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Case Report

Pulmonary lymphangioleiomyomatosis: a case report

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Abstract: Pulmonary lymphangioleiomyomatosis is a rare disease that presents with diffuse progressive destruction of the pulmonary parenchyma. The incidence is less than 1 per million. No effective treatments are currently proposed for this disease. A 29-year-old woman who was diagnosed with pulmonary lymphangioleiomyomatosis received excisional biopsy and symptomatic supportive care. She was diagnosed with pulmonary lymphangioleiomyomatosis and was treated with anti-estrogen therapy and symptomatic supportive care. Pulmonary lymphangioleiomyomatosis is a very rare tumor that cannot be effectively cured.

Keywords: Pulmonary lymphangioleiomyomatosis, pathological examination, immunohistochemistry

Introduction

Pulmonary lymphangioleiomyomatosis is a very rare tumor. Burrell reported the first case of pulmonary lymphangioleiomyomatosis; however, its etiological factors, pathogenesis, and treatment have been recognised only in recent years [1]. An epidemiological survey conducted in seven countries including the United Kingdom and the United States found that the incidence of pulmonary lymphangioleiomyomatosis is 3.4-7.8 per million [2]. PLAM is a rare lung disease of unknown aetiology. It is restricted to females who are generally premenopausal. Pathological features include abnormal smooth muscle cells lining the airways, lymphatics, and blood vessels, leading to airflow obstruction. The parenchyma of the lungs is replaced by cysts.

Abnormal smooth muscle cells are positive for HMB-45. Clinically, the disease is mainly characterised by dyspnea, haemoptysis, recurrent pneumothorax, and celiac disease. This study presents a rare case of pulmonary lymphangioleiomyomatosis and a review of the literature.

Clinical summary

A 29-year-old gravida 0 para 0 woman presented to our hospital on August 12, 2015, with difficulty breathing for 1 day. She had no medical history and no symptoms of tuberous sclerosis complex. On physical examination, her body temperature was 37.5°C. Her superficial lymph nodes were not palpable.

The results of relevant laboratory studies were WBC 16,100/mm^3, RBC 357 × 104/mm^3, Hb 9.2 g/dL, platelet 145,000/mm^3, aspartate aminotransferase 15 U/L, alkaline phosphatase 28 U/L, total bilirubin 0.4 mg/dL, total protein 6.3 g/dL, α-fetoprotein (AFP) 1.0 ng/ml (normal range < 9 ng/ml), carcinoembryonic antigen (CEA) 4.9 ng/ml (normal range < 5 ng/ml), and carbohydrate antigen (CA) 19-9 13.2 U/ml (normal range < 35 U/ml). HBsAg and anti-HCV antibody were both negative. There were no abnormal findings and the patient's medical, surgical, and family histories were unremarkable.

High-resolution CT

A high-resolution CT scan showed that both lungs had an extensive and well-distributed cystic lucent shadows on the whole, the cystic shadow presented with and a uniform, thin-walled complete follicular cavity. Most of the shadows were round or semi-round and surrounded by normal lung tissues. They were evenly distributed in both lungs (**Figure 1**).

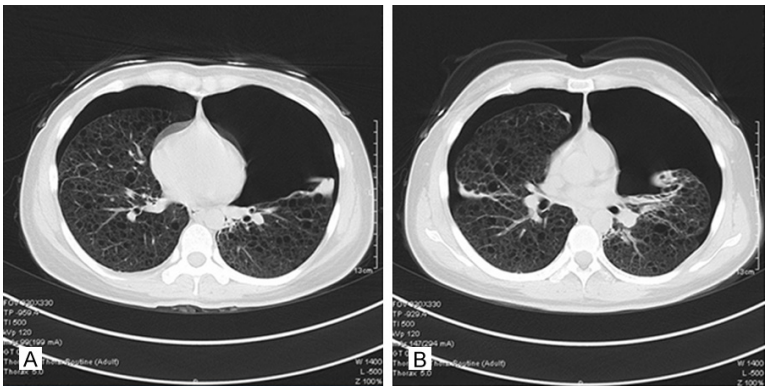

Figure 1. A and B: A high-resolution CT scan showed that both lungs had extensive and well-distributed cystic lucency shadows and uniform, thin-walled complete follicular cavity. Most of the shadows were round or semi-round and surrounded by normal lung tissues. They were evenly distributed in both lungs.

