RADIOLOGY FORUM

Lymphangioleiomyomatosis : A Rare Cause of Breathlessness

B.N. Vinodh, S.K. Sharma, S. Mukhopadhyay[1] and S. Datta Gupta[2]

Departments of Medicine, Radiodiagnosis[1] and Pathology[2], All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India

[Indian J Chest Dis Allied Sci 2004; 46 : 205-208]

CLINICAL SUMMARY

A 24-year-old female presented with complaints of cough with scanty expectoration, breathlessness on exertion and chest pain for the last three years. These symptoms had appeared during the 12th week of her third pregnancy. She was given anti-tuberculosis treatment at another hospital for nine months without any improvement in symptoms. Four years ago she had been diagnosed to have leprosy of borderline variety for which she had received treatment. On examination, she was tachypnoeic with a respiratory rate of 33 breaths per minute. She had clubbing and small, discrete and firm lymph nodes in the anterior cervical region. Chest examination revealed wheezing with bibasilar end-inspiratory crepitations.

INVESTIGATIONS

A plain chest radiograph revealed extensive small cystic lesions involving the entire lung fields on both the sides, large cystic lesions in the right upper lobe, mildly increased lung volume and obliteration of the right costophrenic angle with a small area of calcification in the right lower lobe (Figure 1). Arterial blood gas analysis while breathing room air revealed: pH of 7.35, $PaCO_2$ of 27.8 mmHg, PaO_2 of 93.6 mmHg, HCO_3 of 17.1 meq/l and oxygen saturation of 96.2 per cent. Spirometry revealed FVC 30%, FEV_1 35% and PEFR 75% of the predicted value. FEV_1/FVC 118% with diffusion capacity of the lung for carbon monoxide (DLCO) (steady state method) 21.8% of the predicted value.

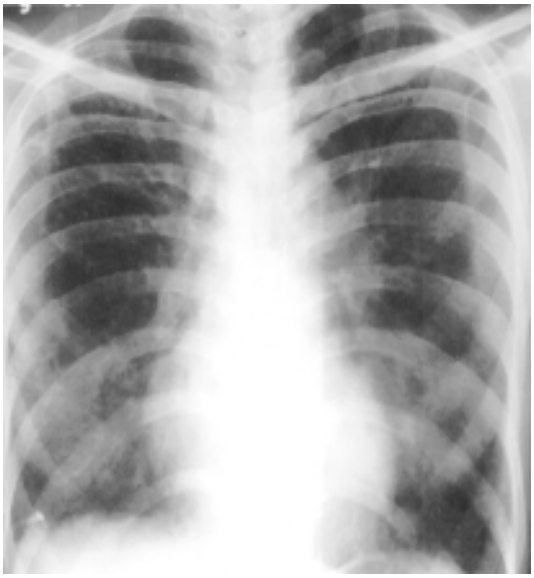

Figure 1. Chest radiograph (PA view) showing the extensive small cystic lesions involving the entire lung fields on both sides.

[Received: November 24, 2003; accepted after revision: April 7, 2004]

Correspondence and reprints request: Dr S.K. Sharma, Professor and Head, Department of Medicine, Chief Division of Pulmonology and Critical Care Medicine, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-110 029, India; Tele.: 91-11-26594415; Telefax: 91-11-26588641; E-mail: <sksharma@aiims.ac.in>.

The high resolution computerised (HRCT) scan of the chest revealed extensive varied sized thin-walled cysts distributed throughout both the lung fields with the cyst size ranging from one millimeter to 3.5 centimeter in diameter. No lung zone was spared. Most of the cysts had perceptible thin wall with the majority of them having round or oval shape and some having irregular outline. The lung parenchyma between the cysts was normal. The main and left pulmonary arteries were enlarged. Few small pre-tracheal and pre-carinal lymph nodes were seen. Mild pleural thickening was observed in the left lower zone (Figure 2).

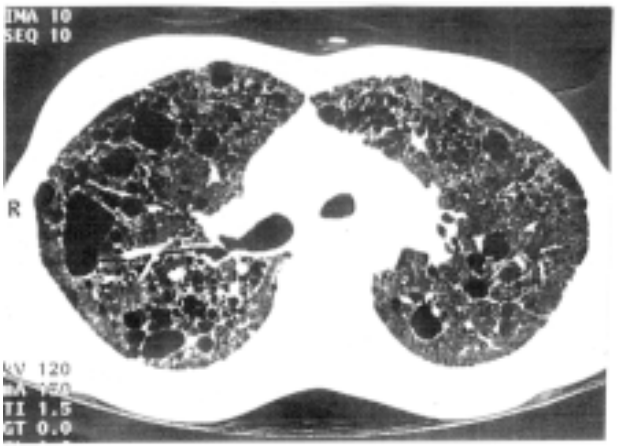

Figure 2. High resolution computerised (HRCT) scan of the chest through upper lobes showing the thin-walled cysts of varying sizes (1 mm to 3.5 cm).

