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CASE REPORT

Total pleural covering technique for intractable pneumothorax in patient with Ehlers–Danlos syndrome

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Abstract We report a patient with vascular-type Ehlers–Danlos syndrome (vEDS) who developed pneumothorax and was treated with a total pleural covering technique (TPC). A 24-year-old man developed repeat pneumothorax with intermittent hemo-sputum. Based on unusual radiological manifestations of lung lesions and physical findings, EDS was suspected as an underlying cause of the pneumothorax. Surgical treatment was performed using a mediastinal fat pad and TPC, and no relapse was seen up to 2 years after surgery. TPC is a less invasive surgical approach for selected patients with vEDS. Accurate underlying diagnosis of vEDS and systemic evaluation of vascular complications are necessary before planning surgery.

Keywords Ehlers–Danlos syndrome · Pneumothorax · Total pleural covering technique

Introduction

Ehlers–Danlos syndrome (EDS) is a genetically heterogeneous collection of disorders characterized by hyperextensible skin, dystrophic scarring, easy bruising, and joint hypermobility. Respiratory manifestations of EDS are uncommon and reports of treatment options for pneumothorax associated with EDS are limited [1, 2]. We report a patient with vascular-type EDS (vEDS) who developed intractable pneumothorax and was successfully treated with a total pleural covering (TPC) technique.

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Case

A 24-year-old man with a history of left pneumothorax 7 years prior developed right anterior chest pain and was diagnosed with right pneumothorax in June 2012, which we treated with surgery. Chest computed tomography (CT) performed just before surgery revealed apical bullae in the right side as well as a small cavity in the parenchyma of the left lower lobe (LLL), thus the right apical bullae were resected using a video-assisted thoracotomy and the postoperative course was uneventful.

Two months after surgery, the patient developed intermittent hemo-sputum. Chest CT revealed cavitary nodules in the right lower lobe (RLL) (Fig. 1a), while the cavity in LLL noted before surgery had shrunk, leaving a small scar-like shadow. Most of the cavitary nodules in the RLL also demonstrated similar spontaneous regression within a few months (Fig. 1b). In October 2012, the patient developed left pneumothorax with cavitary lesions seen in the LLL, which required more than 1 month of thoracic drainage.

The patient showed clubfoot at birth and experienced recurrent dislocation of the shoulder joint in childhood. His family had no relevant medical history. The skin of the patient was not translucent, though rather lax and easily bruised. The small joints of the extremities were slightly hyper-extensive. Based on unusual radiological manifestations of lung lesions and physical findings, EDS was suspected as a cause of the intractable pneumothorax. Then, skin biopsy of the patient was performed for biochemical analysis of EDS.

The patient came to us with repeated left pneumothorax in January 2013, which recurred twice over the next 2 months. Chest CT revealed persistent cavitary lesions in the LLL and the left pneumothorax was thought intractable with conservative treatment (Fig. 2a). A systemic survey of the vascular system showed no abnormality and surgery was performed. The pleura around the cavitary lesions was pale, in which the pleural defect was observed. The pleura was quite frail and required an atraumatic approach. The fragility of the lung tissue was reached to the pleura, and the causative of pneumothoraxes was thought because of the development of pleural defect above the cavitary lesions. We avoided using sutures for repair and overlaid a pericardial fat pad with an instillation of fibrin glue to cover the defects. The majority of the visceral pleura was covered with regenerated oxidized cellulose mesh sheets

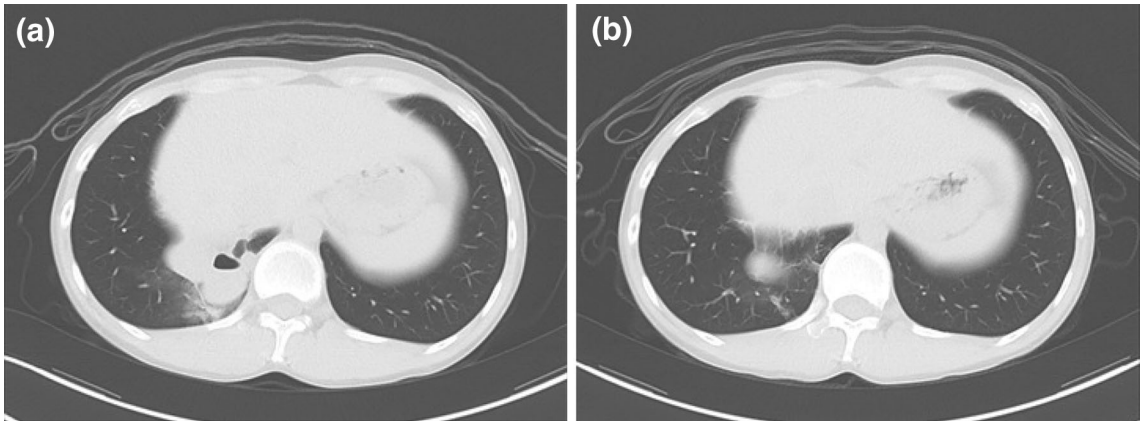

Fig. 1 **a** Chest CT image showing cavitary nodules in the RLL. **b** Chest CT image obtained 2 months after that shown in (**a**) demonstrating a small scar-like shadow remaining in the RLL, suggesting self-regression of the cavitary nodules

