Review Article

Diffuse cystic lung diseases: Imaging spectrum and diagnostic approach using high-resolution computed tomography

Priya Singh, Amit K. Verma, Gaurang Pandey

Department of Radiodiagnosis, King George Medical University (KGMU), Lucknow, Uttar Pradesh, India

ABSTRACT

The lung cyst is an air-containing lucent area surrounded by thin imperceptible walls. Other lucent lung lesions like centrilobular emphysema, cavity, cystic bronchiectasis, honeycomb cyst, and pneumatoceles are close mimics of a lung cyst on high-resolution computed tomography (HRCT). Various diseases with multiple lung cysts throughout both the lungs are classified as diffuse cystic lung diseases (DCLDs). HRCT is considered the imaging of choice for diagnosis of such diffuse cystic lung diseases. Common DCLDs like lymphangioleiomyomatosis, Birt–Hogg–Dubé syndrome (BHS), Langerhans cell histiocytosis (LCH), lymphocytic interstitial pneumonia (LIP), and desquamative interstitial pneumonia (DIP) can be confidently diagnosed on HRCT without further requirement of histopathological confirmation. The imaging also helps in differentiation of uncommon DCLDs and exclusion of the mimics. This review describes a simple algorithmic approach for DCLDs on HRCT based on scrutinizing the cyst's distribution, size, and shape, background parenchymal changes, and its correlation with clinical features and extrapulmonary imaging findings.

KEY WORDS: Cystic lung disease, high resolution computed tomography, imaging

Address for correspondence: Dr. Amit K. Verma, Assistant Professor (Radiodiagnosis), KGMU, Lucknow - 226 003, Uttar Pradesh, India.
E-mail: drverma.gilbert25@gmail.com

Submitted: 19-Jan-2022 **Accepted:** 29-May-2022 **Published:** 25-Oct-2022

INTRODUCTION

According to the Fleischner Society nomenclature, a lung cyst is a well-defined, air-containing structure within a thin, smooth wall (usually <2 mm in thickness).[1] Contrary to the cyst in other organs, which contain fluid, the lung cyst contains air, but occasionally it may have fluid or solid material.[2] Histopathology resembles the radiological features and shows it as a circumscribed air-filled space surrounded by an epithelial or fibrous wall of variable thickness.[1] Check valve mechanism causing dilatation of distal airspaces, ischemia with necrosis of air space walls, and airway destruction by proteases are the possible pathophysiological mechanism responsible for formation of the lung cyst. Plain chest radiograph is often not very helpful in the detection of smaller lung cysts as the radiographic findings are very subtle. High-resolution computed tomography (HRCT) is the modality of choice for the identification of lung cysts. It helps in excluding lung cysts from other air-containing lung lesions and differentiating different types of diffuse cystic lung diseases.

Depending on pathology, cysts in the lung can be focal, localized, or diffuse. Focal and localized cysts

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/lungindia.lungindia_44_22

How to cite this article: Singh P, Verma AK, Pandey G. Diffuse cystic lung diseases: Imaging spectrum and diagnostic approach using high-resolution computed tomography. Lung India 2022;39:553-61.

are often incidental and a part of the normal aging process. This spectrum also includes some congenital aberrations (bronchogenic cyst and congenital pulmonary airway malformations) or a sequela of other pathological conditions (post-traumatic or post-infective). Diffuse cystic lung diseases (DCLDs) represent multiple cysts scattered in both the lungs, randomly or in a specific pattern, with or without background parenchymal changes. Therefore, a detailed knowledge of DCLDs is very crucial for early diagnosis and management. This state-of-the-art review will give a comprehensive description of various DCLDs with a diagnostic algorithm focused on HRCT appearance and background parenchymal changes in context of clinical course.

LUNG CYST MIMICS: DEFINITION AND DIFFERENTIATION

Air-containing lesions like cystic bronchiectasis, centrilobular emphysema, bulla, cavity, honeycomb cyst, and pneumatoceles have a significant overlap in the imaging features and are often confused with cystic lung diseases. Therefore, exclusion of such overlapping mimics is very crucial to reach a definitive diagnosis of DCLDs [Figure 1].

Bronchiectasis is the localized and irreversible dilatation of the bronchial tree. It is usually associated with infections (acute, chronic, or recurrent), genetic disorders (like cystic fibrosis), or fibrosis. On HRCT, pathological airways appear ballooned, usually exceeding 2 cm in diameter. Visualizing the branching appearance of bronchi with classical tram track and signet ring sign may help differentiate bronchiectasis from the lung cysts. The cluster of grape appearance of the airways may be seen in the region of bronchiectasis.[1] Dynamic scanning may aid differentiation as cystic bronchiectasis can increase in size on inspiration, whereas lung cysts usually remain the same during different phases of respiration. Other ancillary findings like tree in bud appearance of peripheral airways, mucus impaction, volume loss, mosaic perfusion, and air trapping may further aid in diagnosis of bronchiectasis over the lung cyst.

Emphysema is characterized by permanent and abnormal dilation of airways distal to the terminal bronchiole with associated destruction of their walls. Out of different types, centrilobular and sometimes paraseptal emphysema are the closest mimics of lung cysts. On HRCT, an identifiable thin imperceptible wall in pulmonary emphysema is an essential feature that differentiates it from the cystic lung diseases. Increased lung volume and lucency, an upper lobes predominant distribution and a central dot sign representing the pulmonary artery further helps confident detection of emphysema, even though the advanced stage of cystic lung disease with coalescence of the cyst is often challenging to differentiate from emphysema.[1]

