Cystic Lung Disease: Not Just LAM

Stephen Hobbs, MD

Lung Cysts
- Definition:
  - Thin-walled,
  - Well-defined,
  - Air-containing lesion
- Mimics:
  - Emphysema
  - Cystic bronchiectasis
  - Cavitary Nodules
  - Honeycombing

Cysts vs Mimics
- Cysts as the primary abnormality
  - Lymphangioleiomyomatosis
  - Pulmonary Langerhans Cell Histiocytosis
  - Lymphoid Interstitial Pneumonia
    - Birt-Hogg-Dube
    - Neurofibromatosis
    - Amyloid
    - Light Chain Deposition Disease
    - Cystic Metastases
Lymphangioleiomyomatosis

- Proliferation of smooth muscle cells in the bronchioles, small vessels and lymphatics
- Perivascular epithelioid Cell Tumor, PEComa
- Leads to obstruction of the bronchioles, lymphatics and vessels

Lymphangioleiomyomatosis

- Sporadic Form
  - S-LAM
  - Young women only
  - ~50,000
- Tuberous Sclerosis Complex
  - TSC-LAM
  - Males or females
  - 250,000

Lymphangioleiomyomatosis

- Symptoms:
  - Cough
  - Dyspnea
  - Pneumothorax
  - Upwards of 80% lifetime risk
  - Mean time to diagnosis is 3-5 years
  - VEGF-D >800pg/mL

Lymphangioleiomyomatosis

- Treatment:
  - Progesterone
  - Tamoxifen
  - Antiestrogen agents
  - Radiotherapy
  - Oophorectomy
  - Variable outcome
  - Progression typical
  - May require transplant
  - Can recur in transplanted lungs
  - Diffuse, thin-walled cysts
  - Regular in shape
  - Progressively larger as disease progresses
  - Occasional small nodules or groundglass
  - Multifocal Multinodular Pneumocyte Hyperplasia
  - Lymphatic involvement
    - Adenopathy
    - Chylous Effusions
  - Pneumothorax – up to 80%
Lymphangioleiomyomatosis

Tuberous Sclerosis
- Autosomal dominant
- Triad of
  - Seizures
  - Mental Retardation
  - Adenoma Sebaceum
- Angiomyolipomas
- Cardiac rhabdomyomas
- Retinal phacomas

PLCH
- Proliferation of Langerhans cells in the bronchiolar subendothelium resulting in granuloma formation and progressive destruction with bronchiole dilation.
Systemic LCH
- Various organ involvement such as bones and pituitary
  - Histocytosis X
  - Eosinophilic granuloma
  - Letterer-Siwe
  - Hand-Schüller-Christian
- Less frequent pulmonary involvement
  - Children
  - Worse Prognosis
  - No relationship with smoking

PLCH
- Young adults
  - 20 – 40 years old
  - Prior male predilection now more even
- Smoking >90%

PLCH
- Symptoms:
  - Cough
  - Dyspnea
  - Pneumothorax
    - Up to 20%
  - Weight loss
  - Fever
  - Night Sweats
  - Anorexia

PLCH
- Treatment:
  - Smoking cessation
  - Steroids
    - 50% of patients stabilize
    - 25% progress
    - 25% regress

PLCH
- Early:
  - Small nodules
  - Centrilobular predominant
  - Upper lung predominant
  - Costophrenic angle sparing
  - Anterior RML and distal lingual sparing
- Mid:
  - Nodules will progressively cavitate
- Late:
  - Cavitating nodules result in cysts
  - Bizarre and irregular

PLCH
- Early Nodular Disease
- Mixed nodules and cysts
Late Cystic Disease

Lymphocytic Interstitial Pneumonia
- Alveolar interstitium is permeated by polyclonal lymphocytes and plasma cells.
- Idiopathic disease is rare
- Most frequently underlying Sjögren syndrome
- Other causes:
  - Immunodeficiency, bone marrow transplantation, and HIV (especially children)

LIP
- Treatment:
  - Progesterone
  - Tamoxifen
  - Antiestrogen agents
  - Radiotherapy
  - Oophorectomy
  - Variable outcome
- Progression typical
- May require transplant
- Can recur in transplanted lungs

LIP
- Groundglass opacity
- Poorly defined centrilobular nodules
- Reticular Opacity
- More commonly Cysts
- Up to 80%
  - Lower lung predominant
  - Perivascular
LIP

- Non Cystic

Birt-Hogg-Dube

- Autosomal-Dominant
- Folliculin gene
  - Tumor suppressor
- Fibrofolliculomas
  - Face, Neck, Upper chest
- Renal Tumors
  - Renal Cell Carcinomas, Oncocytomas
- Colonic polyps, chorioretinal disease

- Pulmonary Cysts:
  - Thin walled
  - Lower lung predominant
  - Elongated
  - Along pleura and mediastinum
**Neurofibromatosis**

- Variable Thoracic Manifestations
- Ribbon Ribs
- Rib notching
- Neurofibromas
  - Cutaneous
  - Intercoastal
  - Mediastinal

- Pulmonary Disease:
  - Rare
  - 25% of cases are cysts
  - More commonly
    - Upper lung bullae
    - Lower lung fibrosis

**Protein Deposition Diseases**

- Amyloid
  - Usually lambda
  - Congo Red Positive

- LCDD
  - Usually kappa
  - Congo Red Negative

- Both
  - Clinically Similar
  - High Association with multiple myeloma or macroglobulinemia
  - Renal Failure
  - Death >75% for both

- Amyloid
  - Nodules
    - SPN 60%
    - Calcified in 1/3rd
  - Interlobular Septal thickening
  - Honeycombing
  - Groundglass
  - Lymphadenopathy
  - Tracheobronchial thickening
  - Lung cysts
    - Frequent relation to LIP
Amyloid

Cystic Metastasis

- Need appropriate history of a primary malignancy
- Most frequently epithelial origin
  - Leiomyosarcoma
  - Angiosarcoma
  - Synovial cell sarcoma
  - Epithelioid cell sarcomas
  - Endometrial stromal sarcoma

Summary

- PLCH
  - Smoker
  - Centrilobular nodules progressing to bizarre cysts
  - CPA sparing
- LAM
  - Premenopausal women
  - Diffuse uniform cysts, chylous effusions, Renal AMLs
- LIP
  - Sjogren disease
  - Lower lung, perivascular cysts
Summary

• Neurofibromatosis
  – Skin lesions, neurofibromas
  – Diffuse cysts

• Birt-Hogg-Dube
  – Skin lesions
  – Lower lung, subpleural and paramediastinal cysts
  – Renal Cell Carcinomas and Oncocytomas

• Protein Deposition
  – Multiple myelomas and macroglobulinemia
  – Nodules and cysts

• Cystic Malignancy
  – History of epithelioid sarcomas

References and Further Reading


