Respiratory Medicine Case Reports 13 (2014) 19–23

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Acute exacerbation of airspace enlargement with fibrosis

Tomoyuki Kakugawa [a], Kazuhiro Tabata [b], Daiki Ogawara [a], Tomoshi Tsuchiya [c], Shintaro Hara [a], Noriho Sakamoto [a], Yuji Ishimatsu [a, *], Kazuto Ashizawa [d], Takeshi Nagayasu [c], Junya Fukuoka [b], Shigeru Kohno [a]

[a] Second Department of Internal Medicine, Nagasaki University School of Medicine, Nagasaki, Japan
[b] Department of Pathology, Nagasaki University Hospital, Nagasaki, Japan
[c] Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan
[d] Department of Clinical Oncology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Keywords:
Acute exacerbation
Airspace enlargement with fibrosis
Smoking-related interstitial lung disease

A B S T R A C T

In 2008, Kawabata et al. described a lesion which they termed “airspace enlargement with fibrosis” that could be included on the spectrum of smoking-related interstitial lung diseases. This group also reported that patients with airspace enlargement with fibrosis but without coexisting interstitial pneumonia of another type had no acute exacerbations and favorable prognoses on clinical follow-up. Here we describe the first case, to our knowledge, of acute exacerbation of airspace enlargement with fibrosis without coexisting interstitial pneumonia of another type. An 82-year-old man was referred to our department for worsening dyspnea and new alveolar opacities on chest radiograph following left pulmonary segmentectomy (S6) for cancer. A diagnosis of acute exacerbation of airspace enlargement with fibrosis without coexisting interstitial pneumonia of other types was made, based on pathological evidence of airspace enlargement with fibrosis and organizing diffuse alveolar damage. Treatment with high-dose methylprednisolone followed by tapered oral prednisolone resulted in gradual improvement of the clinical condition and chest radiographic findings. Clinicians should be aware that patients with airspace enlargement with fibrosis may experience acute exacerbation.

Introduction

Smoking is associated with chronic obstructive pulmonary diseases and lung cancer. Recently smoking has been implicated as a cause of interstitial lung disease, in what is called “smoking-related interstitial lung disease” [1–5]. It has been reported that pathologically significant but clinically unrecognized interstitial fibrosis occurs commonly in cigarette smokers [1–5]. In 2008, Kawabata et al. [6] described a lesion which they termed “airspace enlargement with fibrosis (AEF)” that could be included on the spectrum of smoking-related interstitial lung diseases. The lesion is frequently located in a bronchiolocentric location in the setting of emphysema, and is characterized by a fibrous and frequently hyalinized interstitium with structural remodeling, but lacking foci of fibroblasts. These incidental histologic findings in smokers are not regarded as a distinct form of idiopathic interstitial pneumonia (IIP) [5], but AEF includes more interstitial fibrosis than described for the classic definition of emphysema [7]. Yamada et al. [8] suggested that the histological features of AEF differed significantly from usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), and centrilobular emphysema (CLE) and that the mechanism of fibrosis of AEF is different from that of UIP and NSIP. They also reported that patients with AEF but without coexisting interstitial pneumonia of another type had no acute exacerbations and favorable prognoses on clinical follow-up [6,8]. They speculated that their observation suggested that the AEF and UIP patterns might be fundamentally different, perhaps related to the fact that foci of fibroblasts are not a feature of AEF [6]. However, the natural disease course of AEF has not been fully understood.

