Ehlers-Danlos Syndrome Type IV with Bilateral Pneumothorax

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Abstract

A 17-year-old teen was hospitalized with bilateral pneumothorax. After the bilateral lungs were expanded using catheter tubes, he fully recovered and he was discharged from our hospital. He had a history of colon perforation. Ehlers-Danlos syndrome (EDS) was suspected due to the combination of colon perforation and pneumothorax, and EDS type IV was confirmed after a genetic study identified a c.1511g>a mutation in the COL3A1 gene. This is the first report of bilateral pneumothorax caused by EDS type IV. Clinicians should consider EDS type IV in the differential diagnosis for bilateral pneumothorax in conjunction with distinct previous histories and radiological findings.

Key words: Ehlers-Danlos syndrome, vascular type, bilateral pneumothorax, COL3A1 gene


Introduction

Ehlers-Danlos syndrome (EDS) is an inherited connective tissue disorder that manifests as hyperextensibility of the skin, hypermobility of the joints and weakness of the skin and blood vessels. Six subtypes have been established according to clinical and genetic differences. EDS type IV, or vascular EDS, was first described by Barabas in 1967 (1). This form is rare, accounting for approximately 4% of all EDS cases. Patients with EDS type IV frequently die at a young age due to arterial rupture, aortic dissection, or bowel perforation. In comparison with the other subtypes of EDS, patients with EDS type IV have fragile, but inextensible connective tissues.

Several cases of EDS with respiratory manifestations have been reported (2). To the best of our knowledge, no previous reports have described bilateral pneumothorax in association with EDS type IV. Because the amount of type III collagen in the lung is reduced in patients with EDS type IV (3), bilateral pneumothorax may occur.

We herein describe the case of a patient with EDS type IV causing bilateral pneumothorax.

IV causing bilateral pneumothorax.

Figure 1. A chest X-ray shows free air spaces at bilateral apical portions of the lungs. Pleural effusion was found bilaterally.
A 17-year-old teen presented to our hospital complaining of chest pain. He was a high school student and had never smoked. He had atopic dermatitis and a history of colon perforation at 16 years of age.

His height was 165 cm and his weight was 47 kg. Chest auscultation was nearly normal, and he had a respiratory rate of 14 breaths/min. The skin surface was mildly hard, but with normal elasticity. No hyperextension or thinning of the skin was apparent, and no joints were hyperextensive. Internal bleeding was identified at the right axilla. No retinal detachment, blue sclera, or corneal abnormalities were found on an ophthalmologic examination.

Laboratory tests showed the following: white blood cell count, 5,130/μL (eosinophils, 17%); hemoglobin, 15.0 g/dL; platelet count, 253,000/μL; and immunoglobulin E, 2,482 IU/mL. The results of liver function tests and the C-reactive protein level were all within normal limits.

Free air spaces were identified at the apical portions of bilateral lungs on a chest X-ray, and diffuse ground-glass opacities and bilateral pleural effusions were seen on chest computed tomography (CT) (Fig. 1, 2). We speculated that this pattern suggested an intrapulmonary hemorrhage. Diffusely distributed cavities and a few calcified lesions were also apparent on CT. The patient was admitted with a diagnosis of bilateral pneumothorax.

Catheter tubes were inserted into the bilateral intrathoracic spaces and bloody pleural effusion was confirmed. Because it was difficult to achieve hemostasis, the patient required aspiration for approximately 5 minutes. After both lungs achieved full expansion, the patient was discharged from our hospital.

Pneumohemothorax, hemorrhagic tendency and perforation of the colon suggested the possibility of EDS. We therefore performed chromosomal testing using the G-banding stain on the peripheral blood, however, no chromosomal divisions were identified in the sample. We then reevaluated the tissues removed at the operation for colon perforation. Marked degeneration of the collagen fibers was evident in the submucosal layer. Degeneration and rupture of the collagen fibers was recognized using Elastica van Gieson staining and type III collagen immunostaining. Atypical thickening of the vascular walls and degenerated and ruptured elastic fibrils (Fig. 3) suggested EDS type IV. A skin biopsy showed reduced amounts of type III collagen and ruptured elastic fibrils (Fig. 4).

In addition, a mutation analysis of the \textit{COL3A1} cDNA sequence revealed that the patient had a point mutation, c.1511g>a in exon 23, and the collagen production capacity using the cultured patient’s skin fibroblasts revealed that type III collagen α1 protein production was 12.3% of normal (Fig. 5). Therefore, we diagnosed the patient to have EDS type IV. The details of these results were previously reported by Shimaoka et al. as Case 3 (4).

**Discussion**

The present case report describes a case of EDS type IV with bilateral pneumothorax. To the best of our knowledge, no reports have described bilateral pneumothorax in EDS type IV patients. Respiratory complications are not common.
The major clinical complications of EDS type IV include visceral and arterial rupture, as well as rupture of the gravid uterus. The location of arterial hemorrhage determines the presenting symptoms, such as stroke, intra-abdominal or intrathoracic bleeding, or compartmental syndrome. The incidence of spontaneous pneumothorax in EDS type IV is reported to be 16% (6). The fragility of the pleural tissues may cause the formation of blebs and rupture, which may lead to pneumothorax. In previous reports, unilateral pneumothorax in EDS was not fatal (2). Hemorrhagic pulmonary complications are less described (5, 13, 14). The connective tissue of the vessel walls and internal organs, particularly that of the liver and lung, shows distinct hypoplasia, and type III collagen is significantly reduced (3). This may cause increased fragility of the lungs and may present characteristic radiological findings, such as distributed cavities, fibrous nodules, and calcified lesions (5, 15). Furthermore, pleural rupture may lead to pneumothorax or pneumohemothorax. Awareness of the risk of pneumothorax is thus warranted in patients with EDS, particularly those with type IV.

In conclusion, we herein described the first case of bilateral pneumothorax in a patient with EDS type IV. Clinicians should consider EDS type IV when they examine a patient presenting with bilateral pneumothorax in addition to distinct previous histories and radiological findings.

The authors state that they have no Conflict of Interest (COI).

References


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