Pulmonary Lymphangiomyomatosis in Childhood? — Marked Smooth Muscle Cell Proliferation of the Lung in a Preadolescent Girl with Repeated Pneumothorax and Progressive Dyspnea

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ABSTRACT

A 13-year-old girl with repeated spontaneous pneumothorax and progressive dyspnea is described. The biopsy specimen of the lung showed marked proliferation of smooth muscle cells in the thickened bullous wall and alveolar septa, which was similar to the findings of the pulmonary lymphangiomyomatosis. Pulmonary lymphangiomyomatosis is one of the diseases which should be considered when children have progressive dyspnea, chylous effusions and repeated spontaneous pneumothorax.

Key words: Pulmonary lymphangiomyomatosis, Smooth muscle cell proliferation

It is well known that hypertrophy and hyperplasia of smooth muscle occur in many types of chronic pulmonary disease including interstitial fibrosis, emphysema and pulmonary lymphangiomyomatosis (PLM). Among these PLM is a rare disease characterized by focal proliferation of smooth muscle involving alveolar septa, and peribronchial, perivascular, perilymphatic regions in the lung5). The most frequent problem reported in patients with PLM is progressive dyspnea. Pneumothorax, chylous effusions and hemoptysis are frequent complications. Clinical observations suggest that steroid hormones play an influential role in the biologic behavior of PLM. The patients are women of reproductive age and exacerbation related to menstruation and pregnancy has been reported1,7).

In this paper, we describe a preadolescent girl with repeated spontaneous pneumothorax and progressive dyspnea. Marked proliferation of the smooth muscle was found in the lung biopsy specimen.

CASE REPORT

A 13-year-old girl was referred to us for further evaluation of dyspnea. She was the product of a normal pregnancy and delivery. She showed almost normal development until the age of 9 years and 9 months when she first had dyspnea. Chest roentgenograms revealed right pneumothorax and she made an apparently uneventful recovery. At the age of 10 years and 3 months she again contracted pneumothorax of the right lung. Tomogram of the chest showed the bulla comparable to honeycombs at the bilateral lungs. A lung biopsy was performed, but an established diagnosis was not made. Because of repeated pneumothorax she was operated on for the bulla of the bilateral lungs. During her illness general fatigue gradually increased and physical development was retarded. The patient was of normal intelligence without any history of seizures.

On physical examination, she was a small and slender girl with pale skin and clubbing of the fingers. Examination of the blood revealed a hemoglobin of 13.5 g/dl, and a white cell count of 8,300 /cmm, with 57% neutrophils. Her arterial blood gas levels on room air were: pH, 7.415; Po2, 46.9 mmHg; Pco2, 30.5 mmHg. Her vital capacity decreased to 0.77 L (38.1 percent predicted). A chest radiogram showed hyperinflation of the lungs and diffusely abnormal lung fields with a linear pattern throughout. The level of serum estradiol was below 5.0 pg/ml. Levels of serum progesterone, LH and FSH were also within the prepubertal levels. Computed tomogram of the chest showed remarkable emphysematous areas, like honeycombs in the bilateral lungs (Fig. 1). The biopsy specimen was re-evaluated (Fig. 2). An increased amount of smooth muscle cells proliferating in the thickened bullous wall was found, which
was focal and far in excess of what was observed in an ordinary bulla. There was evidence of diffuse proliferation of the smooth muscle cells in the thickened alveolar septa. These pathological features were similar to those of PLM. However, a lymphangiomatic area was not found in the specimen available.

Ultrasonography of the kidney, liver and spleen showed no abnormal findings. Computed tomography of the head and abdomen revealed nothing unusual. There were no findings that suggested tuberous sclerosis. She was treated with medroxyprogesterone acetate 200 mg p.o. every 2 weeks for 6 months without improvement of clinical symptoms.

DISCUSSION

The clinical observations in our patient are consistent with those of PLM. Unfortunately, lymphangiomatic area necessary for the histological diagnosis of PLM was not found in the specimen available and an established diagnosis of PLM was not made. However, the pulmonary myoproliferation in our patient was focal rather than uniform and was more remarkable than that of other diseases, suggesting that our patient contracted PLM.

It is of interest to note that our patient was preadolescent. The predominant occurrence of this disease in women of reproductive age suggests an association between steroid-hormone metabolism and lymphangiomyomatosis; the proliferation of smooth muscle cells is dependent on estrogen. The existence of specific saturable receptors for estrogen, progesterone and glucocorticoid in the specimens of PLM lung has been reported. Therefore, hormonal manipulation by the use of progesterone, tamoxifen and oophorectomy has been documented.

There have been no reports concerning the initiation of smooth muscle proliferation in PLM. Because our patient is preadolescent and menarche has not occurred, the initial proliferation of smooth muscle may not be associated with increase in the estrogen levels. It is likely that the beginning of the proliferation of the smooth muscle occurs early before reproductive age and the symptoms of PLM become apparent after adolescence on account of the accelerated growth of the smooth muscle. However, the possibility that smooth muscle proliferation found in our patient was independent of estrogens could not be excluded.

PLM is a rare, very possibly underdiagnosed disorder in women. Marked proliferation of the smooth muscle of the lung in our patient raises the issue of the existence of PLM in childhood. The outlook is poor for PLM patients as they usually die within ten years. The results of currently known hormonal therapies for PLM have been controversial. The lack of sustained effect is most likely attributable to the patient status far advanced at the start of therapies. Treatment at an early stage will clarify a true role of hormonal manipulations in
PLM. Therefore, PLM is a disease which should be taken into consideration when children have progressive dyspnea, chylous effusions and repeated spontaneous pneumothorax.

(Received June 1, 1989)
(Received July 8, 1989)

REFERENCES