CHEST

A 19-Year-Old Man With Relapsing Bilateral Pneumothorax, Hemoptysis, and Intrapulmonary Cavitary Lesions Diagnosed With Vascular Ehlers-Danlos Syndrome and a Novel Missense Mutation in *COL3A1*

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A 19-year-old sportsman experienced a right-sided pneumothorax and hemoptysis after having had an intermittent cough and blood-tinged sputum for 2 months. A chest CT scan revealed small cavitary lesions in both lungs. The relapsing pneumothorax was treated with a chest tube twice, as well as surgically after the second relapse. Two months after surgery, the patient developed a cough, fever, and high C-reactive protein levels. At that time, large consolidations had developed in the right lung, while the left lung subsequently collapsed due to pneumothorax. The patient's physical appearance and anamnestic information led us to suspect a genetic connective tissue disease. A sequencing analysis of the *COL3A1* gene identified a novel, de novo missense mutation that confirmed the diagnosis of vascular Ehlers-Danlos syndrome (EDS). This atypical presentation of vascular EDS with intrathoracic complications shows that enhanced awareness is required and demonstrates the usefulness of the genetic analyses that are clinically available for several hereditary connective tissue disorders.

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ABBREVIATIONS: EDS = Ehlers-Danlos syndrome

Spontaneous pneumothorax is a well-known complication for several different pulmonary conditions; most common in young adults are rupture of subpleural blebs, cystic fibrosis, malignancy, or necrotizing pneumonia. Hemoptysis in adults may have its origin in airway diseases, such as bronchial infections or neoplasms. Pulmonary parenchymal involvement such as pneumonia and inflammatory and immune disorders may also cause hemoptysis, but it is important to consider connective tissue diseases, specifically the vascular type of Ehlers-Danlos syndrome (EDS).[1-3]

Vascular EDS is a rare, autosomal dominantly inherited collagen disorder affecting the connective tissue in several organ systems.[4,5] Vascular EDS carries a serious

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prognosis because of the tendency of vital organs and blood vessels to rupture. In 90% of cases, vascular EDS presents with an extrathoracic arterial dissection or rupture.[6] Pneumothorax is the most common respiratory complication of the disorder, and the incidence of spontaneous pneumothorax in vascular EDS is reported to be 16%.[7] Here, we describe the primary findings and clinical course in a young man with vascular EDS who was diagnosed after an unusual presentation with bilateral pneumothorax and pulmonary findings.

Case Report

A 19-year-old sportsman experienced an acute, massive hemoptysis, shortness of breath, and dizziness after approximately 2 months of an intermittent cough with blood-tinged sputum. In the local hospital, he was diagnosed with a right-sided pneumothorax and treated with a chest tube. After 1 month, the pneumothorax relapsed, and he was readmitted to hospital and again treated conventionally with an intercostal drain. In the following month, the right-sided pneumothorax relapsed once more and chest CT scans were performed that revealed bilateral, small cavitary lesions (Fig 1) of an unknown genesis. Because of the repeated relapses of pneumothorax, the patient was referred for surgery. A resection of subpleural bullae and pleural rubbing were performed by an experienced surgeon, but due to a prolonged leakage of air on the pleural drain, the operation was carried out a second time. During the second operation, an open-lung biopsy specimen was obtained, and the surgeon observed a fragility of the lung, extensive bleeding, and an unusual texture of the pulmonary tissue. Therefore, a pleural decortication was not performed. No relapse of the right-sided pneumothorax was observed, and the patient was discharged from hospital.

A histopathologic investigation of the lung biopsy specimen gave no explanation for the radiologic findings (Fig 2), and because of the suspicion of an underlying disease, fiber-optic bronchoscopy was performed after surgery. This revealed a diffuse and scarce bleeding. Serology tests for antinuclear antibody, antineutrophil cytoplasmic antibody, and rheumatic factor were negative.

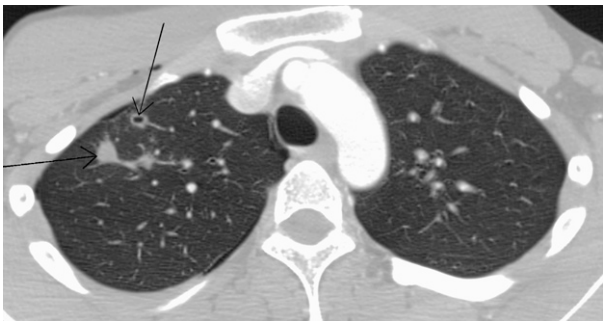

Figure 1 – *CT scan of lungs before pneumothorax surgery, showing right-sided pneumothorax and small cavitary lesions (arrows).*

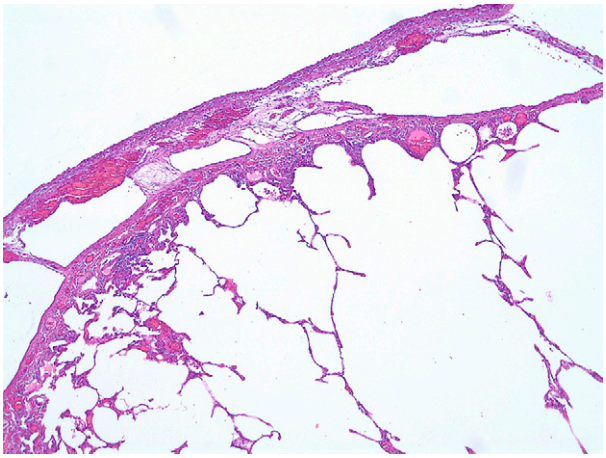

Figure 2 – *Lung biopsy specimen was unspecific with pleural fibrosis, signs of old and new bleeding, and subpleural bullae (hematoxylin and eosin, magnification ×4 objective lens).*

Two months after surgery, the patient developed fever, high C-reactive protein levels, anemia, a persistent productive cough, and hemoptysis. Furthermore, he experienced a left-sided pneumothorax that was not treatable with pleural tubes alone (Fig 3), and was then referred to the university hospital. Upon arrival at the Department of Pulmonary Medicine, the patient was in a generally poor condition, and a chest CT scan demonstrated large, abscess-like structures in the right lung (Figs 4, 5).

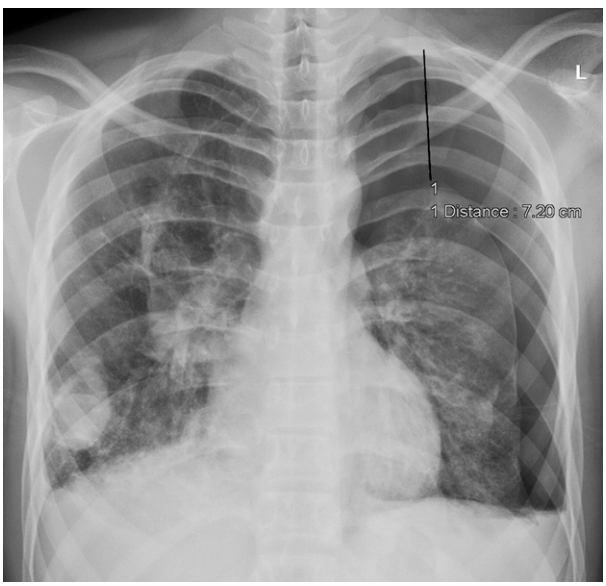

Figure 3 – *Chest radiography 4 mo after surgery, showing a total pneumothorax on the left side and abscess-like structures in the right lung.*