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Case Report

Two Kinds of Cystic Lung Lesions with Pulmonary Lymphangioleiomyomatosis in a Male

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A 34-year-old male with frequent recurrence of right pneumothorax was admitted to our hospital. He was a current smoker and outwardly male without genital aplasia. He was diagnosed as tuberous sclerosis complex (TSC) at 2 year-old and underwent transcatheter arterial embolization for right renal hemorrhage due to renal tumor 2 years ago. Chest Computed Tomography showed that he had multiple tiny round cystic lesions with thin wall in both lungs. The recurrent pneumothorax was expected to be associated with TSC-Lymphangioleiomyomatosis (LAM). Video-assisted thoracic surgery was successfully performed. The operative and histological findings revealed that the bullae were classified into two groups; emphysematous bullae and bullae due to LAM. His postoperative course was uneventful. TSC-LAM is extremely rare, but in some cases the clinical recognition might be escaped due to subtle findings of bullae in early LAM, resulting in diagnosis as spontaneous pneumothorax.

Keywords: lymphangioleiomyomatosis, tuberous sclerosis complex, pneumothorax, video-assisted thoracic surgery, emphysematous bullae

Introduction

Lymphangioleiomyomatosis (LAM) is rare disease that has been reported to occur exclusively in reproductive women.[1)] To our knowledge, pulmonary LAM in men is extremely rare and only five cases have been histologically diagnosed and reported in the past. We herein report a case of pulmonary LAM in a male that had two kinds of cystic lung lesions which was clearly discerned during video-assisted thoracic surgery (VATS).

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Case Report

A 34-year-old male complained of the right chest pain and dyspnea. He was diagnosed as the right pneumothorax based on chest X-ray, and underwent tube thoracotomy in the right chest cavity. He was cured of the pneumothorax in a week, but the right pneumothorax relapsed three times after the discharge. He was referred by his primary care physician and admitted to our hospital. His laboratory data including estrogen and progesterone was within normal limit. His body height was 180 cm and weight was 90 kg, and he was outwardly male without genital aplasia. He was a current smoker, and the number of pack-year of smoking was more than 15. He was diagnosed as tuberous sclerosis complex (TSC) for facial skin lesions at 2 year-old, and underwent transcatheter arterial embolization for right renal hemorrhage due to renal tumor 2 years ago. The chest computed tomography (CT) showed that he had multiple tiny round cystic lesions with thin wall in both lungs (**Fig. 1A**). To consider all of the finding together, the

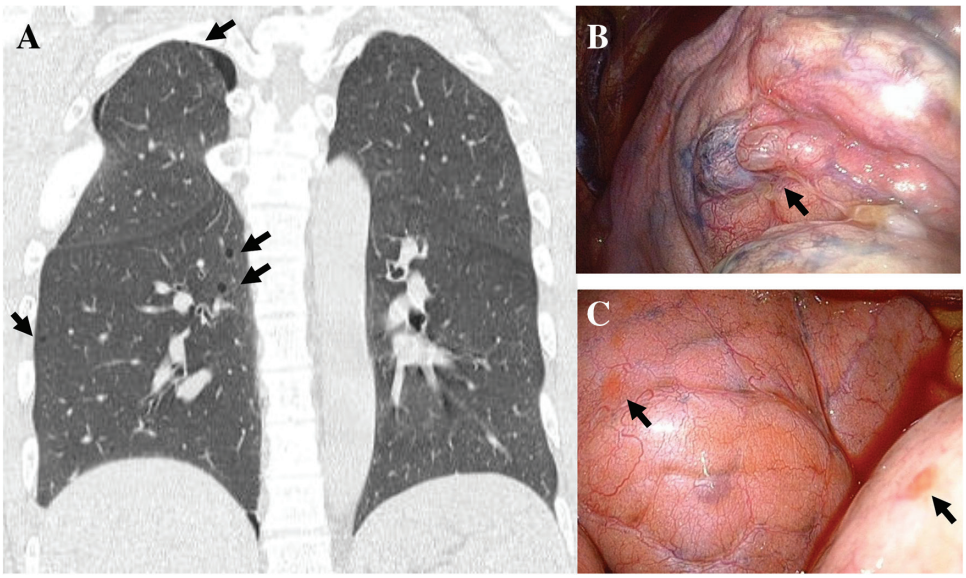

Fig. 1 (**A**) A coronal section of Chest CT. There are a lot of small cysts with thin cystic wall (arrows). (**B**) Thoracoscopic findings. There are projecting bullae with anthracosis on the right S1 (arrows). (**C**) Thoracoscopic findings. There exists reddish, small and flattened bullae on the right middle and lower lobe (arrows).

