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Pulmonary Lymphangioleiomyomatosis in a Male

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Pulmonary lymphangioleiomymatosis has been obseved almost exclusively in women, usally in their reproductive years. Exacerbations with pregnancy and after hormonal manipulation have been documented, and it has been suggested that its pathogenesis is due to the influence of hormonal(estrogenic) stimulus. The clinical, roentgenographic, and histopathologic features of this case of pulmonary lymphangioleiomyomatosis in a 22-year-old male are all characteristic of those described in prior reports, except for the patient's sex. With the following case of pulmonary lymphangioleiomyomatosis in a male, we suggest the possibility of the existence of an additional pathogenetic mechanism.

Key Words : *Lung, Lymphagioleiomyomatosis, Male, Interstitisal disease.*

INTRODUCTION

Pulmonary lymphangioleiomyomatosis is a rare disease that affects only women, primarily those in their reproductive years (Kane et al., 1978 : Kitzsteiner et al., 1980 ; Corrin et al., 1975). It has distinctive histopathologic characteristics such as a widespread linear or nodular proliferation of the smooth muscles that line the lymphatics in the pulmonary interstitium (Kane et al., 1978 ; Corrin et al., 1975 ; Vazquez et al., 1976). It occurs with respiratory insufficiency in the majority of cases (Kane et al., 1978 ; Corrin et al., 1975). Other initial clinical manifestations include spontaneous pneumothorax, chylous pleural effusion, and hemoptysis. There is no successful treatment for it, and many patients undergo a fatal course within 10 years of the initial onset of symptoms. We experienced an exceptional case of pulmonary lymphangioleiomyomatosis in a male, which is pathogenetically unexplainable in light of current concepts. We hereby report it with an additional possible hypothesis of its pathogenesis.

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CASE REPORT

A 22-year-old male was admitted to Soonchunhyang University Hospital in November 1989. He complained of dyspnea, which was aggravated spontaneously during this time. Up until 6 months prior to his admission, he underwent closed thoracotomy 3 times for relieving pneumothorax. About 4 years ago he had recovered form pulmonary tuberculosis. There was no medical history of mental retardation or seizure. His only remarkable physical finding was the absence of breathing sounds in the left hemithorax. Chest P-A upon admission revealed increased interstitial densities with honeycombing in both lungs and a moderate degree of pneumothorax in the left hemithorax (Fig.1). A chest CT scan showed pneumatic thin-walled cysts replacing the entire lung fields, especially in both upper lung fields (Fig.2). He had a 59.5% fall in FEV1/FVC ratio and a 64.5% fall in FVC

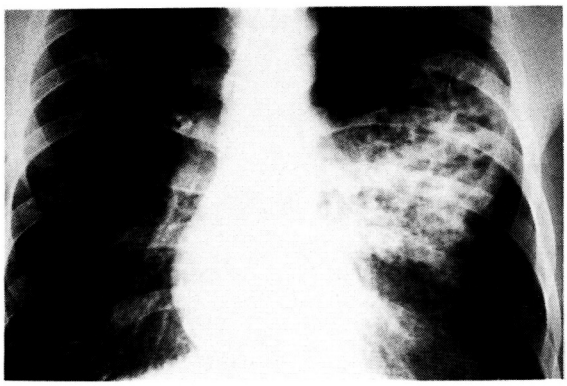

Fig. 1. Increased interstitial markings and scattered honeycombings are noted in both lung fields.

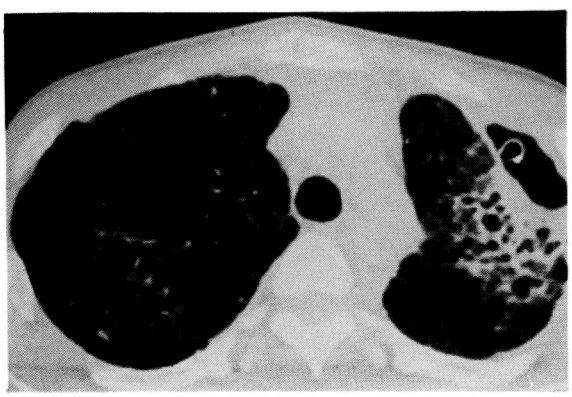

Fig. 2. Entire lung fields were replaced by pneumatic thin-walled cysts. pneumothorax with chest tube is also noted in the left hemithorax.

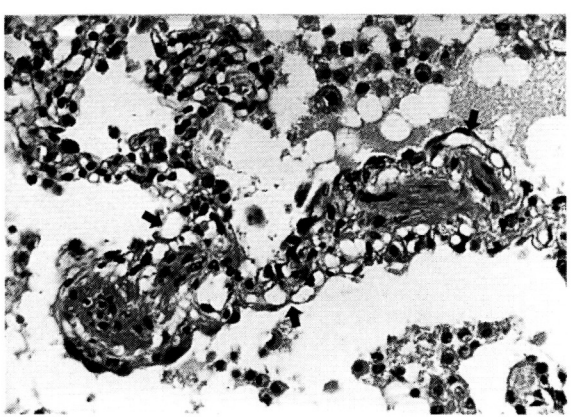

Fig. 3. Microscopic nodular proliferation of smooth muscle with myriads of subsidiary lymphatic channels(arrows) is shown(H&E, ×200)

