation in the tuberous sclerosis complex (TSC) genes TSC1 and TSC2 leads to the cyst formation. Based on the most recent European Respiratory Society guideline in 2010 [17], a VEGF-D > 800 pg/ml with typical CT findings is diagnostic for LAM. According to the American Thoracic Society and Japanese Respiratory Society guidelines, presence of tuberous sclerosis complex, elevated serum VEGF-D > 800 pg/mL, renal angiomyoplipoma (Fig. 10), lymphangioleiomyoma, or chylous effusion in women with LAM compatible cystic lung disease does not require biopsy to confirm LAM [18]. By European guidelines, greater than 10 cysts are required for "definite LAM" and 2–10 cysts for "probable LAM".

During the early stages, CT will show small, thin-walled cysts scattered diffusely throughout the lung parenchyma without parenchymal destruction (Fig. 11). As the disease progresses, cysts may increase in number and size, leaving almost no normal lung behind. The disease itself would not cause nodules or ground glass appearance, but as disease progresses, concomitant lung infection and post infectious parenchymal

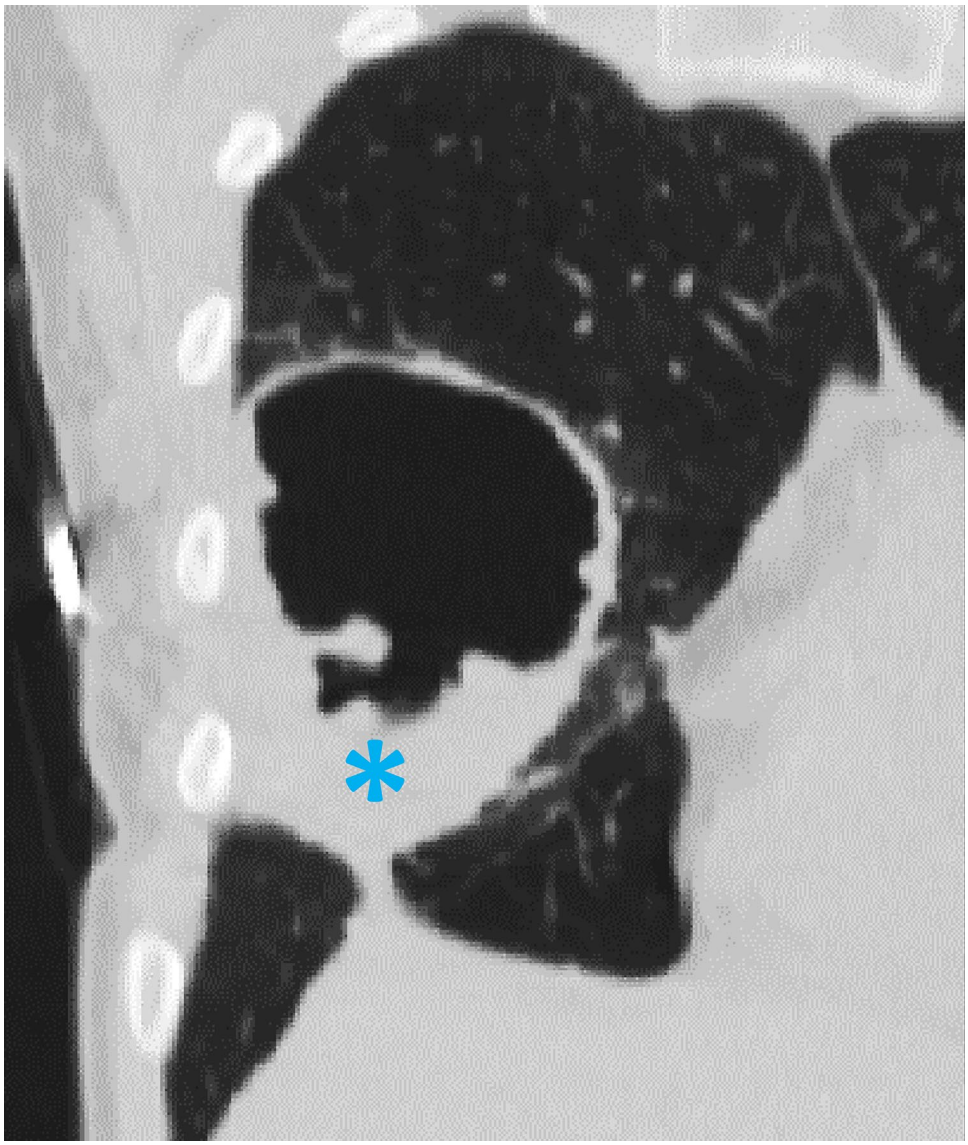

Fig. 4 CT image of a thick-walled cavity in patient with granulomatosis with polyangiitis. Note the nodular soft tissue thickening of the wall (asterisk)

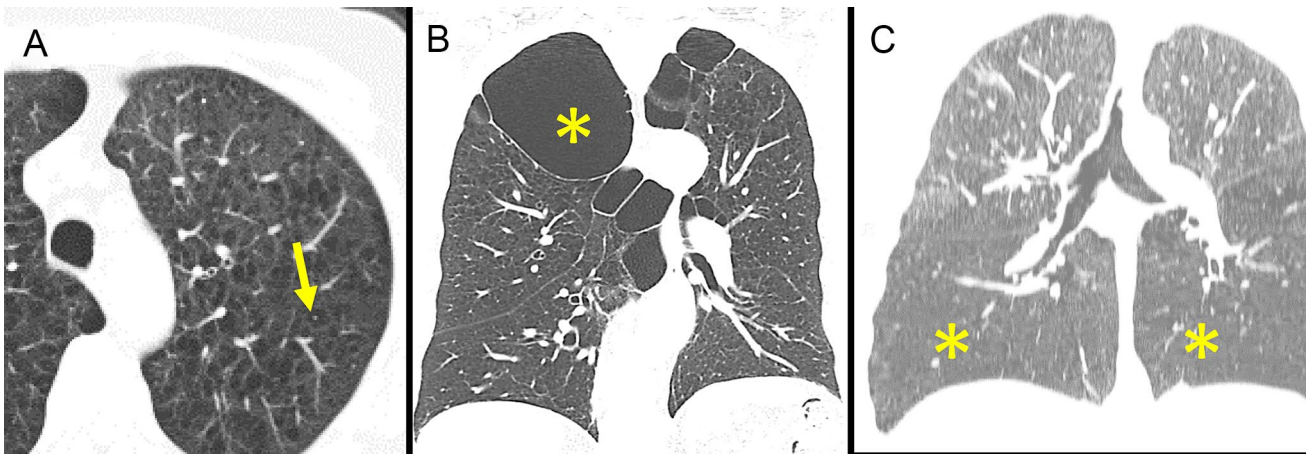

Fig. 5 Categories of Emphysema. **A** Centrilobular emphysema: Note the central dot sign (arrow). **B** Paraseptal emphysema: Note the subpleural distribution of bleb and bullae (asterisk). **C** Panacinar emphysema: Note the lower lung predominant emphysema (asterisk) in a patient with Alpha-1 antitrypsin deficiency