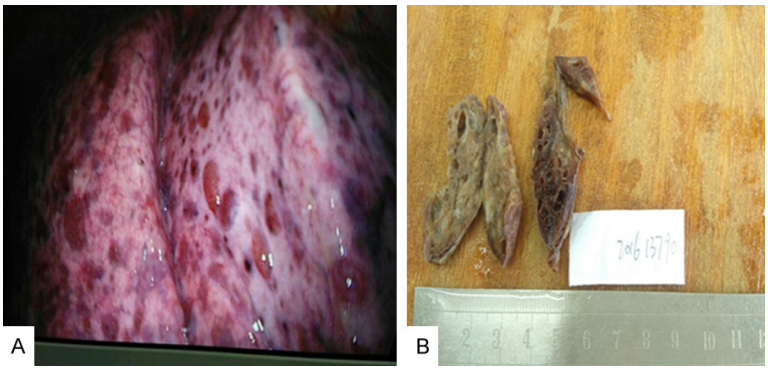

Figure 2. A: Diffuse miliary nodules were seen on the surface of the lungs. Some were vesicular, and Diffuse distribution of cystic nodules approximately 0.1 cm in diameter, and the upper lobe segment and lower lobes had a visible bullous structure approximately 0.5 cm in diameter. Part of the lung resection yielded 5.0 × 3.5 × 3.0 cm specimens. B: The sections were grey red, grey brown, and multi-cystic.

Pathological findings

There was a diffuse distribution of cystic nodules approximately 0.1 cm in diameter, and the upper lobe segment and lower lobes had a visible bullous structure approximately 0.5 cm in diameter. Part of the lung resection yielded 5.0 × 3.5 × 3.0 cm specimens. Diffuse miliary nodules were seen on the surface of the lungs. Some were vesicular, and the sections were grey red, grey brown, and multi-cystic. One section was a polycystic honeycomb, and there was a 0.1-0.5 cm cyst on the smooth wall of the capsule (**Figure 2**).

Pathological features showed abnormal smooth muscle cells lining the airways, lymphatics, and blood vessels, leading to airflow obstruction. The parenchyma of the lungs was replaced by cysts (**Figure 3**).

The malignant cells were positive for D2-40, Ki-67 (approximately 5% positive), SMA, HMB-45, ER, PR, and TTF-1 (**Figure 4**).

Discussion

Pulmonary lymphangioleiomyomatosis belongs to the vascular epithelial cell tumor lineage, which is a rare diffuse interstitial pulmonary disease of unknown cause. It is likely related to an increase in estrogen because it is extremely rare in children and men. The disease is most common in women of childbearing age [4], with an average age of 32 ± 8.9 [3]. The present case was similar to the literature. Treatment with reduced estrogen can improve the condition.

Clinically, the disease is categorised by dyspnea, hemoptysis, recurrent pneumothoraces, and chylous effusions. It has been reported that approximately 50% of patients have spontaneous pneumothorax as the initial symptom [5]. Pulmonary lymphangioleiomyomatosis should be considered when women of childbearing age have increasing dyspnea that cannot be relieved, similar to emphysema. The European Respiratory Society published the world's first pulmonary lymphangioleiomyomatosis guide in 2010 [6]. However, treatment needs improvement.

In cases of lymphangioleiomyomatosis, high-resolution CT scan shows multiple thin-walled cysts distributed evenly throughout the bilateral lung fields with normal intervening lung parenchyma and recurrent pneumothorax or chylothorax. The diameter of the capsule is 0.3-

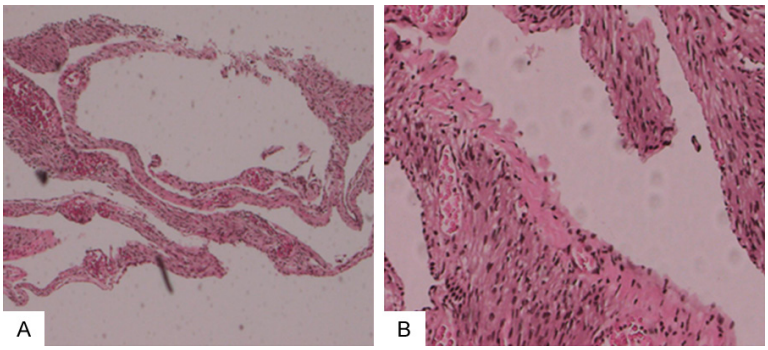

Figure 3. A and B: Pathological features showing abnormal smooth muscle cells lining the airways, lymphatics, and blood vessels, leading to airflow obstruction. A: H&E × 100. B: H&E × 200.

