Distal Acinar Emphysema and Interstitial Pneumonia in a Patient with von Recklinghausen’s Disease:
Five-Year Observation Following Quitting Smoking

Akihito Yokoyama, Nobuoki Kohno, Kimiko Sakai, Kei-ichi Kondo, Yutaka Hirasawa and Kunio Hiwada

Cystic lesion, malignancy and interstitial pneumonia are well-known as pulmonary complications of patients with von Recklinghausen’s disease. We report herein an unusual patient with distal acinar emphysema and interstitial pneumonia of prominent hypercellularity demonstrated by transbronchial biopsy and broncho-alveolar lavage fluid (BALF). Six months after quitting smoking, the total cell count of BALF was remarkably reduced. This patient remains stable under 5-year observation in terms of symptoms and findings of both BALF and pulmonary function tests. Quitting smoking may have facilitated a favorable prognosis for the particular lung disease complicated in this patient.

Key words: neurofibromatosis, desquamative interstitial pneumonia, bronchoalveolar lavage, smoking

Introduction

von Recklinghausen’s disease is a relatively common autosomal disorder linked to chromosome 17. The pulmonary manifestations of neurofibromatosis consist of diffuse interstitial fibrosis and bullae, either alone or in combination (1). Respiratory symptoms are usually mild, but about 20% of affected patients develop disabling disease. We treated a patient with the characteristic feature of distal acinar emphysema on chest computed tomography (CT) and histologically-proven interstitial pneumonia. To our knowledge, no patient with a complication of distal acinar emphysema in von Recklinghausen’s disease has been reported. Therefore, we report this case together with the result of a 5-year observation.

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Case Report

In 1991, a 48-year-old man was admitted to our hospital for resection of skin tumors with tenderness. A diagnosis of neurofibromatosis had made on the basis of multiple cafe-au-lait spots, multiple histologically-proven neurofibromas and a family history of neurofibromatosis. In the preoperative investigations, his chest roentgenogram revealed diffuse reticular shadow and bullae in the bilateral upper lobes, though he had no respiratory symptoms. A chest CT demonstrated low-attenuation area with comb-like remnant interstitium in the peri-pleura with upper lobe-dominant distributions (Fig. 1). These findings are characteristic of a diagnosis of distal acinar emphysema. Pulmonary function tests revealed slight airway obstruction on his flow-volume curve (V25/HT: 55%) and 150% increased residual volume, but otherwise repeatedly within normal limits including DLco (%VC: 107%; FEV1: 77.5%; %DLco: 126%). He smoked 1 pack of cigarettes per day for 20 years. 67Ga-citrate scintigraphy revealed slightly increased uptake in both lungs. The specimens obtained by transbronchial biopsy showed interstitial pneumonia with lymphocyte-dominant infiltration, and increased numbers of intra-alveolar macrophages (Fig. 2). The gross appearance of the bronchoalveolar lavage (BALF) was darkgreen especially in the second and third aliquots, and the total cell count (TCC) of BALF revealed a marked increase (220×10⁴/ml) (Fig. 3) with 99% macrophages (more than 99% CD1a-negative demonstrated by immunohistochemical staining).

Because he had no symptoms, he was advised to quit smoking and no further treatment was performed. Six months
Figure 1. A–D) Photographs of chest CT obtained in 1996, showing bulla and distal acinar emphysema with upper lobe predominance with some centrilobular emphysema. These findings are essentially the same as in 1991.

Figure 2. Histological findings of a specimen obtained by transbronchial biopsy (HE stain, original magnification, ×20).

later, TCC of BALF were reduced to 41.8% (92×10⁴/ml) (Fig. 3). At the same time, the concentration of albumin in BALF and KL-6 in serum were both decreased from 194 μg/ml to 67 μg/ml, and from 333 U/ml to 179 U/ml, respectively. Examinations revealed that these markers fluctuated to some extent, but did not return to the initial levels (52–76×10⁴/ml for TCC, 59–82 μg/ml for BALF albumin, and 180–260 U/ml for BALF KL-6). He remains symptomless with no remarkable changes in objective examinations at present, 5 years from the first evaluation.

Discussion

The present patient showed characteristic pulmonary manifestations of von Recklinghausen’s disease; i.e., interstitial pneumonia and cystic lesions (1). In addition to the cystic lesions commonly observed in patients with centrilobular emphysema, his chest CT showed a remarkable peri-pleural low-attenuation with upper lobe predominance, which suggested a diagnosis of distal acinar emphysema (2). These attenuation areas could not be due to fibrosis because the finding of honeycombing fibrosis, which is in direct contrast to the definition of
emphysema (3), was not seen. In consideration of his smoking history, this patient has distal acinar emphysema independent of interstitial pneumonia.

The interstitial pneumonia complicated in patients with von Recklinghausen’s disease is generally indistinguishable from that of known or unknown etiology (1, 4). One of the characteristic features of the present patient was a marked hypercellularity in BALF. In fact, the total cell count of this patient was the most numerous that we have seen in our experience. Since the increased numbers of intra-alveolar macrophages were observed in both BALF and TBLB specimens, and this finding is not infrequently observed in patients with von Recklinghausen’s disease (5), a diagnosis of desquamative interstitial pneumonitis (DIP) may be suggested. The pulmonary function tests revealed no deterioration during the 5-year follow-up observation. This fact favors the diagnosis of DIP rather than usual one, although open lung biopsy is necessary for a definitive diagnosis.

In the present patient the number of macrophages in BALF was markedly reduced following quitting smoking. This fact indicated that smoking likely contributed to the extremely increased alveolar macrophages of this patient. Smoking is well-known to increase alveolar macrophages (6); they produce elastase which destroy lung elastin, and then contribute to the pathogenesis of emphysema (7). Therefore, this scheme could be applied to this patient. The fact that he was of a relatively younger age (<50 years old) and an unusual type of the disease would need the modification in this patient. Interstitial pneumonia, a well-known complication of von Recklinghausen’s disease, may influence the development of emphysema in this patient. There is a possibility that von Recklinghausen’s disease itself may increase the sensitivity to smoking, though it has not been proved. Furthermore, Motoyama et al mentioned in their report (8) that nerve growth factor, whose serum levels were reported to be increased in patients with von Recklinghausen’s disease (9), has protease activity, and may contribute to the pathogenesis of emphysema in patients with von Recklinghausen’s disease. In anyway, quitting smoking seemed beneficial in this patient. This notion is supported by both the reduced serum KL-6 level and the albumin concentration in BALF. The idea of the former has been studied by us and is known to be useful for evaluating the disease activity of pneumonitis (10, 11). The latter is a sensitive marker for inflammatory damage to the air-blood barrier (12). Further careful observation of this patient will determine the prognosis of these particular lung complications.

References