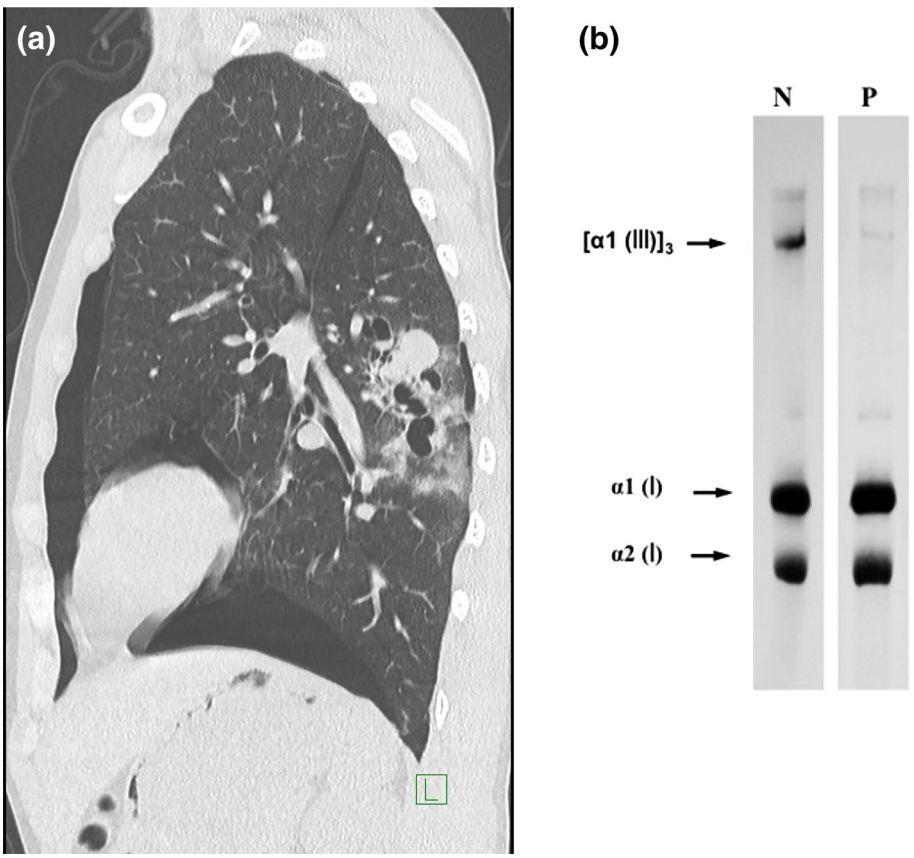

Fig. 2 **a** Chest CT images (sagittal view) obtained just prior to surgery showing cavitary nodules in the LLL containing fluid. **b** Sodium dodecyl sulfate-polyacrylamide gel electrophoresis analysis of procollagen from fibroblasts cultured from the patient (P) and a normal volunteer (N). The synthesis of type III procollagen was significantly decreased in the patient sample

(ROCM; SURGICEL®, 4 × 8 inch, Original Hemostat, Ethicon, Tokyo, Japan) for prevention of pneumothorax. Air leakage was successfully controlled. The patient repeated mild pneumothorax in the right side after bullectomy in 2012, while no relapse of left pneumothorax was seen for up to 2 years after surgery.

Electron microscopy and biochemical analysis of a skin specimen were used to confirm the diagnosis of EDS. Electron microscopic analysis revealed irregularities in the diameter of the collagen fibers. In addition, a fibroblast culture using the skin sample showed a decreased production of type III collagen, suggesting vEDS (Fig. 2b).

Discussion

vEDS is a recessively inherited serious connective tissue disorder and affected patients have a worse prognosis as compared to those with other subtypes of this syndrome. The reported prevalence of EDS is 1 in 100,000 and vEDS accounts for 5–10 % of all EDS cases [3].