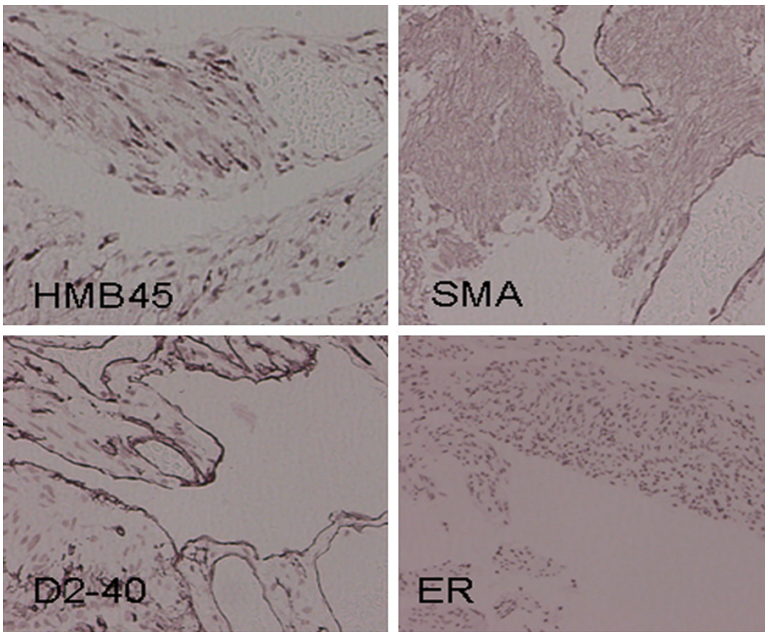

Figure 4. HMB-45, SMA, D2-40, ER were expressed in the spindle tumor cell areas. IHC × 200.

0.5 cm. Advanced lung tissue can be completely replaced by vesicles. Lung tissue biopsy is the optimal diagnostic confirmation method.

In general, the image of the tumor's growth pattern indicated it had divided into three types: a type of cystic change, perivascular epithelioid hyperplasia, and a combination of both.

Pulmonary lymphangioleiomyomatosis is a type of perivascular epithelioid cell tumor. Common traits include tumor cells that are epithelioid or fusiform and form around thin-walled vessels. They are arranged in a bundle or nest. The cells proliferate around the walls, leading to stenosis of the airway. It has been postulated that the proliferation of pulmonary lymphangioleiomyomatosis cells and hemosiderin can exist simultaneously [7]. Patients' immunohistochemical staining is positive for HMB-45, SMA, D2-40, Ki-67 (approximately 5% positive), ER, PR, and TTF-1, which are derived from the spindle tumor cells. Due to the small number of cases, its treatment remains controversial. No effective treatments are currently proposed for this disease.

Pulmonary lymphangioleiomyomatosis occurs almost exclusively in women of childbearing age, indicating that it is closely associated with estrogen. Pregnancy is thought to aggravate the condition [8], and it can improve after menopause [9]. Estrogen directly activates early phase ERK through non-genetic pathways [10]. The main treatment is to reduce estrogen. In the later stages of the disease, the main treatment is lung transplantation. Lymphangitic smooth muscle cells are likely to develop in the lung tissue after transplantation. Double-lung transplantation led to a one-year survival rate of 86% (68/79), a three-year survival rate of 76% (60/79), and a five-year survival rate of 65% (51/79) [11]. Patients with pulmonary lymphangioleiomyomatosis have a poor prognosis; the natural course of illness leads to death from respiratory failure within 10 years after the onset of symptoms.

The postoperative course was uneventful. A surgical biopsy was ordered to confirm the disease diagnosis. Anti-estrogen and symptomatic supportive therapies are currently the main methods of clinical treatment. The patient is still alive three years after the operation.

Conclusions

In summary, we here present an unusual case of a woman with pulmonary lymphangioleiomyomatosis have a poor prognosis; the natural course of illness leads to death from respiratory failure within 10 years after the onset of symptoms. Early diagnosis and prevention is an important problem.

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Disclosure of conflict of interest

None.

Abbreviations

PLAM, pulmonary lymphangioleiomyomatosis.

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