Sporadic Lymphangioleiomyomatosis Presented with Bilateral Pneumothorax

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Abstract

A 41-year old lady in a reproductive age group presented to us with bilateral pneumothorax. She gave history of right sided pneumothorax prior to this episode which prompted us to further investigate which revealed multiple bilateral cystic lung changes on high resolution computed tomography of the thorax. Transbronchial cryobiopsy of the lung confirmed the diagnosis of lymphangioleiomyomatosis. She was treated conservatively due to financial constraints and discharged two months later once prolonged air leak resolved. This case illustrates the need to investigate the underlying cause of recurrent pneumothorax especially in females due to therapeutic and prognostic implications.

Keywords

Cystic lung disease, Lymphangioleiomyomatosis, Recurrent pneumothorax

Introduction

Cystic lung diseases are uncommon and represent a diagnostic and therapeutic challenge. The differential diagnosis is broad and includes pulmonary lymphangioleiomyomatosis (LAM), langerhans cell histiocytosis, lymphoctic interstitial pneumonia, Birt-Hogg-Dube disease, neurofibromatosis and papillomatosis. We report a case of sporadic LAM confirmed by transbronchial lung cryobiopsy in a non-smoker female who presented with recurrent pneumothorax.

Case History

A 41-year old non-smoker Sri Lankan lady presented with history of fever for five days, and gradually worsening of shortness of breath associated with minimal blood stained cough. There were no constitutional symptoms, night sweats, and no contact with tuberculosis patients. Her past medical history was significant for a right-sided spontaneous pneumothorax 2 years ago in Sri Lanka requiring a chest tube insertion. Both the pneumothorax occurred after she completed her menstrual cycle. She is single, nulliparous, and works as an operator in electronic manufacturing company in Malaysia for the past 6 months. She is a registered Sri Lankan refugee.

On physical examination, she has a thin built, non cachetic, with no syndromic features. She was alert, conscious, not in distress and was able to talk in full sentences. Vital signs were stable and she was not hypoxic and afebrile. Her lungs showed reduced chest expansion, reduced breath sounds and hyperresonance on percussion more prominent on the left lung. Other systems were unremarkable.

Chest radiograph (Figure 1) showed bilateral pneumothoraces. Bilateral chest tube was inserted. Investigation for tuberculosis was negative and sputum and blood cultures were negative.

High resolution computer tomography (HRCT) of the thorax (Figure 2) showed numerous diffuse thin wall cysts of various sizes bilaterally surrounded by normal lung parenchymal. Based on history and HRCT findings, a working diagnosis of lymphangioleiomyomatosis (LAM) was made. Histopathological examination (HPE) obtained through transbronchial cryobiopsy of the lung was initially reported as non-specific and showed moderate lymphocytic infiltration and focal emphysematous changes with dilatation of alveolar spaces. However, a re-look of the HPE by a thoracic pathologist confirmed the diagnosis of LAM. Further imaging looking for renal angiomyolipoma were not done in view of her financial limitations. During multidisciplinary team meeting attended by cardiothoracic surgeon, respiratory physician and radiologist; surgical pleurodesis was not offered in view of diffuse cystic lesions.

Her hospital stay was eventful in which she was intubated and ventilated for 9 days due to respiratory distress and subsequently developed ventilator-associated pneumonia. Methicillin Resistant Staphylococcus Aureus (MRSA) was isolated from tracheal aspirate in which she responded with intravenous linezolid acid. The left lung successfully expanded and subsequently she received talc slurry pleurodesis; while the right lung remains with residual pneumothorax. As patient also could not afford a heimlich valve (Pneumostat); she had a prolonged hospital stay with slow recovery in terms of clinical symptoms and oxygen requirement. With lung rehabilitation and nutritional support, she gradually recovered. Her right lung slowly expanded and chest tube was removed. She was discharged after 2 months of hospitalization without requiring oxygen supplementation. Subsequently, she was lost to our follow-up.