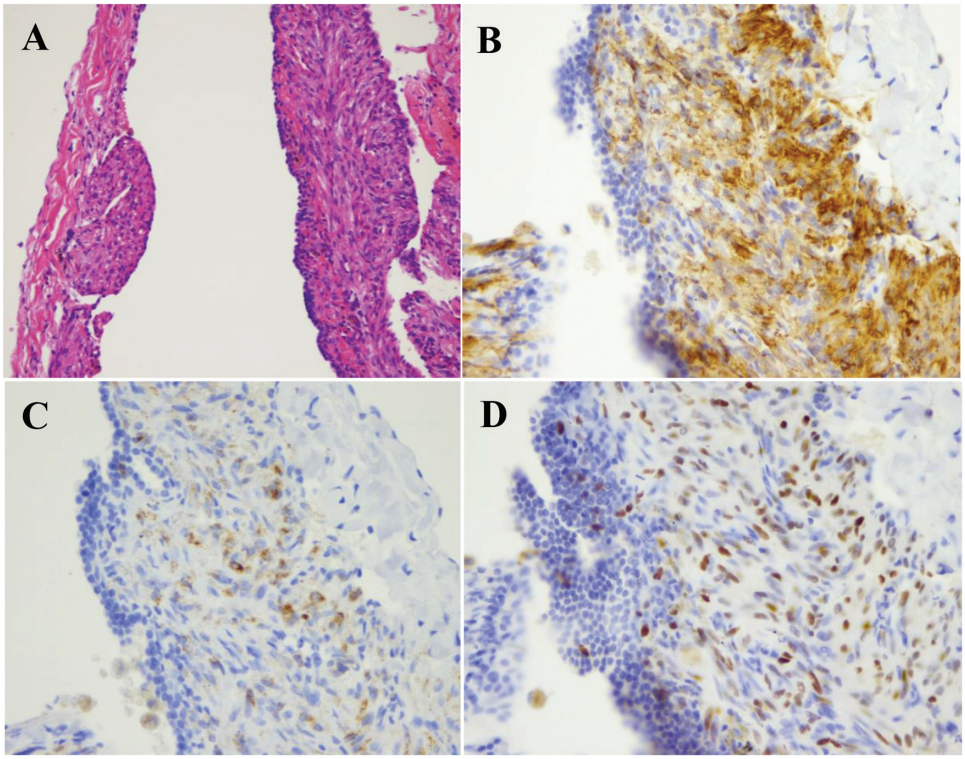

Fig. 2 Histologiocal findings of bullae on the right middle lobe. Bullae have thickness of cystic wall with spindle cells ((**A**) H.E. stain X100.) which were immunohisitochemically positive for anti-SMA antibody ((**B**) X200), anti-HMB45 antibody ((**C**) X200), anti-ER antibody ((**D**) X200). SMA: smooth muscle actin; HMB45: human melanin black 45; ER: estrogen receptor

