CASE REPORT

Usual interstitial pneumonia associated with primary biliary cirrhosis

Hiroshi Ishii*, Atsuko Iwata, Jun-ichi Kadota

Department of Respiratory Medicine, Oita University Hospital, 1-1 Idaigaoka, Yufu-city, Oita 879-5593, Japan

Received 3 April 2008; accepted 1 May 2008

Summary
We herein describe the first case, to our knowledge, of surgical biopsy-proven usual interstitial pneumonia (UIP) as the pulmonary manifestation in primary biliary cirrhosis (PBC). A 56-year-old male was admitted to our hospital because of the identification of bilateral reticular infiltrate on a chest roentgenogram. He was histologically confirmed to have PBC without definite signs of Sjögren’s syndrome at age 47. His chest CT scan showed bibasilar reticular opacities without a honeycomb appearance, while a bronchoalveolar lavage fluid analysis revealed no lymphocytosis. A surgical lung biopsy specimen revealed evidence of a UIP pattern. The patient’s condition has remained stable for a follow-up period of two years without treatment. Our case indicates that the UIP pattern is an additional form of diffuse interstitial pneumonia/fibrosis that may develop in association with sporadic PBC.

Introduction
Primary biliary cirrhosis (PBC) is a chronic, cholestatic liver disease characterized by the inflammatory destruction of the intrahepatic bile ducts, eventually leading to cirrhosis. PBC is thought to be an autoimmune disorder, and such patients demonstrate autoantibodies to mitochondria. Pulmonary manifestations in PBC have been reported since 1970, and include a decreased vital capacity or diffusion capacity for carbon monoxide, lung granulomas, lymphocytic bronchitis/bronchiolitis, lymphocytic interstitial pneumonitis, and other fibrosing interstitial pneumonias. However, PBC may be associated with other autoimmune disorders, such as Sjögren’s syndrome (SjS) and rheumatoid arthritis (RA), and a majority of the previously reported interstitial pneumonia cases mentioned above had a history of SjS. In addition, there is no report of a usual interstitial pneumonia (UIP) pattern confirmed by a surgical lung biopsy in a patient with PBC without either definite signs of SjS or RA, since the concept of UIP, which is distinct from non-specific interstitial pneumonia (NSIP), was first established in 1994.

* Corresponding author. Tel.: +81 97 586 5804; fax: +81 97 549 4245.
E-mail address: hishii@med.oita-u.ac.jp (H. Ishii).

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doi:10.1016/j.rmedc.2008.05.004
Case report

A 56-year-old male was admitted to our hospital because of a bilateral reticular infiltrates on a chest roentgenogram. He was histologically confirmed to have PBC at age 47, while a stable condition for PBC, including the biological liver function and histological findings by repeated liver biopsy, had been maintained since age 51. He was asymptomatic and had taken no medications prior to the illnesses. He did not smoke or have a history of exposure to dust or birds. There was no finger clubbing, but minimal fine crackles were detected in the lower lung fields. The laboratory tests revealed a normal blood count and routine chemistry findings including the liver function. The serum levels of KL-6 and surfactant protein-A were 421 U/ml (normal value <500 U/ml) and 52.1 ng/ml (<43.8 ng/ml), respectively. The examination of the autoantibodies showed a positive antinuclear factor, anti-centromere, and anti-mitochondria, but were negative for the others. The Schirmer and Rose Bengal dye tests were negative. No signs of other collagen-vascular disease including CREST syndrome were present. The arterial blood gas analysis revealed no hypoxemia. Pulmonary function tests demonstrated neither a restrictive impairment nor airway obstruction, but a reduced percent diffusion capacity for carbon monoxide of 64.2%. The chest computed tomography (Fig. 1) revealed peripheral reticulonodular shadows without a honeycomb appearance, predominantly in the dorsal sub-pleural area of the whole lung. The bronchoalveolar lavage fluid demonstrated a normal cell proportion. The examination of surgical lung biopsy specimens obtained from the left lower lobe revealed histopathologic features characteristic for UIP (Fig. 1), and of microscopic honeycombing and mononuclear infiltrations with some lymphoid follicles. At two years after the lung biopsy, his clinical condition remains stable without therapeutic intervention.

Discussion

Pulmonary manifestations have been recognized in PBC since 1970, while most early reports relied on radiologic findings or pulmonary function testing but not necessarily histopathology. According to the report by Lucey et al. in 1986, 2.17% of the patients (out of all the subjects including 230 cases of PBC) were complicated by fibrosing alveolitis. However, it was unclear what methods were used to reach this diagnosis. In addition, PBC is known to be one of the most frequent hepatic diseases associated with SjS and RA. Interstitial pneumonias in PBC occur with SjS or RA. Rodriguez-Roisin et al. stated that lung involvement in PBC was the result of the associated connective tissue disease. But, SjS or keratoconjunctivitis sicca was not the case in our patient, in whom the clinical examination for these diseases was negative.

UIP is a pathologic pattern characterized by the presence of a wide range of damage in the same tissue specimen ranging from normal alveolar walls to fibrosis and end-stage lesion. The concept of UIP being distinct from NSIP was first established in 1994. The UIP pattern has also been recognized in association with collagen-vascular diseases, such as RA and scleroderma. As in the present case, the UIP pattern in patients with collagen-vascular diseases seems likely to be associated with lymphoid follicles in the lung, compared with that in idiopathic pulmonary fibrosis (IPF), but this remains unclear. The histopathologic changes in the lung of patients with SjS have been recently documented, in which NSIP was the most frequent finding documented in 33 patients and none had a UIP pattern. To
our knowledge, the association between UIP and PBC without any other collagen-vascular disease has not been previously published. Park et al.\textsuperscript{10} reported that UIP in patients with RA had a significantly worse prognosis in comparison to UIP with non-RA-collagen-vascular diseases (not including PBC) and NSIP with other collagen-vascular diseases. The present case demonstrated a clinically stable condition for 2 years without any treatment, however, the prognosis of UIP in PBC remains unclear.

In conclusion, we herein described the first case of UIP in PBC, although these two disorders may have only been coincidentally associated. The ultimate impact of interstitial pneumonia, such as UIP, on patients with PBC therefore remains to be clarified. It may thus be very important to further investigate pulmonary involvement as a prognostic factor in cases accompanied by sporadic PBC.

Acknowledgement

We thank Dr. Y. Kawabata (Division of Pathology, Saitama Cardiovascular and Respiratory Centre, Ohsato, Saitama) and K. Kashima for valuable assistance in the pathological diagnosis.

Conflict of interest statement

None of the authors have a conflict of interest to declare in relation to this work.

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