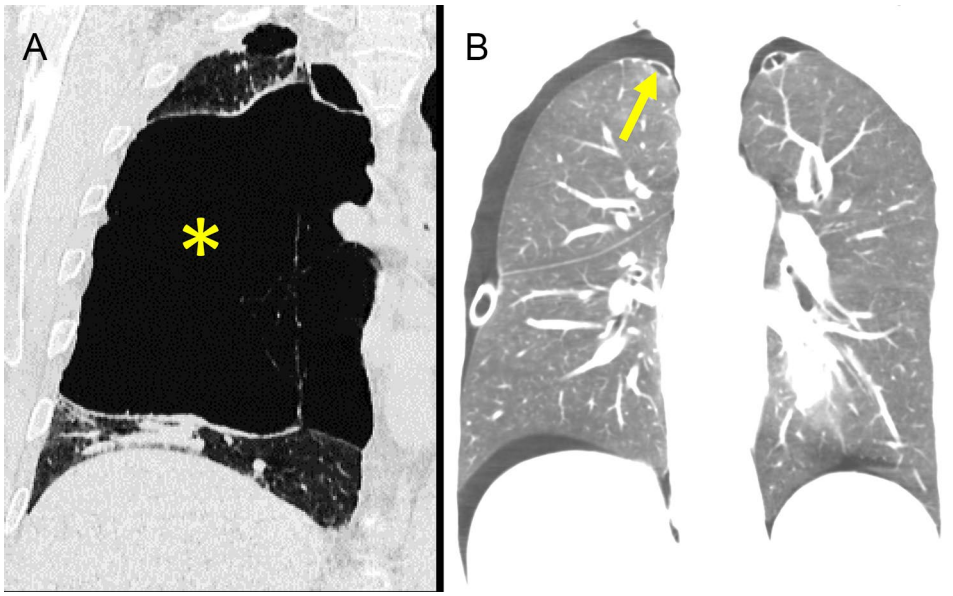

Fig. 6 **A** Bulla. The coronal CT image demonstrates a large loculated lucency in the lung parenchyma (asterisk) which causes mass effect on adjacent normal lung. **B** Bleb. The subcentimeter air-filled spaces underneath the visceral pleura (arrow) in a young patient resulted in spontaneous pneumothorax from a bleb rupture

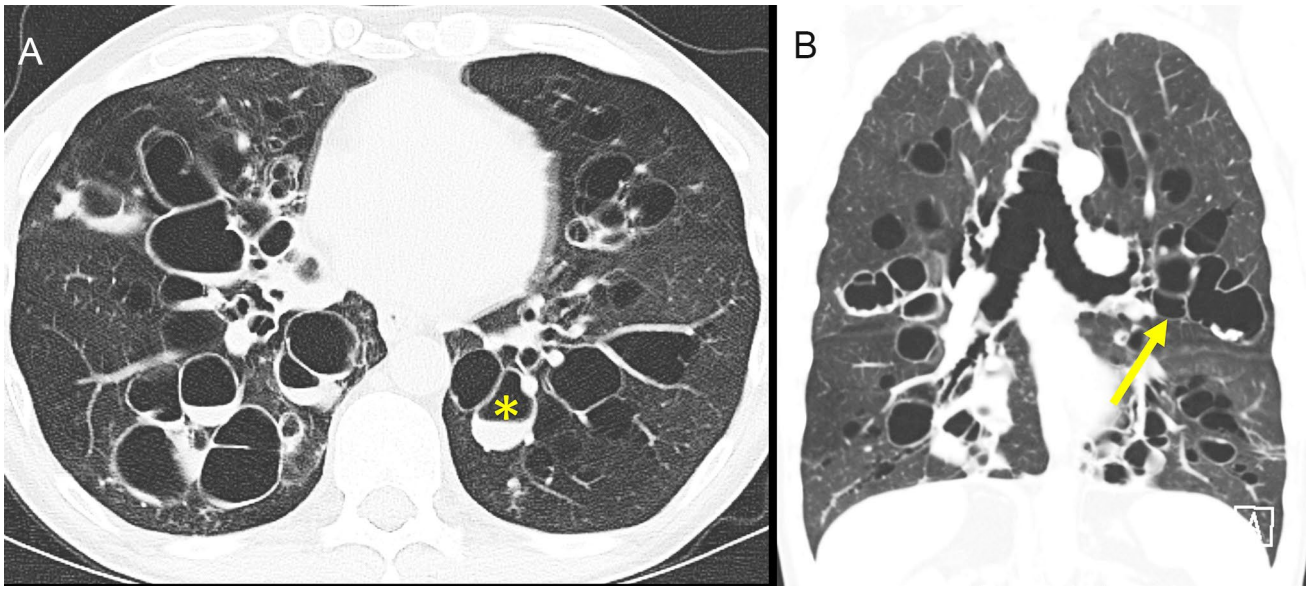

Fig. 7 75-year-old man with Mounier-Kuhn syndrome. CT chest with axial (**A**) and coronal (**B**) images demonstrate bilateral cystic structures with air-fluid levels (asterisk). These structures can be seen in continuity with the bronchi (arrow) consistent with bronchiectasis and not cystic lung disease

changes could lead to variable appearances on CT. Cyst rupture can lead to spontaneous pneumothorax in patients with LAM.

Thoracic lymphatic manifestations (Fig. 12) are common among LAM patients due to infiltration of lymphatic system by the LAM cells. These include septal line thickening, chylothorax, pericardial effusion, thoracic duct enlargement, mediastinal lymphadenopathy, and rarely, cystic lymphangiomas.

In TSC-LAM patients, proliferation of type 2 alveolar epithelial cells may occur and is known as multifocal micronodular pneumocyte hyperplasia (MMPH) which manifests as ground glass nodules on CT (Fig. 13).

(ii) Light Chain Deposition Disease (LCDD)

LCDD is a rare disorder characterized by the abnormal deposition of monoclonal immunoglobulin light chains in various organs leading to organ dysfunction.

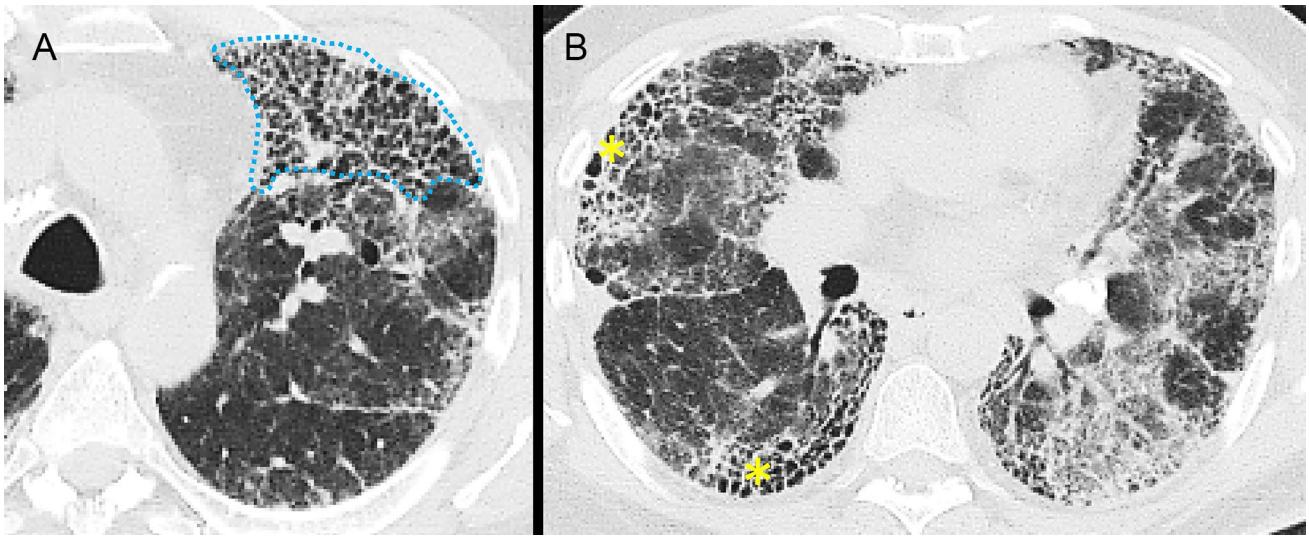

Fig. 8 80-year-old man with idiopathic pulmonary fibrosis. **A** and **B** CT chest images demonstrate honeycombing as stack of subpleural lucencies (dotted line in **A** and asterisk in **B**)

