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Cystic Lung Lesions - The Pathologist says “My Approach is…:”

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My approach….

• Build on prior approaches
• Must include everything (almost) that results in holes in the lung
• Recognize that rad/path literature correlations very loose and confusing!
Objectives

At the end of the lecture, participants should be able

1. To define what is meant by the word “cyst” in respiratory medicine/pulmonary pathology
2. List locations of the most common cysts
3. Discriminate between cysts associated with neoplasms from those without neoplasms
4. Summarize the types of ancillary clinical testing that might be necessary in patients with cystic lung disease
Cyst- Pathology Definition

• Cyst: uni- or multi-locular epithelial lined cavity of various etiologies that contains liquid or gaseous material

• Pseudocyst- non-epithelial lined cavity
Classification of Lung Cysts

• Location

• Mural cellularity
  • None
  • Without neoplasms
  • With neoplasms
Location of Lung Cysts/Holes

- Pleural
  - Blebs
- Subpleural
  - Distal acinar emphysema/bullae
  - Honeycomb
Location of Lung Cysts/Holes

- Lymphatic/paraseptal
  - Birt - Hogg Dube (BHD)
  - LAM
- Peribronchhiolar/bronchiolocentric
  - LIP
  - PLCH
  - Smoking-related
Location of Lung Cysts/Holes

- Random
  - Amyloid/light chain deposition disease
  - Ehlers Danlos syndrome
  - COPA syndrome
  - Infection
  - Congenital
  - Age-related: 25% of pts > 75 yrs
  - Metastases
Mural Cellularity

- None
- BHD
- Ehlers Danlos syndrome
- Smoking related
- Congenital
- Age related
Birt-Hogg Dube
Ehlers Danlos
Emphysematous Holes
Ehlers Danlos: Cystic Holes
Smoking Related Diffuse Cystic Lung Disease, n=4

• ? LAM: women 31-53 yrs, mean 44 years.
• Dyspnea, cough, none with p’thorax
• 75% active smokers, 5-32 pack yrs, mean 18; one with heavy second hand smoke
• Other cystic disease excluded
• ? Pathogenesis

Gupta N et al Chest 2018:154; e31-35
Smoking Related Diffuse Cystic Lung Disease

• Different from emphysema
• Some cysts associated with small airways
• Associated findings
  • Respiratory bronchiolitis
  • Mild obliterative bronchiolitis/mural fibrosis
  • Intraluminal foam cells and mucostasis

Gupta N et al Chest 2018:154; e31-35
59 yr old woman with dyspnea, 1 ppd smoker
Extensive work up for cystic lung disease negative
27 year old woman
Asymptomatic
Motor vehicle accident
? Congenital
Mural Cellularity

- Fibrous
  - Honeycomb
  - Traumatic/post infectious
  - Bleb

- Cellular-non neoplastic
  - PLCH
  - LIP
  - COPA syndrome
? Trauma vs Infection
Bleb-Intrapleural
Distal Acinar Emphysema

Centriacinar Emphysema
Mural Cellularity

- Fibrous
  - Honeycomb
  - Traumatic/post infectious
  - Bleb

Cellular-non neoplastic
- PLCH
- LIP
- COPA syndrome
Bronchiolar centered cellular stage
LCH cells, eos, lymphs, smoker’s macs

“Cyst” Formation
Due to location, ?necrosis

Fibrosis of nodules
Paracicatricial airspace enlargement,
Endstage cystic fibrosis
Lymphocytic Interstitial Pneumonia/LIP
Lymphocytic Interstitial Pneumonia/LIP
COPA Syndrome

- Monogenic AD autoimmune disorder
- Mutations in COPA gene (encodes for α-subunit of COPA-1 protein-vesicular transport)
- Symptoms: begin in childhood, < 12 yrs
  - Arthritis
  - Pulmonary symptoms

Tsui JL et al ERJ Open Res 2018;4:00017-2018
Taveira-Silve AM et al J Med Gen 2018;0:1-5
COPA Syndrome

- Follicular bronchiolitis
- Diffuse alveolar hemorrhage +/- capillaritis
- Cysts
- Emphysema
- DIPNECH/carcinoid
- Non-UIP fibrosis

Tsui JL et al. ERJ Open Res 2018;4:00017-2018
Taveira-Silve AM et al. J Med Gen 2018;0:1-5
Mural Cellularity

- Cellular-Neoplastic
  - Metastases
    - Cellular dermatofibroma
    - DFSP
    - Endometrial stromal sarcoma
    - LAM/LAM-like change
  - Amyloid/light chain deposition (MALT lymphoma)
Metastatic Cellular Dermatofibroma

Factor XIIIa
Metastatic DFSP
Lymphangioleiomyomatosis (LAM)
Macrocysts

Microcysts

HMB45
Clear Cell Proliferation with LAM-like Change
Light Chain Deposition Disease

More fibrillar than amyloid

CR negative
Light Chain Deposition Disease

- 2/3 with multiple myeloma
- Nodules, cysts, diffuse
- Congo red negative
- Amorphous material more fibrillar than amyloid
- $K >> \lambda$
- Diffuse, worse prognosis

Kato T et al Chest 2018;153:e105-112
IHC Work-Up of Lung Cysts

• LAM: ER, PR, MART-1, HMB-45, MiTF, Beta catenin
• ESS: ER, CD10
• DF and DFSP: Factor XIIIa
• PLCH: CD1a, Langerin, S-100 protein, BRAF V600E
Clinical Work-Up of Lung Cysts

• $\alpha$-1 antitrypsin levels
• VEGF-D levels (LAM)
• Pelvic CT
• History of trauma, infection, skin lesions, smoking (incl. MJ), prior GYN surgery
• Genetic evaluation: COPA, EDS
• Serum and urine electrophoresis
No Mural Cellularity

EDS
Smoking related
Congenital
Age related
Cellular: Fibrous Walls

Bleb
Honeycomb
Post-traumatic
Post-infectious
Cellular: Non-Neoplastic

© MAYO CLINIC
Cellular: Neoplastic

LAM

Metastases
DF
DFSP
ESS
PeCOMA

Amyloid
Light Chain Deposition
Things I still don’t understand about cystic lung disease

- 30% of patients with DIP have cysts, said to be “reversible!”
- Cysts in hypersensitivity pneumonitis - 10%
Pathologist’s role

- Confirm the biopsy done for “cystic” lung disease contains cysts
- Classify the cysts
- Give differential when specific diagnosis not possible- Suggest additional testing to narrow differential
- Realize some cases still insoluble
Merci beaucoup, Nice Nice!