Pregnancy Unmasking Lymphangioleiomyomatosis

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Abstract
A 30 year-old housewife presented with cough and shortness of breath which progressed during her ensuing pregnancy, culminating in a still-birth at 9 months of gestation and requiring her hospitalisation in the immediate postpartum period. HRCT scan of the thorax showed thin-walled cysts and open lung biopsy confirmed the clinical impression of lymphangioleiomyomatosis. She was put on oral medroxyprogesterone acetate. After disease flare-up in the postpartum period her symptoms have stabilised.

INTRODUCTION

Pulmonary lymphangioleiomyomatosis (LAM) is a rare disease of unknown aetiology characterised by proliferation of unique, smooth muscle-like cell type (LAM cell) involving the small airways, the pulmonary microvasculature and the lymphatic structures leading to airway obstruction, cystic changes in the lung parenchyma (hallmark of this disease), pulmonary haemorrhages, chylous pleural effusion and pneumothorax. This disease occurs primarily in pre-menopausal women and hormonal factors have been suspected of have an important role to play.1-4 We report here a case of lymphangioleiomyomatosis in a young woman who presented with insidious onset of cough and shortness of breath that worsened during her pregnancy and immediate post-partum period.

CASE REPORT

A 30 year-old housewife presenting with worsening of shortness of breath and cough after a still-birth at nine months of pregnancy was admitted for evaluation.

She was apparently well till about 18 months back when, after a brief febrile illness, she developed cough with scanty expectoration followed by shortness of breath on moderate exertion without any wheeze, orthopnoea, paroxysmal nocturnal dyspnoea, haemoptysis or chest pain. On the basis of chest radiograph, local doctors prescribed antitubercular drugs, which she took for the next six to seven months without much symptomatic relief.

Two months into her illness she developed pregnancy during the course of which her cough and shortness of breath worsened requiring frequent medical consultations. At 9 months of pregnancy she delivered a macerated stillborn fetus. Within 10 days of delivery she was admitted in the medical ward with cough, expectoration, severe shortness of breath, oliguria and features of overt right ventricular failure. ECHO cardiogram suggested pulmonary hypertension with tricuspid regurgitation and HRCT scan of the thorax was reported to show ‘extensive cystic bronchiectasis.’ She improved with O2, antibiotics and diuretics and was discharged after 20 days but was later admitted in our ward for re-evaluation.

The patient had no h/o exposure to pets, farm animals, dusts or chemicals; no h/o diabetes, hypertension, rash, arthritis, seizures, addiction or any risk factor for HIV infection. Her previous pregnancies at 5 and 7 years were uneventful.

On physical examination, the patient had digital clubbing but no peripheral oedema, lymphadenopathy, cyanosis or skin lesions. The JVP was not raised, she was afebrile, the pulse 100/min regular, respiration 20/min and BP 110/70 mmHg. There were bilateral end-inspiratory crackles, more on both lung bases. There was RV apex and loud P2.

Her chest X-ray (Fig. 1) showed prominent cystic changes in addition to reticulo-nodular markings with well-preserved lung volumes and mild cardiomegaly.

Her sputum was repeatedly negative for AFB and Bactec culture for Mycobacterium tuberculosis showed no growth. Her peripheral blood count and liver and renal function tests were normal. Serum ANF and rheumatoid factor were negative and serum angiotensin-converting enzyme level was normal. Spirometry showed moderate, mixed, obstructive and restrictive ventilatory defect and S_pO_2 on room air was 90%.

The HRCT scan of thorax on review (Fig 2), showed thin-walled cysts 2-10 mm in diameter distributed throughout the lung fields without any lymphadenopathy or pleural abnormality. A CT scan of the abdomen was normal.
An open-lung biopsy (Figs. 3, 4) showed dilated alveolar spaces (emphysematous) with smooth muscle tissue in their walls, perivascular smooth muscle proliferation, aggregates of lymphoid cells and dilated lymphatic spaces. No granuloma or malignancy was seen. The features are consistent with early lesions of lymphangioleiomyomatosis.

The patient was put on medroxyprogesterone acetate 10 mg orally daily and future pregnancies were discouraged.

She is on regular follow-up over the last 8 months. She is symptomatically better with stable radiological appearance and can perform her daily household activities.