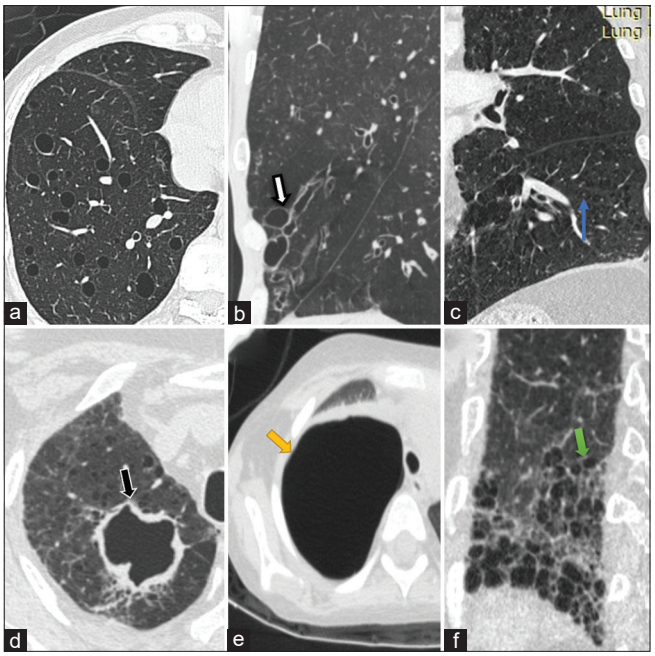

Figure 1: Lung cyst mimics. (a) Cyst: Multiple air-containing lesions having smooth and thin wall. (b) Cystic bronchiectasis: Tubular and cystic dilatation of bronchi (white arrow) with branching pattern. (c) Emphysema: Areas of decreased lung attenuation having thin imperceptible walls and a central dot representing pulmonary artery branch (blue arrow). (d) Cavity: An air-filled lesion having thick and irregular wall (black arrow). (e) Pneumatocele- A large air-filled lesion (yellow arrow) caused by *Staphylococcus pneumonia*. (f) Honeycomb cysts: Multiple well-defined small cystic spaces having thick shared walls and a multi-layered appearance with subpleural and lower lobe predominance (green arrow)

Cavity is a lesion with a thick irregular wall (generally more than 4 mm) that may form within pulmonary consolidation, a mass, or a nodule. Pulmonary cavities can be congenital or secondary to infection, malignancy, previous trauma, and non-infective granulomatous pathology (as in rheumatoid nodules). The wall thickness, characteristics of its inner lining (whether smooth or irregular) and other pulmonary and extrapulmonary findings enable differentiation between the two entities.[1] Cavities may have contents like fluid, mycetoma, or debris. Knowledge of the duration of the disease further helps to narrow the diagnosis. Acute pulmonary cavities generally occur secondary to infections while chronic cavitary diseases may be secondary to chronic illnesses, such as tuberculosis, primary lung cancers, metastasis and autoimmune disorders.

Pneumatoceles is a transient parenchymal cyst with a thin wall formed secondary to lung infection, trauma, aspiration of chemical or barotrauma. They are more commonly seen in children. Acute bacterial pneumonia caused by *Staphylococcus aureus*, *Klebsiella*, *Pneumococcus*, or *Pneumocystis jirovecii* sometimes produces pneumatoceles. Imaging appearance of the pneumatocele is often similar to a cyst; however, they are fewer in number and associated with adjacent consolidation or ground glass opacity as a sign

of prior or resolving infection. Moreover, pneumatoceles are transient and mostly resolve on follow-up.

In **honeycomb cysts**, cystic changes may also be seen in fibrosing interstitial pneumonia in the form of honeycombing. Honeycombing represents the late stage of interstitial lung disease with severe fibrosis, and is characteristic of usual interstitial pneumonia. On HRCT, honeycomb cysts are characterized by well-defined cystic space of size ranging from 3 to 10 mm, having thick shared walls and a multi-layered appearance. They are clustered in the subpleural region, often with a basal predominance.[1] Associated architectural distortion, traction bronchiectasis, and volume loss can be seen. The imaging findings in combination of disease course is quite diagnostic and differentiates them from the cystic lung diseases.

COMMON DIFFUSE CYSTIC LUNG DISEASE

Lymphangioleiomyomatosis: Lymphangioleiomyomatosis (LAM) is a rare progressive disorder that occurs predominately in women of childbearing age. It is characterized by cystic destruction of lungs, renal angiomyolipomas and lymphatic obstruction. Amongst two different forms, the sporadic lymphangioleiomyomatosis (S-LAM) is more common compared to the rare form which is associated with tuberous sclerosis (TSC-LAM).[3] About 30% of women and 10%–15% of men with tuberous sclerosis develop TSC-LAM, but S-LAM occurs exclusively in women.[4,5] In both the types of LAM, there is mutational inactivation of TSC1 or TSC2 genes leading to an uncontrolled proliferation of atypical smooth muscle cells along the terminal bronchiole, alveolar wall, lymphatics, and pulmonary vessels.[6] Obstruction of a terminal bronchiole by these abnormal cells is considered as a responsible factor for dilatation of distal air spaces and lung parenchymal destruction causing cyst formation.[7]

Imaging plays a most important role in the diagnosis. Though not very sensitive, plain radiographs of the chest may show nonspecific reticular-interstitial pattern with increased lung volume. On HRCT, multiple symmetrically and uniformly distributed well-defined, thin-walled rounded, 2–10 mm cysts are seen in bilateral lungs [Figures 2 and 3].[8] The number and size of the cyst increases with progression of the disease. Intervening residual lung parenchyma in LAM is usually normal; however, small centrilobular nodules and ground glass opacities might develop in the highly cellular form. Air trapping is absent in LAM, except in the advanced stage with total cystic replacement of the lung. Rupture of a subpleural cyst causing recurrent pneumothorax (70% patients) is a common presentation, requiring urgent intervention. Large and recurrent chylous effusions are also not uncommon. Other pulmonary manifestation includes pulmonary hemorrhage (in 8%–14%) producing ground glass attenuation, dilatation of thoracic duct, and enlarged mediastinal ganglia.[9] Imaging diagnosis of LAM is further supported by the presence of ancillary abdominal findings, which include renal angiomyolipomas (in 20%–54%), lymphangioleiomyoma, and chylous ascites. Raised serum VEGF-D levels with typical imaging features makes the diagnosis of LAM almost certain.[10] Confirmation of LAM can be done on surgical lung biopsy with histology showing diffuse proliferation of atypical smooth muscle cells along the wall of cysts, which are positive for smooth muscle actin and melanoma-associated (HMB-45) antigens on immunohistochemistry. Lung transplantation is the definitive treatment of LAM in significantly symptomatic patients.