Here we describe an AEF patient without coexisting interstitial pneumonia of another type in whom the natural disease course and sequential changes on chest high-resolution computed

* Corresponding author. Second Department of Internal Medicine, Nagasaki University School of Medicine, 1-7-1 Sakamoto, Nagasaki, Nagasaki 852-8501, Japan. Tel.: +81 95 819 7273; fax: +81 95 849 7285.
E-mail addresses: kakugawa@nagasaki-u.ac.jp (T. Kakugawa), t-kaz@nagasaki-u.ac.jp (K. Tabata), bomb0416@yahoo.co.jp (D. Ogawara), tomotsuchiya@hotmail.com (T. Tsuchiya), hara_shin123@me.com (S. Hara), nsakamot@nagasaki-u.ac.jp (N. Sakamoto), yuji-i@nagasaki-u.ac.jp (Y. Ishimatsu), ashi@nagasaki-u.ac.jp (K. Ashizawa), nagayasu@nagasaki-u.ac.jp (T. Nagayasu), fukuokaj@nagasaki-u.ac.jp (J. Fukuoka), s-kohno@nagasaki-u.ac.jp (S. Kohno).

http://dx.doi.org/10.1016/j.rmcr.2014.07.005

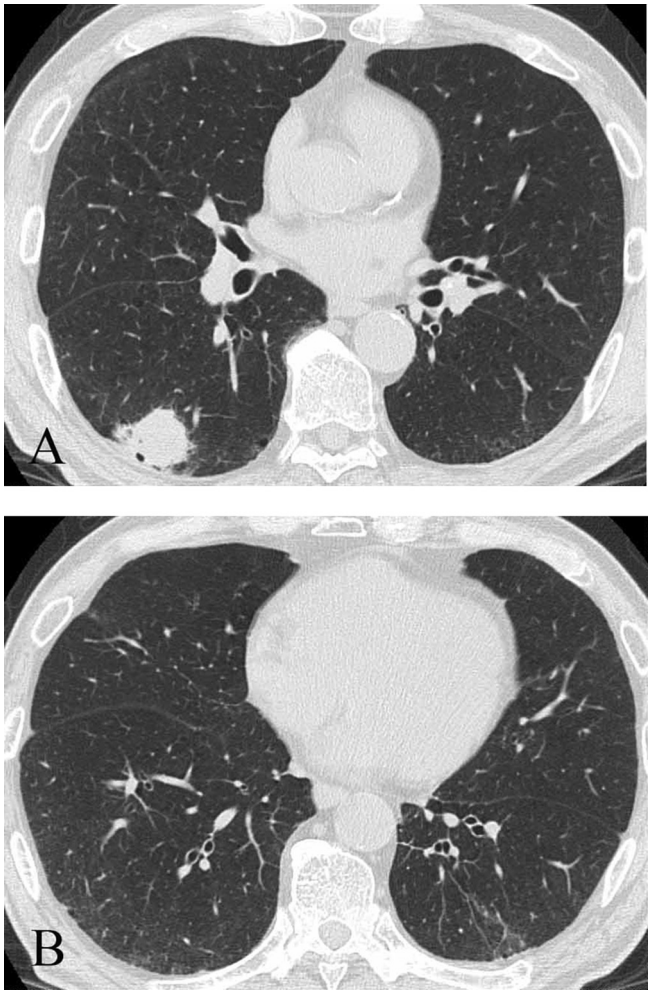

Fig. 1. High-resolution computed tomography (HRCT) before the first surgery. HRCT of the chest revealed a nodule in the right lower lobe (A) and ill-defined centrilobular small nodules and ground-glass opacities, in addition to low attenuation areas and small cysts, in the subpleural areas bilaterally (B).

tomography (HRCT) findings were precisely observed, and who finally experienced acute exacerbation. To our knowledge, this is the first reported case of acute exacerbation of AEF in a patient without coexisting interstitial pneumonia of another type.

