Lung Transplantation for Pleuroparenchymal Fibroelastosis After Chemotherapy

Fengshi Chen, MD, Kousaku Matsubara, MD, Aya Miyagawa-Hayashino, MD, Kimihide Tada, MD, Tomohiro Handa, MD, Tetsu Yamada, MD, Masaaki Sato, MD, Akihiro Aoyama, MD, and Hiroshi Date, MD

Departments of Thoracic Surgery, Diagnostic Pathology, Respiratory Medicine, Kyoto University Graduate School of Medicine, Kyoto, and Departments of Pediatrics and Respiratory Medicine, Nishi-Kobe Medical Center, Kobe, Japan

We report the youngest patient ever reported in the literature to exhibit pleuroparenchymal fibroelastosis (PPFE) as a late-onset pulmonary toxicity after treatment with anticancer chemotherapy. The patient was diagnosed with mature B-cell leukemia at age 14. He was successfully treated with intensive chemotherapy; however, 7 years later, he experienced recurrent pneumothoraces. He was clinically diagnosed with upper lobe pulmonary fibrosis. At age 28, he underwent single left lung transplantation. Histologic examination of the resected lung revealed PPFE in the upper lobe and constrictive bronchiolitis obliterans in the lower lobe, which implied a close relationship between PPFE and constrictive bronchiolitis obliterans.


Improvements in therapies for childhood cancer during the last four decades have resulted in significant increases in 5-year survival rates for most malignancies. However, considering the long life expectancy of childhood cancer patients, attention is now being focused on the late sequelae of cancer treatments on vital organ function, especially cardiac and pulmonary conditions, and secondary cancer [1]. Considering pulmonary toxicity, reduced pulmonary function is associated with chemotherapy, but it is usually subclinical. Life-threatening lung damage is rare unless patients receive radiotherapy or hematopoietic stem cell transplantation (HSCT) in combination with chemotherapy [2].

Pleuroparenchymal fibroelastosis (PPFE) is among the new entities of idiopathic interstitial pneumonias [3]. To date, PPFE as a pulmonary toxicity after anticancer chemotherapy has rarely been reported [4]. Herein, we report, to our knowledge, the youngest patient ever reported in the literature to exhibit PPFE as a late-onset pulmonary toxicity after treatment with anticancer chemotherapy; he was subsequently treated with lung transplantation successfully.

Comment

Noninfectious pulmonary complications after HSCT are a serious concern because of their poor prognosis [6]. Thus, most hematologists prefer performing only intensive chemotherapy if HSCT is not required. Although it is true that even chemotherapy alone could cause pulmonary toxicity, pulmonary toxicity manifesting as PPFE after intensive chemotherapy is very rare. Only 1 patient has been reported with this lethal complication after chemotherapy alone; a 65-year-old woman exhibited PPFE after chemotherapy for breast cancer [4]. To our knowledge, our patient is the first reported case with a late-onset pulmonary complication manifesting as PPFE after treatment with chemotherapy for childhood cancer. This late-onset lung toxicity after anticancer chemotherapy tends to be less common in pediatric patients, and it is very rare for PPFE to develop in a young adult.

A 14-year-old boy was hospitalized because of a 1-month history of headache and malaise. A bone marrow examination on admission showed marked infiltration of lymphoblast cells, with expression of CD10, CD19, CD20, HLA-DR, and surface immunoglobulin M. Cerebrospinal fluid examination showed pleocytosis (10 cells/μL) containing blast cells. On the basis of these results, the patient was diagnosed with mature B-cell acute lymphoblastic leukemia complicated by central nervous system involvement. He received multidrug chemotherapy according to the group D regimen of the Japan Association of Childhood Leukemia Study NHL-98 for the treatment of B-cell non-Hodgkin lymphoma and mature B-cell acute lymphoblastic leukemia in childhood [5]. The total dose of chemotherapeutic agents included 66 g/m² of cyclophosphamide, 0.9 g/m² of etoposide, 18 g of methotrexate, 36 g/m² of cytarabine, and 200 mg/m² of pirarubicin. He has remained in first complete remission; therefore, he did not undergo radiotherapy or HSCT. However, 7 years later, an abnormality was observed on a chest radiograph (Fig 1A), although he did not show any symptoms. He subsequently experienced recurrent pneumothoraces. During the next 3 years, upper lobe pulmonary fibrosis became evident (Fig 1B). Autoimmune disease, chronic pulmonary infection, and ankylosing spondylitis were unlikely possible causes of this pulmonary complication. His respiratory condition also deteriorated gradually, and he was subsequently listed for lung transplantation at the age of 26 (Fig 1C). While he was on the waiting list, his respiratory condition deteriorated progressively. Two years later, he successfully underwent left single lung transplantation. The postoperative course was uneventful. Currently, 4 months after lung transplantation, he is well (Fig 1D). Pathologic examination of the extracted lung revealed a thickened pleura as well as prominent subpleural and paraseptal fibrosis with a mixture of elastic tissue in the upper lobe (Fig 2A). Constrictive bronchiolitis obliterans (CBO) was also observed in the lower lobe (Fig 2B).

Address correspondence to Dr Chen, Department of Thoracic Surgery, Kyoto University Graduate School of Medicine, 54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan; e-mail: hdate@kuhp.kyoto-u.ac.jp.
Idiopathic PPFE is an unusual type of pulmonary fibrosis that was first proposed in 2004 [4], and it is similar to idiopathic pulmonary upper lobe fibrosis, which was proposed in 1992 [7]. Although recurrent infections, autoimmunity, and genetic predisposition have been advocated, the etiology of PPFE is still unknown. Recently, much interest has been focused on the relationship between PPFE and CBO. In lung transplantation, the close relationship between CBO and PPFE has been documented [8], and both lung lesions may share a common pathway to chronic lung injury. Although the injury to the pulmonary parenchyma may be multifactorial, the coexistence of PPFE and CBO in our patient supports the close relationship between PPFE and CBO, which might suggest a common pathway to drug-induced lung disease.

In conclusion, pulmonary toxicity occurred only after intensive anticancer chemotherapy in a very young
adult patient, although HSCT was not performed after chemotherapy. However, the patient was successfully treated with single lung transplantation.

References