INTRODUCTION

The vascular type of Ehlers-Danlos syndrome (vEDS) is an uncommon inherited disorder characterized by abnormalities in type III collagen, presenting itself as arterial dissection or rupture. We report a case of an isolated pulmonary hematoma mimicking a lung tumor in an 18-year-old man which turned out to be the initial finding of vEDS. Pneumothorax and hemothorax occurred repeatedly for 15 months following the surgical removal of the mass, and were treated by repeated left upper and lower lobectomy and thoracotomy. The diagnosis of vEDS was confirmed by pathologic and genetic studies.

Case Report

An 18-year-old man, who had been in good health, was referred to our hospital from another hospital due to recurrent scanty hemoptysis. Physical examination revealed a normal appearance of the face and skin. His parents were healthy without relevant past medical history. The results of laboratory examinations including coagulation study were normal. Chest radiograph showed a well-defined mass in the medial aspect of the left upper lung zone (Fig. 1A). Chest computed tomography (CT) demonstrated a well-defined, non-enhancing mass of relatively high attenuation (about 75 Hounsfield units) in the left upper lobe (Fig. 1B). The initial impression was a benign tumor that had originated from lung parenchyma. On the lung CT scan, the adjacent lung parenchyma was clear and there was no evidence of blood aspiration or bronchiectasis. For pathological confirmation of the diagnosis, surgical removal of the mass was performed using video-assisted thoracoscopic surgery which revealed an old hemorrhage and benign fibrosis. There were no complications during or immediately after surgery. Six months
after discharge, the patient revisited the hospital due to dyspnea, and his chest radiograph revealed a left-sided pneumothorax (Fig. 1C). A chest tube was inserted, and chest CT showed a huge cavity with internal air-hemorrhage level in the left lower lobe, and a smaller cavity surrounded by patchy ground-glass opacity in the left upper lobe (Fig. 1D, E). A large amount of blood was continuously drained (> 150 mL/min) through the inserted chest tube, and the huge hemorrhagic cavity was shown to almost completely occupy the left lower lobe, for which the patient underwent a left lower lobectomy. Immediately after this surgical procedure, hemothorax and massive hemoptysis developed, which were treated with an additional operation of a left upper lobectomy and thoracic drainage. The lung specimen revealed an organized hematoma with cavity formation, and an old and fresh intraparenchymal hemorrhage. There was no evidence of vasculitis or bronchiectasis. A genetic study was performed in order to determine the fragility of the underlying lung tissue that may have caused the recurrent hematoma and pneumothorax. An analysis of the type III collagen gene (COL3A1) was performed after obtaining informed consent from the patient. A heterozygous mutation in exon 13 at c.889 of the COL3A1 gene from guanine to adenine (c.899G > A) was detected (Fig. 1F). This mutation converted glycine to aspartate at amino acid position 300 (Gly300Asp). Based on these findings, a diagnosis of vEDS was made.

Eleven months after the initial presentation, the patient developed dyspnea and the chest radiograph at this time showed a right-sided pneumothorax. He was treated via chest tube insertion without any complications. He again developed dyspnea with hemoptysis after 2 months, and a large hematoma with surrounding hemorrhage was detected on chest radiography (Fig. 1G). A chest CT scan detected small air cavities in the large hematoma accompanied with pneumothorax (Fig. 1H). Because the patient’s vital signs were unstable, he was managed only by conservative therapies, such as controlling blood pressure by keeping him in an absolute bed rest state in the intensive care unit. Operation or endovascular treatment was not considered at this point. After receiving conservative manage-
treatment for about 1 month, the patient was discharged from the hospital. On serial follow-up chest radiography, the size of the hematoma was decreased but not completely resolved. Also, repetitive pneumothorax and other small hematomas developed. Currently, the patient is under close observation with his blood pressure under control at the cardiovascular department of our hospital.

