Case Report

Recurrent Pneumothorax in a Premenopausal Filipino Female: A Case Report

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ABSTRACT

Lymphangioleiomyomatosis (LAM) is a rare progressive multisystemic cystic lung disease. It commonly presents as fatigue, progressive dyspnea, and spontaneous pneumothorax which can progress to chronic respiratory failure. Previously, patients were diagnosed with LAM through histopathological testing. In 2017, new guidelines were released by the American Thoracic Society allowing the clinical diagnosis of LAM. This is the case of a 46-year-old female with a history of recurrent pneumothorax and progressive dyspnea. During episodes of pneumothorax, she underwent multiple chest tube insertions. High-resolution chest CT scan revealed a small right pneumothorax with septations, pleurodiaphragmatic adhesions, minimal pleural effusion, diffuse cystic lung disease, and a fat-containing right renal nodule consistent with an angiomyolipoma thereby fulfilling the clinical criteria for the diagnosis of LAM. The patient eventually underwent talc pleurodesis and was started on sirolimus. LAM should be considered in women of childbearing age without co-morbidities presenting with spontaneous pneumothorax.

Keywords: lymphangioleiomyomatosis; LAM; pneumothorax; cystic lung disease; progressive dyspnea

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INTRODUCTION

Lymphangioleiomyomatosis (LAM) is a progressive disease that affects premenopausal women and is characterized by cystic lung lesions, renal angiomyolipomas (AML), and lymphatic involvement. It commonly presents as fatigue, progressive dyspnea, and spontaneous pneumothorax. There are two main types of LAM: sporadic LAM and LAM associated with tuberous sclerosis complex (TSC). The pathogenesis of LAM involves inappropriate cell growth and proliferation of abnormal smooth muscle cells, abnormal angiogenesis, and lymphangiogenesis leading to the migration of LAM cells and deposition in the pulmonary parenchyma resulting in progressive cystic destruction of the lung tissue.[1] Limited studies have reported its exact prevalence. In the United States, United Kingdom, and Switzerland, the incidence of LAM ranges from 0.23-0.31 per million women every year.[2] The epidemiology of the disease in Asia or the Philippines has not been well-documented. In the Philippines, only three case reports have been published, all of which have undergone histopathological diagnosis.[3-5] However, recent developments in the diagnosis of LAM favor a less invasive approach which allows its clinical diagnosis using nonpathological tests. This facilitates early recognition and timely intervention to avoid rapid decline of pulmonary function.

CASE PRESENTATION

This is the case of a 46-year-old female, non-smoker, who presented with recurrent pneumothorax. She was healthy and had no previous admissions. In 2011, she presented with sudden dyspnea. She was tachypneic with decreased breath sounds at the right lung field. Chest radiography revealed a pneumothorax in the right hemithorax, where a chest tube was inserted. There were also apical infiltrates and the patient was managed as a case of tuberculosis. In the interim, she had episodes of dyspnea relieved by rest.

In 2018, the patient had a sudden onset of difficulty of breathing not associated with cough and fever. On physical examination, the patient was in respiratory distress, tachycardic, and tachypneic with desaturations as low as 80% and she was hooked to nasal cannula at 4 liters per minute. There were decreased breath sounds in the right upper lung field and a pneumothorax in the right apex was seen on chest radiograph (Figure 1). Chest computed tomography (CT) scan revealed a small right pneumothorax with septations, minimal pleural effusion, diffuse cystic lung disease (Figure 2A) and an angiomyolipoma, a fat-containing right renal nodule measuring 0.8 x 0.8 cm (Figure 2B). Unfortunately, due to limited resources, measurement of serum vascular endothelial growth factor-D (VEGF-D) was not done. Screening for tuberous sclerosis was also not done as the patient did not have any family history or dermatological features such as subungual fibromas, facial angiofibromas, hypomelanotic macules and shagreen patches, hence, lessening the suspicion for such. The patient was clinically diagnosed with LAM in accordance with the 2017 American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines (ATS/JRS CPG) wherein a clinical diagnosis of LAM can be made based on the combination of characteristic high-resolution CT (HRCT) features plus one or more of the following: presence of TSC, angiomyolipomas, chylous effusions, lymphangioleiomyomas, or elevated serum VEGF-D greater than or equal to 800 pg/ml.[6]

