Case Report

**Pulmonary Manifestations and Management of Proteus Syndrome**

*Chia-Ying Li,1 Yih-Leong Chang,2 Wei-Chou Chen,1 Yung-Chie Lee1*

Proteus syndrome is a very rare, sporadic and congenital condition that is characterized by postnatal mosaic overgrowth. This disorder is thought to be caused by a somatic gene mutation, but the exact etiology is unknown. Commonly involved tissues include connective tissue, bone, skin and the central nervous system. Another less common symptom involves pulmonary emphysematous changes. This report documents a 25-year-old man with Proteus syndrome who presented with progressive exertional dyspnea and asymmetric overgrowth of his extremities. He underwent left pneumonectomy and his postoperative course was uneventful. Lung tissue showed emphysematous changes with multiple bulla formation and scattered calcification. We also review recent literature related to pulmonary manifestations and management of Proteus syndrome.

**Key Words:** bullous lesion, mutation, pneumonectomy, pneumothorax, Proteus syndrome

Proteus syndrome (PS) is a complex disorder that consists of asymmetric and mosaic overgrowth that can include connective tissue, the skeleton, blood vessels, central nervous system and many other tissues. It was originally named by Wiedemann in 1983 after the Greek sea god Proteus, who possessed the ability to transform himself into any shape. Proteus thus refers to polymorphism.1 While children with the disorder have a normal appearance at birth, features of PS appear during the first year of life and progress subsequently. As a result of the great variability in presentation and rarity of this syndrome, it remains rather difficult to diagnose. However, clearer guidelines have recently been proposed.2 Pulmonary bullous changes are a specific criterion for diagnosis. Only a few studies have mentioned surgical intervention for pulmonary dysmorphology.3,4 We describe a case with emphysematous bullae who underwent left pneumonectomy.

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1Division of Thoracic Surgery, Department of Surgery, 2Department of Pathology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan.

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*Correspondence to:* Dr Yung-Chie Lee, Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, 7 Chung-Shan South Road, Taipei, 100 Taiwan.
E-mail: yclee@ntuh.gov.tw
Case Report

A 25-year-old man had an underlying history of asymmetric, bilateral overgrowth of the fingers since the age of 5 months, along with varicose veins of the left leg since he was 8-years-old. He underwent amputation for the deformed digits several times (Figure 1). He suffered from dyspnea at 19 years of age, and emphysematous changes in the left lung were noted by radiography. Exertional dyspnea progressed gradually; he experienced dyspnea after climbing more than two flights of stairs.

On admission, lung perfusion revealed an almost total absence of perfusion radioactivity in the left lung. Chest radiography and computed tomography demonstrated diffuse bullous lesions in the left lung, with severe deviation of the mediastinum to the right side, and compression of the right lung (Figures 2 and 3). Laboratory data were within the normal range, except for elevated C-reactive protein levels (5.04 mmol/L). Spirometry revealed severe restrictive ventilatory defects, as demonstrated by forced vital capacity (FVC) of 1.62 L (37.6% of predicted FVC) and a forced expiratory volume at 1 second (FEV1.0) of 1.24 L (32.4% of predicted FEV1.0). He underwent left pneumonectomy. Multiple lobulated bullae in the left lower lobe, with full occupation of the left thoracic cavity, were noted. The upper-left lobe was compressed, with atelectatic changes.

Microscopically, the lung parenchyma showed diffuse emphysematous changes with multiple bulla formation (Figure 4A). Scattered foamy cell aggregates (Figure 4B), calcification and ossification were seen sporadically. After surgery, a geneticist was consulted for specific manifestations, and he was diagnosed with PS. During a 6-month follow-up, the patient lived an active life and was fully-functional, with an FVC of 2.53 L (58% of predicted FVC) and FEV1.0 of 2.29 L (59.1% of predicted FEV1.0).
Discussion

Patients with PS can present with disproportionate and asymmetric overgrowth of tissues. Although limb overgrowth is the most common anomaly, many tissues can be involved.³ According to the diagnostic criteria, findings of mosaic somatic overgrowth, sporadic occurrence, progressive course, cerebriform connective nevus over the bilateral palms, venous malformation, and pulmonary emphysematous changes lead to the diagnosis.²,³,⁵ Happle has hypothesized that PS results from a postzygotic mutation that leads to mosaic effects that are lethal if the mutation is carried in a non-mosaic fashion.³,⁵ There are no documented cases involving affected offspring. Thus a negative family history can be meaningful for differential diagnosis.⁵ Although it has been claimed that several cases have involved phosphatase and tensin homolog gene mutations, patients usually have a normal chromosome complement.²,⁴ In our case, no obvious family history was noted and phosphatase and tensin homolog gene testing was negative.

Pulmonary emphysematous bullous changes have been noted in 9–13% of cases, but it could be higher because the pulmonary manifestations might not be obvious when other features of PS become prominent.⁴,⁵ The distribution of these bullae could be unilateral or bilateral. There is no preference for any particular lobe. The cause of this is unknown and could be related to deficiencies or abnormalities of muscular, elastic or fibrous connective tissue. These patients might develop symptoms of pulmonary insufficiency, persistent atelectasis or pneumonia. Such changes can be relentless and lead to death. Computed tomography can be useful for accurate diagnosis.⁴,⁵

In young adults, this disease presents similar symptoms to conditions such as bronchopulmonary dysplasia, cystic adenomatoid malformation, intrapulmonary bronchogenic cysts, postinfectious pneumocele, cystic bronchiectasis, cystic fibrosis, hydatid disease, histiocytosis X, Marfan’s syndrome, neurofibromatosis pneumoconiosis, α1-antitrypsin deficiency, sarcoidosis and tuberous sclerosis. However, most of these diseases involve just a few focal bullous changes and do not progress over time.⁴,⁶

PS treatment focuses on minimizing further lung damage and avoiding infection. If the distribution is localized, resection of the lesion site might be an option. If the lesion is too extensive, lung transplantation might be needed.⁴

Other thoracic findings include rib overgrowth, bronchial hamartoma, chest wall masses (lymphangioma, hemangioma, or lipoma) and spinal abnormalities, which can cause respiratory distress.⁴ In this situation, surgical intervention should be considered.³

In conclusion, patients with PS have highly variable symptoms that make diagnosis and treatment...
complicated. When pulmonary bullous changes occur, surgical resection should be considered for the prevention of further pulmonary insufficiency or infection.

References