Birt–Hogg–Dubé syndrome- Birt–Hogg–Dubé syndrome (BHD) is a rare inherited autosomal dominant disorder characterized by a triad of multiple pulmonary cysts, skin lesions, and renal neoplasm of different histological types.[11] Germline mutations in the tumor suppressor gene *FLCN* located on chromosome 17p11.2, encoding the protein folliculin, is responsible for BHD.[12,13] BHD usually affects the 20–85 years age group individuals with no sex predilection. Most patients present clinically with multiple skin lesions and symptoms due to recurrent pneumothorax.

HRCT findings show multiple pulmonary cysts which are irregular in shape and variable in size seen in more than 85% of patients with BHD [Figures 4 and 5]. Cyst in BHD are thin-walled, frequently have lobulated, lentiform, or elongated shape, and internal septations with lower zone, subpleural and paramediastinal predominance. There is a 50-times higher risk of spontaneous pneumothorax in patients with BHD syndrome than in the general population. Lung parenchyma surrounding the lung cyst is normal in BHD syndrome. Compared to LAM, cysts in BHD are less in number, more oversized, irregular in shape and usually do not increase in size with time.[14] Data from different studies suggest that compared to other cystic lung disease, BHD does not usually progress to respiratory insufficiency.[15]

Renal involvement (about 30%) in BHD represents multifocal or bilateral renal tumors which are usually oncocytoma, chromophobe, or papillary type of renal cell carcinoma.[16] Fibrofolliculoma and trichodiscomas are common hamartomatous skin lesions associated with BHD. Thus, HRCT finding of multiple pulmonary cysts having a family history of similar disease or recurrent pneumothorax associated with renal and skin findings predict the diagnosis of BHD syndrome. Finally, a genetic evaluation is required to confirm the diagnosis.[17] As there is no definitive treatment for BHD syndrome, management in BHD includes thoracostomy followed by pleurodesis for recurrent pneumothorax and treatment of renal tumors.

Langerhans cell histiocytosis: Langerhans cells are a type of dendritic cell which is a part of our immune system. Their function is to phagocytize foreign antigens and activate T

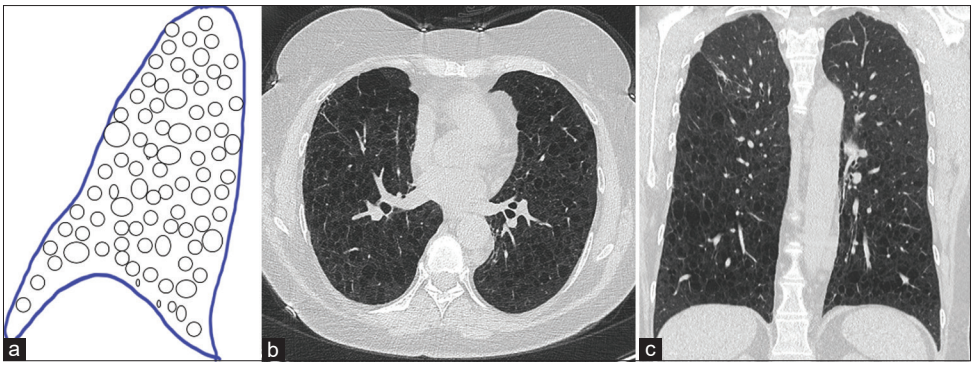

Figure 2: Lymphangioleiomyomatosis. (a) Schematic diagram, (b) and (c) Axial and coronal high resolution CT images demonstrates diffuse thin-walled cysts with intervening normal lung parenchyma. Cysts are round or ovoid in shape and relatively small and uniform in size. There is diffuse involvement with no lobar predominance

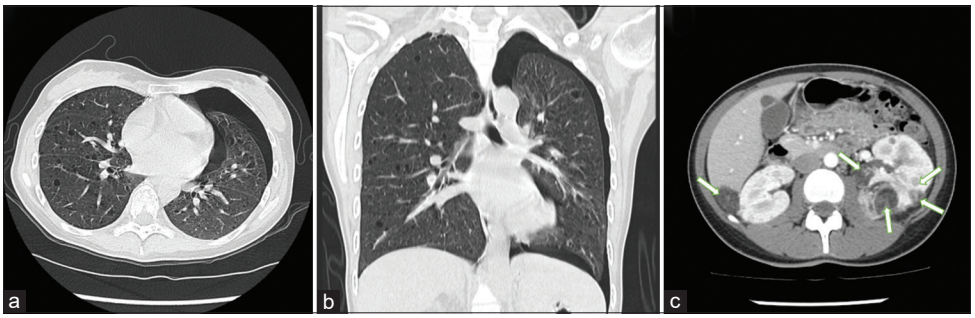

Figure 3: Lymphangioleiomyomatosis. (a and b) Axial and coronal high resolution CT images demonstrates multiple small thin-walled cyst with intervening normal lung parenchyma associated with left pneumothorax. (c) Contrast enhanced CT axial image demonstrates fat containing and heterogeneously enhancing lesions (white arrows) in bilateral kidneys suggestive of renal angiomyolipomas