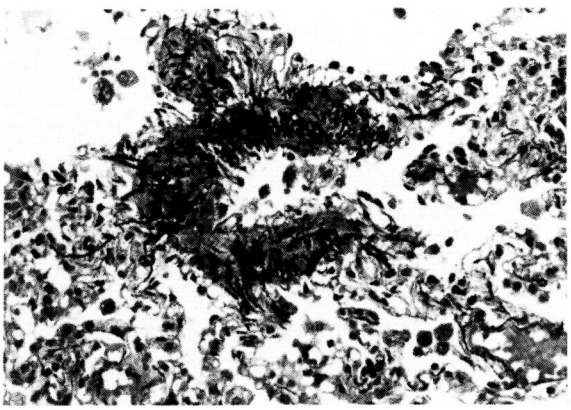

Fig. 4. Vascular spaces totally obliterated by nodular proliferation of smooth muscle were easily identified (Elastic stain, ×400)

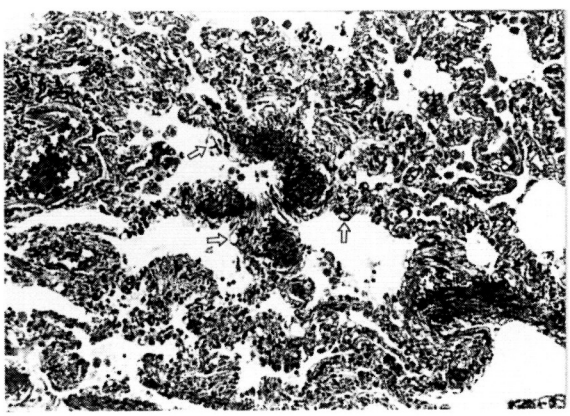

Fig. 5. Bundles of smooth muscle with numerous ectatic small lymphatics lined by endothelium(arrows) were noted(Masson's trichrome stain, ×400)

on pulmonary function test performed after relief of pneumothorax. Under the clinical impression of interstitial lung disease, open lung biopsy was performed. The outer surface of the lung was, for the most part, replaced with widespread subpleural blebs. A 1.5㎝ wedge of parenchyma was excised from the left upper lobe. After fixation with 10% buffered formalin, the tissue was embedded in paraffin. Sections were stained with hematoxylin-eosin, masson's trichrome, and elastic stain for obliterated vessel wall. Microscopically, the major alteration in this biopsy specimen (a sine quanon for outright lymphangioleiomyoma) was a proliferation of smooth muscle along the lymphatic route in the pulmonary interstitium, especially prominent in

pleura and septa. Alveolar spaces were diffusely obliterated by bundles of smooth muscle with myriads of subsidiary irregulay lymphatic channels (Fig.3). Numerous intra-alveolar hemosiderin laden macrophages were also found. Individual smooth muscle cells were spindle to oval and occasionally pleomorphic with nuclear hyperchromasia. They have abundant eosinophilic cytoplasm with no mitoses. But nuclear hyperchromasia or pleomorphism were not so prominent in the smooth muscle cells surrounding the small ectatic lymphatics in nodular fashion as in which surrounding the large irregular lymphatics, especially in the subpleural region with diffuse infiltrative pattern. Masson's trichrome stain confirmed the nature of the smooth muscle around numerous lymphatic channels (Fig. 4). Vascular spaces were totally obliterated by nodular proliferation of the smooth muscle, but they were easily identified in elastic stain (Fig. 5). Interstitial inflammatory reactions were multifocal and mild, admixed with nodular proliferation of smooth muscle bundles. Moderate degree of interstitial fibrosis and focal giant cells were found only in the subpleural region which may results from thoracotomy.

DISCUSSION

The patohgenesis of pulmonary lymphangioleiomyomatosis has been the subject of many studies but is still uncertain. Theories proposed for the pathogenesis of pulmonary lymphangioleiomyoma include hormonal imbalance and a forme fruste of tuberous sclerosis. The properties of the disease that only affects women in their reproductive years and which is exacerbated with pregnancy or after hormonal manipulation are highly suggestive of the possibility of hormonal influence (Kane et al., 19 78 ; Kitzsteiner et al., 1980). Kitzsteiner and mallen (1980) report a successful case of early oophorectomy as a means of treatment. Some authors who regard pulmonary lymphangioleiomyoma sa a forme fruste of tuberous sclerosis have emphasized that several characteristics of pulmonary lymphangioleiomyoma, such as sex and age distribution, histologic features, the presence of renal angiomyolipomas, and the involvement of lymphatics and lymph nodes, are similar to those of tuberous sclerosis (Corrin et al., 1975 ; Valensi, 1973 ; Stovin et al., 1975). Stovin and coworders (1975) claim that vascular smooth muscle proliferates in tuberous sclerosis and that the perilymphatic cells are involved in lymphangioleiomyoma ; that both axial and peripheral structures are involved in tuberous sclerosis, whereas only axial structures are involved in lymphangioleiomyoma ; and that localized nodular proliferations of smooth muscle occur in tuberous sclerosis, as opposed to the more diffuse proliferation in lymphangioleiomyoma.

The clinical, roentgenographic, and histopathologic features of the disease seen in this patient were all characteristic of pulmonary lymphangioleiomyoma, except for the patient's sex. This case involving a male patient was beyond the former concept of hormonal imbalance. He had neither a history of hormonal therapy nor endocrinologic symptoms or signs. There was no evidence of tuberous sclerosis, e.g., mental retardation, seizure, or adenoma sebaceum. Therefore, we considered the possibilithy of the existence of new etiologic factors. He had a history of multiple thoracotomy, tuberculosis, and longstanding emphysema. Such conditions may act as a significant irritant in pulmonary lymphatics and may give rise to lymphatic obstruction and engorgement, as well as hypertrophy of the smooth muscle around the lymphatic spaces in the pulmonary interstitium.

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