Video-assisted thoracoscopy of the right lung revealed a shrunken fibrotic lung with multiple cysts all over the lung fields. A biopsy taken from the right lung showed alveoli with thickened walls with inflammation and muscularisation around slit like spaces. Special staining with Masson's trichrome stain showed smooth muscle bundles around vascular spaces with some lymphocytes (Figure 3). However, immunofluorescence study with HMB-45 was negative. Based on these features, a diagnosis of lymphangioleiomyomatosis (LAM) was made and the patient was started on monthly medroxyprogesterone 450 mg i.m. The patient was followed up for four years. She had one episode of spontaneous pneumothorax, which was managed with underwater seal drainage. Her breathlessness increased gradually and the

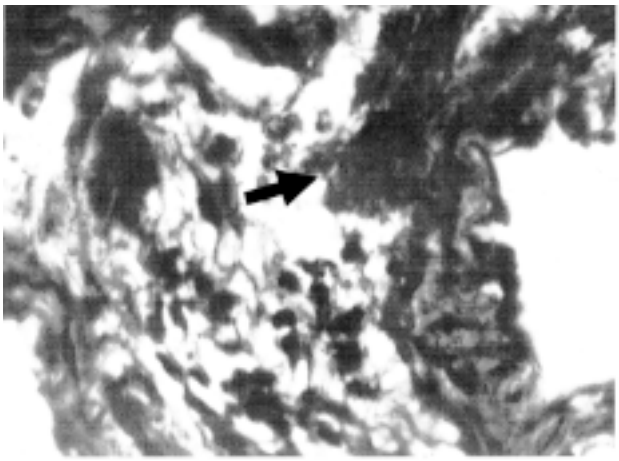

Figure 3. Higher power showing smooth muscle bundles (arrow) around vascular spaces with some lymphocytes (Masson's Trichrome x 40).

patient became breathless even at rest by the end of the fourth year. A repeat lung function study and HRCT scan of the chest during the third year of follow-up did not show any change from the earlier findings. She developed features of chronic cor-pulmonale by the end of four years. A repeat arterial blood gas analysis with the patient breathing room air revealed: pH of 7.394, $PaCO_2$ of 35.0 mmHg, PaO_2 of 58.4 mmHg, HCO_3^- of 17.1 meq/l and oxygen saturation of 89.5 percent. Patient was put on continuous domiciliary oxygen therapy at four litre per minute and is being followed up.

DIAGNOSIS

Lymphangioleiomyomatosis (LAM)

DISCUSSION

Lymphangioleiomyomatosis (LAM) is a rare disease of unknown cause, first described in 1937[1,2]. It predominantly occurs in women of reproductive age group. It occurs frequently in association with tuberous sclerosis (TSC) and is characterised by alveolar smooth muscle proliferation and cystic destruction of the normal lung parenchyma. To date more than 445 cases have been reported[3]. The prevalence of LAM in TSC population is estimated to be

between one to three percent[3]. Except for occasional case reports no epidemiological reports are available from the Indian subcontinent[4].

LAM commonly presents with dyspnoea (often due to spontaneous pneumothorax and pleural effusion), chronic cough, haemoptysis, wheeze, chest pain and *ascites*. About 50% of the patients present with recurrent pneumothorax. Our case did not have pneumothorax at the time of presentation. However during the follow-up period, she developed one episode of pneumothorax that was managed with under-water seal drain. The pulmonary function tests (PFT) in LAM show wide range of patterns from normal to obstructive through a mixed picture to restrictive with the obstructive pattern being common. The PFT in our patient revealed a restrictive pattern. It also revealed a markedly decreased DLCO which is the most frequent abnormality seen in LAM. Our case developed type 1 respiratory failure and cor-pulmonale at the end of four years. These along with cyanosis are the complications seen at the end stages of LAM.

The chest radiographic features of extensive small cystic lesions involving the entire lung fields on both the sides with increased lung volumes as seen in this case are the frequent findings described in LAM. However in the initial stages, chest radiograph may be normal. In such cases HRCT scan may show the abnormalities, as it is a more sensitive indicator of early disease[5]. The presence of numerous thin walled cysts ranging from one millimeter to several centimeters in size involving the lungs diffusely is characteristic. These characteristic features on HRCT scan can obviate the need of a lung biopsy to establish the diagnosis.

Langerhans cell histiocytosis, idiopathic pulmonary fibrosis and emphysema were the differential diagnosis in our case. However, the characteristic type and distribution of lesions helped in differentiating LAM from these entities.

Light microscopy findings of the lungs are characterised by diffuse interstitial proliferation of bundles of "immature" smooth muscle cells. These cells have a benign appearance and immunohistochemistry shows smooth muscle cells. These cells have a benign appearance and immunohistochemistry shows smooth muscle actin and melanoma associated antigens. These antigens are called HMB-45 antigens and are useful for diagnosis of LAM because LAM is the unique smooth muscle cell proliferation in the lung that expresses such antigen[5]. However, in our case this was negative.

Management of LAM is mainly symptomatic and includes the symptomatic treatment of wheezing, pneumothoraces and pleural effusions. It is not uncommon for these patients to be treated as tuberculosis, as was seen in our case, because of the lack of awareness and facilities of a diagnostic lung biopsy in India[4]. Since LAM is usually seen in women of reproductive age group hormonal factors are thought to be involved in its pathogenesis. Hence hormonal manipulations, like progesterone, oophorectomy, tamoxifen and gonadotrophin releasing hormone agonists have been used to prevent the progression of the lung disease but with mixed results. A meta-analysis of 30 cases, which included eight patients treated with progesterone alone, has demonstrated a success rate (improvement or stabilization) of 50% with progesterone use[6]. Hence, progesterone therapy is considered as the first-line therapy for LAM. The presence of chylous effusion or *ascites* is correlated with the responsiveness to medroxyprogesterone[6]. Unfortunately our patient continued to deteriorate despite being on medroxyprogesterone. Lung transplantation is the best therapeutic option in these cases in the event of failure of medical treatment and in end stage disease[7]. However, recurrence of LAM has been described in the allograft also[8,9]. The overall long-term prognosis of LAM is poor. Most of the patients deteriorate relentlessly after the appearance of symptoms and succumb to death due to respiratory failure by the end of 10 years.

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