**DISCUSSION**

The prevalence of lymphangioleiomyomatosis (LAM), a rare condition affecting the lungs of premenopausal women, is reported around one per million in the UK, France and the U.S. Reported prevalence in Asian countries is lower, in Singapore it being 0.24 and in Korea 0.03 per 100,000 of population.

LAM is exclusively confined to women, the mean age of onset being around 34 years. Patients present most commonly with shortness of breath, cough and pneumothorax. Chylous pleural effusions and haemoptysis are less common. Nonspecific clinical features with unremarkable chest radiographs at presentation lead to a delay in diagnosis typically between 3 and 5 years or an incorrect diagnosis. In our country, high prevalence of tuberculosis can lead to a misdiagnosis of LAM as pulmonary or miliary tuberculosis as in our case. Worsening of the respiratory symptoms and respiratory function has been noted during pregnancy with acceleration of the disease process. Symptoms worsened in our patient during pregnancy and immediate post-partum period leading to hospitalisation. Investigations including CT scan of thorax made a comparatively early diagnosis possible. After her post-partum flare-up, her symptoms stabilised. Extra-pulmonary features, including lymphnode masses, chylous ascites, uterine fibroids and renal angiomyolipomas, were not present in our patient, neither were there any findings to suggest tuberous sclerosis. Obstructive and combined obstructive-restrictive ventilatory defects with impaired gas transfer are commonly observed in patients with LAM.

The most common radiographic findings in LAM are...
bilateral reticular or reticulo-nodular pattern involving all lung zones with preserved or increased lung volumes. Cystic changes may also be identified.1

Our patient's chest X-ray (Fig. 1) showed diffuse shadowing, cystic changes with preserved lung volumes - findings which can be also seen in Langerhan's cell histiocytosis (LCH), sarcoidosis and extrinsic allergic alveolitis.2 Pneumothorax and pleural effusions are also common at presentation.

The characteristic HRCT (of thorax) findings consist of thin-walled cysts 2-20 mm or more in diameter distributed throughout the lung fields with normal parenchyma between the cysts1,2,4 as in our case (Fig. 2). The cysts can be differentiated from honey-combing due to interstitial lung disease (ILD) by their diffuse distribution (subpleural location in ILDs4) and the presence of relatively normal intervening parenchyma. In LCH the cysts occupy mid and upper lung zones sparing the bases and are often of irregular shape; and there are usually multiple pulmonary nodules.1,2

Although transbronchial biopsy with HMB 45 staining (monoclonal antibody which in the lung stains only LAM cells) can be sufficient to make a diagnosis of LAM, open-lung biopsy has been the gold standard.2

LAM is thought to be hormonally dependent and hormonal manipulation in the form of progesterone supplementation or antioestrogen measures like ovarian irradiation, tamoxifen, LHRH or oophorectomy have been used.1,2,3,4 The natural history of inexorable clinical deterioration has been significantly altered only in very rare instances. Progesterone, either oral or IM depot preparation, has been the most frequently used medical treatment of the disease.2 Beneficial effects have been noted on chylothorax or chylous ascites, whereas pulmonary parenchymal changes are suggested to be stationary or progressive.1 The poor results of medical therapy have prompted lung transplantation in patients with end-stage LAM and the outcome is similar to the figures following transplantation for other lung diseases.3

For a disease whose first description appeared in literature in 1937,4 the aetiology is still eluding us. The disease should be considered in premenopausal women seeking medical attention for worsening dyspnoea, pneumothorax or chylous fluid collections and should be included in the differential diagnosis of chronic interstitial lung-diseases. Being hormone dependent the disease is often exacerbated by pregnancy leading to complications. The disease being rare, definite data regarding survival, diagnostic criteria, optimal methods of therapy are not available, all of which need to be answered by well-designed studies.

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REFERENCES

Announcement
The 4th Annual Clinical Course in HIV Medicine

January 10th-21st, 2005 at Department of HIV Medicine, Ruby Hall Clinic, Pune.

Organized by Center for Health/AIDS Research and Training (CHART) (An Indo-American initiative by University of South Florida, Tampa, USA) and Department of HIV Medicine, Ruby Hall Clinic

- Course format includes lectures, case discussions, hands-on clinical training and laboratory and research work.
- Only 30 candidates.
- National and international faculty teaching basic and advanced principles of HIV management.
- Certificate of participation.
- The deadline for receipt of applications is 30th November, 2004.

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