Spectrum of Cystic Lung Disease and its Mimics

Kathleen Jacobs MD and Elizabeth Weihe MD
UC San Diego Medical Center, Department of Radiology
No Financial Disclosures
Learning Objectives

1. Review the pathologic and radiologic definition of a lung cyst
2. Illustrate classic and distinguishing HRCT features of cystic lung disease
3. Review common mimics of cystic lung disease
4. Discuss the underlying pathology of each entity
Definition of a Lung Cyst

- **Pathology:** Any round, circumscribed space surrounded by an *epithelial or fibrous wall* of variable thickness.

- **Radiography or CT:** *Round* parenchymal *lucency* or low attenuating area with a *well-defined interface* with normal lung. Cysts are usually thin-walled but can have variable wall thickness (<2 mm).

Diffuse Cystic Lung Disease

- **Syndromic**
  - Neurofibromatosis
  - Tuberous Sclerosis (TS)/ Lymphangioleiomyomatosis (LAM)
  - Birt Hogg Dube

- **Smoking-Related**
  - Pulmonary Langerhans Histiocytosis
  - Desquamative Interstitial Pneumonia

- **Immune-Mediated**
  - Chronic Hypersensitivity Pneumonitis
  - Lymphocytic Interstitial Pneumonia

- **Post-Infectious**
  - Pneumocystis Pneumonia
Neurofibromatosis Related Diffuse Lung Disease (NF-DLD)

- Specific to Neurofibromatosis type-1
- Ground glass (50%)
- Basilar reticulation/fibrosis (37%)
- Cysts (25%); upper lobe predominant
- Emphysema (25%)
- Other thoracic findings: cutaneous/subcutaneous neurofibromas, ribbon deformity of ribs, focal thoracic scoliosis, posterior vertebral scalloping
- NF-1 has increased sensitivity to cigarette smoke with early development of emphysema-like changes which may be a risk factor for NF-ILD
- Pathology: Lymphoplasmocytic inflammation and fibrosis in the alveolar septa, similar to NSIP

Cutaneous neurofibromas

Small cysts

Subpleural, basilar reticulation
Sporadic Lymphangioleiomyomatosis (S-LAM)

- Almost exclusively in women of childbearing years
- Diffuse thin wall ovoid cysts surrounded by normal lung
- Cysts measure 2-5 mm (up to 25-30 mm)
- Uniform cyst distribution
- Interlobular septal thickening (interstitial edema from lymphatic obstruction)
- Associated with chylous effusion, recurrent pneumothorax, lymphadenopathy
- Pathology: Smooth muscle proliferation in the pulmonary interstitium (affects vessels, airways, lymphatics, alveolar septa, pleura)

Note:
--Uniform distribution of cysts
--Predominantly small cysts

Bilateral apical pneumothoraces
Tuberous Sclerosis Complex (TSC) Associated LAM

- TSC is autosomal dominant, characterized by hamartomas, seizures, mental retardation
- 26% of women with TSC have LAM
- Usually less severe than S-LAM
- Thin wall cystic lesions 2-5 mm in size (up to 25-30 mm)
- Associated with
  - Cortical tubers/subependymal nodules
  - Renal angiomyolipomas
  - Facial angiofibroma
- Pathology: Same as S-LAM

Note:
--Same morphology as S-LAM, but less severe
--Normal intervening lung parenchyma
Birt-Hogg-Dube Syndrome

• Rare, autosomal dominant syndromes characterized by skin hamartomas, renal tumors (chromophobe RCC), pulmonary cysts (80-90%)
• Thin walled cysts
  – Vary widely in size
  – Enlongated/oval, multiseptated
  – Subpleural
  – Basal predominant
• Associated bullous emphysema
• Increased risk of PTX
• Pathology: Folliculin gene mutation leads to alveolar de-arrangement

Note:
--Variable-sized cysts, some with septated appearance (arrow)
--Many cysts are subpleural
--Basal predominance
Pulmonary Langerhans Histiocystosis (PLCH)

• +Smoking history

• Symmetric, upper lobe predominant cysts
  – Irregular small cysts (<10mm), some with thicker walls
  – Intervening parenchyma with nodules, architectural distortion, reticulation

• Temporal heterogeneity

• Pathology: Reactive polyclonal process induced by antigens in cigarette smoke → peribronchiolar infiltration of specific histiocytes called Langerhans cells (Birbeck granules) → stellate interstitial nodules → cavitation → thick/thin wall bizarre cysts

• Treatment: Smoking cessation and steroids

Note:
--Variable cyst morphology, but majority small cysts
--Some cysts with thicker walls (arrow)
--Upper lobe predominant
Nodules in addition to cysts
Desquamative Interstitial Pneumonitis (DIP)

- Strong association with smoking
- Small cysts (< 2cm) represent focal bronchiolectasis and dilated alveolar ducts
- Associated with patchy ground glass opacities (80%)
- Basilar and peripheral distribution
- Pathology: Pigmented macrophages fill the alveolar spaces
- Treatment: Worse prognosis than RB-ILD; ~66% will stabilize or improve with steroid therapy

