

Cystic Lung Diseases

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HARVARD
MEDICAL SCHOOL

Postgraduate
Medical Education

Disclosure

No conflict of interest

Learning Objectives

- Identify causes of cystic lung diseases
- Awareness of linkage between cystic lung disease and genetic inheritable disorders

Cystic lung diseases

Centrilobular emphysema

Pulmonary metastasis

Subacute (?chronic) hypersensitivity pneumonitis

Desquamative interstitial pneumonia

Barotrauma/ ARDS

Pulmonary infection- pneumatoceles

Necrobiotic nodules

Light chain disease

Lymphangiomyomatosis

Langerhans cell histiocytosis

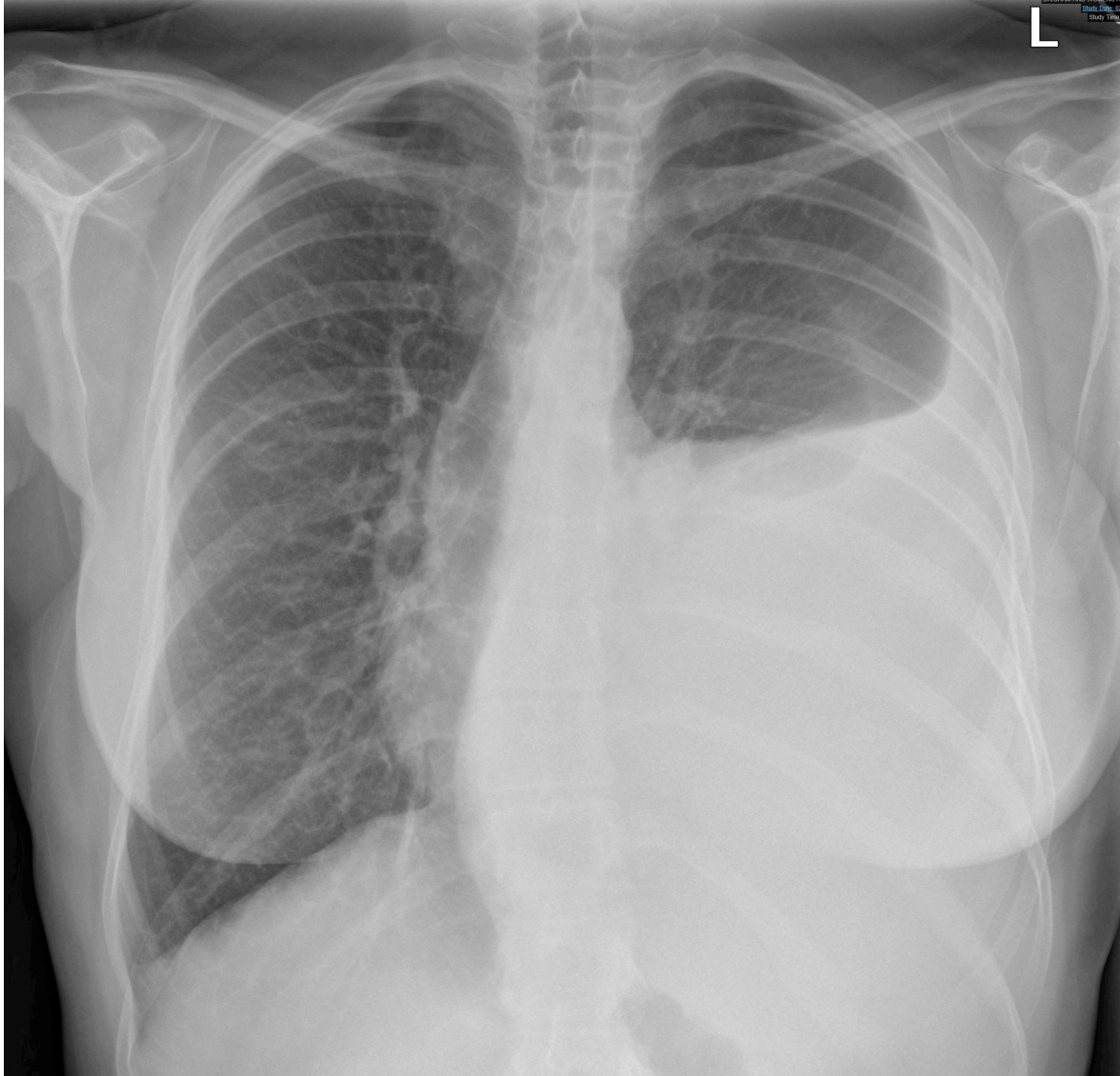
Birt Hogg Dube syndrome

Lymphoid interstitial pneumonia

Cystic lung changes in LAM



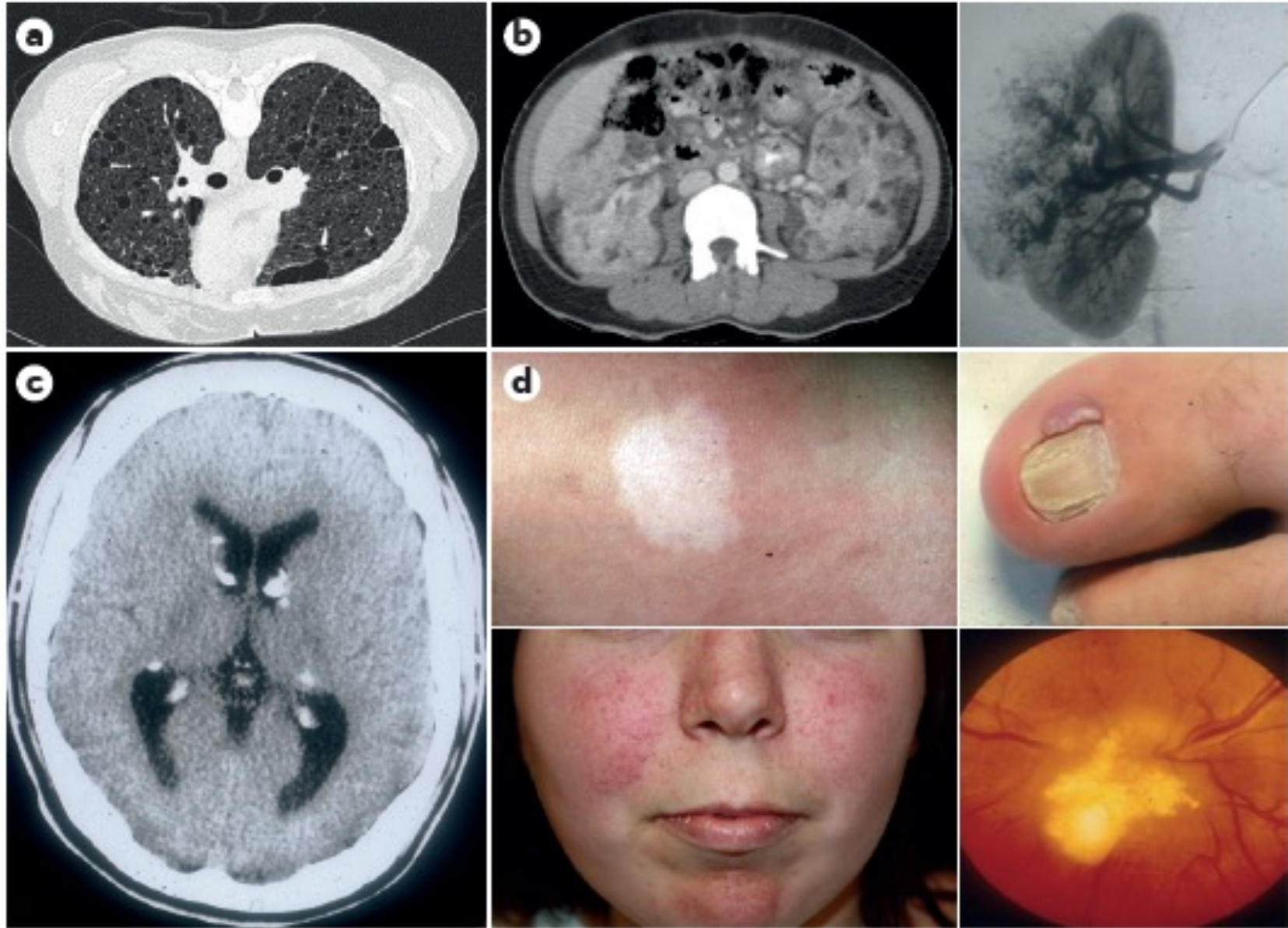
Chylous effusion



Screening for TSC

- Personal and family history
- Skin lesions
- Bilateral AML
- Brain lesions

Tuberous Sclerosis Complex



Angiomyolipoma (AML)



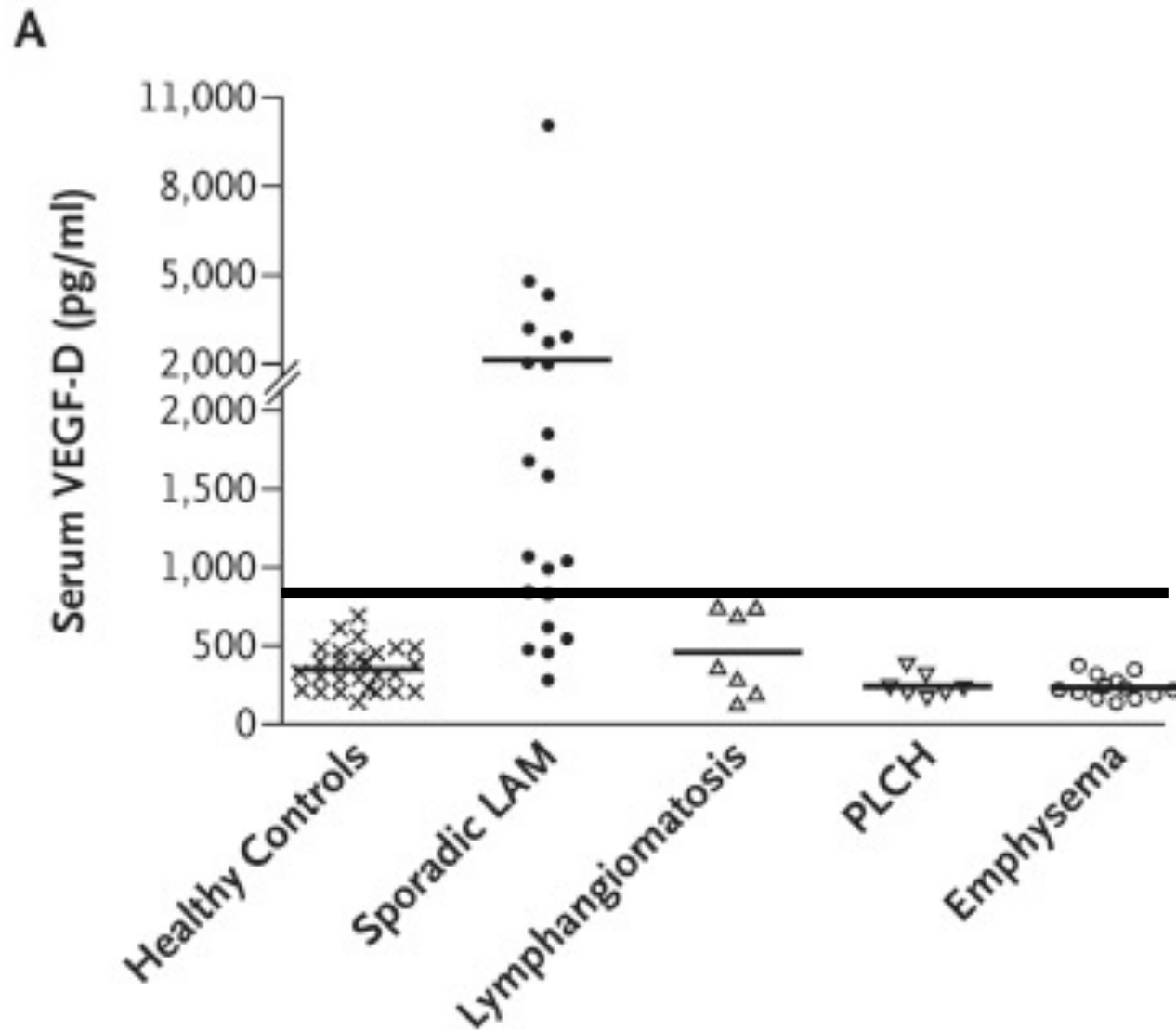
Pneumothorax



Pneumothorax

- 40% at the time of diagnosis
- 60% at some point
- Risk of recurrence high (>70%)

