Turk J Gastroenterol 2010; 21 (1): 60-62

Successful treatment of primary Sjögren's syndrome complicated with primary biliary cirrhosis and lung involvement

Primer biliyer siroz ve akciğer tutulumu ile seyreden primer Sjögren sendromunda başarılı tedavi

Akif ALTINBAŞ[1], Güneş ARIK[1], Umut KALYONCU[2], Ali AKDOĞAN[2], Ömer KARADAĞ[2], Bünyamin KISACIK[2], A. İhsan ERTENLİ[1,2]

Departments of [1]Internal Medicine, [2]Rheumatology, Hacettepe University, School of Medicine, Ankara

A patient with primary Sjögren's syndrome complicated with primary biliary cirrhosis and lymphocytic interstitial pneumonia is presented. She was 38 years old and was admitted to our hospital for generalized pruritus, xerostomia, xerophthalmia, fatigue, and reticulonodular changes on her chest X-ray. With the findings of ground-glass attenuation and centrilobular nodules in high resolution computerized tomography, the diagnosis of lymphocytic interstitial pneumonia was made. Oral methylprednisolone 1 mg/kg/day and ursodeoxycholic acid 15 mg/kg/day were started. At the 6th month follow-up, she had no complaints, and pulmonary function tests and high resolution computerized tomography were normal. This is the first case of Sjögren's syndrome, primary biliary cirrhosis and lymphocytic interstitial pneumonia in the English literature.

Key words: Primary Sjögren's syndrome, primary biliary cirrhosis, lymphocytic interstitial pneumonia

38 yaşında kadın, hastaneye jeneralize kaşıntı, kserostoma, kseroftalmi, halsizlik şikayetleri ile başvurdu. Arka-ön akciğer grafisinde retikülonodüler değişiklikler, yüksek çözünürlüklü akciğer tomografisinde buzlu cam dansitesi ve sentrilobüler nodüller tespit edilmesi üzerine primer biliyer siroz ve lenfositik interstisiyel pnömoni tanısı ile oral 1 mg/kg/gün metilprednizolon ve 15 mg/kg/gün dozunda ursodeoksikolik asit başlandı. Hastanın altıncı ay kontrolünde hiç bir şikayetinin kalmadığı, solunum fonksiyon testlerinin normal olduğu, yüksek çözünürlüklü akciğer tomografisindeki değişikliklerin tamamen düzeldiği saptandı. Primer biliyer siroz, lenfositik interstisiyel pnömoni ve primer Sjögren sendromu birlikteliği daha önce tanımlanmamıştır.

Anahtar kelimeler: Primer Sjögren sendromu, primer biliyer siroz, lenfositik interstisiyel pnömoni

INTRODUCTION

Sjögren's syndrome (SS) is a chronic autoimmune exocrinopathy. It is characterized by lymphoplasmacytic infiltrates in the salivary and lacrimal glands. Similar lymphocytic infiltrates may invade visceral organs, including bronchi and lungs. The bronchopulmonary manifestations reported in SS are xerotrachea, follicular bronchitis/bronchiolitis, cystic lesions, and lymphocytic interstitial pneumonia (LIP). Less common manifestations include bronchiolitis obliterans with organizing pneumonia and pulmonary hypertension (1). SS has also been associated with primary biliary cirrhosis (PBC), autoimmune hepatitis and cryptogenic cirrhosis. The overall incidence of liver disease in patients with SS was reported as 6% (2).

In this report, we present a patient with primary SS (pSS) complicated with both PBC and LIP.

CASE REPORT

A 38-year-old female admitted to our hospital for generalized pruritus, xerostomia, xerophthalmia, fatigue, and reticulonodular changes on her chest X-ray. Her medical history was significant for PBC and pSS for six months, based upon the presence of anti-mitochondrial antibodies (AMA), antinuclear antibodies (ANA), a liver histology suggesting PBS stage II/IV, and parotis histology sug-

Address for correspondence: Akif ALTINBAŞ
Hacettepe University, Medical Faculty
Department of Internal Medicine
Sıhhıye 06100 Ankara, Turkey
Phone: + 90 312 305 30 71/305 15 38 • Fax: + 90 312 311 72 08
E-mail: akifa@hacettepe.edu.tr