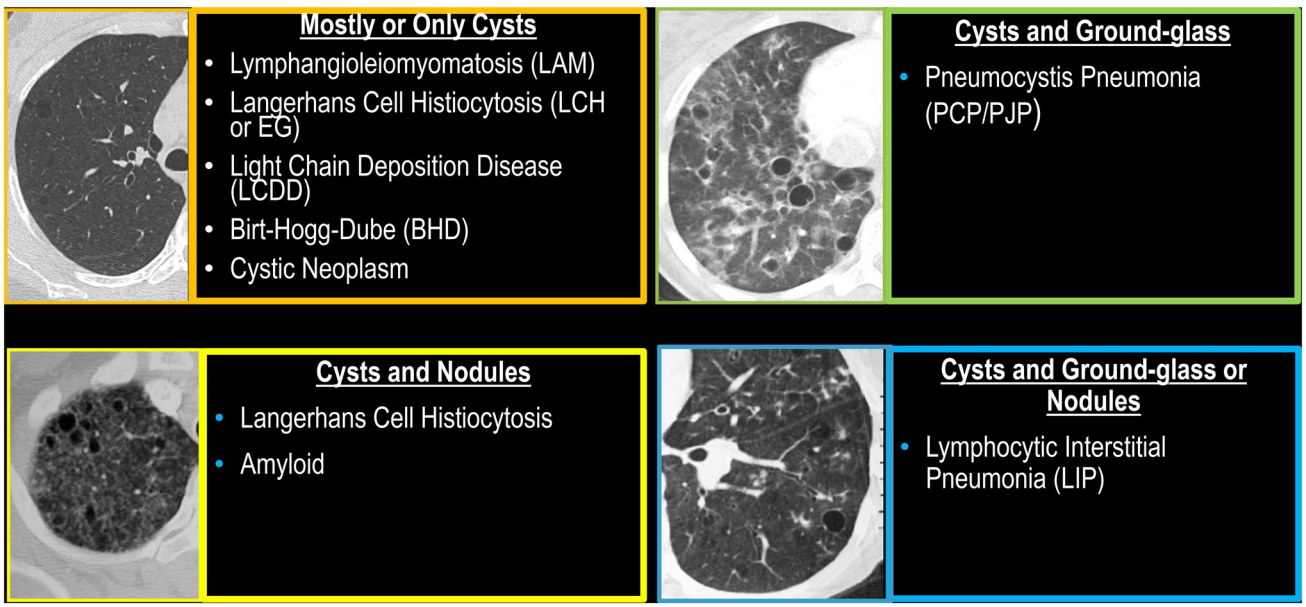

Fig. 9 Classification of common cystic lung disease discussed in this review based on their imaging features

Those light chains are of a nonfibrillary material without β-pleated sheet configuration and do not bind to Congo red, different from amyloidosis. The majority of LCDD occurs in association with multiple myeloma or a lymphoproliferative disease, especially Waldenström macroglobulinaemia [19].

Lung involvement is rare in systemic LCDD. Characteristic CT features include thin-walled cysts (Fig. 14) with vessels inside or traversing the wall (Fig. 15). Calcified pulmonary nodules associated with the cysts are rare and are more suggestive of amyloid [20, 21].

(iii) Birt-Hogg-Dubé syndrome (BHDS)

Also known as Hornstein-Knickenberg syndrome, BHDS is a rare genetic disorder characterized by skin fibrofolliculomas, pulmonary cysts, and renal tumors (especially oncocytomas and renal cell carcinomas). The pathophysiology of BHDS involves mutations in the folliculin (FLCN) gene. The current European BHD Consortium criteria for diagnosing BHDS includes one

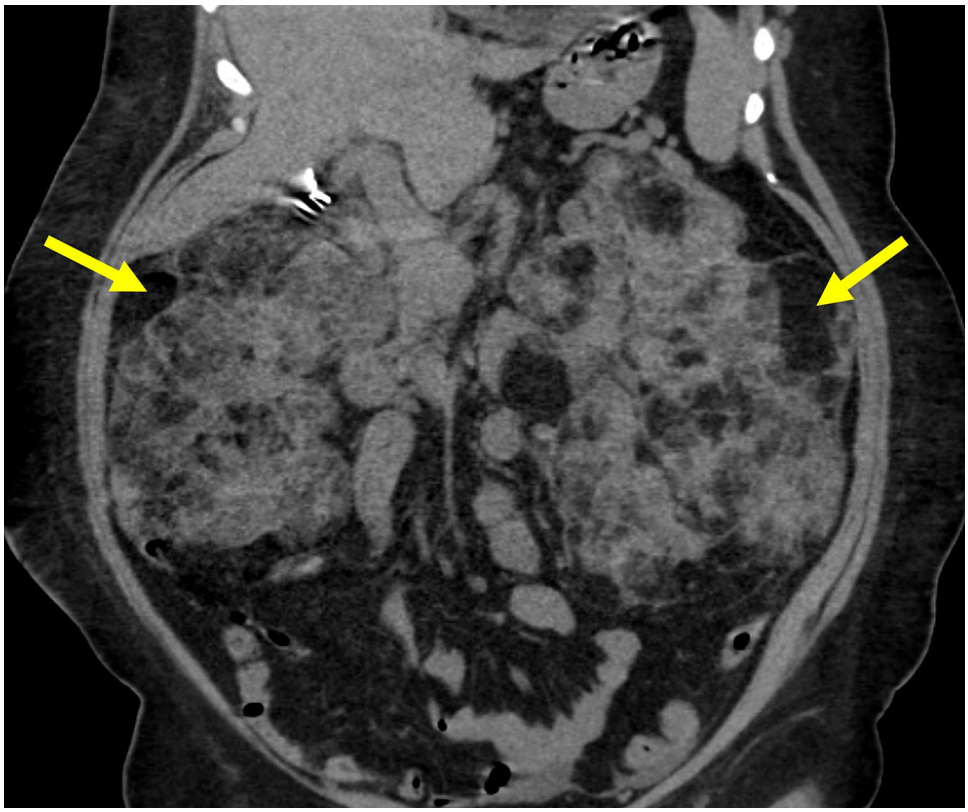

Fig. 10 Coronal CT of the abdomen in a patient with LAM demonstrates bilateral fat-containing soft tissue lesions in the kidneys (arrows) consistent with renal angiomyolipomas

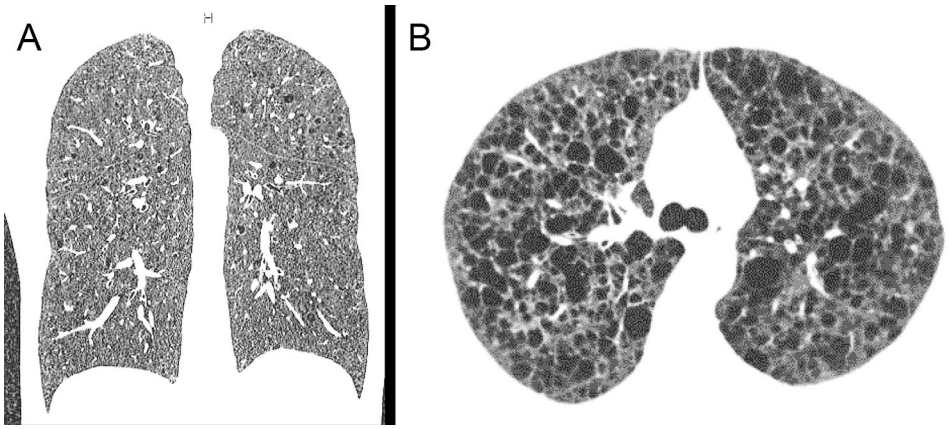

Fig. 11 Two patients with LAM. **A** 36-year-old woman with sporadic LAM. Coronal CT chest demonstrates innumerable thin wall cysts scattered through out the lung parenchyma. **B** 55-year-old woman with slightly advanced LAM in the setting of tuberous sclerosis complex

major criteria and two minor criteria. Pulmonary cysts are considered a minor criteria along with renal cell cancer (Fig. 16), and first degree relative affected with BHD; whereas, pathogenic FLCN gene mutation and 5 adult onset fibrofolliculomas are considered major criteria [22].

The pulmonary cysts have lower zone predominance with paramediastinal predilection. As the disease progresses, these cysts may enlarge with variable cyst morphology with multilobulated or multiseptated appearance on CT.

(iv) Cystic lung cancer

Lung cancers associated with cystic airspaces are less common than solid tumors, but they are easier to miss. Their small size and thin walls make biopsy a challenge. Cystic type lung cancer is different from the cavitating lung cancer in that the wall in these lesions are extremely thin.