VEGF-D a biomarker for LAM



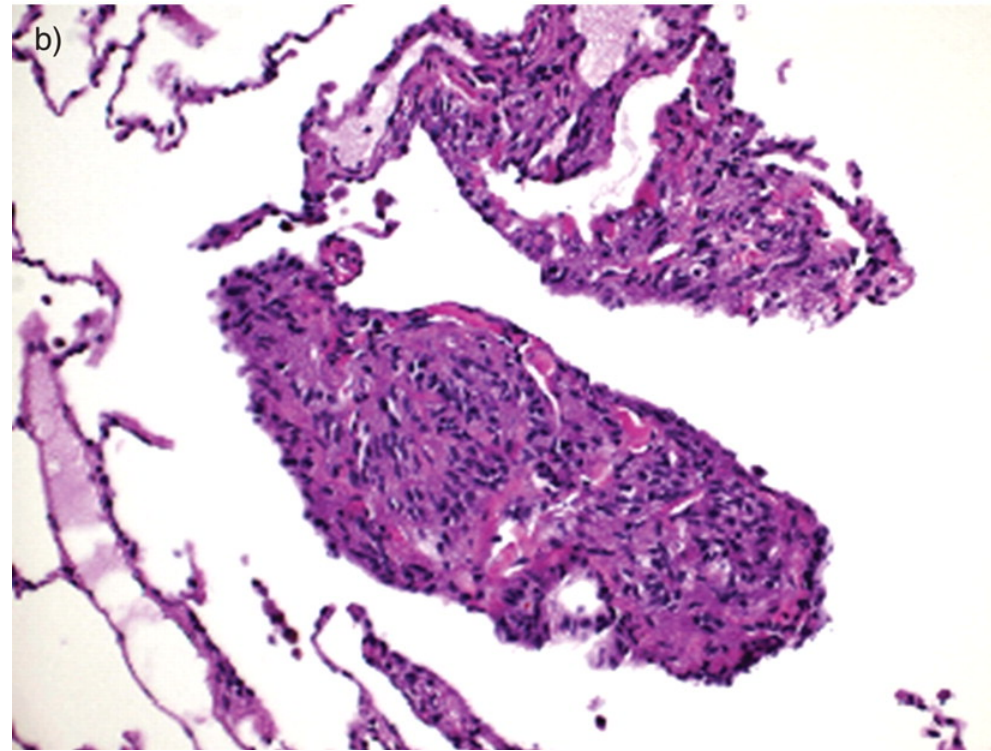
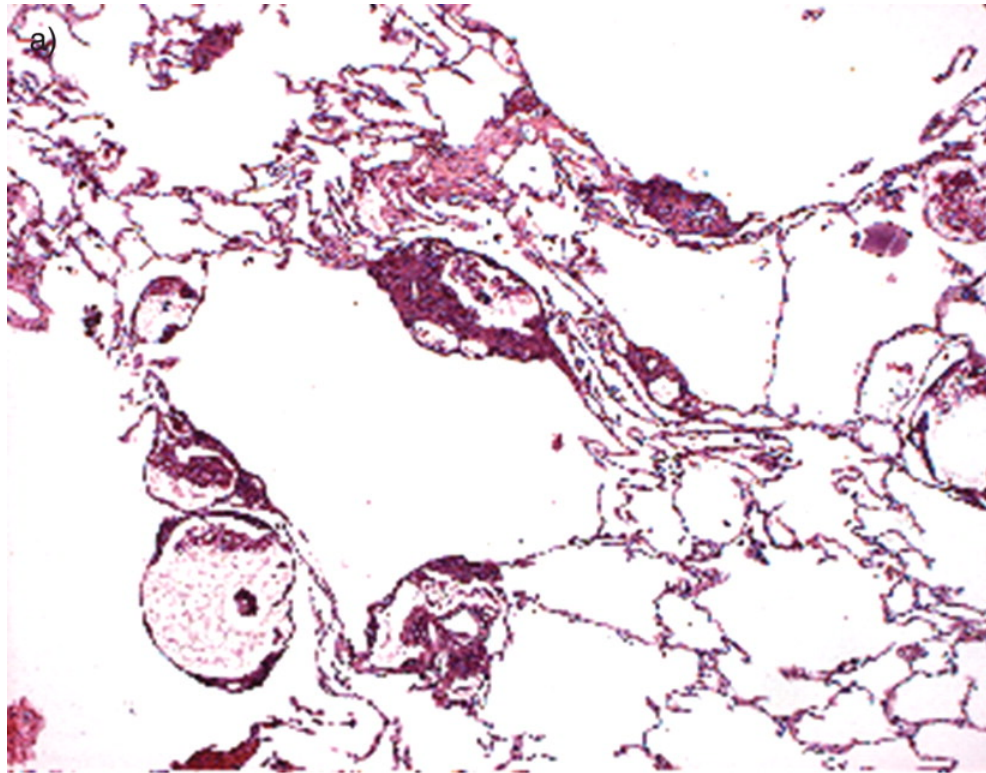
Diagnostic criteria of LAM