Case report

An 82-year-old man was referred to our department for worsening dyspnea and new alveolar opacities on chest radiograph following left lung segmentectomy (S6). He was an ex-smoker (20 cigarettes a day for 57 years) who had quit smoking 5 years previously. He had been diagnosed with squamous cell carcinoma of the lung 4 years previously and had undergone combined right middle and lower lobectomies (first surgery). Before the first surgery, HRCT of the chest revealed ill-defined, centrilobular, small nodules and ground-glass opacities (GGOs), in addition to low attenuation areas and small cysts, in the subpleural areas bilaterally (Fig. 1). However, 20 months after the first surgery, GGO appeared along the subpleural area of the right residual lung on HRCT and gradually changed to consolidation with bronchiectasis (Fig. 2). Subsequently, 3 years after the first surgery, HRCT revealed a new nodule in the left lower lobe (S6) that gradually increased in size, suggesting the possibility of recurrence of the lung cancer. Therefore, he underwent segmentectomy (S6) of the left lung 4 years after the first surgery. Interstitial opacities were not evident in the left lung on HRCT 2 months before that second surgery. Consolidation with bronchiectasis was evident along the subpleural area in the right residual lung (Fig. 3). The chest radiograph obtained before the second surgery showed no GGOs in the left lung (Fig. 4). The patient did not complain of worsening dyspnea before the second surgery, and the respiratory status was stable before, during, and just after that procedure. The patient presented to our department 10 days after the second surgery complaining of worsening dyspnea for 2 days. There was no history of exposure to any infectious, toxic, or environmental agent that could cause interstitial lung disease. Physical examination revealed that he was afebrile. Fine crackles were detected bilaterally on chest auscultation. Results of arterial blood gas analysis on 2 L/min O_2 via nasal cannula were pH 7.468, PaO_2 83.9 Torr and $PaCO_2$ 36.0 Torr. Laboratory examinations on admission revealed a white blood cell count of 12,800/mm^3 with 90% neutrophils. C-reactive protein was elevated (6.43 mg/dL). Serum lactate dehydrogenase level was elevated (426 IU/L). Serum Krebs von den Lungen-6 (KL-6) and surfactant protein-D levels were elevated (881 U/mL and 717 ng/mL, respectively). Anti-nuclear antibody and other autoantibodies to specific antigens were all negative. Pneumococcal and *Legionella* urinary antigens were negative. Cultures of blood to detect bacteria, fungi, and mycobacteria were all negative. Results of serological tests for *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae,* and *Chlamydophila psittaci* were negative; test results for β-D glucan and cytomegalovirus antigen were also negative. Echocardiography demonstrated no evidence of heart failure. Chest radiograph showed bilateral GGOs in both lower lung fields (Fig. 5). HRCT showed bilateral non-homogenous GGOs with traction bronchiectasis and bronchiolectasis with basilar predominance (Fig. 6). The left lung S6 segmentectomy tumor specimens contained pleomorphic carcinoma that had components of sarcomatoid carcinoma and adenocarcinoma. The surrounding, uninvolved area had emphysematous changes with interstitial and peribronchiolar fibrosis, but without histological features of IIPs, such as UIP or NSIP

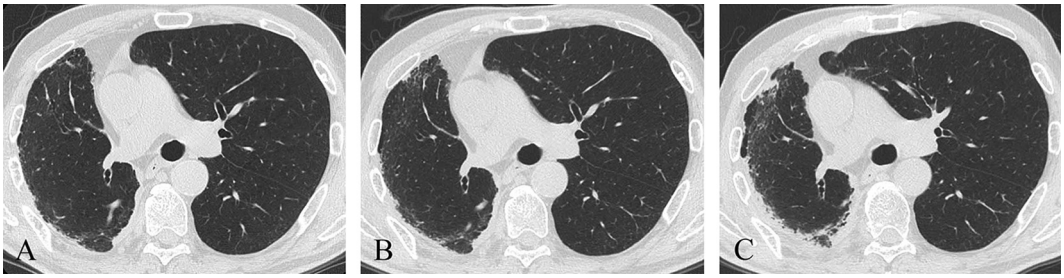

Fig. 2. High-resolution computed tomography (HRCT) after the first surgery. Ground-glass opacities appeared along the subpleural area of the right residual lung 20 months after the first surgery (A), and then gradually changed to consolidation with bronchiectasis on HRCT: 26 months after the first surgery (B); 38 months after the first surgery (C).