Cystic lung malignancy can be primary (less common) or metastatic (more common) and can be solitary or multiple. If cystic lung lesions are seen in patients with known malignancy, metastatic disease should be

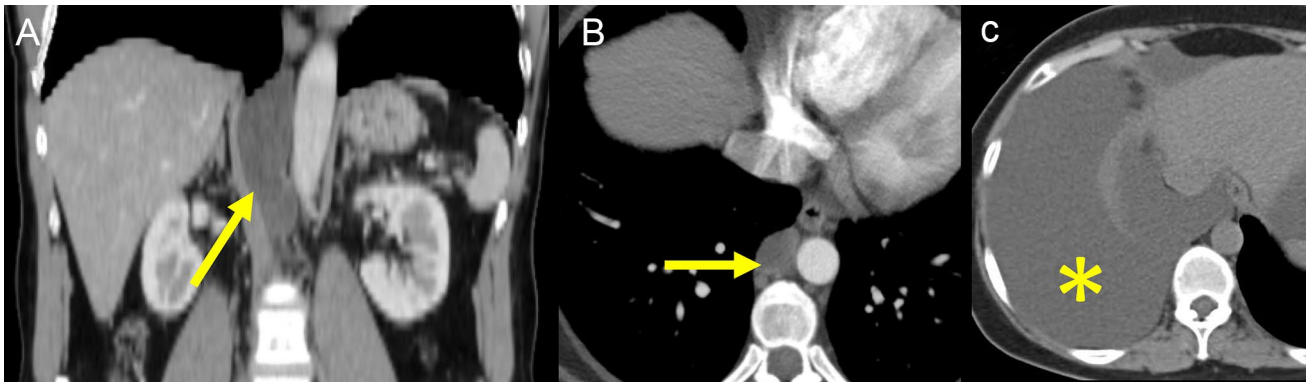

Fig. 12 Three patients with LAM associated thoracic lymphatic manifestation. Patient **A** and **B** have a dilated thoracic duct or lymphocele (arrow); whereas Patient **C** demonstrates a homogeneously low attenuating pleural effusion, the pleural fluid analysis revealed chylothorax (Asterisk)

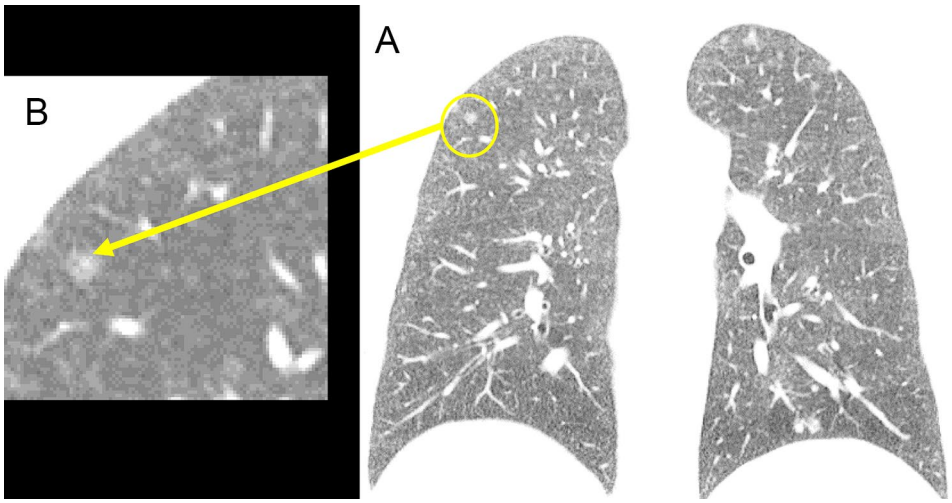

Fig. 13 30-year-old with tuberous sclerosis with no LAM. However, the coronal CT (**A**) demonstrates multiple ground-glass nodules compatible with MMPH. One such nodule is magnified in panel (**B**)

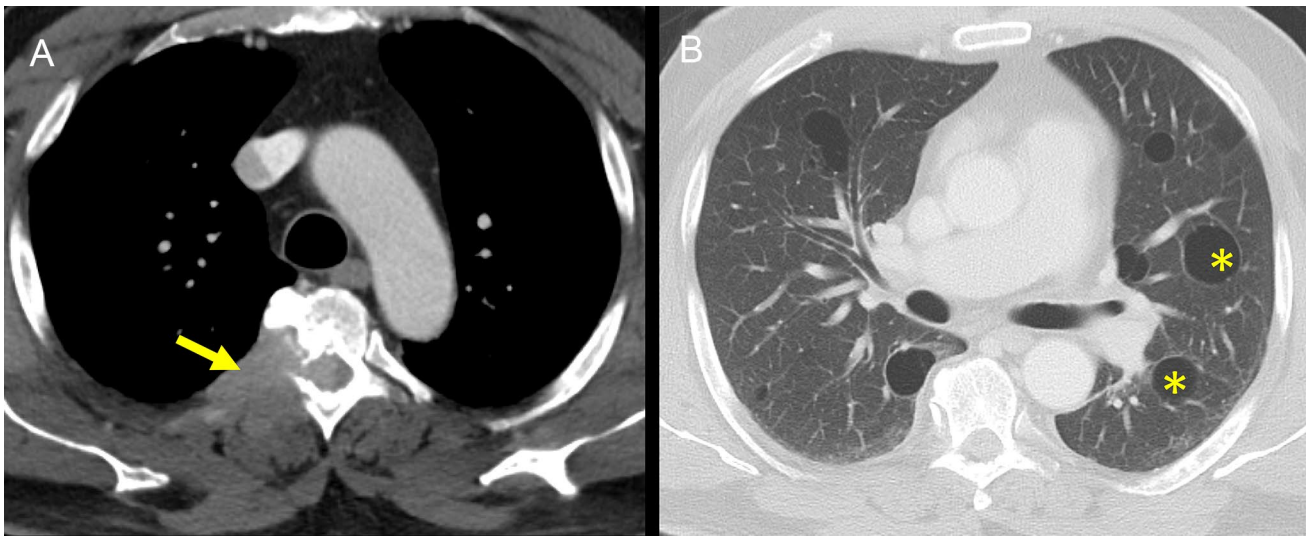

Fig. 14 55-year-old man with multiple myeloma and light chain deposition in the lungs. CT chest on mediastinal (**A**) and lung (**B**) windows demonstrate multiple thin-walled cysts (asterisk) consistent with cystic lung disease. Note the CT chest demonstrates a plasmacytoma extending into spinal canal (arrow)

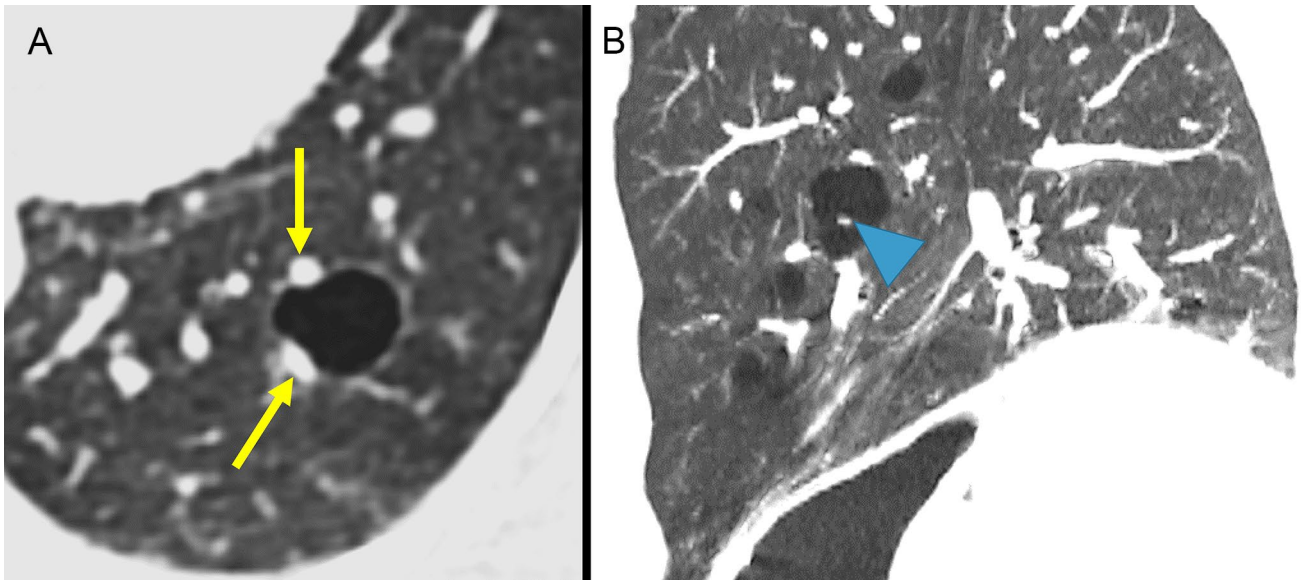

Fig. 15 75-year-old man with pulmonary light chain deposition disease. Axial (**A**) and sagittal (**B**) CT chest demonstrates characteristic feature of the pulmonary cyst with vessel traversing the wall (arrow in A) and center of the cyst (arrowhead in B)