Manuscript received: 22.05.2007 **Accepted:** 11.09.2009

doi: 10.4318/tjg.2010.0051

gesting SS. Schirmer test was 4 mm in both eyes, and anti-Ro and anti-La antibodies were negative. Ground-glass attenuation and centrilobular nodules were found in high resolution computed tomography (HRCT) before admission. In our hospital, her liver function tests were compatible with cholestasis (alkaline phosphatase [ALP]: 664 U/L, normal range: 35-129; gamma glutamyl transpeptidase [GGT]: 305 U/L, normal range: 5-40; serum bilirubin and transaminase levels were within normal limits). ANA (1/320 titers) and AMA (1/80 titers) were positive. In HRCT examination, the diagnosis of LIP was made with ground-glass attenuation and centrilobular nodules (Figure 1). A mild restrictive profile was present in pulmonary function tests, and mild decrease in DLCO (78%) was noted, while she denied any pulmonary symptom. Hence, she refused bronchoscopy. Oral methylprednisolone 1 mg/kg/day and ursodeoxycholic acid 15 mg/kg/day were started. Methylprednisolone was then tapered. On the follow-up visit three months later, there was improvement regarding cholestasis (ALP: 125 U/L and GGT: 325 U/L), and HRCT revealed only cylindrical bronchiectasis in the left upper lobe without any evidence of alveolitis (Figure 2). Her methylprednisolone therapy was gradually switched to an alternate-dose regimen, and ursodeoxycholic acid was continued as 15 mg/kg/day. Six months later, she had no complaint, pulmonary function tests were normal, and DLCO was 95%, while mild cholestasis was still present (ALP: 91 U/L and GGT: 159 U/L). She is still taking methylprednisolone 35 mg on alternate days and ursodeoxycholic acid 15 mg/kg/day.

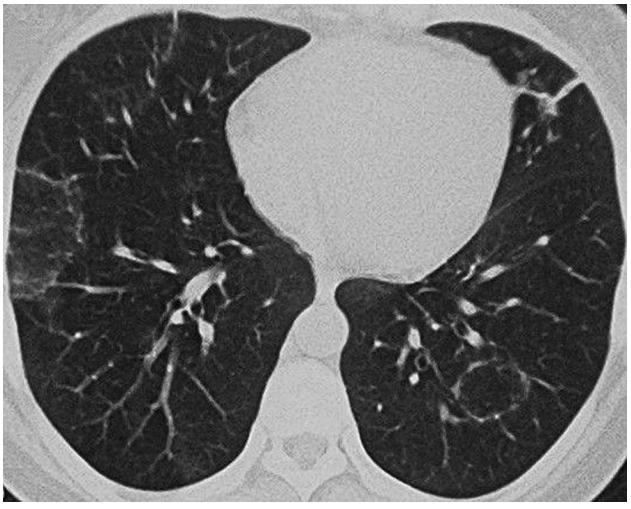

Figure 1. HRCT (pre-treatment): ground-glass attenuation and centrilobular nodules.

DISCUSSION

The frequency of lung involvement in SS is estimated to range between 9-75% of the patients depending on the diagnostic modalities. On the other hand, LIP appears much less commonly in SS. Constantopoulos et al. (4) reported 3 LIP in 343 SS patients (0.9%). However, recent reports suggest that the frequency of LIP may be higher in SS. Taouli et al. (1) found that 31 of 35 SS patients have lung involvement on chest CT, and 5 of those 31 were diagnosed as LIP. The main HRCT findings in LIP are ground-glass attenuation, poorly defined centrilobular nodules, thickening of bronchovascular bundles, and lymph node enlargement (1). Pulmonary biopsy may be required to exclude differential diagnoses including usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP) with fibrosis. However, HRCT is a useful new tool in evaluating lung parenchyma in pSS, and HRCT findings correlate with histopathologic diagnosis (6, 11). Likewise, the HRCT of our patient was highly suggestive for LIP with ground-glass attenuation and centrilobular nodules. She was asymptomatic regarding pulmonary symptoms. Accordingly, for ethical reasons, we did not perform invasive procedures including lung biopsy.