**DISCUSSION**

EDS is an uncommon inherited disorder characterized by abnormalities in the components of the extracellular matrix such as collagen, which cause hyperextensibility of the skin, hypermobility of large joints and easy bruising (1). The frequency of this syndrome is reported to be 1 in 10000 (2). EDS was classified into the following six types in a conference at Villefranche in 1997, drawing upon the accumulated clinical experience and advances in molecular genetics: the classic type, the hypermobility type, the vascular type, the kyphoscoliosis type, the arthrodysplasia type and the dermatosparaxis type (3).

The vEDS is an autosomal dominant inherited disease caused by a single allele mutation in the COL3A1 gene coding for type III collagen, which results in qualitative or quantitative abnormalities of mature type III collagen protein (1). The vEDS accounts for less than 4% of all EDS patients and has the worst prognosis (4). The most common initial complications in vEDS patients are arterial dissection or rupture and gastrointestinal perforation (10). Pregnancy should be closely monitored due to an increased risk of death from uterine rupture (5).

There are some controversies regarding the therapeutic options for vEDS, due to a broad spectrum of disease manifestations. Conservative management with regulation of blood pressure is the treatment traditionally recommended for vEDS patients with asymptomatic complications. Patients with frank bleeding require emergent operative repair or catheter-directed embolization (11). Currently, there is no effective method to prevent the complications associated with vEDS. Further studies are required to determine how to prevent these complications using gene therapy (1).

We had made two mistakes during the process of diagnosis and treatment of the present case. First, we should have considered a follow up imaging study with conservative treatment or CT guided transthoracic needle biopsy instead of surgical resection for the solitary mass. Second, after excision of the mass, the specimen showed only an old hemorrhage with fibrotic tissue. At that time, we should have evaluated the cause of hemorrhage through a genetic study, and determine the treatment plan with consideration of the background connective tissue disorder.

In summary, we report here a rare case of vEDS with a unique initial presentation of an isolated pulmonary hematoma. Although the diagnosis of vEDS depends on pathologic and ge-
Vascular Ehlers-Danlos Syndrome

The vascular type.

REFERENCES

1. Watanabe A, Shimada T. Vascular type of Ehlers-Danlos syndrome. J Nippon Med Sch 2008;75:254-261
2. Abel MD, Carrasco LR. Ehlers-Danlos syndrome: classifications, oral manifestations, and dental considerations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:582-590
3. Beighton P, De Paeppe A, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers-Danlos syndromes: revised nosology, Villefranche, 1997. Ehlers-Danlos National Foundation (USA) and Ehlers-Danlos Support Group (UK). Am J Med Genet 1998;77:31-37
4. Germain DP. Clinical and genetic features of vascular Ehlers-Danlos syndrome. Ann Vasc Surg 2002;16:391-397
5. Pepin M, Schwarze U, Superti-Furga A, Byers PH. Clinical and genetic features of Ehlers-Danlos syndrome type IV, the vascular type. N Engl J Med 2000;342:673-680
6. Selim B, Lane CR, Rubinowitz AN, Siner JM. Spontaneous hemothorax and recurrent hemoptysis in a 26-year-old man with skin lesions. Chest 2010;137:480-483
7. Herman TE, McAlister WH. Cavitary pulmonary lesions in type IV Ehlers-Danlos syndrome. Pediatr Radiol 1994;24:263-265
8. Ishiguro T, Takayanagi N, Kawabata Y, Matsushima H, Yoshii Y, Harasawa K, et al. Ehlers-Danlos syndrome with recurrent spontaneous pneumothoraces and cavitary lesion on chest X-ray as the initial complications. Intern Med 2009;48:717-722
9. Dimsdale JE, Nelesen RA. French-horn hypertension. N Engl J Med 1995;333:326-327
10. Sykes EM Jr. Colon perforation in Ehlers-Danlos syndrome. Report of two cases and review of the literature. Am J Surg 1984;147:410-413
11. Oderich GS, Panneton JM, Bower TC, Lindor NM, Cherry KJ, Noel AA, et al. The spectrum, management and clinical outcome of Ehlers-Danlos syndrome type IV: a 30-year experience. J Vasc Surg 2005;42:98-106