CASE REPORT

Anti-synthetase syndrome with lung involvement associated with primary biliary cirrhosis: A case report

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\textbf{Summary}

We here report a case of association between primary biliary cirrhosis and anti-synthetase syndrome with exclusive interstitial lung involvement. The patient developed exertional dyspnoea 14 years after being diagnosed with primary biliary cirrhosis. Search for autoantibodies showed positivity for anti-Jo-1. No clinically evident myositis was present. HRCT scan showed bilateral interstitial pulmonary involvement, and the BAL yielded an alveolar lymphocytosis with low CD4/CD8 ratio. Treatment with systemic corticosteroids led to rapid improvement of the clinico-radiological picture. Although primary biliary cirrhosis had been previously found in association with polymyositis, no previous reports of its association with anti-Jo-1 syndrome with prominent pulmonary involvement are known.

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\textbf{Introduction}

A 73-year-old female, non-smoker, with diabetes mellitus, no history of allergies, no significant occupational exposures, was admitted to the hospital in October 2006 for evaluation of progressive exertional dyspnoea. She had been
diagnosed with primary biliary cirrhosis (PBC) in 1991 based on liver biopsy and presence of serum anti-mitochondrial antibodies. In 1990, she had been treated surgically (hemicolecction) for colonic cancer. She had no fever and no joint or muscle pain. Raynaud’s phenomenon was absent. Muscle strength was normal. No skin lesions were present. The chest examination revealed basal bilateral crackles.

Laboratory tests showed normal hemogram, increased alkaline phosphatase (506 UI/mL), gamma-glutamyl transferase (259 UI/mL) and total cholesterol (232 mg/dL). Creatine phosphokinase was not elevated. Positivity for HBs antibody and HBc antibody was detected, indicating previous Hepatitis B infection. The patient also tested positive for the homozygous H63D mutation of the hemochromatosis gene (HFE), but blood iron and ferritin were not altered. Search for autoantibodies showed positivity for anti-Jo-1 and anti-SS-A/R0. High resolution CT scan of the chest showed reticular opacities and ground-glass areas mainly localized in both upper lobes, consistent with a non-specific interstitial pneumonia (NSIP) pattern (Figure 1). Lung function tests Figure 2 showed mild restrictive deficit (forced vital capacity (FVC) 71% of predicted value, forced expiratory volume in 1s (FEV1) 81% of predicted, FEV1/FVC% 80), with reduced lung transfer factor for CO (TLCO 57% of predicted value). Low arterial oxygen saturation was detected at rest (85%), requiring oxygen therapy (2 L/min). Bronchoalveolar lavage (BAL) was then performed, yielding a lymphocytic inflammation, with a low CD4/CD8 ratio. Due to the presence of respiratory failure a decision was made not to proceed with a lung biopsy, and to immediately start treatment with prednisone (0.5 mg/kg/day). The therapy led to gradual improvement of symptoms. Simultaneously, therapy with ursodeoxycholic acid (600 mg twice daily) was begun, as the patient had never been treated before for PBC, resulting in a marked improvement of the cholestasis indices. High-resolution computed tomography (HRCT) scan performed 7 months after the diagnosis showed almost complete resolution of the reticular pattern and marked reduction of ground-glass opacities (Figure 1). In light of the significant clinical and functional improvement it was possible to discontinue the oxygen therapy and to reduce the dose of prednisone to 0.25 mg/kg/day, and the conditions of the patient have remained stable up to now.

Discussion

The anti-synthetase syndrome (AAS) is a relatively uncommon clinical entity of autoimmune nature, found more frequently in adult female patients, and characterized by positivity to serum antibodies directed against aminoacyl-tRNA synthetases and a variable combination of myositis, interstitial pneumonia, arthritis, Raynaud’s phenomenon, mechanic’s hands. This condition is considered a subset of idiopathic inflammatory myopathies. There have been rare reports of AAS cases in which the lung involvement was the main, sometimes exclusive, manifestation at the onset. Among the anti-synthetase antibodies more frequently associated with lung involvement the anti-Jo-1 is one of the better known. It is noteworthy that, when present, the lung disease is the main determinant of survival in patients with AAS. In the present case study, we report the association of PBC and anti-Jo-1 syndrome with predominant interstitial lung disease. To our knowledge, such an association has not been reported before, although there are few documented cases of PBC associated with polymyositis with typical muscle involvement and no lung disease. The chest HRCT in our case showed a NSIP pattern,
and, while not confirmed bioptically in our case, this finding is consistent with the observed, prompt response to corticosteroids which is typical of this type of interstitial lung disease. Moreover, among the patterns of interstitial pneumonia found in association with polymyositis, NSIP is relatively common. In our patient, the pattern of pulmonary inflammation as evidenced by the BAL was consistent with previous reports of lung disease in AAS (2), as it presented mainly a lymphocytosis with low CD4/CD8 ratio. Although the main features of lung involvement in our patient did not differ from previously described cases of AAS, a potential role of the coexisting PBC in the pathogenesis of lung disease cannot be excluded; PBC itself has been found in association with a spectrum of pulmonary abnormalities, from subclinical alveolar lymphocytosis to interstitial fibrosis, although a definite interstitial pneumonia has been reported only rarely in PBC patients. We conclude that the presence of anti-synthetase and anti-mitochondrial antibodies should be always tested, among other auto-antibodies, in all patients who develop interstitial lung disease in absence of known causes of pulmonary fibrosis.

Conflict of interest statement

None of the authors is involved in any actual or potential conflict of interest concerning the subject matter.

References