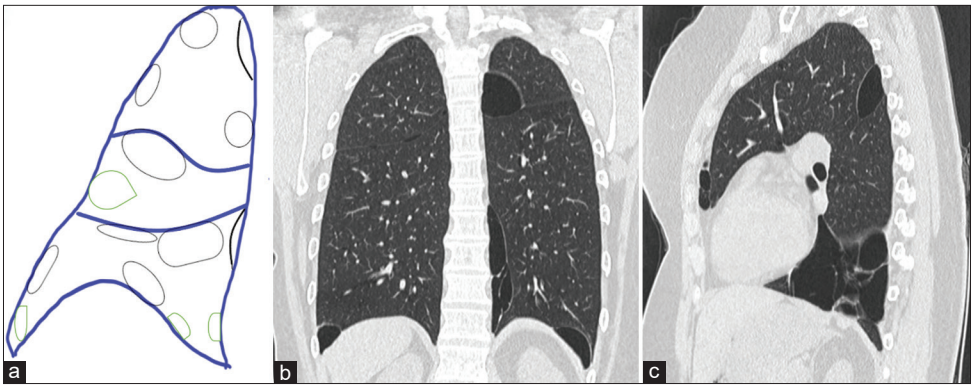

Figure 4: Birt–Hogg–Dubé syndrome. (a) Schematic diagram, (b) and (c) Coronal and sagittal high-resolution CT images demonstrates scattered thin-walled cysts with intervening normal lung parenchyma. Cysts are irregular in shape and variable in size. There is subpleural, para-mediastinal and lower lobe predominance of cysts

or B cell immunity. Langerhans cell histiocytosis (LCH) is an abnormal proliferation of non-malignant monoclonal Langerhans cells that can involve either one or multiple organs.[18] The disease is exclusively seen in smokers in 3rd to 4th decade of their life with no definitive gender predilection.[19] LCH has a characteristic gradual temporal progression with a different appearance in the imaging features at a different stage of evolution.

In the early stage, small and irregular-shaped nodules develop in the bilateral lung. In addition to nodules, irregular cavitation within the nodules and air-filled cysts develops with disease progression.[20,21] In advanced stage, cysts predominate with few or minimal residual nodules. Extensive cysts can give a honeycombing appearance with reticulations. Cysts in LCH are non-uniform in size (1–20 mm) and shape, ranging from round or oval shape to bizarre configurations like bilobed, septated, or cloverleaf. Similarly, the cyst can have variable wall thickness, depending on the degree of cavitation. There is an apicobasal gradient in distribution of the nodules and cyst. These are more predominant in bilateral upper and middle

lobe with relative sparing of medial tips of medial lobe or lingula, lower lobes, and costophrenic angles. Thus, HRCT findings of multiple bizarre-shaped cysts with upper lobe predominance associated with background of nodules and cavitating nodules in a young smoker suggest pulmonary Langerhans cell histiocytosis (PLCH) [Figures 6 and 7]. Extrapulmonary manifestations of the LCH include cystic bone disease, diabetes insipidus, and skin changes (nearly in 20% of patients).[22] Transbronchial or surgical lung biopsy is confirmatory in suspicious cases. Smoking cessation usually improves clinical symptoms and may produces spontaneous regression of the nodular lesions.[22] Lung transplantation is required in cases with rapid deterioration.

Lymphocytic interstitial pneumonia: Lymphocytic interstitial pneumonia **(**LIP) has been classified as a type of interstitial lung disease associated with immune system dysregulation and is characterized by lymphocytic infiltration along the alveolar septa.[23,24] FB and LIP can be idiopathic or associated with some immunological abnormality. Sjögren's syndrome (SS) has been described as the most common association of LIP. Other less commonly associated autoimmune disorders include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Hashimoto thyroiditis, or immunodeficiency states such as HIV and common variable immune deficiency.[24]

Women are more commonly affected compared to men, and the mean age at onset of symptoms is between 40 and 70 years. HRCT in LIP shows a mixture of ground glass opacities, irregular centrilobular and subpleural nodules, septal thickening, and multiple bilateral lung cysts [Figures 8 and 9]. Sometimes lymphadenopathy can also be seen, while pleural effusion and consolidation are rare. Ground glass opacities (GGO) are the predominant finding in the early stage of the disease. With disease progression, GGO gradually subsides, and bilateral cysts predominate in chronic LIP. 68% of the LIP patients have cysts on HRCT. Cyst in LIP vary in shape, are thin-walled, and fewer in number than LAM and LCH.[25] The size of these cysts is variable but usually <3 cm and are distributed diffusely in both lungs with subpleural and peri-broncho-vascular predominance.[25,26] In Sjögren's syndrome, 58%–90% of patients have HRCT findings, with cystic changes seen in 12%–46%.[27] Thus, cystic lung disease associated with SS or any other immunological disease favours LIP. Histopathological evaluation is required to confirm the diagnosis. Conversion of LIP to lymphoma is infrequent, although described; therefore, any consolidation or GGO increasing in size on follow-up needs a biopsy to rule out malignant transformation.[28] The prognosis usually depends on underlying systemic or autoimmune disease. Most of the patients respond to steroids and immunosuppressive drugs, while few progresses to fibrosis, end-stage lung disease, and respiratory failure.

Desquamative interstitial pneumonia: Desquamative interstitial pneumonia (DIP) is a rare type of idiopathic interstitial pneumonia associated with smoking. DIP primarily occurs in smokers in about 90% of the cases in their 4th or 5th decade of life. Other conditions like exposure to organic dust, drugs, viral illness, and autoimmune

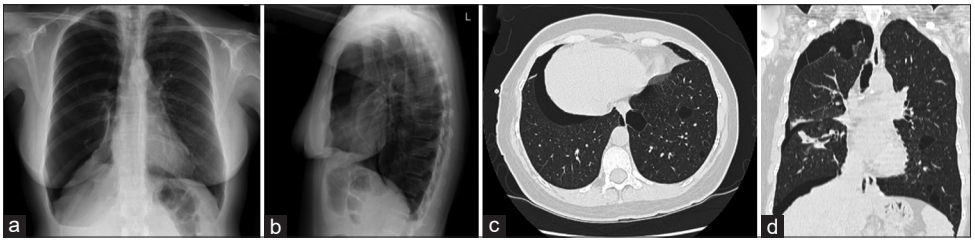

Figure 5: Birt–Hogg–Dubé syndrome. (a and b) Chest radiograph in PA and lateral view demonstrates right pneumothorax and fine linear opacities in left lung. (c and d) Axial and coronal high resolution CT images demonstrates right pneumothorax and few irregular shaped subpleural cyst in left lung with intervening normal lung parenchyma