- Typical cystic changes

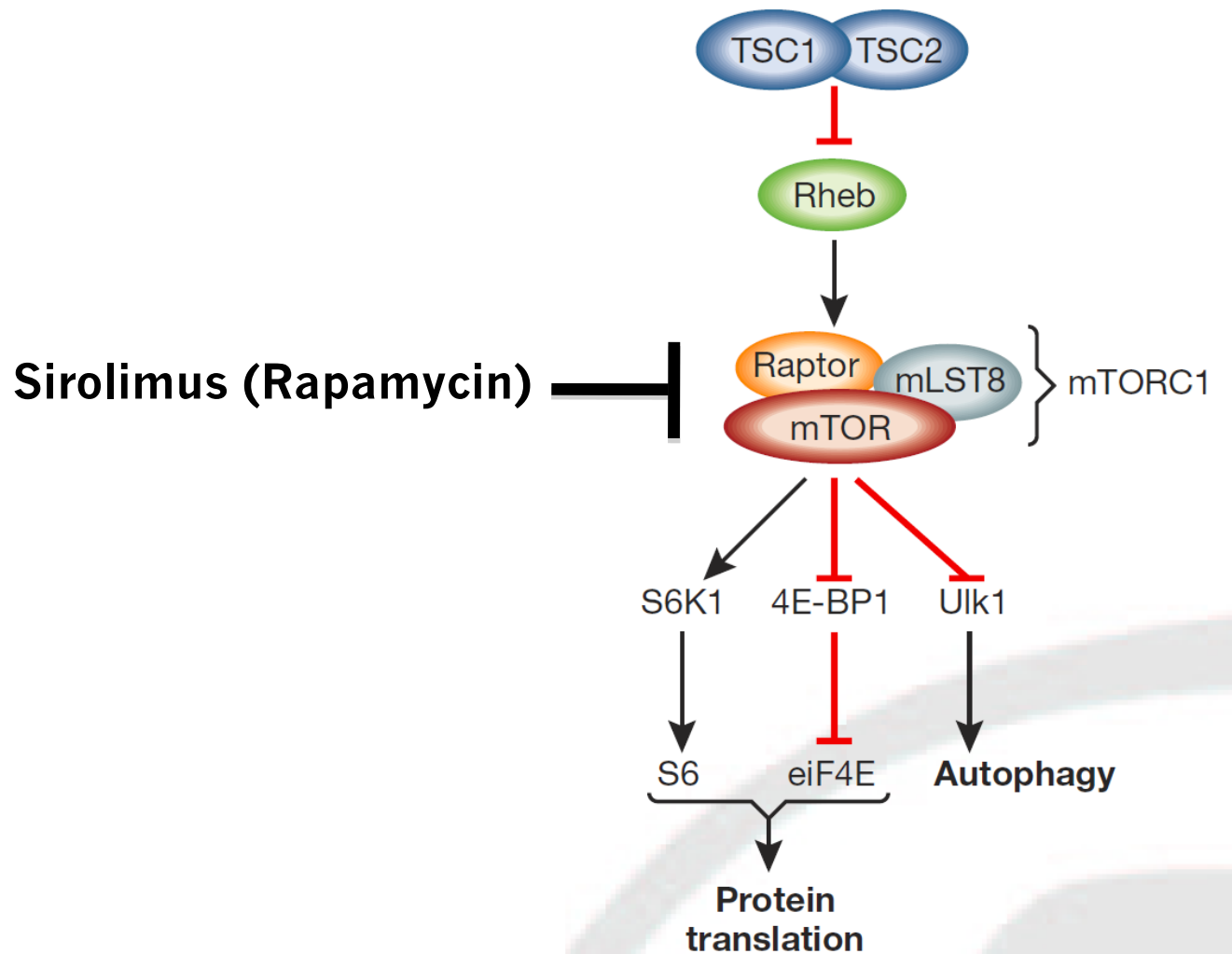
+ **any**

- AML
- Chylous effusion
- VEGF-D $>800\text{pg/ml}$

Lung biopsy

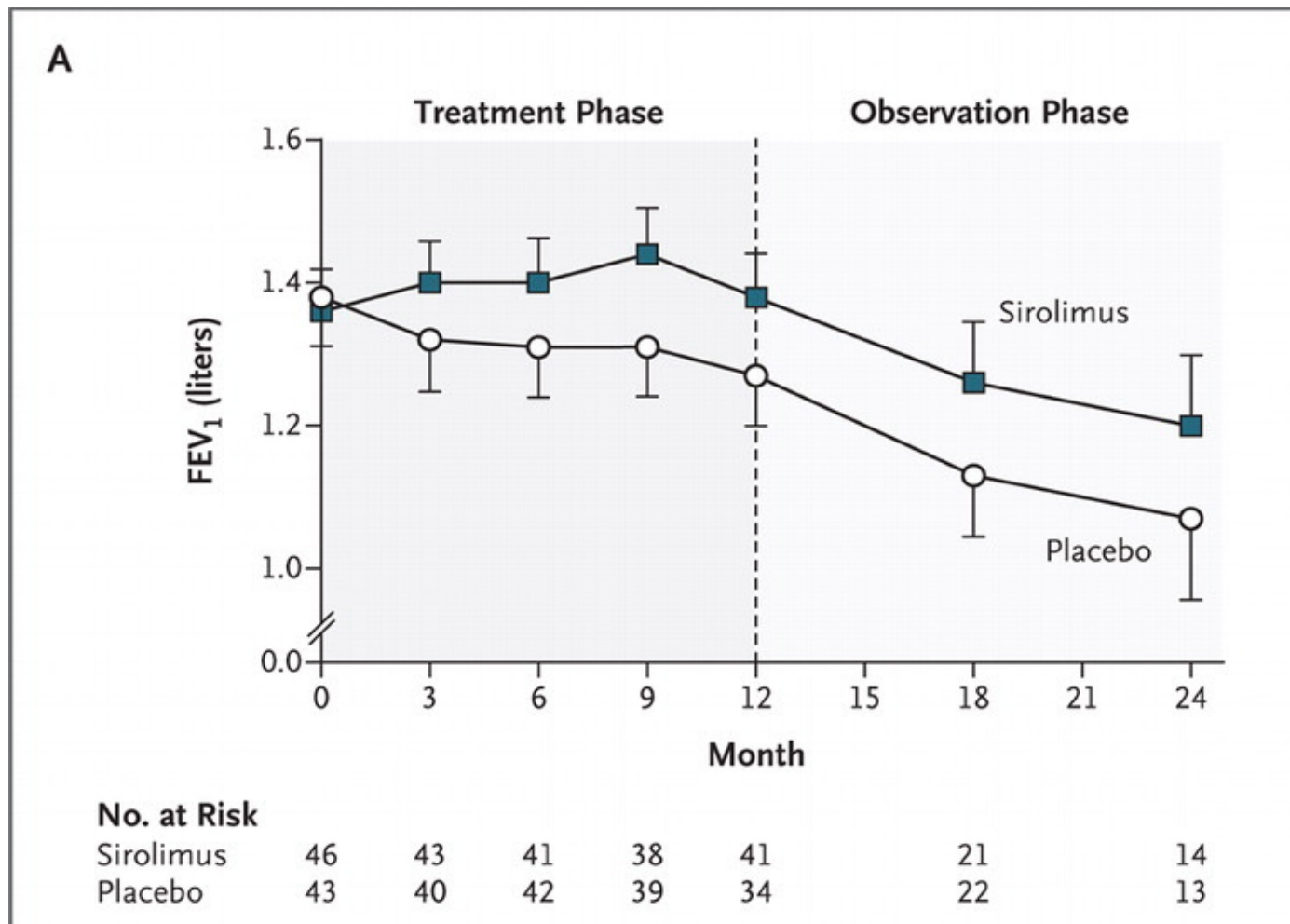


mTOR Kinase is Activated in LAM Cells



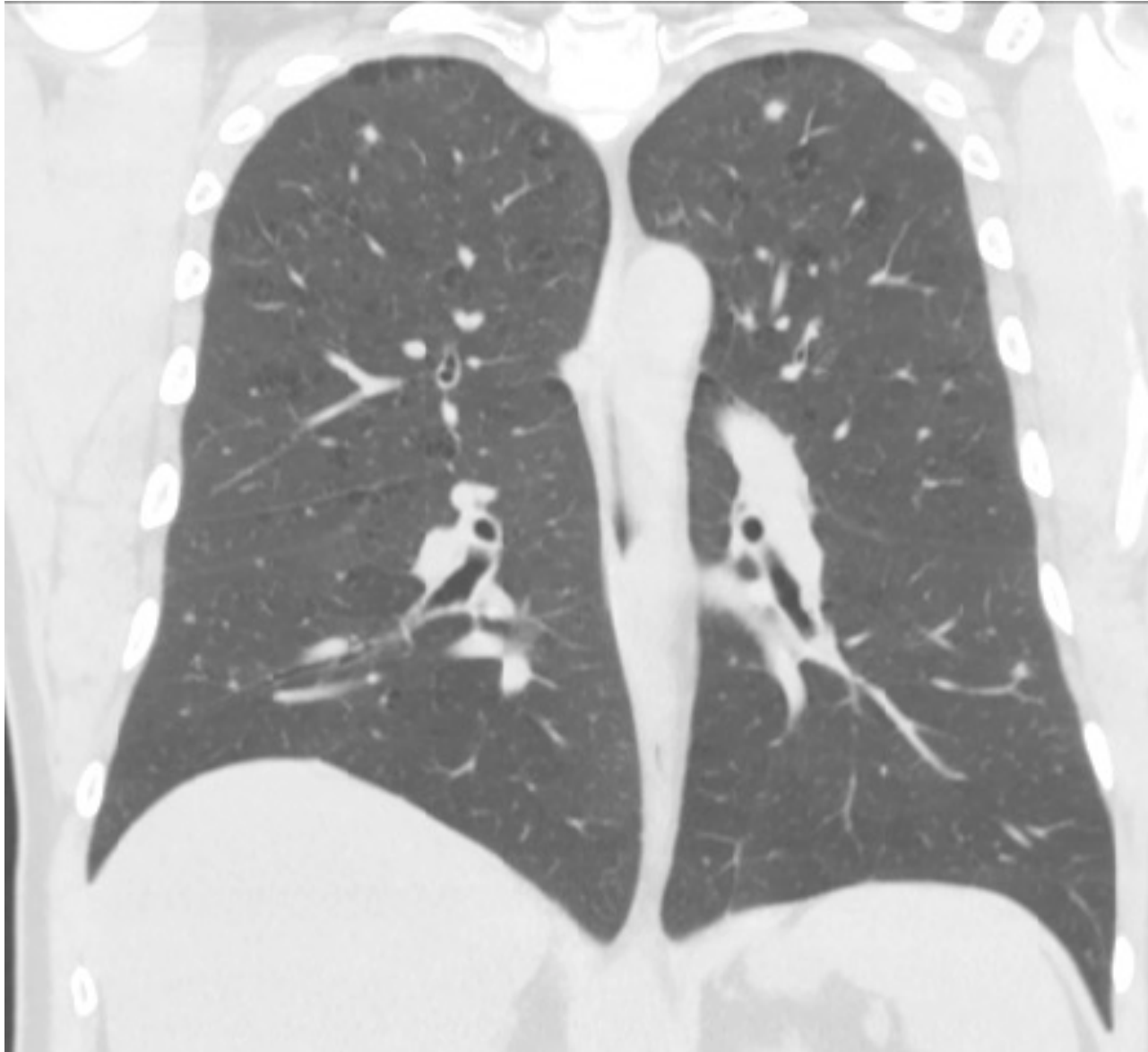
Rapamycin

- It works (MILES trial)



Langerhans cell histiocytosis

Langerhans Cell Histiocytosis



Langerhans Cell Histiocytosis

- Systemic disease or single organ
- Unknown true prevalence (3-5% of all diffuse lung disease?)
- M=F
- >90% smokers
- Cannabis?