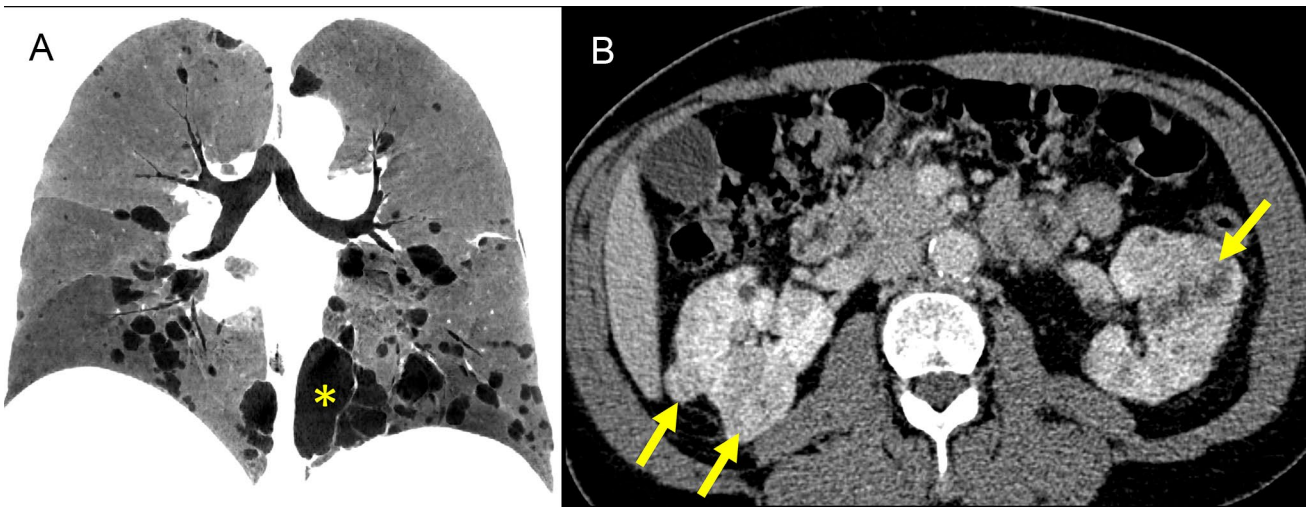

Fig. 16 45-year-old man with BHD syndrome. Coronal minIP reconstruction of the CT chest (**A**) demonstrates multiple lower lung predominant cysts with paramediastinal location (asterisk). Axial CT of the abdomen with contrast (**B**) demonstrates multiple renal masses (arrow) which were compatible with renal cell neoplasms

suspected. Cystic neoplasms are usually adenocarcinomas, whether they be primary (Fig. 17), or metastatic (Fig. 18). In the age of immunotherapy and targeted therapies, many types of treated neoplasm may appear as cystic.

In primary lung cancer, pleuropulmonary blastoma (PPB) and pulmonary adenocarcinoma can manifest as multilocular cystic lesions. PPB is mostly seen in pediatric patients mostly as a pulmonary manifestation of DICER1 syndrome.

As previously stated, adenocarcinoma is the most common primary lung cancer associated with cystic airspaces [23]. The mechanism of cyst formation includes a check-valve mechanism obstructing the small airways, lepidic growth of adenocarcinoma on emphysematous lung parenchyma, cyst formation of tumor and tumor growth along the wall of a pre-

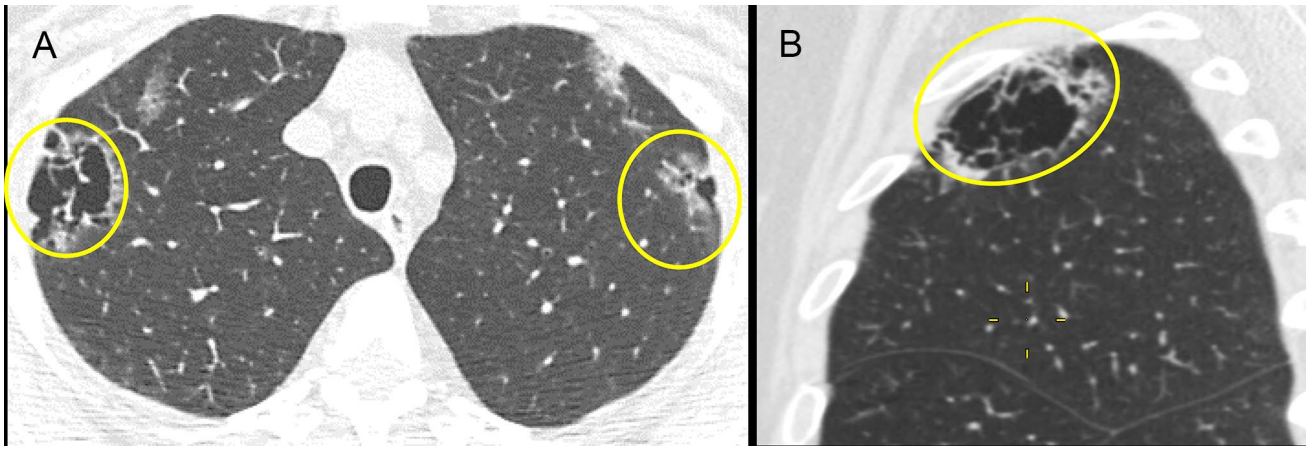

Fig. 17 66-year-old man with multifocal primary lung adenocarcinoma lesions (encircled). Axial (**A**) and sagittal (**B**) CT chest demonstrates clustered cystic spaces with thick walls (an imaging feature seen with cystic adenocarcinomas of the lung)

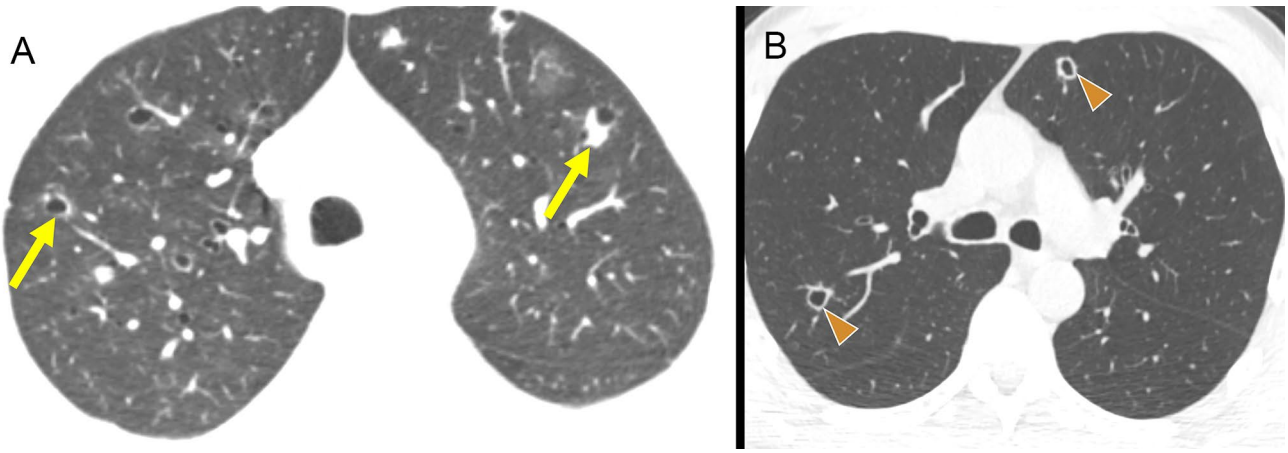

Fig. 18 **A** 65-year-old man with history of adenocarcinoma of the gallbladder. Axial CT of the chest demonstrates cystic lesions bilateral (arrow) which were later biopsy-proven metastases. **B** 44-year-old man with history of colon adenocarcinoma. Axial CT of the chest demonstrates cystic lesions bilaterally (arrowhead) which were later biopsy-proven metastases

existing bulla [8]. The key of identifying them at early stage is progressive wall thickening or nodularity along a cystic wall especially for high risk patients [24]. In Cowden's syndrome, with multisystem hamartoma formation, lung cysts and cystic adenocarcinomas may be seen. The patients are at increased risk for additional malignancies as well (Fig. 19).