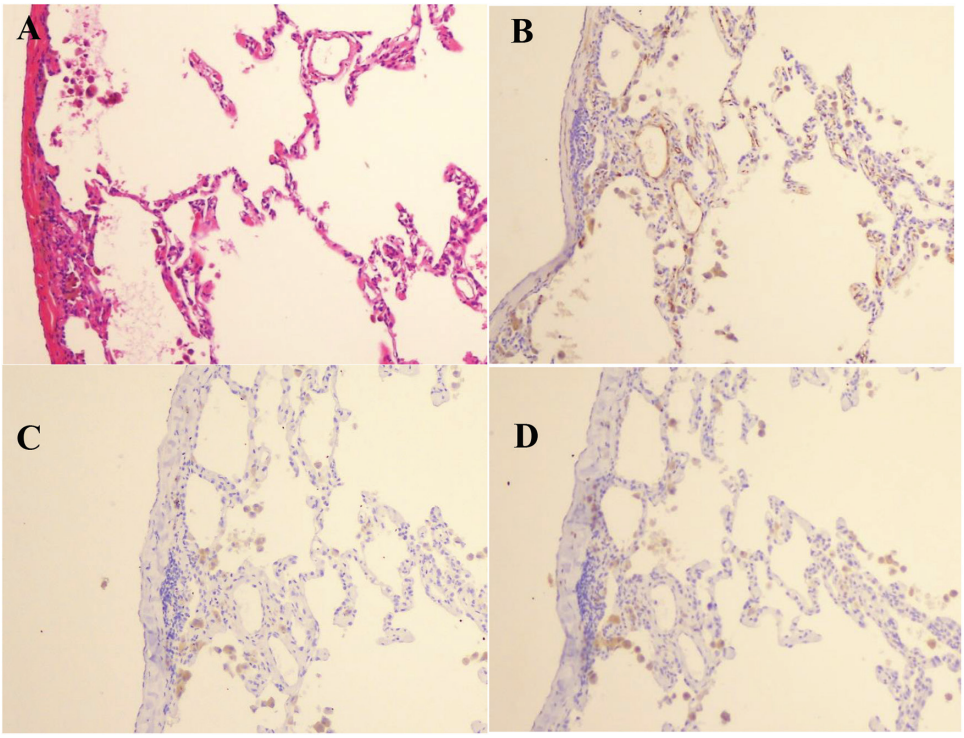

Fig. 3 Histologiocal findings of bullae on the right upper lobe. There are not apparent spindle cells ((**A**) H.E. stain X100) and cystic wall is immunohisitochemically negative for anti-SMA antibody ((**B**) X100), anti-HMB45 antibody ((**C**) X100), anti-ER antibody ((**D**) X100). SMA: smooth muscle actin; HMB45: human melanin black 45; ER: estrogen receptor

recurrent pneumothorax was expected to be associated with TSC-LAM. VATS was underwent, and the operative findings revealed that there were projecting bullae with anthracosis at the right apical portion of lung and they had tendency to fuse together with growth of capillaries on thickened cyst walls (**Fig. 1B**). It was also discovered that reddish small flattened bullae were existed in the right middle and lower lobe (**Fig. 1C**). They did not have tendency to fuse together and any findings of inflammation. The culprit lesion seemed to be apical bullae, and both of lesions were resected with automatic suture instruments (ENDOGIA™ Ultra Universal, COVIDIEN, Boulder, CO) for histologically diagnosis. The histological findings revealed that bullae in apex of the right upper lobe were emphysemoatous lesions and bullae of the right middle lobe attributed to LAM. The latter showed thickness of cyst wall with spindle cells which were immunohistochemically positive for anti-smooth muscle actin (SMA) antibody, anti-human melanin black 45 (HMB45) antibody, anti-estrogen receptor (ER) antibody and progesterone receptor (PgR) antibody, so that they were diagnosed as LAM cells (**Fig. 2**). On the other hand, bullae in apex of the right upper lobe did not have apparent spindle cells and the cyst wall of bullae was immunohistochemically negative for LAM (**Fig. 3**). It was implied that emphysematous bullae due to smoking caused the recurrence of the right pneumothorax. His postoperative course was uneventful, and no recurrence of the pneumothorax has happened for 10 months post-surgery. We could not undergo genetic tests for TSC and karyotyping because of the absence of his agreement.

Discussion and Conclusion

LAM is rare disease that has been reported to occur in reproductive women. Prevalence is estimated 1.2 to 2.3 per million in Japan. Pulmonary LAM in men is extremely rare, and there have been reported only five cases in the past.[2–6] Clinical manifestations in LAM are pneumothorax, dyspnea on effort, hemosputum, chylothorax, and abdominal effusion. Among them, pneumothorax tends to show frequent recurrences. Lung is frequently damaged, therefore the lung lesions closely concern about patients' prognosis. Disease progression varies in each case. Once respiratory failure happens, lung transplantation is eventually considered.[1] According to statics providing by Japanese study, 173 cases of LAM have registered, and 145 cases was sporadic LAM. Mean age when first

symptom occurred was 31.6 ± 8.8 year-old, and mean age at diagnosis was 34.0 ± 8.8 year-old. 126 cases had pneumothorax, and mean recurrent times was 2.1.[1)]

TSC is transmitted in a dominant pattern, and there was no gender difference in the incidence of TSC. It is quite puzzling that there have been a few reports about TSC-LAM in male. Adriaensen et al reported that CT for TSC patients demonstrated pulmonary thin-walled cysts in the lung bases in 28% of patients and pulmonary cysts were detected in 42% of female patients and in 13% of male patients.[7)] Most of the reported cases of LAM in male including ours were early stage with mild symptoms and their cystic lesions were small.[4–6)] Cyst size is significantly associated with pneumothorax in LAM. Patients with cyst size of more than 0.5 cm are more likely to have pneumothorax than patients with those of less than 0.5 cm.[8)] As for possible explanation for sex distinction, TSC-LAM in male can have small cystic lesions in lung, but tiny cysts might not cause pneumothorax. Actually, TSC-LAM in male diagnosed with CT had no symptom of respiratory system.[7)]

Our case has prominent emphysematous bullae due to smoking as well as cyst with LAM cells. Cystic lesions of LAM at early stage are small and obscure so that careful and trained observation are needed to find them during surgery. Our case is of clinical significance and educative. Thoracic surgeon should pay attentions to examine thoroughly all of lung lobes on the occasion of VATS for spontaneous pneumothorax.

Disclosure Statement

No relevant financial relationship exists.

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