Adult LCH

- Single or multisystem disease
 - Seborrheic rash
 - Diabetes insipidus
 - HSM/ Lymphadenopathy

- Single site: Most commonly the lungs
 - Smoking history?
 - Polyclonal

Langerhans Cell Histiocytosis

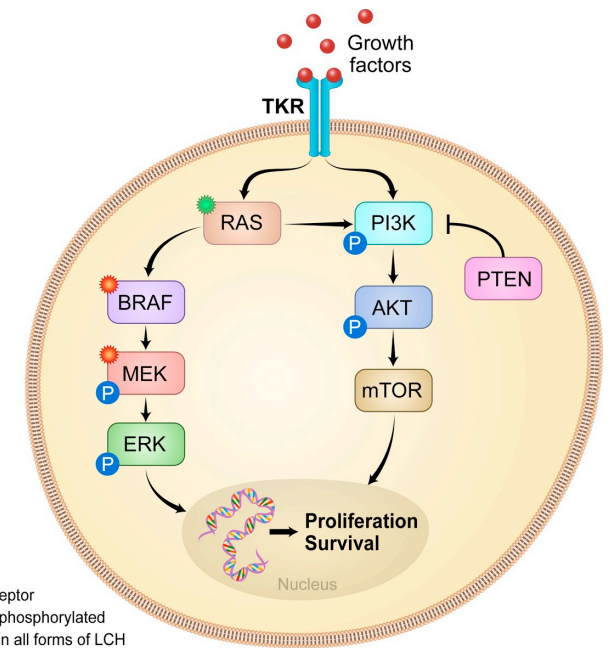
- Lung nodules
- CD1a+ cells (reactive or clonal?)
- Lung destruction
- Smoking

PLCH

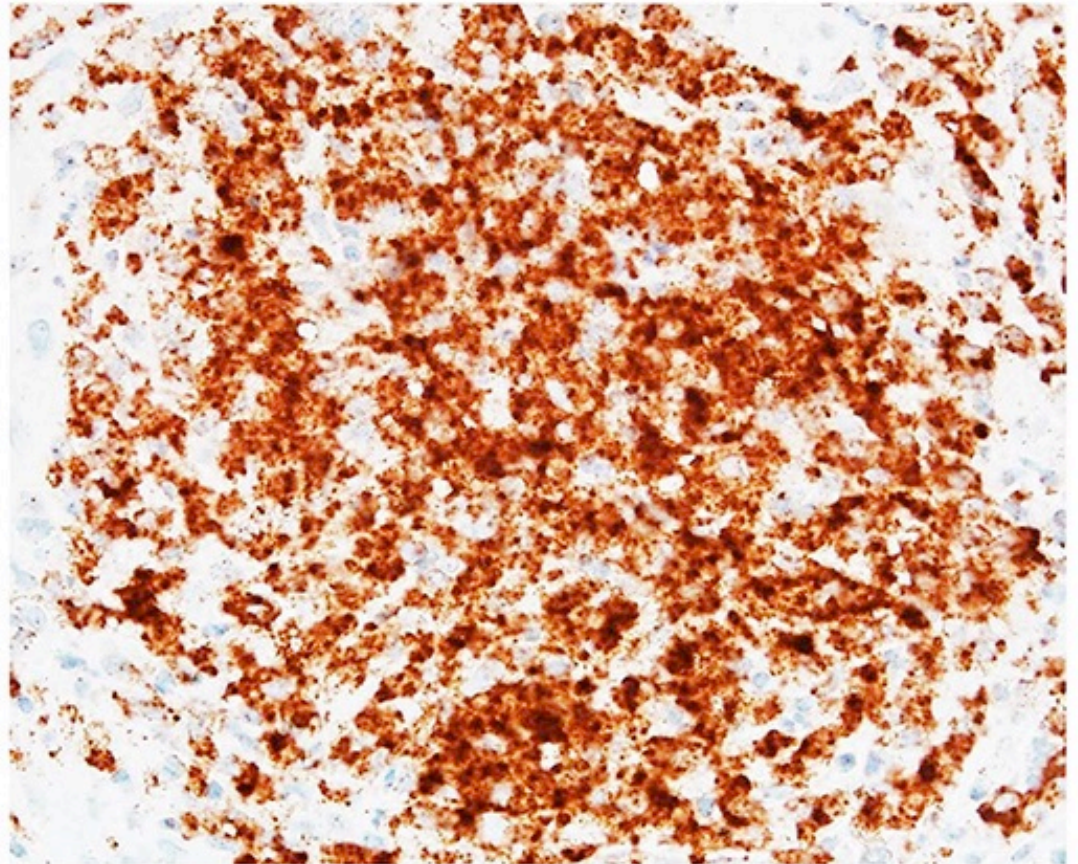
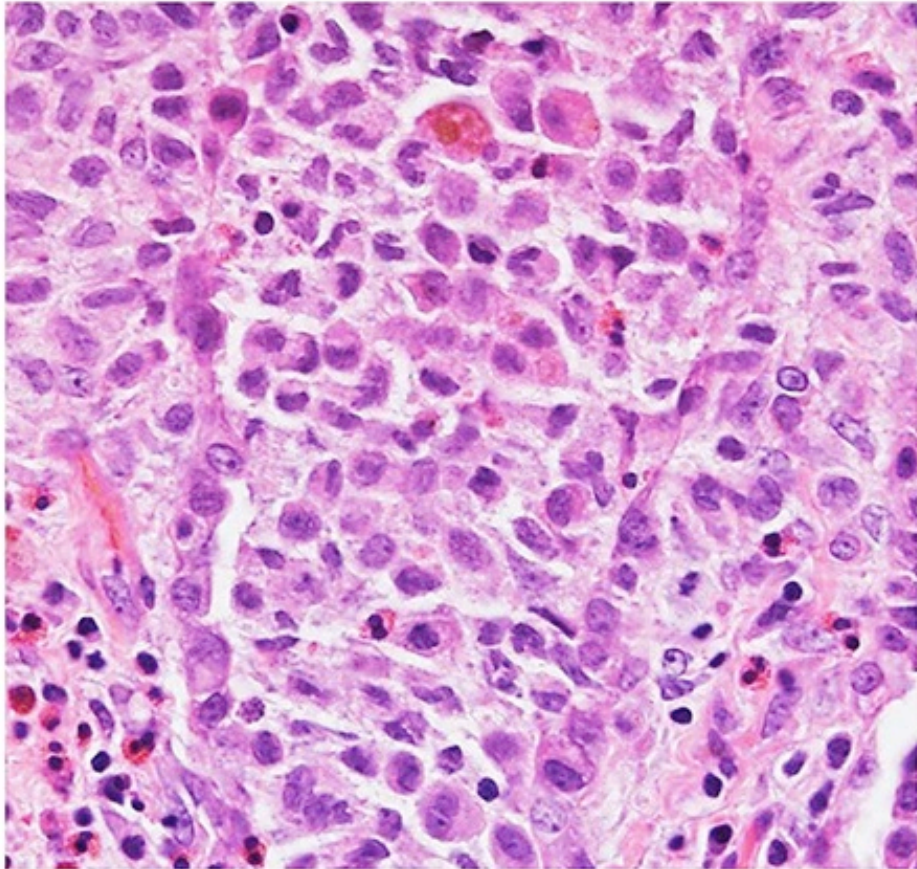
-Mutations in tumor suppressor gene (BRAF)