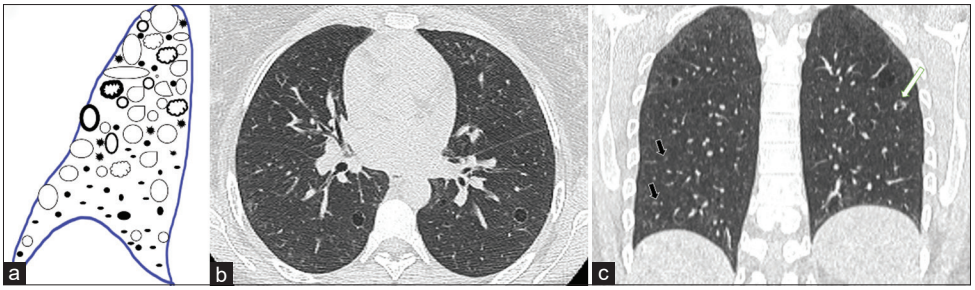

Figure 6: Langerhans cell histiocytosis. (a) Schematic diagram, (b) and (c) Axial and coronal high-resolution CT images demonstrates thick- (white arrow) and thin-walled cysts of various shape and sizes associated with multiple centrilobular nodules (black arrows). There is relative upper lobe predominance. Cyst in Langerhans cell histiocytosis are characteristically bizarre shaped, spare costophrenic angles and medial tips of middle lobe/lingula

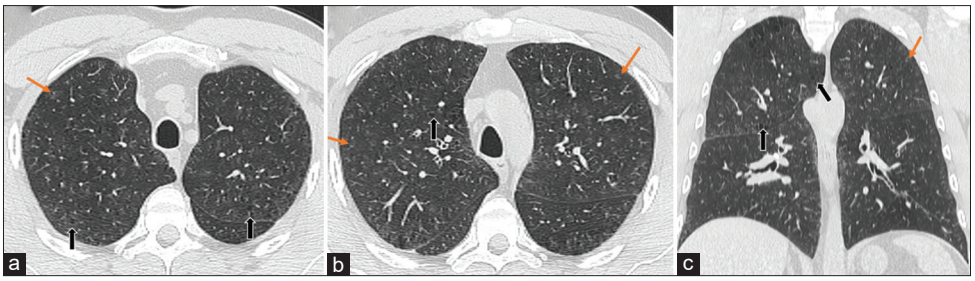

Figure 7: Langerhans cell histiocytosis. (a), (b) Axial, and (c) coronal high-resolution CT images demonstrate multiple irregular nodules (coloured arrows) with cavitation forming small cysts (black arrows) with upper lobe predominant distribution

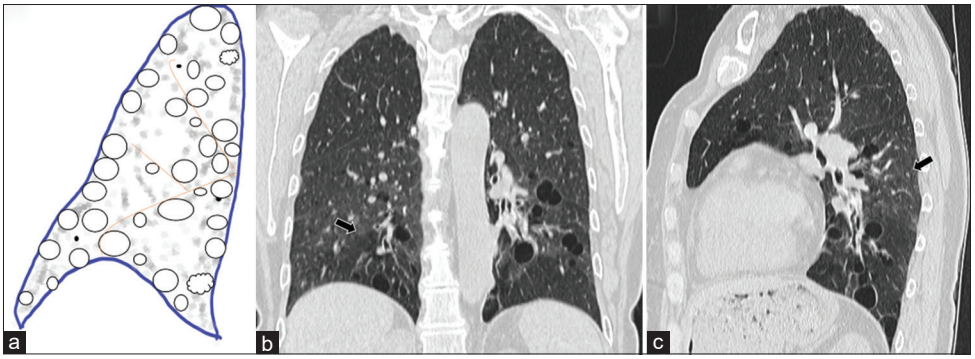

Figure 8: Lymphocytic interstitial pneumonia. (a) Schematic diagram, (b) and (c) Coronal and sagittal high-resolution CT images demonstrates few thin-walled cysts of variable size and shape in bilateral lungs with subpleural and peri-broncho-vascular predominance. Associated patchy areas of ground glass opacification are present in bilateral lower lobes (black arrows)

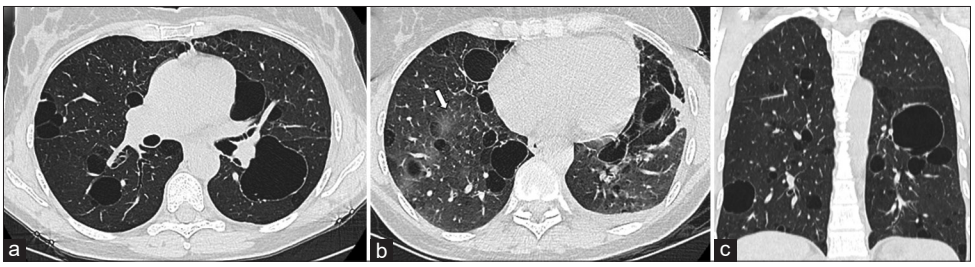

Figure 9: Lymphocytic interstitial pneumonia. (a), (b) Axial, and (c) coronal high-resolution CT images demonstrates few thin-walled cysts of variable size and shape in bilateral lungs with subpleural and peri-broncho-vascular predominance Associated patchy areas of ground glass opacification (white arrow) are present in bilateral lungs

disorders are reported as rare associations that can potentially cause DIP.[29] Males are more commonly affected compared to females. The disease is considered as a more severe pathomorphological continuum of respiratory bronchiolitis–associated interstitial lung disease (RB-ILD). RB-ILD and DIP are similar to each other both on histopathology and imaging, the only difference being the diffuse nature of DIP and bronchiocentric distribution of RB-ILD.[29] Dyspnoea and dry cough are usual clinical presenting symptoms.

