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Newsletter

HISTOPATHOLOGY UPDATE

A rare cause of cystic lung disease

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Case presentation

A 44-year old non-smoking female was undergoing abdominal x-ray. The radiologist reported basal lung cysts, but the patient was asymptomatic for pulmonary symptoms. Subsequent referral and consultation resulted in a high resolution CT scan of the chest (see Figure 1). Multiple lung cysts were noted to be evenly distributed in the lung parenchyma. A biopsy was undertaken to confirm the radiological differential diagnosis.

The CT scan (Figure 1) show thin walled cysts of variable size, which were bilateral and diffusely distributed. Nodules were not identified. Histology (see Figures 2 & 3) confirmed numerous lung cysts, with the peripheral aspect of the cysts showing small bundles of spindle cells displaying no atypia (arrows in Figures 2 & 3). The spindle cells in certain areas were tangentially sectioned and mimicked smooth muscle cells, which could have been interpreted as resident pulmonary vasculature or of airway origin.

Consultation with the submitting surgeon clarified the radiological differential diagnosis, and the spindle cells at the edge of the cysts stained positive for Desmin (see Figure 4), HMB45 (see Figure 5) and Progesterone receptor (see Figure 6). The case was concluded as LYMPHANGIOLEIOMYOMATOSIS.

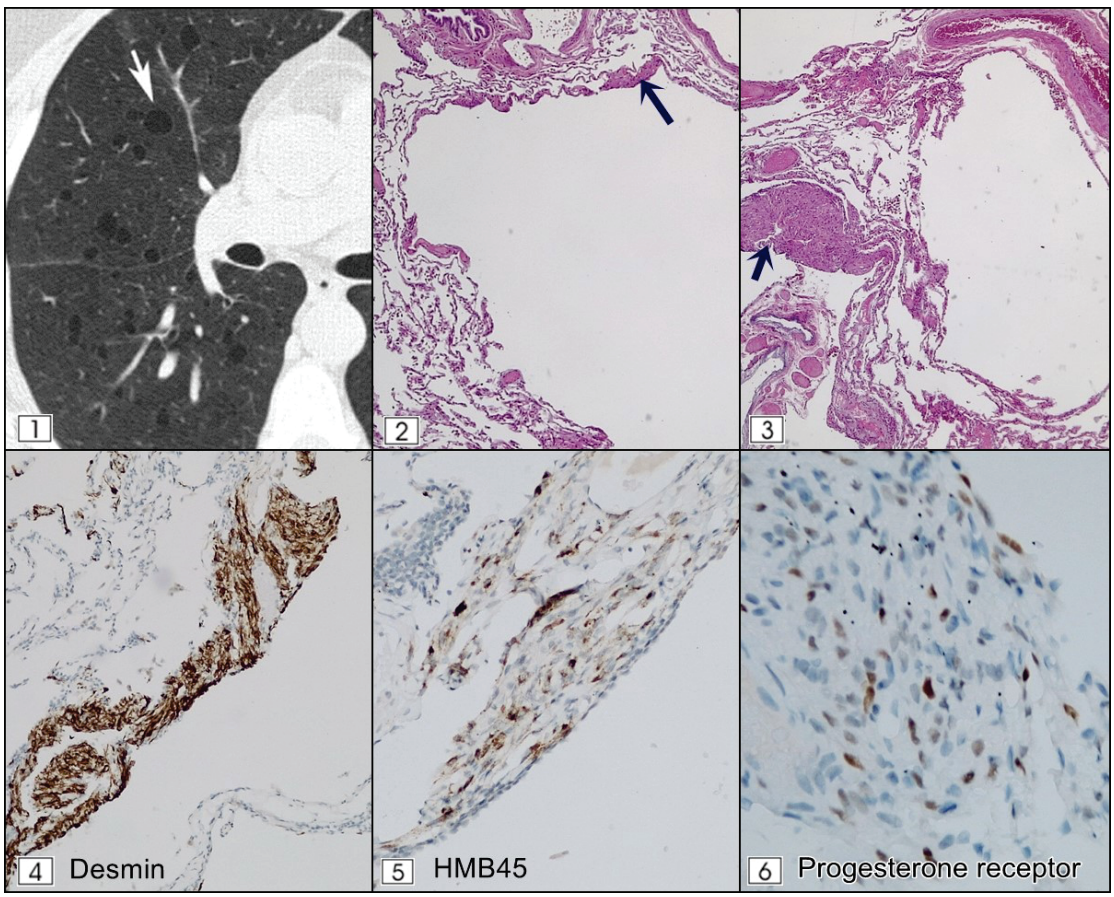

Figure 1 to 6

What is lymphangioleiomyomatosis (LAM)?

- A rare disease characterised by abnormal proliferation of smooth muscle-like cells (LAM cells) in the lungs, kidneys and lymphatics
- LAM is now classified as a form of neoplastic disease
- Can be either sporadic or in association with tuberous sclerosis syndrome (TSC)

INCIDENCE: 3rd to 4th decade, predominantly affects females of reproductive age, no smoking association.

PRESENTING FEATURES:

PULMONARY	EXTRAPULMONARY
Up to one third of TSC patients may show subclinical lung disease	Renal angiomyolipoma
Progressive dyspnoea (chylous effusion, diffuse cystic disease or obstruction) and pneumothorax	Lymphadenopathy
Clinical tests: abnormal lung function tests – decreased CO transfer, hypoxaemia, obstruction	Lymphangioma

GENETICS: the syndromic form is linked to mutations in TSC1 and TSC2 genes, which encode hamartin and tuberin proteins, respectively. The sporadic form shows mutations of TSC2 within tumour cells. These loss-of-function mutations result in unregulated activation of the mTOR signalling pathway.

X-RAY FEATURES: may appear normal in early disease. Typically hyperinflated lung with bilateral reticular opacities. Pneumothorax. Pleural effusion.

HIGH RESOLUTION CT: virtually diagnostic – thin walled cysts of varying size distributed throughout the lung.

PROGNOSIS: variable with no definitive treatment guidelines. No successful medical treatment. Severe disease requires lung transplantation. Hormonal therapy is not currently recommended. Inhibition of activated pathways involved in the disease process are being investigated in various trials (e.g. mTOR and PDGFR inhibitors).

CLINICAL AND RADIOLOGICAL DIFFERENTIAL DIAGNOSIS: Langerhans cells histiocytosis (LCH) – also a form of diffuse cystic lung disease. Usually occurs in smokers of either gender. Combination of diffuse cysts and centrilobular micronodules, with sparing of the costophrenic sulci, are seen with imaging studies. The cysts, in contrast to LAM, have irregular, bizarre shapes.

References

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