Birt-Hogg-Dubé (BHD) Syndrome-Associated Lung Cysts: Histopathological Analysis and Differential Diagnosis from Miscellaneous Cystic Lung Diseases

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Birt-Hogg-Dubé (BHD) Syndrome
Germline mutation of *FLCN* (folliculin: 17p.11.2)

- Lung cysts: 80-98%
- Fibrofolliculoma: 50-90%
- Kidney cancer: 20-30%
Number of papers describing BHD syndrome in science journals [PubMed]
BHD syndrome-associated kidney cancer
<multiple, hybrid tumor, chromophobe RCC >
Skin Manifestations
Fibrofolliculomamas preferentially in face & neck

Adult onset, 2-4 mm sized, no pain no itch
BHD syndrome-associated lung cysts
Pneumothorax (PTX): Major Symptom to suspect BHD syndrome

Lung cysts w/o PTX 8 (4%)

RCC 44 (22%)

PTX 143 (72%)

Unknown, others 5 (2.5%)

Histopathology of typical BHD lung cysts

I) Subpleural cyst

II) Intraparenchymal cyst
I) Histopathology of a subpleural cyst
‘Ruptured subpleural cysts’
PTX-associated remodeling → Bulla/Bleb formation

Mechanical stress-induced inflammation

Mesothelial invagination

Calretinin
BHD vs emphysematous bulla/bleb

II) Histopathology of intraparenchymal cyst

Septum-like structure, connecting bronchovascular bundle, penetrate a cyst

Complex alveolus-like structure budding on or embedded in the BHD cyst wall

mTOR pathway

BHD syndrome
Activated mTOR Signaling in BHD Lung

Possibility of an increased risk of lung cancer in BHD syndrome patients (I) Multifocal case

Possibility of an increased risk of lung cancer in BHD syndrome patients (II) Familial case

Differential diagnosis between BHD and rare cystic lung disease

- Lymphangioleiomyomatosis (LAM)
- Lymphocytic IP
- Follicular bronchiolitis
- Cystic metastases
BHD syndrome

- Skin
  - Fibrofolliculoma
- Lung
  - Cyst
  - Pneumothorax
- Kidney
  - Chromophobe RCC

Familial

LAM/TSC

- Skin
  - Angiofibroma
- Lung
  - Cyst
  - Pneumothorax
- Kidney
  - Angiomyolipoma

50%

De novo

Child onset

Adults
BHD syndrome

- Basilar subpleural
- Lentiform cysts

LAM

- Diffuse uniform distribution
- Chylous effusion

BHD syndrome

LAM
BHD syndrome

LAM

SP-A

HMB45
Recurrent pneumothoraces associated with lymphoproliferative diseases
Multiple lung cysts associated with Sjögren's syndrome
κ chain (ISH)  

λ chain (ISH)
Summary
Diagnostic clues in BHD lung cysts

- No fibrosis/inflammation
- Epithelial-mesenchymal association
- Vascular protrusion
- Near complete epithelial lining
- Pro-SPC
BHD-Net Japan
http://www.bhd-net.jp/

パート・ホッグ・デューベ症候群(Birt-Hogg-Dubé 症候群)情報ネット（BHDネット）
このサイトではBHD症候群の診療に関する情報をみなさまに発信しています。