The most characteristic finding on HRCT is patchy or diffuse GGOs, which have a predilection for the peripheral and lower lobe of the lungs[30] [Figure 10]. Small cysts may develop within areas of GGOs in 32%–75% of patients and usually involve less than 10% of the lung area.[31] Cysts in DIP are usually less than 2 cm in size, uniform, thin-walled, and are surrounded by GGO. Dilatation of bronchioles and alveolar ducts are considered to be responsible for cyst formation. Coexisting centrilobular emphysema can be seen while reticulations and honeycombing are minimal in DIP.[32] Thus, a middle-aged smoker with HRCT findings of uniform thin-walled cyst interspersed within areas of GGO is characteristic for DIP and differentiates it from smoking-associated LCH where cysts are more bizarre shaped, upper lobe predominant, and rarely associated with GGO. The primary treatment for DIP is smoking cessation which often leads to regression of lung lesions.

UNCOMMON DIFFUSE CYSTIC LUNG DISEASE

Amyloidosis: Although uncommon, diffuse cystic lung diseases can also develop in amyloidosis, where lung cysts are multiple (usually >10), round or lobulated, thin-walled,

and variable in size [Figure 11].[33,34] Other pulmonary findings include GGO, fibrosis, tracheal wall thickening, and lymphadenopathy. Pulmonary amyloidosis is also associated with Sjögren's syndrome, LIP, and mucosa-associated lymphoid tissue lymphoma.[34] The confirmation of amyloid-associated cystic lung disease requires a histopathological diagnosis.

Light chain disease: HRCT findings of light chain deposition disease (LCDD) include multiple small-to-large-sized round cyst in a diffuse distribution associated with reticulonodular opacities.[35]

Hypersensitivity pneumonitis: Few scattered cysts may be seen in up to 13% of subacute and rarely in the chronic phase of hypersensitivity pneumonitis (HSP).[36] These cysts are seen interspersed in predominant lung findings of GGOs, centrilobular nodules, areas of decreased lobular attenuation, and fibrosis. The cysts are few, uniform, and small in size, and resemble that of LIP.

Pneumocystis pneumonia: Characteristic HRCT finding for pneumocystis pneumonia (PCP) includes bilateral symmetrical GGOs predominantly affecting central part of the lung with subpleural sparing. Smaller group of the patients (nearly 10%–34%) may also show a predominant cystic pattern associated with or without pneumothoraxes on HRCT common in the upper lobes.[37]

Cystic metastasis: Metastasis from peripheral sarcomas, angiosarcoma and mesenchymal tumors can show cystic changes and are complicated by pneumothorax. Low-grade mucosa-associated lymphoid tissue lymphomas rarely present as cystic lesions.[38] Thus, in patient with known malignancy, the appearance of a new cyst on HRCT is worrisome and requires a biopsy to rule out metastasis.

Recurrent respiratory papillomatosis: Recurrent respiratory papillomatosis (RRP) is caused by the human papillomavirus and is characterized by multiple squamous cell papilloma, which mainly affects the upper airways.[39] Rarely diffuse lung cysts can develop, especially in cases with bronchopulmonary spread.[40] The pulmonary spread in RRP shows thin-walled cysts, multiple cavities, and nodules predominant in lower-zone on HRCT.

Approach to diffuse cystic lung disease on HRCT

The common DCLDs can be classified based on the presence or absence of associated parenchymal abnormalities and/or the predominant abnormalities on HRCT thorax. Further characterization is based on patterns of the cyst distribution, shape and size of the cysts, their wall thickness, extrapulmonary imaging findings, in context with clinical course of the disease and its association. A simple algorithmic approach for diagnosis and differentiation of various common and uncommon diffuse cystic lung diseases (DCLDs) is mentioned in Figure 12.

LAM and BHD are amongst the DCLDs with multiple cysts and normal background parenchyma. These cysts are nearly of similar size, in diffuse and symmetrical

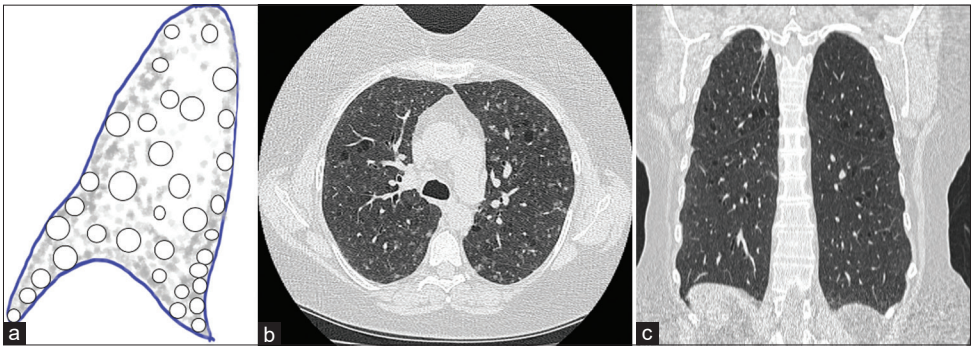

Figure 10: Desquamative interstitial pneumonia. (a) Schematic diagram, (b) and (c) Coronal and sagittal high-resolution CT images demonstrates small uniform round-shaped thin-walled cysts interspersed with patchy areas of ground glass opacities. Ground glass opacities in desquamative interstitial pneumonia shows peripheral and lower lobe predominance

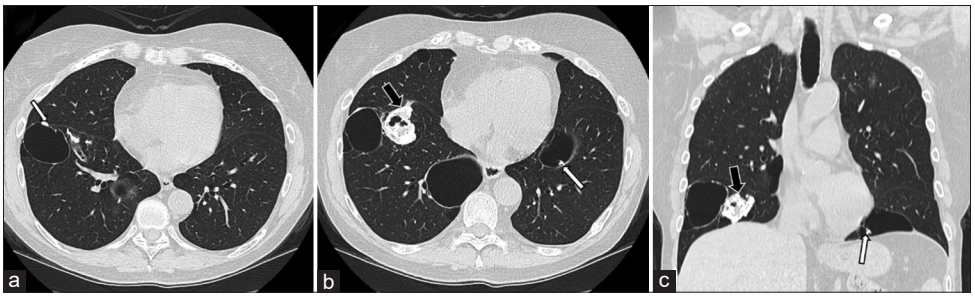

Figure 11: Amyloidosis. (a), (b) Axial and (c) coronal high-resolution CT images demonstrates few thin-walled cysts of variable size in bilateral lungs associated with eccentric calcified nodule (white arrows). Note a partially calcified cavitating nodule (black arrows) in right lung