(v) Neurofibromatosis-associated cystic lung disease (NF-CLD)

NF-CLD is a pulmonary manifestation of Neurofibromatosis-1 (NF-1) or von Recklinghausen's disease, with non-specific respiratory symptoms and a characteristic pattern of upper lobe cystic and basilar interstitial lung disease on CT. Smoking may be a risk factor for NF-CLD, but the occurrence of these lung changes in nonsmokers with NF-1 suggests that NF-CLD is a unique clinical entity possibly related to the underlying mesenchymal defects associated with neurofibromatosis (Fig. 20) [25]. Other features in NF-CLD include lateral thoracic meningoceles, Kyphoscoliosis, Pulmonary hypertension, Cor pulmonale, and mediastinal neurofibromas [26].

(B) CLD with cysts and nodules

(i) Langerhans Cell Histiocytosis (LCH)

LCH is the most common histiocytic neoplasm characterized by the proliferation and accumulation of abnormal Langerhans cells in various tissues. Identification of BRAF and MAP2K1 mutations in up to 50% of cases [27]. LCH can affect the lungs as single system

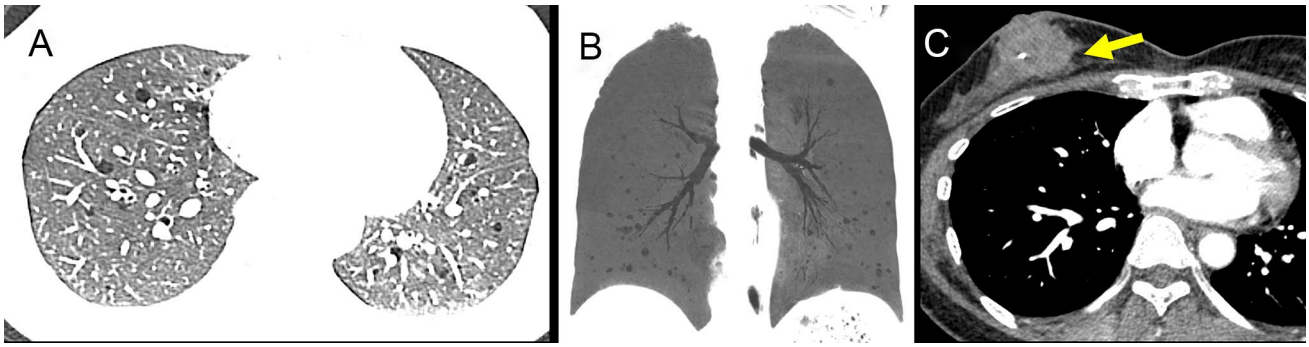

Fig. 19 34-year-old woman with Cowden syndrome. Axial CT of the chest (**A**) with minIP coronal (**B**) demonstrates bilateral scattered thin-walled pulmonary cysts. Also note the right breast mass which was biopsy-proven breast cancer (arrow) on soft tissue windows of CT chest (**C**)

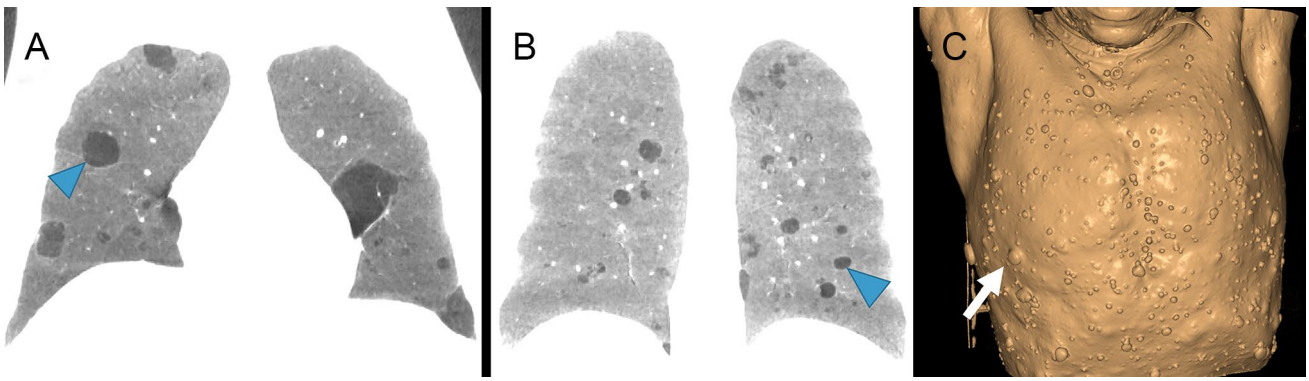

Fig. 20 55-year-old man with NF-1. Coronal minIP reconstruction of CT chest (**A**, **B**) with 3D volume rendering (**C**) demonstrates bilateral scattered thin-walled pulmonary cysts (arrowhead). Also note innumerable skin neurofibromas (arrow)

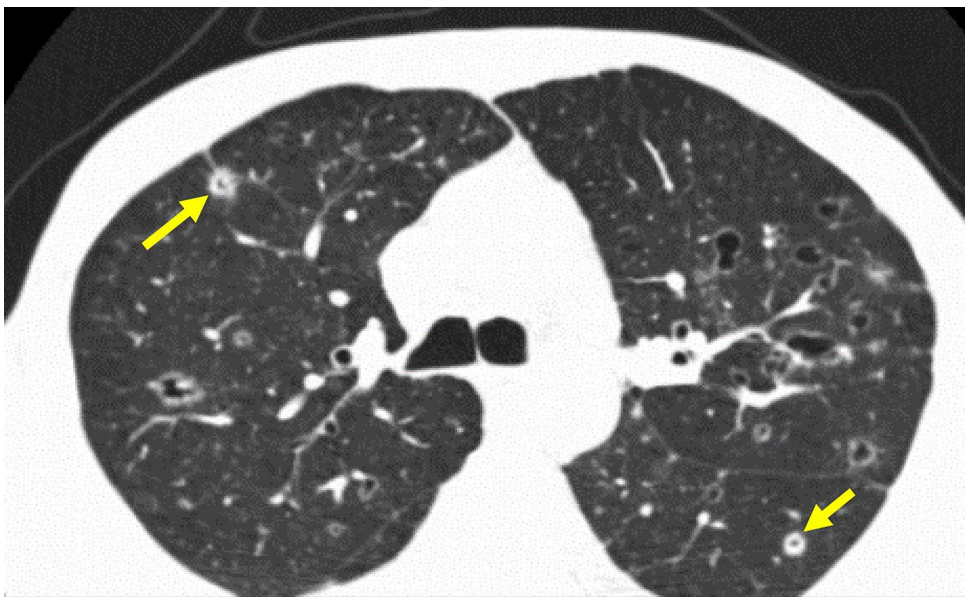

Fig. 21 34-year-old man with smoking-associated Langerhans cell histiocytosis (LCH). Axial CT chest demonstrates multiple bilateral thick-walled cavitary nodules (arrows) in keeping with LCH