Patients with vEDS can display translucent skin with highly visible subcutaneous vessels, easy bruising, a characteristic face (acrogeria), and skin laxity of varying degrees, while clubfoot can be present at birth. The syndrome features severe arterial, digestive, and uterine complications, such as spontaneous rupture of the arteries or bowel, which account for 90 % of the initial manifestations, while initial complications occurring in other organs were in only 5 % of reported cases [1]. Although respiratory manifestations of vEDS are not common, pneumothorax, hemoptysis, bleb formation, and hemorrhagic cavitary lesions of the pulmonary parenchyma might be observed [2, 4, 5]. In the present case, repeated pneumothorax occurred with self-remittent hemorrhagic cavitary lesions in the lung. These unusual changes suggested the underlying disease and led to our preoperative diagnosis of vEDS.

The biochemical abnormality leading to vEDS is a defect in type 3 collagen, encoded by the COL3A1 gene [6, 7]. Type 3 collagen is a key element in the structure of arterial walls, viscous organs, and lung parenchyma. The pathogenesis of associated respiratory complications is unclear, though they are thought to result in fragility of the lung structures [8]. This deficit of type 3 collagen that constitutes the vascular walls and lung parenchyma may lead to pulmonary artery rupture or tears in the lung parenchyma, which may appear as characteristic changes of the lung in vEDS cases [4, 5, 9].

A diagnosis of vEDS is based on clinical findings, and confirmed by biochemical or genetic tests of type 3 collagen [1]. Biochemical analysis of type III procollagen production using cultured fibroblasts from affected individuals is also widely used for detection of vEDS. Detection of a causative mutation in COL3A1, which encodes type 3 collagen, can be used to confirm the diagnosis of vEDS with a genetic method, while morphological analysis with electron microscopic images can display atrophic change in collagen fibers [10].

As there is no specific treatment for vEDS, pneumothorax can recur during the course of disease progression. For treatment of pneumothorax from vEDS, it is best to consider not only management of the air leakage but also prevention of recurrence. TPC is a technique used for pleural reinforcement of the entire lung with the aim to control and prevent pneumothorax, and was initially reported as a treatment option for intractable pneumothorax in lymphangioleiomyomatosis (LAM) cases [11, 12]. With this technique, the visceral pleura is covered with ROCM expecting pleural thickening. As the reports on TPC are limited, the adverse effect is still unclear [11, 12]. Kurihara et al. reported promising results with TPC for the intractable pneumothorax so far. They underwent TPC for more than 30 patients with LAM and the recurrence occurred in two patients in 6 years [12]. In the present case, to avoid pleural damage during surgery, we used mediastinal fat tissue to cover the pleural defect with an instillation of fibrin glue and also used TPC expecting prevention of pneumothorax. We think these procedures are less traumatic for the fragile lung tissue of vEDS patients as compared to pleural plication. To the best of our knowledge, this is the first repot of surgical treatment with TPC for pneumothorax associated with vEDS. Pneumothorax has not recurred in the left lung after TPC so far in our case, though more experiences are needed to see how TPC contribute to the prevention of pneumothorax in vEDS. There are reports of pneumothorax in vEDS-developed thoracic hemorrhage which could be a fatal complication [13]. Regarding the disease progression of vEDS which may complicate the lung lesions, we used ROCM covering not only for the area with cavitary change in LLL but for the entire lung expecting preventive effect for pneumothorax. Considering from the disease progression and the fragility of the lung tissue in vEDS, TPC in combination with mediastinal fat pad could be an acceptable option in surgical treatment of pneumothorax.

Because of systemic problems and the fragility of lung tissue associated with vEDS, surgical treatment has potential risks of hemorrhage and secondary damage, thus the benefits of an invasive approach should be carefully assessed [1, 10]. It is unknown whether fragility of the tissue proceeds homogeneously in the lung or differ in the parts in vEDS. In our case, we could recognize that pleural change telling the fragility of the lung tissue at the time of TPC. However, at the time of the right bullectomy in 2012, no pleural change was observed apart from apical

bullae and it was difficult to tell the fragility of lung from its appearance. Although the right bullectomy was performed without complication in our case fortunately, we still concern bullectomy can be a traumatic procedure in vEDS patients. We consider that an operation using a mediastinal fat pad with TPC is rather atraumatic, thus may be applied in selected patients with relatively mild disease. Nevertheless, accurate diagnosis of underlying vEDS and systemic evaluations of vascular complications are necessary before planning surgery.

Conclusion

We report a vEDS patient who developed pneumothorax with hemorrhagic cavitary lesions in the lungs. Intractable pneumothorax was surgically treated with use of a mediastinal fat pad and TPC, which represent a less invasive surgical approach for selected patients.

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Conflict of interest All authors have declared no competing interest.

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