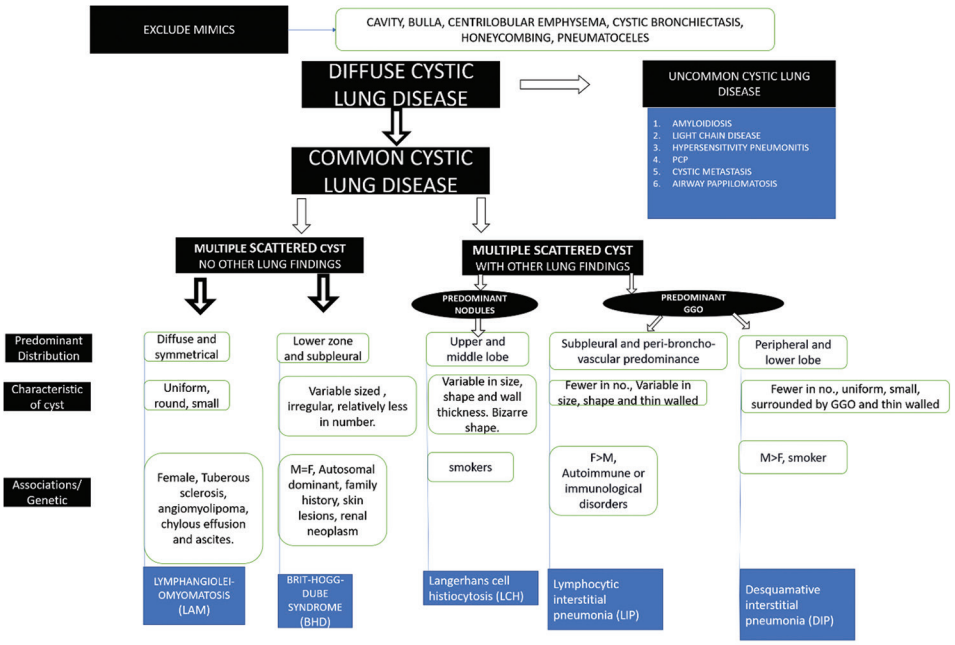

Figure 12: A simple algorithmic approach for diagnosis and differentiation of diffuse cystic lung diseases (DCLDs)

distribution in the LAM. While in BHD, the cysts are of variable sizes with subpleural, peri-fissural and lower lobe predominant. Unlike LAM and BHD, other common DCLDs (LCH, LIP and DIP) also have background parenchymal changes in association with multiple lung cysts. Nodules are the predominant parenchymal abnormality in LCH, while GGOs are more common in LIP and DIP. The cysts are of bizarre shape and in upper lobe predominance distribution in LCH, while more uniform, in peri-broncho-vascular and lower lobe predominance in LIP, and DIP. Other DCLDs have thin cyst walls but can have variable shapes. Further correlation of imaging diagnosis with patient's sex, smoking history, family history, clinical history of autoimmune disorders, and extrapulmonary findings is extremely important for a definitive diagnosis. In uncommon DCLDs, multiple cysts are rare presentation, and diagnosis is usually made with clinical correlation. Therefore, we believe that a proper knowledge of the disease spectrum and clinical course, put together in this HRCT algorithmic approach can facilitate the diagnostic differentiation of the common DCLDs which usually leads to a definitive diagnosis without the need of histological confirmation.

CONCLUSION

Diffuse cystic lung diseases are a group of complex disorders that often have an overlapping clinical presentation, but different underlying pathological processes. On HRCT, they can have a spectrum of imaging findings with variable degrees of overlap, making their diagnosis difficult. However, considering the cyst's characteristics, distribution, ancillary and background parenchymal findings, in association with clinical context and associated extrapulmonary findings, HRCT still remains the imaging of choice for the diagnosis of common diffuse cystic lung diseases (LAM, BHD, LCH, LIP, and DIP). Awareness of the spectrum of imaging findings of DCLDs on HRCT and using a stepwise approach can be extremely helpful in narrowing the differentials and to reach a definitive diagnosis.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Hansell D, Bankier A, MacMahon H, McLoud T, Müller N, Remy J. Fleischner society: Glossary of terms for thoracic imaging. Radiology 2008;246:697-722.
2. Cantin L, Bankier A, Eisenberg R. Multiple cystlike lung lesions in the adult. Am J Roentgenol 2010;194:W1-W11.
3. Henske E, McCormack F. Lymphangioleiomyomatosis — a wolf in sheep's clothing. J Clin Investig 2012;122:3807-3816.
4. Costello L, Hartman T, Ryu J. High frequency of pulmonary lymphangioleiomyomatosis in women with tuberous sclerosis complex. Mayo Clin Proc 2000;75:591-94.
5. Adriaensen M, Schaefer-Prokop C, Duyndam D, Zonnenberg B, Prokop M. Radiological evidence of lymphangioleiomyomatosis in female and male patients with tuberous sclerosis complex. Clin Radiol 2011;66:625-628.
6. Carsillo T, Astrinidis A, Henske E. Mutations in the tuberous sclerosis complex gene TSC2 are a cause of sporadic pulmonary lymphangioleiomyomatosis. Proc Natl Acad Sci 2000;97:6085-90.
7. Corrin B, Liebow A, Friedman P. Pulmonary lymphangiomyomatosis: A review. Am J Pathol 1975;79:348-82.
8. Pallisa E, Sanz P, Roman A, Majó J, Andreu J, Cáceres J. Lymphangioleiomyomatosis: Pulmonary and abdominal findings with pathologic correlation. Radiographics 2002;22(suppl_1):S185-98.
9. Avila N, Dwyer A, Moss J. Imaging features of lymphangioleiomyomatosis:

Diagnostic pitfalls. Am J Roentgenol 2011;196:982-6.
10. Gupta N, Vassallo R, Wikenheiser-Brokamp K, McCormack F. Diffuse cystic lung disease. Part I. Am J Respir Crit Care Med 2015;191:1354-66.
11. Birt A. Hereditary multiple fibrofolliculomas with trichodiscomas and acrochordons. Arch Dermatol 1977;113:1674-7.
12. Khoo S, Bradley M, Wong F, Hedblad M, Nordenskjöld M, Teh B. Birt-Hogg-Dubé syndrome: mapping of a novel hereditary neoplasia gene to chromosome 17p12-q11.2. Oncogene 2001;20:5239-42.
13. Kennedy J, Khabibullin D, Henske E. Mechanisms of pulmonary cyst pathogenesis in Birt–Hogg–Dube syndrome: The stretch hypothesis. Semin Cell Dev Biol 2016;52:47-52.
14. Tobino K, Hirai T, Johkoh T, Kurihara M, Fujimoto K, Tomiyama N, *et al*. Differentiation between Birt–Hogg–Dubé syndrome and lymphangioleiomyomatosis: Quantitative analysis of pulmonary cysts on computed tomography of the chest in 66 females. Eur J Radiol 2012;81:1340-6.
15. Lee J, Jeon M, Song J, Chae E, Choi J, Kim G, *et al*. Birt-Hogg-Dubé syndrome in Korean: Clinicoradiologic features and long-term follow-up. Korean J Intern Med 2019;34:830-40.
16. Gupta N, Sunwoo B, Kotloff R. Birt-Hogg-Dubé syndrome. Clin Chest Med 2016;37:475-86.
17. Menko F, van Steensel M, Giraud S, Friis-Hansen L, Richard S, Ungari S, *et al*. Birt-Hogg-Dubé syndrome: Diagnosis and management. Lancet Oncol 2009;10:1199-206.
18. Abbott G, Rosado-de-Christenson M, Franks T, Frazier A, Galvin J. From the archives of the AFIP. Radiographics 2004;24:821-41.
19. Friedman P, Liebow A, Sokoloff J. Eosinophilic granuloma of lung. Medicine 1981;60:385-96.
20. Colby T, Lombard C. Histiocytosis X in the lung. Hum Pathol 1983;14:847-56.
21. Brauner M, Grenier P, Tijani K, Battesti J, Valeyre D. Pulmonary Langerhans cell histiocytosis: Evolution of lesions on CT scans. Radiology 1997;204:497-502.
22. Vassallo R, Ryu J, Schroeder D, Decker P, Limper A. Clinical outcomes of pulmonary Langerhans'-cell histiocytosis in adults. N Engl J Med 2002;346:484-90.
23. Johkoh T, Müller N, Pickford H, Hartman T, Ichikado K, Akira M, *et al*. Lymphocytic interstitial pneumonia: Thin-section CT findings in 22 patients. Radiology 1999;212:567-72.
24. Swigris J, Berry G, Raffin T, Kuschner W. Lymphoid interstitial pneumonia. Chest 2002;122:2150-64.
25. Cha S. Lymphoid interstitial pneumonia: Clinical features, associations and prognosis. Eur Respir J 2006;28:364-9.
26. Watanabe M, Naniwa T, Hara M, Arakawa T, Maeda T. Pulmonary manifestations in Sjögren's syndrome: Correlation analysis between chest computed tomographic findings and clinical subsets with poor prognosis in 80 patients. J Rheumatol 2009;37:365-73.
27. Nicholson A. Lymphocytic interstitial pneumonia and other lymphoproliferative disorders in the lung. Semin Respir Crit Care Med 2001;22:409-22.
28. Yousem S, Colby T, Gaensler E. Respiratory bronchiolitis-associated interstitial lung disease and its relationship to desquamative interstitial pneumonia. Mayo Clinic Proc 1989;64:1373-80.
29. Lynch D, Travis W, Müller N, Galvin J, Hansell D, Grenier P, *et al*. Idiopathic interstitial pneumonias: CT features. Radiology 2005;236:10-21.
30. Akira M, Yamamoto S, Hara H, Sakatani M, Ueda E. Serial computed tomographic evaluation in desquamative interstitial pneumonia. Thorax 1997;52:333-7.
31. Attili A, Kazerooni E, Gross B, Flaherty K, Myers J, Martinez F. Smoking-related interstitial lung disease: Radiologic-clinical-pathologic correlation. Radiographics 2008;28:1383-96.
32. Chew K, Clarke M, Dubey N, Seet J. Nodular pulmonary amyloidosis with unusual, widespread lung cysts. Singapore Med J 2013;54:e97-e99.
33. Baqir M, Kluka E, Aubry M, Hartman T, Yi E, Bauer P, *et al*. Amyloid-associated cystic lung disease in primary Sjögren's syndrome. Respir Med 2013;107:616-621.
34. Colombat M, Stern M, Groussard O, Droz D, Brauner M, Valeyre D, *et al*. Pulmonary cystic disorder related to light chain deposition disease. Am J Respir Crit Care Med 2006;173:777-80.
35. Franquet T, Hansell D, Senbanjo T, Remy-Jardin M, Müller N. Lung cysts in subacute hypersensitivity pneumonitis. J Comput Assist Tomogr 2003;27:475-8.
36. Boiselle P, Crans C, Kaplan M. The changing face of Pneumocystis carinii pneumonia in AIDS patients. Am J Roentgenol 1999;172:1301-9.
37. Ioachimescu O, Sieber S, Walker M, Rella V, Kotch A. A 35-year-old woman with asthma and polycystic lung disease. Chest 2002;121:256-60.
38. Yogi A, Miyara T, Ogawa K, Iraha S, Matori S, Haranaga S, *et al*. Pulmonary metastases from angiosarcoma: A spectrum of CT findings. Acta Radiologica 2015;57:41-6.
39. Soldatski I, Onufrieva E, Steklov A, Schepin N. Tracheal, bronchial, and pulmonary papillomatosis in children. Laryngoscope 2005;115:1848-54.
40. Zawadzka-Głos L, Jakubowska A, Chmielik M, Bielicka A, Brzewski M. Lower airway papillomatosis in children. Int J Pediatr Otorhinolaryngol 2003;67:1117-21.