In March 2022, the patient was admitted for talc pleurodesis on the right but had a sudden onset of dyspnea with desaturations as low as 85%. The right chest tube was reinserted. The patient also had an anaphylactic reaction to ampicillin-sulbactam which resulted in a further delay in her scheduled pleurodesis. In June 2022, she was started on sirolimus and trough levels were maintained within target range. Between March and October 2022, four more episodes of pneumothorax were recorded. In October 2022, the patient underwent talc pleurodesis. After pleurodesis and while on sirolimus, she had another pneumothorax in May 2023 but no recurrence has been reported since then. Figure 3 shows a timeline of the recurrence of her pneumothorax.

The patient is relatively young with no known comorbidities. She is a non-smoker which reduces the likelihood of airway inflammation and respiratory bronchiolitis which can cause recurrent primary spontaneous pneumothorax.[7] In addition, smokers are predisposed to chronic obstructive pulmonary disease which is also the most common cause of secondary spontaneous pneumothorax.[8] The patient also has no family history of spontaneous pneumothorax. This makes inherited conditions such as Birt-Hogg-Dubé syndrome,

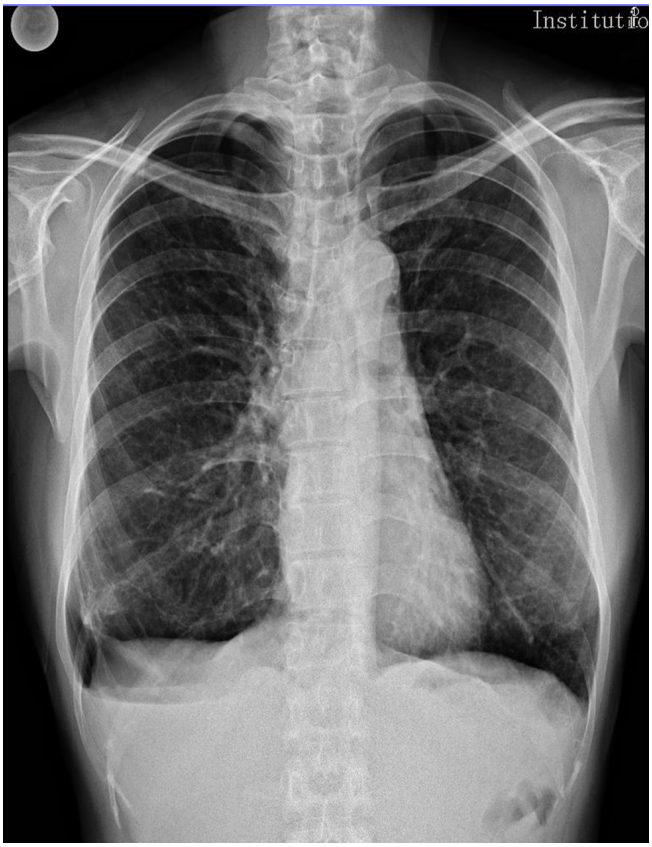

Figure 1. Chest x-ray showing minimal pneumothorax in the right apex

hyperhomocysteinemia, alpha-1 antitrypsin, and Marfan syndrome less likely.[9-10] The apical infiltrates seen on radiograph led to a differential diagnosis of pulmonary tuberculosis. With a history of recurrent pneumothorax, another consideration for this patient was a catamenial pneumothorax secondary to thoracic endometriosis. In thoracic endometriosis, symptoms begin within 72 hours after the onset of menstruation.[11] However, for this patient, the symptomatology and recurrence of pneumothorax were not related to her menstrual cycle.