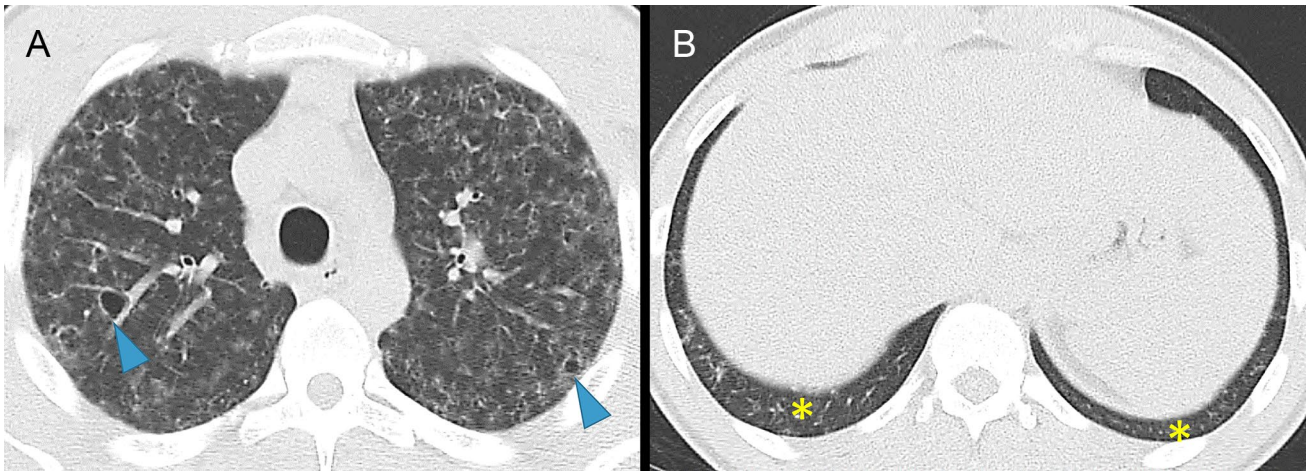

Fig. 22 29-year-old man with smoking-associated Langerhans cell histiocytosis (LCH). Axial CT chest of the upper lung (**A**) demonstrates multiple bilateral cysts (arrowhead) with associated ground-glass (which was related to smoking related respiratory bronchiolitis). Note the sparing of the extreme bases (asterisk in **B**)

involvement or as part of a multisystem disease. In the revised classification of histiocytosis and neoplasms of the macrophage-dendritic cell lineages, the former is considered LCH single system with lung involvement (LCH-SSL) and the latter is classified under LCH multiple system (LCH-MSL). The incidence of LCH-SSL is mostly identified in young adults (20–40 years of age) with a history of current or previous cigarette smoking in up to 95% of cases. Smoking cessation often results in stabilization, regression, and sometimes complete resolution [28].

On CT, the involved lung has a predilection for the mid to upper zones with regional sparing of the costophrenic recesses, right middle lobe and lingula. In the early stages, bronchiolocentric nodules will be a dominant feature with irregular margins referred to as the "stellate nodule" (Fig. 21). The nodules may cavitate, but the surrounding lung parenchyma is usually normal. As LCH-SSL progresses, thin-walled cysts will appear sparing the extreme bases (Fig. 22). Confluence of 2 or more cysts may result in bizarre shapes. Pleural effusions and lymphadenopathy are quite rare with LCH.

(ii) Pulmonary Amyloidosis

Amyloidosis is a group of disorders characterized by the extracellular accumulation of abnormal protein aggregates known as amyloid fibrils. Pulmonary amyloidosis most commonly involves the deposition of AL (primary) amyloid, and less likely to be seen with the other types (AA and ATTR). Four different patterns of noncardiac intrathoracic amyloid deposition have been described: tracheobronchial, mediastinal/hilar lymphadenopathy, pleural effusion, and lung parenchymal [29]. When the lung parenchyma is affected, the most common described pattern is nodular or interstitial deposition, with cyst formation often in association with Sjögren syndrome [30, 31].

Cysts are commonly numerous (often > 10), thin walled with or without heterogeneously calcified small peripheral nodules, mostly involving mid and lower lung zones, often are in the peribronchovascular or subpleural areas (Fig. 23) [32]. MALT lymphoma should be suspected if there is any nodule growth [32].

(C) CLD with cysts and ground glass

(i) Pneumocystis jirovecii Pneumonia (PJP, formerly PCP pneumonia)

PJP/PCP is a form of pneumonia caused by the fungal organism Pneumocystis jirovecii. It is most often seen in patients with weakened immune systems, such as those with HIV/AIDS (CD4 < 200 cells/mm3), cancer patients undergoing chemotherapy who are immunosuppressed, and transplant recipients on immunosuppressive medications.

On CT, diffuse or patchy ground-glass opacities are the most common finding, representing alveolar filling with the organism and inflammatory exudates. Cystic lesions can occur particularly in patients with HIV/AIDS receiving aerosolized prophylaxis [33]. These cysts are thin-walled and can be scattered throughout the upper lungs (Fig. 24). The mechanism of cyst formation is thought to be related to the accumulation of organisms within the alveoli, leading to alveolar wall tension and subsequent rupture, creating air-filled cysts.

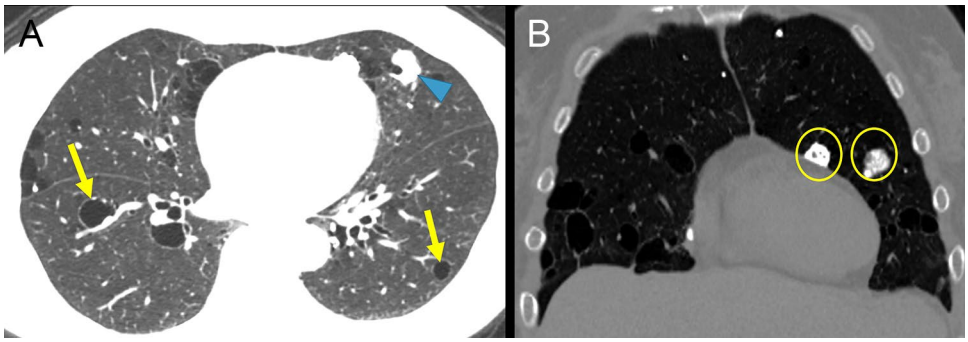

Fig. 23 61-year-old woman with biopsy-proven pulmonary amyloidosis. CT chest with axial (**A**) and coronal (**B**) images demonstrate bilateral cysts (arrow) and nodules (arrowhead). Note the calcification in the nodules on coronal CT (circle)

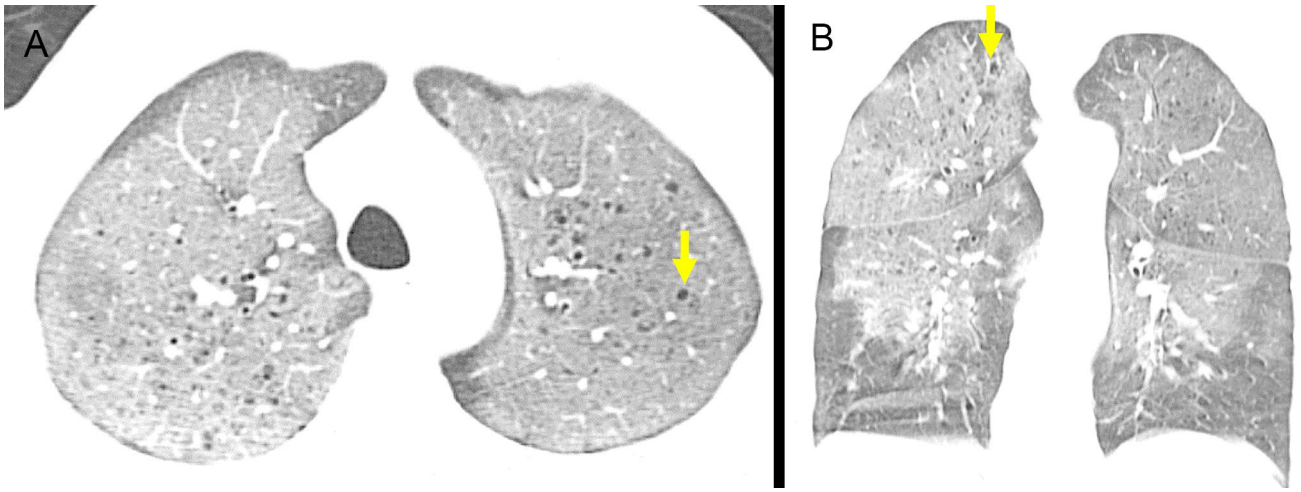

Fig. 24 21-year-old man with HIV/AIDS presented with shortness of breath and fever. Axial (**A**) and coronal (**B**) CT chest images demonstrate bilateral ground-glass opacities with subpleural sparing and an upper lung predominance. Note multiple tiny thin-walled cysts (arrow) associated with ground-glass