-Potential targeted therapy.

-Circulating cell with mutation in BRAF or NRAS



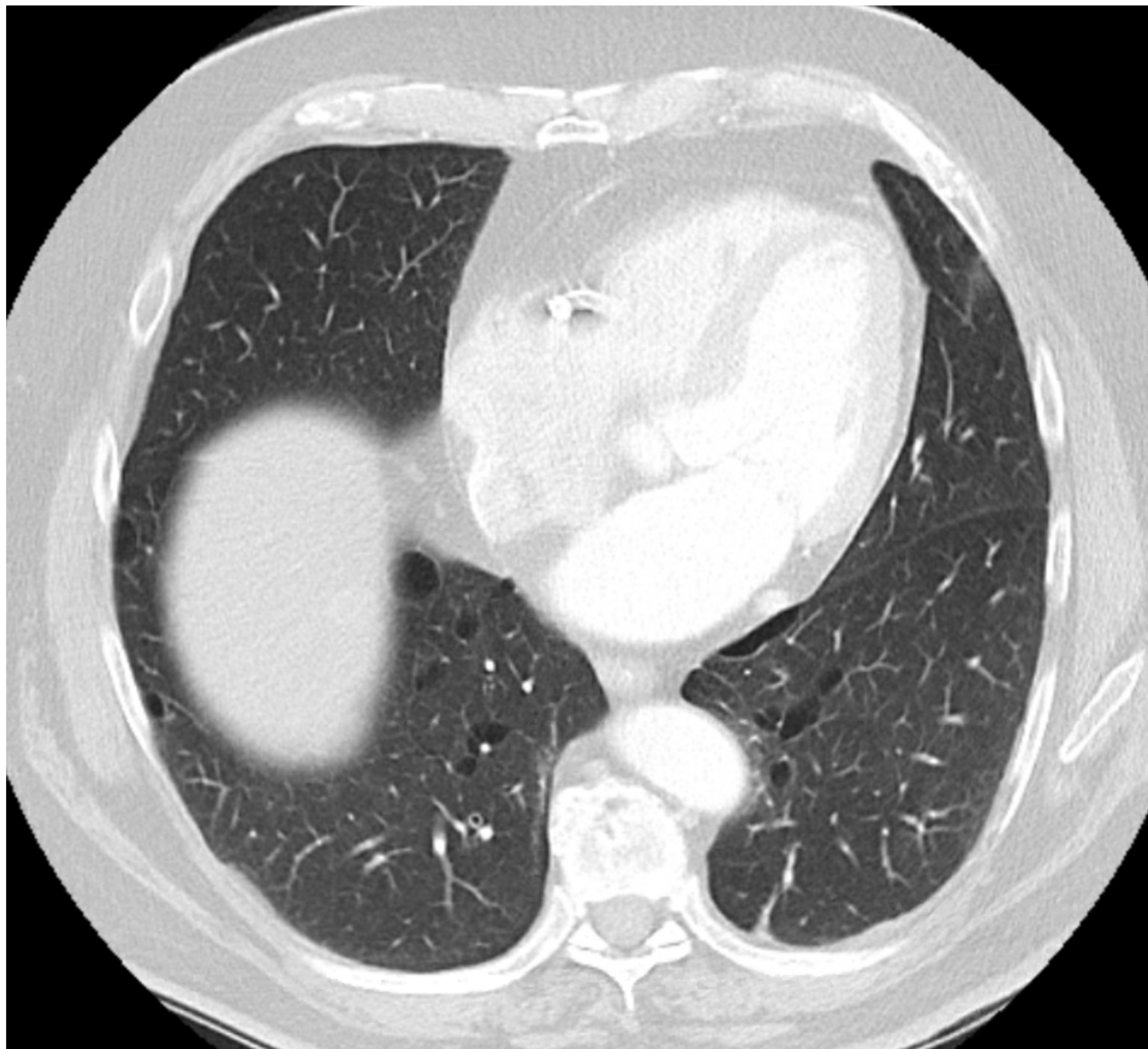
Lung biopsy



Treatment and prognosis

- 40-50% spontaneous resolution
- 60% decline over time.
 - Isolated decline in DLCO look for PH
- Smoking cessation

Birt Hogg Dube Syndrome



Birt Hogg Dube

- Autosomal dominant
- Penetrance for lung cysts ~80% by age 50
- 25-75% pneumothorax
- High recurrence rate