The patient is currently maintained on sirolimus and has fewer episodes of dyspnea on exertion. The last pneumothorax episode was in May 2023. She no longer requires oxygenation and can now regularly exercise and perform routine daily activities. She was advised pulmonary rehabilitation and continuous professional counselling to aid in her mental and emotional well-being.

DISCUSSION

The diagnosis of LAM should be established using a stepwise approach from the least to the most invasive method, in accordance with the 2017 ATS/JRS CPG. The algorithm states that for patients with clinical suspicion of LAM and HRCT chest findings of multiple, bilateral, uniform, round, thin-walled cysts - a detailed clinical evaluation must be done to first check for the presence of TSC. If there is no clinical suspicion for such, serum VEGF-D, non-contrast CT or MRI of the abdomen/pelvis, or chylous fluid/node/mass aspiration is obtained. If any of the following is present – serum VEGF-D greater than or equal to 800 pg/ml, renal AML or lymphangioleiomyomas, or positive cytology - the diagnosis of LAM is confirmed. In cases where the findings fail to reveal features consistent with LAM, individualized decision-making on whether to do transbronchial lung biopsy or simple close monitoring of the patient should be done. Surgical lung biopsy is done as a last resort if transbronchial lung biopsy is unable to reveal a diagnosis.[6] This will minimize unnecessary intraoperative risks and lessen possible iatrogenic complications. In our local setting, measurement of serum VEGF-D is unavailable. Histopathological diagnosis is costly and most patients have difficulty proceeding with such diagnostic interventions. This results in the delay of diagnosis and management which would greatly impact the prognosis of the disease.

The annual decline in forced expiratory volume in one second (FEV1) in untreated LAM patients has been reported to range from 40 to 120 mL/year and higher.[12] The median survival for these patients is 23 years from diagnosis.[13] Approximately two-thirds of patients with LAM develop pneumothorax. The risk of recurrent pneumothorax is approximately around 70%.

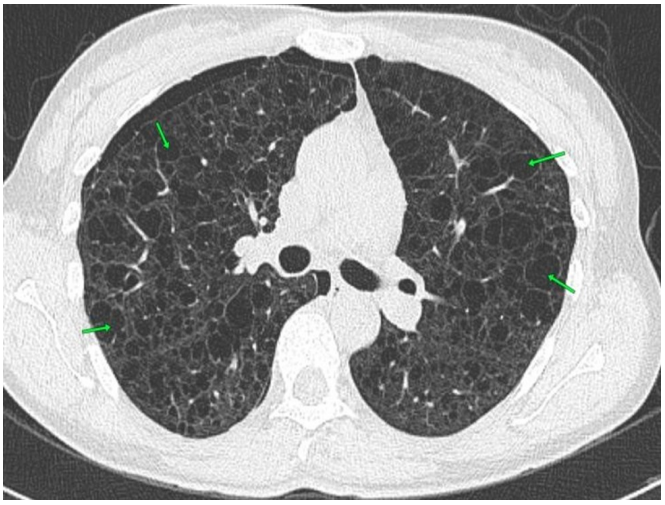

Figure 2A. Transverse cut of chest CT scan showing numerous, thin-walled, air-filled cysts of varying sizes (green arrows) with surrounding normal parenchyma signifying a diffuse cystic lung disease