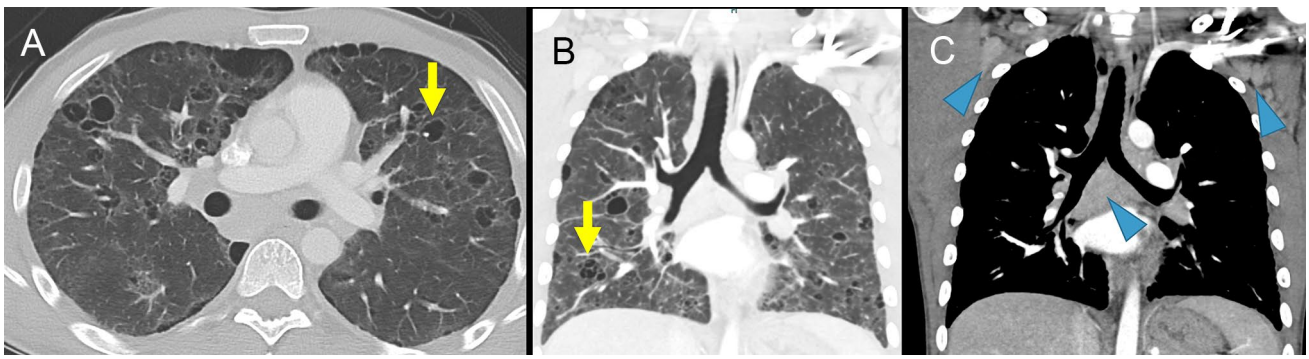

Fig. 25 33-year-old man with multicentric Castleman's disease without HIV. Axial (**A**) and coronal (**B**, **C**) CT of the chest demonstrates bilateral cysts in peribronchovascular distribution (arrow) with mid to lower lung predominance. Also note the enhancing mediastinal and axillary lymphadenopathy (arrowhead)

(D) CLD with ground glass and nodules

(i) Lymphocytic Interstitial Pneumonia (LIP)

LIP is a lymphoproliferative disorder arising from a spectrum of pathological abnormalities involving the mucosa-associated lymphoid tissues [34]. Histologically, LIP demonstrates diffuse interstitial cellular infiltrates predominantly by lymphocytes, plasma cells, and histiocytes, resulting in widening of alveolar and interlobular septa [35]. Most LIP patients are women with an age range of 40 to 70 years. LIP exhibits a strong association with systemic diseases including autoimmune diseases such as Sjogren syndrome or systemic lupus erythematosus [35].

CT usually demonstrates bilateral typical thin-walled cysts in the background of GGO. Cysts are generally perivascular in a mid to lower lung distribution (Fig. 25).

Conclusion

Pulmonary cysts and cysts mimics are a common finding in clinically asymptomatic and symptomatic individuals. Distinguishing between a true cyst and cyst mimic is a crucial step in distinguishing between non-CLD (incidental cysts vs cyst mimics) and CLD. CLD's represent a diverse spectrum of pathological process and are summarized in Table 2. Over the past decade, several advances have been achieved in our understanding of CLD, including underlying pathophysiology as well as improvements in clinical treatments. In this review, we provide an imaging primer as well as a systemic approach (Fig. 26) to identifying features of CLD, with the goal of aiding the radiologist in diagnosing CLD and optimizing management in patients with CLD, as earlier recognition of disease and treatment is associated with better outcomes.

Table 2 Clinical summary of common cystic lung diseases

Cystic Lung Disease	Patient characteristics	Cyst distribution	HRCT association	Clinical association
LAM	Female predominance	Diffuse	Thin-walled cysts, no GGO or nodule	Tuberous sclerosis, hamartomas in other organs
LCDD	Often with plasma cell dyscrasias	Variable, Often diffuse	Septal thickening, no GGO, can have nodules	lymphoproliferative disorders
BHD	Autosomal dominant inheritance	Lower lung zone, paramediastinal predilection	Multiple cysts, no specific GGO or nodule pattern	Skin fibrofolliculomas, renal tumors, FLCN gene mutation
Cystic neoplasm	Often adenocarcinomas	Primary (can be anywhere), metastatic (random and diffuse)	Cystic masses, possibly with GGO or nodules depending on the neoplasm type	Primary lung cancer (cystic variety), some genetic syndromes (DICER-1 and Cowden syndrome) can cause pleuropulmonary blastomas and increased risk for pulmonary adenocarcinoma with cystic spaces
NF-CLD	4th or 5th decade, earlier in tobacco users	Upper lung predominant	Basilar interstitial lung disease	NF-1, spontaneous pneumothorax
LCH	Commonly affects young adults who smoke	Upper and mid lung zones, sparing costophrenic angles	Nodules (which may cavitate), cysts, GGO in early disease	Lung cancer, BRAF-mutation predisposes to secondary malignancy (often hematological)
Amyloidosis	Female, 6th decade	Peribronchovascular or subpleural, mid and lower lung zones	Nodules, calcified lesions	Sjögren syndrome, lymphoproliferative disease
PJP	Immunocompromised, CD4 < 200 cells/mm3	Upper lung predominance	Diffuse GGO (often sparing lower lung zones)	HIV/AIDS, immunosuppression (for example; bone marrow transplant recipients)
LIP	Female, 4th-6th decade	Lower lung zones	GGO, peribronchovascular nodules	autoimmune diseases (Sjögren syndrome, Lupus. Castleman disease), rarely in HIV/AIDS

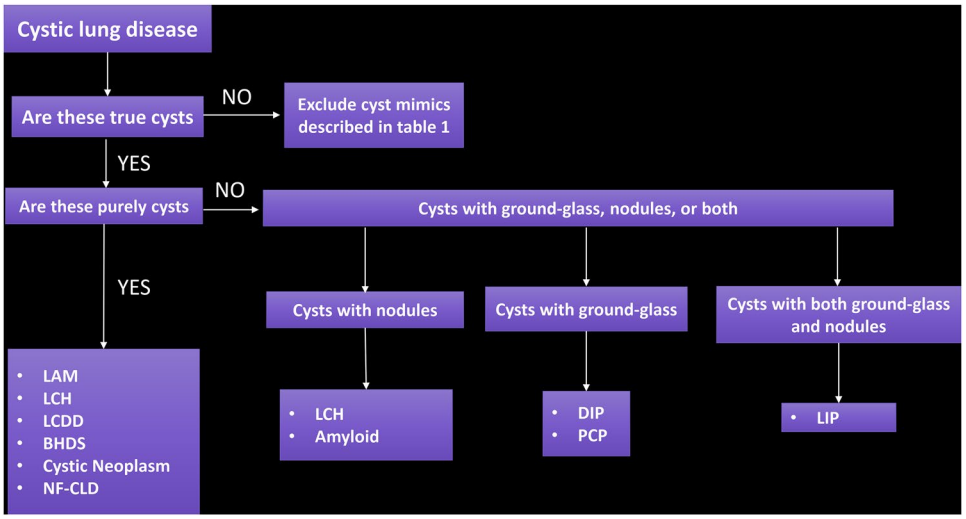

Fig. 26 Flow chart summary

Author Contributions MB, SB, MN: Conceptualize and wrote the layout MB, SB, MN: Images contribution CW, CS, KO: Original Draft CW, CS, KO, MB, SB, MN: Revision and finalization of manuscript CW, CS, KO, MN: Figure legend generation and table generation.

Data Availability No datasets were generated or analysed during the current study.

Compliance with Ethical Standards

Conflict of Interests The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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