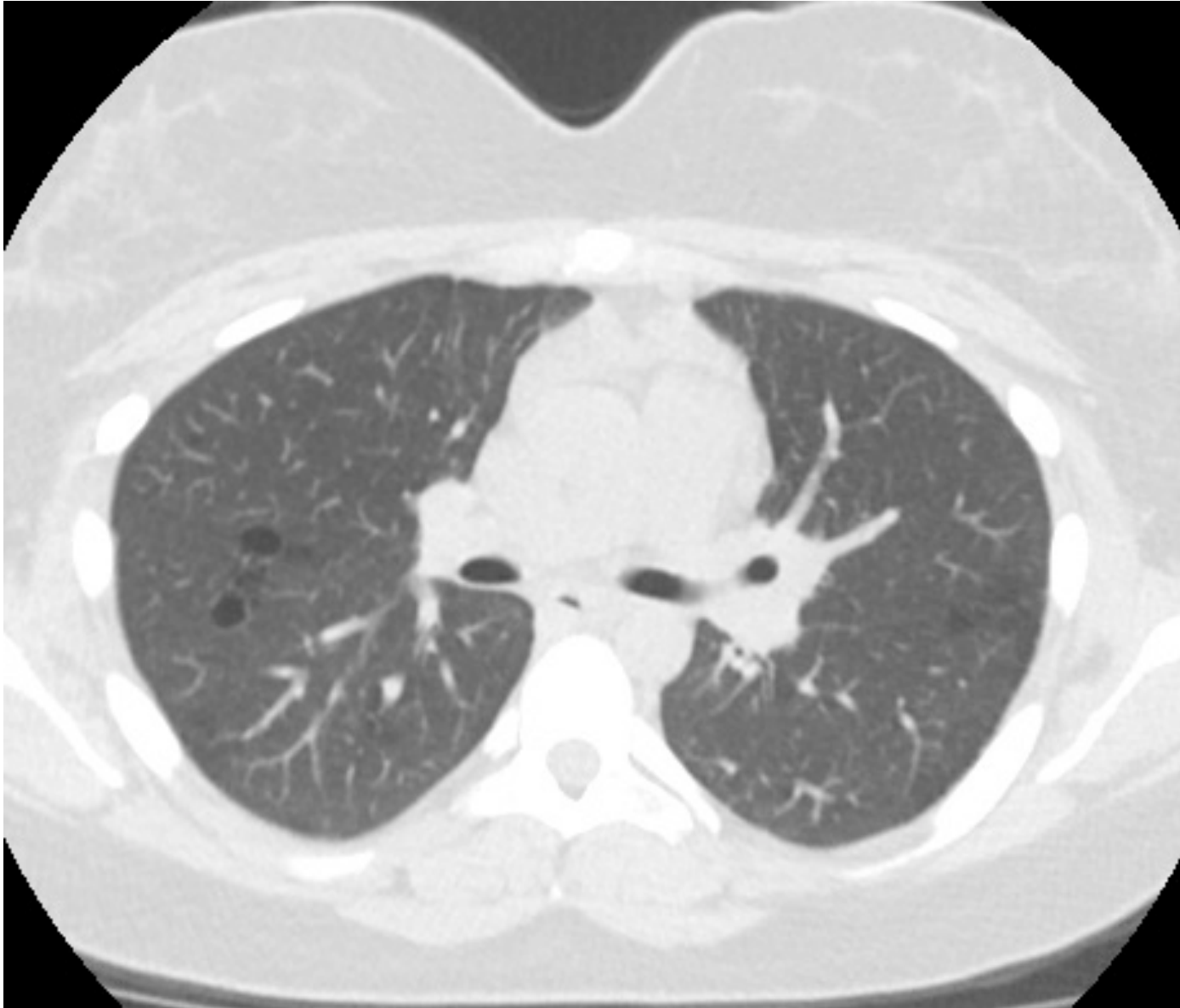
Fibrofolliculomas



Birt Hogg Dube

- Kidney cancer in ~25%
- Different histological subtypes. Can be bilateral and multifocal
- FLCN gene mutation

Prematurity



Summary

	LAM	PLCH	BHD
HRCT	Round Thin- walled Diffuse	Irregular Sparing angles Nodules	Ellipse Lower lobes pleura
Other features	Women Chylous effusion Angiomyolipoma VEGF-D > 800 pg/ml	Diabetes insipidus Skin and bone lesions	Kidney cancer
Pneumothorax	60%	10-20%	25-75%
Genes	TSC1 or TSC2	BRAF or MEK	FLCN

Question #1

30 years old female presenting with shortness of breath and dyspnea on exertion. Chest radiograph shows a right sided pneumothorax. A CT scan of the chest confirms the presence of pneumothorax and shows cystic lung disease in addition to a fat rich kidney tumor. The treatment is:

- a) No need to be concerned about lung function, it will not decline overtime
- b) Steroids
- c) No available therapies
- d) Rapamycin

Question #1

Answer d) Rapamycin.

This is a patient who has LAM. The presence of cystic lung disease and an angiomyolipoma is diagnostic of LAM. In this setting there is no need for a lung biopsy. Other features that could have confirmed the diagnosis are the presence of chylous effusions and a high VEGF-D level ($>800\text{pg/ml}$).

If a patient with LAM requires therapy, the treatment as an mTOR inhibitors such as rapamycin. This has been shown in the MILES trial.

Question #2

30 years old female presenting with shortness of breath and dyspnea on exertion. Chest radiograph shows a right sided pneumothorax. A CT scan of the chest confirms the presence of pneumothorax and shows cystic lung changes. A careful skin examination shows facial fibrofolliculoma. The next best step

- a) Start rapamycin
- b) Steroids
- c) Lung biopsy
- d) CT scan of the abdomen

Question #2

d) CT scan of the abdomen. This patient has BHD. The presence of facial fibrofolliculoma is pathognomonic of BHD. The major risk in BHD is renal cell carcinoma. A CT scan of the abdomen should be obtained to screen for kidney tumors. BHD

References

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