Note:
--Background of ground glass opacities
--Basilar predominance
Chronic Hypersensitivity Pneumonitis

- More common in nonsmokers
- Thin-walled cysts, few in number: ~10% in subacute stage and ~40% in chronic stage
- More common to see ground glass opacities, centrilobular nodules, air trapping (head-cheese sign)
- Mid/upper lobe predominant fibrosis (no or minimal honeycombing as opposed to UIP)
- Type III/Type IV hypersensitivity response
- Pathologic hallmark: Chronic interstitial infiltrates
  - Lymphocytes, plasma cells, occasional multinucleated giant cell and histiocytes
- Treatment: Exposure removal and steroids

Air trapping

Scattered, small cysts

Note:
--Background of subpleural reticulation/fibrosis
Lymphocytic Interstitial Pneumonia

- Associated with Sjogrens, AIDS, Lupus, DIP
- Cystic airspaces in 68%, variable size 1-30mm, thin-walled
- Lower lobe predominant
- Fewer cysts than LAM/PLCH
- Associated with LAD, bronchovascular thickening, poorly defined centrilobular and subpleural nodules
- Absence of pleural effusion
- Pathology: Diffuse interstitial proliferation with polyclonal small lymphocytes/plasma cells

Note:
--Scattered, lower lobe cysts
Pneumocystis Pneumonia

- Associated with T-cell immunodeficiency
- Ground glass opacities characteristic (+/- crazy paving)
- Cysts/pneumatoceles in 10-34%
  - Small, thin walled
  - Can coalesce into bizarre shapes
- LAD (< 10%)
- Pleural effusions rare
- Spares the periphery
- Pathology: Peri-bronchiolar inflammation results in obstruction with cyst formation via a ball-valve effect
- Treatment: Steroid and antibiotics (Bactrim)
  - Improve or resolve within 5 months of treatment

Boddu et al. *Pathology Research International* 2017; 1-17.
Lee et al. *J of Computer Assisted Tomography* 2002;26:5-12.
Note:
--Upper lobe cysts and ground glass opacities
--Relative subpleural sparing
Focal Cystic Disease: Pneumatocele

- Post-infectious pneumatocele associated with Staph Aureus (most common) and Strep Pneumo
- Usually transient but can last for years
- Pathology: Combination of parenchymal necrosis and ball-valve mechanism (airway obstruction by inflammatory exudates)

Quigley at el. AJR 1988;150:1275-1277.
Extensive basilar consolidation with areas of cavitation

Bronchiectasis

Large pneumatocele
Focal Cystic Disease: Congenital Pulmonary Airway Malformation

- Mixed solid/cystic mass
- Type 1 – large cysts
- Type 2 – numerous small cysts (0.5-1.5 cm)
- Type 3 – microcysts
- Type 4 – large cysts with mass effect
- No systemic vascular supply (as opposed to pulmonary sequestration)
- Distinguish from other congenital focal cystic disease: congenital lobar emphysema (involved lung is expanded) and pulmonary sequestration.
- Pathology: Bronchiolar proliferation and columnar/epithelium lined micro- and macrocysts

Boddu et al. *Pathology Research International* 2017; 1-17.
Increased lucency of the right lower lobe with multiple small cysts
Mimics of Cystic Lung Disease

- Emphysema/Bullae
- Cavitary Nodule/Consolidation
- Honeycombing
- Bronchiectasis
Cyst versus Bullae/Cavity

- Bullae (>1cm) and Blebs (<1 cm): cystic air spaces contiguous with the pleura and often associated with bullous emphysema

- Cavity: a gas-filled space, seen as a lucency or low attenuation area, within pulmonary consolidation, mass, or nodule.
  - Usually thicker walled (>4mm)

Tracheobronchopapillomatosis with cavitating nodules (arrow)
Cavitary/Cystic Metastatic Disease

- Cavitary mets rare <5%
- Usually epithelial origin (squamous)
- Peripheral
- Feeding vessel sign
- Mesenchymal (sarcomas) less frequent
  - Can produce thin-walled cysts difficult to distinguish from LAM
  - Stain for HMB45 and CD34 in mets

Lee et al. *J of Computer Assisted Tomography* 2002;26:5-12.
Emphysema
- imperceptible wall
- polygonal shaped lucency

Honeycombing
- stacked lucencies
- architectural distortion
Bronchiectasis

e.g: Cystic Fibrosis
-Lucencies contiguous with airways (arrows)
-adjacent pulmonary artery
Conclusion

• Differential diagnosis for cystic lung disease can be narrowed by considering the following:
  – Cyst or Mimic?
  – Distribution (diffuse vs focal, lobar predominance)
  – Size/shape of cysts
  – Patient sex/age/history (young female?, smoker?)
  – Secondary imaging findings (ground glass opacities?, skin nodules?)
Author Contact

Kathleen Jacobs: kjacobs@ucsd.edu