

A Rare Case of Pulmonary Lymphangiomyomatosis with Recurrent Pneumothorax

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Abstract: Lymphangiomyomatosis (LAM) is a multisystem disorder, predominantly affecting women. It is characterized by cystic lung lesions, abdominal angiomyolipomas (AML) and lymphatic abnormalities. Our patient was admitted with dyspnea, anorexia, left side chest pain and history of recurrent pneumothorax. She was evaluated with HRCT Thorax & Bronchoscopic biopsy for histopathology and immunohistochemistry. She was diagnosed LAM. She was started on Oral Medroxyprogesterone acetate.

Keywords: Lymphangiomyomatosis, cystic lung disease, tuberous sclerosis

1. Introduction

Lymphangiomyomatosis (LAM) is a chronic disease mostly affecting women of reproductive age group with a life expectancy spanning decades. It is uncommon occurring in approximately 4.9/1,000,000 women. It is a benign multisystem disorder characterized by cystic lung lesions, abdominal angiomyolipomas (AML) and lymphatic abnormalities. It is caused by the proliferation of a neoplastic smooth muscle-like LAM cell that also has characteristics of melanocytes. The lung develops cysts ranging in size from 0.2 to 2 cm. LAM cells grow in the walls of cysts and along blood vessels, lymphatics, and bronchioles causing airways narrowing, vascular wall thickening, lymphatic disruption, and venous occlusion. Focal hemosiderosis may be present.

2. Case Report

A 36 years old female of Indian descent from middle socioeconomic class presented with complain of chest pain in left side since 3 days. Patient also had mild non-productive cough, dyspnoea on exertion, anorexia and weight loss for at least 15 days. She had no complain of fever or haemoptysis. She didn't have any addiction, bad habits, occupational exposure or history of using oral contraceptive pills. She had no similar family history. She has one 12 year old healthy child & no history of miscarriages.

Patient had similar past history 2 months ago. She had right sided pneumothorax and ICD was inserted & kept for 6 days. She again developed right sided pneumothorax just within 2 days after removal of ICD and it was reinserted and kept for 20 days. After this period pleurodesis was done using povidone iodine.

On physical examination air entry was decreased bilaterally but more on left side than right. Rest of the lung field was clear on auscultation. All other systems were normal on examination. Chest x-ray P/A view showed bilateral pneumothorax, more on left side than right.

HRCT Thorax was done. In that both lungs showed multiple well defined thin walled cysts involving all segments with bilateral symmetrical distribution. No zonal predominance was noted. Right mild pneumothorax and minimal effusion with internal septations was noted. Left minimal pneumothorax noted. No evident bone erosion was seen. These findings suggested LAM. (Fig 1, 2 & 3)

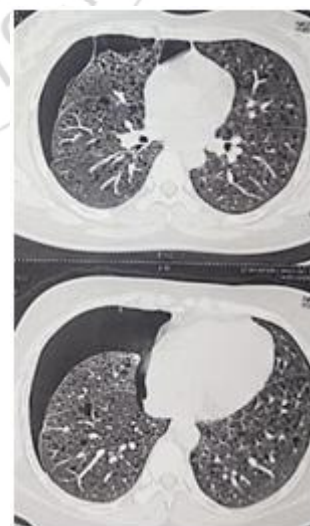


Figure 1: HRCT Thorax showing multiple cysts and right pneumothorax

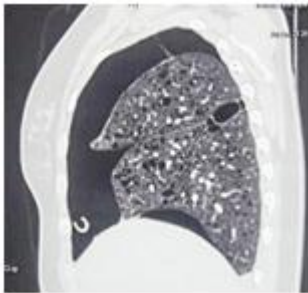


Figure 2: HRCT Thorax coronal view

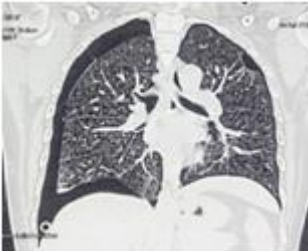


Figure 3: HRCT Thorax sagittal view

Bronchoscopy was done and transbronchial lung biopsy was taken. Histopathological examination showed cystic spaces surrounded by proliferation of atypical spindle cells and tiny fragments of respiratory epithelium & cartilage tissue were also seen, suggesting LAM. Immunohistochemistry examination showed HMB45 was positive in many cells. HMB45 appears to provide a highly specific and highly sensitive diagnosis for LAM in females, specially when radiological & histopathological findings are s/o LAM thus confirming the diagnosis.

