Pregnancy Complicated by Lymphangioleiomyomatosis

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Lymphangioleiomyomatosis, a multisystem disease characterized by cystic lung lesions can result in respiratory failure and is considered to be sex hormones related. No effective treatment for lymphangioleiomyomatosis is currently available. We report a 35-year-old patient in her second pregnancy. She also had experienced five episodes of spontaneous pneumothorax at the age of 30. Despite excessive estrogen production during pregnancy she had mild non-progressive exertional dyspnea without limitation of daily activities during pregnancy without deterioration of respiratory status.

Keywords: Lung diseases • lymphangioleiomyomatosis • pregnancy

Introduction

Lymphangioleiomyomatosis (LAM) is a rare lung disorder that occurs mainly in women and most commonly during childbearing years. It provokes various symptoms and signs such as dyspnea, chest pain, hemoptysis, pneumothorax, chylos pleural effusion, and eventually respiratory failure. Extra-pulmonary manifestations include abdominal and pelvic masses occurring along the axial lymphatics, chylous ascites, and renal angiomyolipomas. It is characterized by non-neoplastic proliferation of atypical smooth muscle cells that may lead to airway, lymphatic, and blood vessel obstruction overtime.

LAM cells are frequently positive for estrogen and progesterone receptor proteins, suggesting the hormonal sensitivity of this disease. Indeed, several reports have shown exacerbation of LAM during pregnancy. We report a rare case of a 35-year-old woman in her second pregnancy with pulmonary LAM. Her first pregnancy was complicated by acute abruptio placenta and fetal death at the 27th weeks of gestation. To the best of our knowledge it is the first confirmed report of this disease in Iran.

Case Report

A 35-year-old patient was admitted to prenatal clinic in her second pregnancy. Her first pregnancy had ended in a stillbirth at the 27th weeks of gestation because of acute abruptio placenta two years earlier. She became pregnant spontaneously. Her antenatal course was uneventful with no exacerbation of respiratory status in the second pregnancy. The patient also had experienced five episodes of spontaneous pneumothorax at the age of 30 and had been diagnosed as having sub pleural emphysematous change based on histologic finding of specimen obtained by open lung biopsy.

Her chest radiographs showed ground glass opacities and high resolution chest computed tomography (CT) showed innumerable thin-walled cystic air spaces of different sizes throughout the lung parenchyma (Figure 1). Insertion of chest tubes, pleurodesis and open lung biopsy were performed. On admission (eight weeks of gestation), no abnormality of breath sounds was noted. Neurologic findings were normal. There was no history of seizure. Laboratory findings...
were normal too. The patient was neither smoker nor oral contraceptive user.

Ultrasound examination demonstrated a single eight weeks viable fetus. Uterus, ovaries, abdomen, and kidneys looked normal.

The patient was referred to the pulmonary outpatient clinic for further evaluation. Revision of the lung biopsy showed LAM (Figure 2).

Pulmonary function tests revealed mild restrictive lung disease. She had mild non-progressive exertional dyspnea without limitation of daily activities during pregnancy. Frequent fetal assessments during pregnancy were normal. At the 37th weeks of gestation, she underwent elective cesarean section by using spinal anesthesia. A male baby weighing 2800 g was delivered with Apgar scores of 9 and 10 in the first and 10th minutes, respectively. Her postoperative course was uneventful. She was referred to the pulmonary outpatient clinic on day 5 of postoperation and was followed up with no deterioration of the disease. Remarkable changes in computed CT findings of the lung were not noted in comparison with the prepregnancy period.

**Discussion**

Pulmonary LAM is characterized by hamartomatous proliferation of immature smooth muscle cells in the alveolar walls and around the lymphatic vessels, veins, and the bronchiolar tree of the lungs. Extrapulmonary features, including

**Figure 1.** Chest radiography of the patient shows ground glass opacities. Tomogram shows numerous small thin walled cysts that are distributed through the lung.

**Figure 2.** Open lung biopsy compatible with lymphangioleiomyomatosis. The oval and spindle cells are positive for MB45 and negative for CD31. Some of them reveal cytoplasmic but not nuclear staining for S100.
lymph node masses, chylous ascites, uterine fibroids, and renal angiomyolipomas, were not present in our patient.

The name LAM reflects the different components of the disease. Lymph and angio refer to the lymph and blood vessels that are involved and leiomyo refers to the smooth muscle.

The prevalence of pulmonary LAM as a rare lung disease affecting primarily young women of childbearing age is reported one per million in the UK, France, and the USA. The prevalence in Asian countries is reported lower. In Singapore it is about 0.24 per 100,000 of population.

LAM has been observed almost exclusively in women, the mean age of onset being around 34 years. Common clinical manifestations of pulmonary LAM include progressive dyspnea on exertion, hemoptysis, repeated pneumothorax, chylous effusions, persistent cough, and fatigue.

Abnormal proliferation of smooth muscle cells in the lungs results in the destruction of pulmonary architecture. Patients with this problem eventually suffer from chronic respiratory failure with severe obstructive ventilatory impairment. Lung transplantation is considered as a last resort.

The causes of LAM are unknown. It is not inherited and is not passed on to the children.

Several reports suggest that abnormal proliferation of smooth muscle cells of the lungs is caused or promoted by estrogens. This is further supported by the fact that pulmonary LAM only affects women in their reproductive years. Its exacerbation with pregnancy or after hormonal manipulation are highly suggestive of the possibility of hormonal influence. Kitzteiner and Mallen reported a successful case of early oophorectomy as means of treatment. Eliasson et al. also revealed in their meta-analysis that oophorectomy with the administration of progesterone was the most effective therapeutic modality.

Most treatments in pulmonary LAM have been directed towards sex hormones manipulations such as reducing or blocking estrogen activity and early induction of menopause. However, two recent reports on a large number of patients concur that anti-estrogen therapy may not be beneficial for most patients. Overall, although these studies have contributed to the understanding of this rare disease, there are still uncertainty about the prognostic factors. The paucity of information on the natural history of pulmonary LAM that may influence the right time for medical intervention should be considered and evaluated.

In most patients, LAM is a chronic disease that span decades. Even severe disease can be stabilized. Because of diversity in the clinical course, there is a need to derive predictive parameter as to which patients will have progressive disease and require specific treatment. Some LAM cells express estrogen and progesterone receptors, which may account for the hormones in disease progression and treatment. In our patient, however, delay in the diagnosis withheld intervention but pregnancy was not associated with a poor prognosis. Immunohistochemistry and biochemical assays have demonstrated the existence of hormone receptors in lung tissues of patients with LAM. This finding is the biologic corollary to the finding LAM respond to hormonal therapy. We have examined lung tissue specimen of our patient for estrogen and progesterone receptors by immunohistochemistry assays. The results were negative. In our patient, it is possible explanation that despite her excessive production of estrogen during pregnancy, her respiratory disease did not deteriorate during this period. Of course it is necessary to do further study for reaching to a definite conclusion.

References


