Atypical Case of Pulmonary Lymphangioleiomyomatosis

Joseph Costa1, Byron Thomashow2, Mary P Rosenblatt3 and Frank D’Ovidio1*

1Department of Surgery, Section of Thoracic Surgery, Columbia University Medical Center, USA
2Division of Pulmonary, Allergy and Critical Care Medicine, Columbia University Medical Center, USA
3Department of Pathology and Cell Biology, Columbia University Medical Center, USA

Abstract

Lymphangioleiomyomatosis is a rare idiopathic disease classically occurring in young women during their reproductive years, associated with diffuse bilateral cystic lung destruction and extrapulmonary manifestations consisting of large cystic lymphatic tumors known as lymphangioleiomyomas and angiomyolipomas commonly affecting the kidneys. Patients presenting initial symptoms consist of dyspnea, spontaneous pneumothorax or less commonly cough hemoptysis or chylous effusions. Radiographic findings demonstrate diffuse bilateral distribution of thin-walled pulmonary cystic changes on CT of the chest. We present an atypical case of a patient with tuberous sclerosis complex, presenting with unilateral pulmonary lymphangioleiomyomatosis.

Introduction

Lymphangioleiomyomatosis (LAM) is a rare, progressive idiopathic multisystem disease, predominantly diagnosed in women of childbearing age with an estimated prevalence of approximately 1 in 1,000,000 people [1]. LAM is much more common in young women with tuberous sclerosis, where signs of the disease can be identified in up to 40% of cases, predominantly characterized by proliferation of atypical smooth muscle cells in the walls of airways, venules and lymphatics, leading to air trapping and progressive cystic destruction of the lungs. Often, predominant pulmonary symptoms include dyspnea, pneumothorax, chyleus pleural effusions, hemoptysis and eventually respiratory failure. LAM presents in two main forms: Sporadic LAM (S-LAM) representing the majority of cases and tuberous sclerosis complex LAM (TSC), a rare autosomal dominant disease with limited pulmonary involvement. Diffuse distribution thin-walled cysts affecting both lungs mainly characterize pulmonary LAM manifestations. Wenaden et al. described the first known case in a patient with atypical unilateral LAM [2]. We present another atypical case of unilateral pulmonary LAM in a young female with a history of TSC.

Case Presentation

A 28 year-old female, non-smoker with a history of childhood asthma, presented to our emergency room complaining of shortness of breath which began during takeoff and descent of her flight returning home the same day. On admission, she was stable and asymptomatic, and found to have what appeared to be a large right-sided pneumothorax and versus significant unilateral bullous disease on chest X-ray. No intervention was initiated because it was felt her symptoms were due to emphysematous changes rather than an acute intrapulmonary process. She was discharged home with follow up plans for further workup. On return for further workup, she denied any symptoms of shortness of breath. CT chest showed a right-sided pneumothorax with extensive bullous disease of the right lung and destruction of the lung parenchyma. Left lung was grossly clear with overall volume loss and a stable mediastinal shift to the left, due to compression from right-sided large bullae (Figure 1). Liver and kidneys were shown to have multiple angiomyolipomas consistent with tuberous sclerosis. Nuclear quantitative perfusion lung scan demonstrated near total absence of ventilation and perfusion of the right lung; however, ventilation and perfusion were well maintained to the left lung. Pulmonary Function Tests (PFTs) demonstrated moderate obstruction and severe restrictive ventilation defect with low lung volumes consistent with residual hyperinflation (FEV1 0.93 (25%), TLC 2.17 (38%), RV 0.84 (56%) and DLCO of 10.9 (34%). Ventilation-perfusion scan showed near total absence of ventilation and perfusion of the right lung. Left lung was perfused throughout, with preferential perfusion to the upper lung. Genetic testing was negative for both TSC1 & TSC2 mutations, however, given the radiologic findings, and history of childhood asthma, diagnosis of TSC-LAM was made. Decision was made to take the patient was taken to the operating room for right sided pneumonectomy. Intraoperative findings showed the right upper lobe and
the right middle lobe to be atrophic and not ventilating. Attempts to ventilate these lobes were unsuccessful. The right lower lobe was severely abnormal, as characterized by extensive giant bullous destruction. Post-operative course was uneventful, and she was discharged home on post-operative day four. Pulmonary function tests repeated at four months showed significant improvement (FEV1 1.73 (47%), TLC 3.61 (64%), RV 1.47 (96%) and DLCO of 14.3 (45%) consistent with previous obstruction no longer being present and severe restrictive defect now moderate. To date, she has done exceptionally well and became pregnant on two occasions with two uneventful deliveries.

Comment

LAM, classically occurring in women of reproductive age, is a rare idiopathic, slowly progressive systemic disease, characterized by infiltration of neoplastic LAM cells having both smooth muscle and melanocyte characteristics into the lungs and lymphatics, resulting in cystic remodeling of the pulmonary parenchyma. Two types of cells comprising LAM lesions are spindle-shaped and epithelioid, both types reacting with antibodies against smooth muscle antigens (Figure 2). Epithelioid cells react with Human Melanin Black antibody (HMB-45). A positive reaction to HMB-45 is virtually diagnostic of LAM [3]. Diagnosis is otherwise made clinically based on findings on high resolution chest CT of round thin-walled cysts of diameters varying from 0.2 cm to 2 cm diffusely affecting both lungs and at least one corroborative feature, such as a lymphangiomyoma, chylothorax, or history of tuberous sclerosis. It often arises spontaneously in patients with no evidence of genetic disease, with approximately one third of women with TSC affected [4]. CT’s findings of bilateral diffuse pulmonary cysts, bilateral fatty renal tumors and bony sclerosis is pathognomonic of TSC. The TSC1 or TSC2 gene is frequently affected, with TSC2 mutations having a higher incidence of cystic formation rate in lungs [5]. In 15% of cases of genetic testing, mutations in TSC1 or TSC2 will not be present, which was our experience with this patient. However, for the majority of cases, 75% to 80% will have a detectable mutation [6], with mutations in TSC2 being most frequently found in 80% to 90% of patients [7]. TSC commonly presents with the classic triad of mental retardation, epilepsy and cutaneous lesions, however clinical features have been known to be variable. In this case, our patient presented atypically in the absence of typical clinical manifestations associated with TSC. Chromosomal testing showed a normal karyotype with no clonal chromosomal abnormalities detected, negative for TSC1 & TSC2 mutations. There have been reports of less severe clinical manifestations associated with TSC1 mutations [7]. Unlike the first reported case of unilateral TSC-LAM by Wenaden and colleagues [2], this case adds another dimension of variation in the presentation of a rare disease, necessitating the importance of recognizing these atypical presentations during the early onset of the disease process.

References