For pneumothorax air tapping was done on left side but yielded no improvement. So ICD was inserted on left side leading to complete resolution of pneumothorax. ICD was kept for 2 days and pleurodesis was done successfully with Doxycycline before removing the ICD.

3. Discussion

Two forms of LAM are described. 1) Sporadic form & 2) Inherited form.

Sporadic LAM is caused by somatic mutations or deletions of the tuberous sclerosis complex-2 (TSC2) gene in an unknown susceptible cell.

LAM also occurs in TSC, an autosomal dominant disorder, resulting from germline mutations in the TSC1 or TSC2 genes (TSC-LAM). The association of TSC and cystic lung disease has long been recognized. The prevalence of cystic lung disease in women with TSC was reported to range from 30% to 40%; in male patients, it has been estimated to be 13%. Males with TSC tend to have milder, subclinical lung involvement.

Two types of LAM cells have been described. 1) Small, spindle-shaped cells predominate in the center of the lung nodules; & 2) Epithelioid cells with large cytoplasm predominate at the periphery.

Both cell types react with antibodies against smooth muscle-cell antigens (e.g., smooth muscle α -actin, vimentin, desmin). The epithelioid cells also react with human melanin black antibody (HMB-45), a monoclonal antibody that recognizes gp100, a premelanosomal protein encoded by the Pmel17 gene. Receptors for estrogen, progesterone, insulin like growth factors, angiotensin II, hyaluronic acid (CD44), chemokines, and erythropoietin have been identified in LAM cells.

A role of estrogens in the pathogenesis of LAM has been suggested by its predominance in premenopausal women, worsening of lung disease during pregnancy or following the administration of estrogens and the presence of estrogen and progesterone receptors in lung and angiomyolipoma LAM cells.

LAM nodules contain MMP2, MMP9, MMP1, and MMP activators (MT1-MMP), and their inhibitors (TIMPs). Levels of TIMP-3, which inhibits some MMP, were reportedly reduced in LAM lesions. Compared with normal subjects, serum levels of MMP-9 were higher in patients with LAM suggesting that an imbalance between MMP and their inhibitors may contribute to lung destruction. The presence of lymphatic spaces in the LAM nodules and strong immunoreactivity towards vascular endothelium growth factor C (VEGF-C), VEGF-D, vascular endothelium growth factor receptor (VEGFR) 3, and podoplanin, markers of lymphatic endothelial cells, led to the hypothesis that disorganized lymphangiogenesis enhances metalloproteinase expression and lung remodelling.

Oophorectomy, tamoxifen, progesterone and GnRH analogues have been used without evidence that they are effective. Recent finding suggesting constitutive activation of the kinase mammalian target of rapamycin (mTOR) has led to trials of mTOR inhibitors including sirolimus & everolimus.

Bilateral or unilateral lung transplant is considered when FEV1 and DLCO are less than 30% predicted, and the patient is on continuous supplemental oxygen.

Patient was discharged with oral medroxyprogesterone acetate 10mg 8 hourly with advice to follow-up monthly. She was instructed to avoid excessive or heavy weight lifting, severe coughing and other strenuous activity. She was also advised to avoid pregnancy due to severe risks involved.

4. Conclusion

LAM is a rare multisystemic disorder mostly seen in females of reproductive age group. In initial stages pulmonary LAM can be misdiagnosed as obstructive lung disease or bronchiectasis. Screening of the patients at risk of the disease can lead to earlier diagnosis with better prognosis and management

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