Discussion

Recurrent pneumothorax in females needs to be further evaluated. Apart from cystic lung diseases, thoracic endometriosis is another differential which needs to be excluded. Thoracic endometriosis can be catamenial and non-catamenial. It is unlikely in the absence of previous symptoms of pelvic endometriosis and the absence of pleural and diaphragmatic nodules in the CT scan [1].

Lymphangioleiomyomatosis (LAM) is a rare disorder resulting from proliferation in the lung, kidney, and axial lymphatics of abnormal smooth muscle-like cells (LAM cells) that exhibit features of neoplasia and neural crest origin causing cystic destruction of the lung [2]. Renal tumours (angiomyolipoma) may be part of the spectrum of the disease. LAM typically occurs in premenopausal women, suggesting the involvement of female hormones in disease pathogenesis. LAM occurs in 30-40% of females with tuberous...
sclerosis complex (TSC) [3,4]. LAM can also occur sporadically in 1 out of 400,000 adult females [3,4]; as in our case. Mutation in TSC1 or TSC 2 gene has been associated with sporadic form of LAM [5].

Histologic changes that is shown in LAM includes spindle-shaped cells with small nuclei, larger epithelioid cells with clear cytoplasm and round nuclei having a smooth muscle cell phenotype, with cyst formation [2]. HMB-45 staining of the LAM cells is a useful marker. With regards to the types of biopsy method to obtain histological diagnosis, Cascante et al. reported a transbronchial lung cryobiopsy using a flexible cryoprobe has a good diagnostic yield compared with using forceps in obtaining histological diagnosis for interstitial lung disease and this technique could avoid a large number of surgical biopsies [6]. Our patient had a transbronchial cryobiopsy performed which was successful in obtaining the diagnosis.

However, in some cases, the diagnosis of LAM can be made with confidence on clinical grounds (without biopsy) in patients with typical cystic changes on high resolution CT scanning of the lung and findings of tuberous sclerosis, angiomyolipoma or chylothorax. There is a proposed definition of LAM according to european respiratory society task force; whereby LAM can be categorised as definite, possible, or probable based on the presence of characteristics or compatible HRCT Thorax, lung biopsy, compatible history, presence or angiomyolipoma or abdominal or chylous effusion [7]. Obstruction of the lymphatic system is the likely mechanism of chylothorax [8].

A prior study has shown that vascular endothelial growth factor-D (VEGF-D) levels are found in lymphangioleiomyomatosis (LAM) but no other cystic lung diseases [9]. Hence, a serologic test for VEGF-D may be useful biomarker for lymphatic involvement and fair predictor for LAM; [9] but otherwise is not available in our setting.

It was a challenge in managing this patient. The estimated rate of recurrence after the first episode pneumothorax in LAM is 75% [10]. Hence chemical pleurodesis is may be performed at first pneumothorax however in patients who failed to respond to initial pleurodesis, they should undergo surgical procedure [7]. In our patient, surgical procedure was not considered following multidisciplinary consensus in view of extensive lung disease. CT abdomen for detection of renal angiomyolipoma which may support the diagnosis and prognosticate the disease was also not done due to her financial limitations. Angiomyolipoma puts the patient at higher risk of bleeding which may require chemoembolization; and periodic imaging by ultrasound is needed if patient is asymptomatic [7]. Patients should be advised against pregnancy on an individual basis as LAM increases further the risk of pneumothorax and chylos effusion [7]. Patients should also avoid oestrogen containing treatments including the combined oral contraceptive pill and hormone replacement therapy[7] as oestrogen may promote the progression of LAM [11]. There are some anecdotal reports of usage of sirolimus in LAM. Recently, a study done in Japan showed that LAM patients who received sirolimus had good drug compliance; and stable quality of life and lung function. However it was also associated with adverse events, including three episodes of pneumonitis [12].

Conclusion

LAM should be considered as a differential in a female with recurrent pneumothorax. Further evaluation with HRCT with/out biopsy is needed to confirm the diagnosis.

References