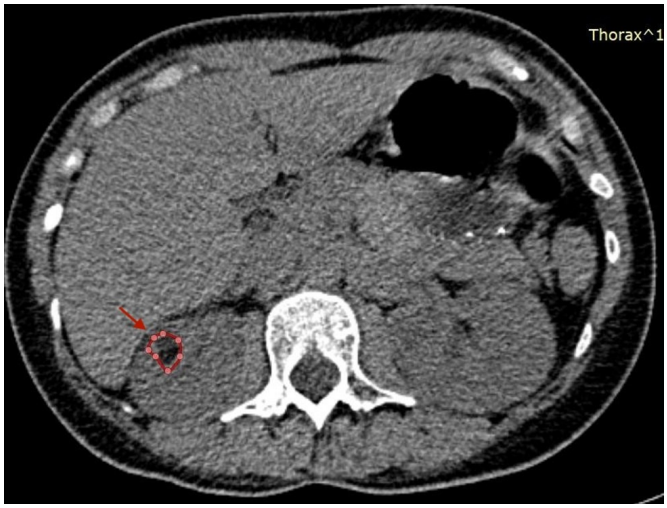

Figure 2B. CT scan showing an angiomyolipoma in the right renal cortex - a nodular focus with fat component (red arrow; lesion encircled)

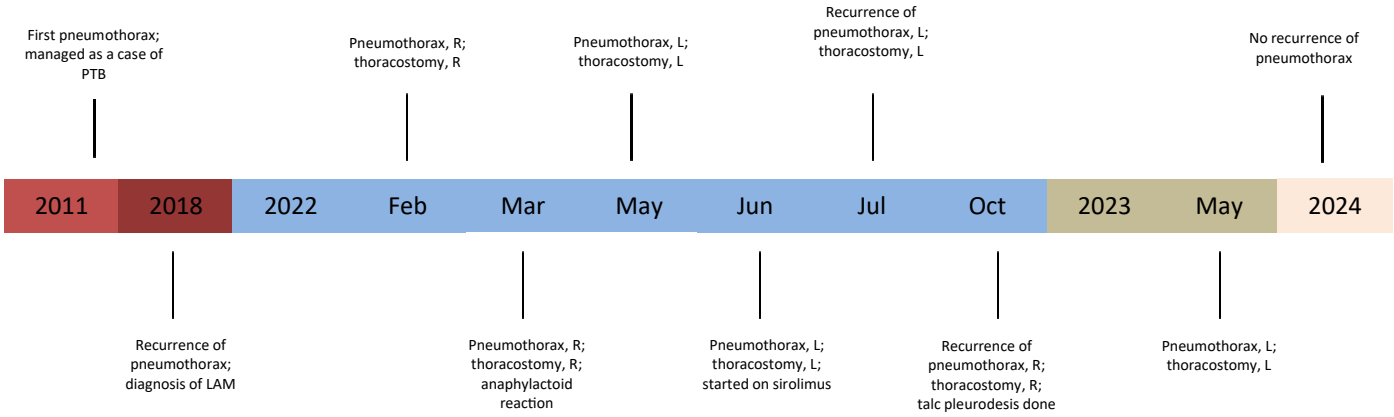

Figure 3. Timeline depicting the frequency and intervals of the patient's pneumothorax. PTB, pulmonary tuberculosis; LAM, lymphangioleiomyomatosis; R, right; L, left

Therefore, pleurodesis after the first pneumothorax is recommended.[6] The treatment for sporadic LAM is inhibition of rapamycin signalling with sirolimus (mechanistic target of rapamycin [mTOR] inhibitor). It is indicated for symptomatic patients with abnormal lung function or those with FEV1<70% of predicted. Treatment with sirolimus is suppressive rather than curative of the disease. It is generally well-tolerated and is continued indefinitely. Monitoring of serum trough levels, complete blood counts, fasting lipids and glucose, liver and renal function, and urine protein every 3 months is recommended.[14-15] However, for patients with an advanced disease, lung transplantation may be the only treatment option.

CONCLUSION

Lymphangioleiomyomatosis is a rare disease, characterized by cyst formation in the lungs and the proliferation of immature smooth muscle in affected organs. Young women presenting with dyspnea and recurrent pneumothorax who are non-smokers should raise the suspicion for LAM. A clinical approach will lead to early recognition and intervention which are crucial in maximizing pulmonary function and slowing down pulmonary decline.

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Ethical Consideration

The authors declared that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Authors' Disclosure

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