Sjögren's syndrome and PBC share many common features. In both conditions, the inflammation starts around the ducts and both epithelial populations inappropriately express class II HLA molecules. CD4-positive T-cells predominate in severe

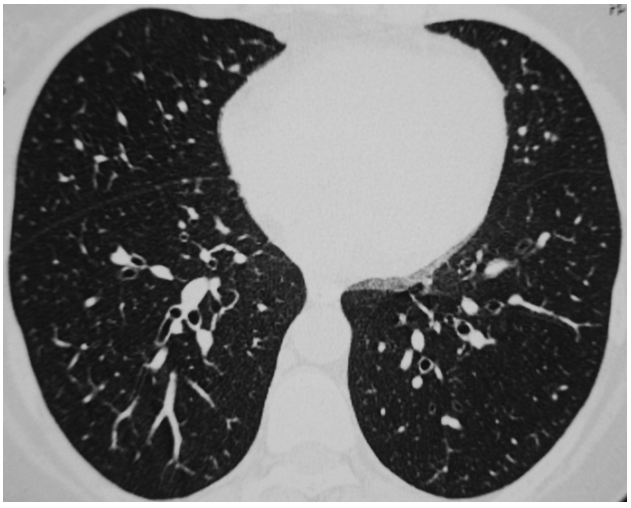

Figure 2. HRCT (3rd month of the treatment): cylindrical bronchiectasis in the left upper lobe.

biliary cirrhosis lesions and salivary gland lesions in pSS (2). Likewise, infiltration of T cells in the alveolar interstitium and areas surrounding lymphoid follicles are the main histopathological findings in LIP (3). An overlap between PBC and pSS has been well known (2). On the other hand, one of the most common (25% of LIP cases) associations of LIP is with pSS (3). There are isolated case reports in the literature demonstrating the association between SS secondary to rheumatoid arthritis, PBC and interstitial pneumonia (8, 9). However, to our knowledge, a patient with pSS complicated with both PBC and LIP has not been reported before.

Long-term use of steroids is commonly associated with significant steroid-associated morbidity. Adverse effects of corticosteroid treatment can be reduced by administering the steroid on alternate days, and alternate-day therapy can be recommended for patients requiring glucocorticoids over a prolonged period of time (10). In a previous study, prednisone 30 mg on alternate days plus piroxicam significantly decreased the serum total protein, IgG, IgA, and sedimentation rate without any improvement in the histological parameters of salivary and lacrimal glands in pSS (12). Hence, the efficacy of alternate-dose steroids in pSS remains to be established. We started steroid therapy with oral methylprednisolone 1 mg/kg/day, and gradually tapered to an alternate-dose regimen to reduce steroid-related toxicity. At the end of a six-month follow-up period, pulmonary function tests and HRCT findings showed significant improvement with this therapeutic approach.

In summary, this paper presents the case of an unusual association between pSS, PBS and LIP, and to our knowledge, this is the first such case reported in the literature. This patient was successfully treated with alternate-dose methylprednisolone and ursodeoxycholic acid for six months.

REFERENCES

1. Taouli B, Brauner MW, Mourey I, et al. Thin-section chest CT findings of primary Sjögren's syndrome: correlation with pulmonary function. Eur Radiol 2002; 12: 1504-11.
2. Abraham S, Begum S, Isenberg D. Hepatic manifestations of autoimmune rheumatic diseases. Ann Rheum Dis 2004; 63: 123-9.
3. Swigris JJ, Berry GJ, Raffin TA, Kuschner WG. Lymphoid interstitial pneumonia. Chest 2002; 122: 2150-64.
4. Constantopoulos SH, Papadimitrioo CS, Moutsopoulos HM. Respiratory manifestations in primary Sjögren's syndrome. A clinical, functional and histologic study. Chest 1985; 88: 226-9.
5. Kim EA, Lee KS, Johkoh T, et al. Interstitial lung disease associated with collagen vascular diseases: radiologic and histopathologic findings. Radiographics 2002; 22: 151-65.
6. Salaffi F, Manganelli M, Carotti M, et al. A longitudinal study of pulmonary involvement in primary Sjögren's syndrome: relationship between alveolitis and subsequent lung changes on high-resolution computed tomography. Br J Rheum 1998; 37: 263-9.
7. Nishio A, Bass NM, Luketic VA, et al. Primary biliary cirrhosis: from induction to destruction. Semin Gastrointest Dis 2001; 12: 89-102.
8. Miyamoto H, Azuma A, Taniguchi Y, et al. Interstitial pneumonia complicated by Sjögren's syndrome, Hashimoto's disease, rheumatoid arthritis and primary biliary cirrhosis. Intern Med 2000; 39: 970-5.
9. Hiraoka A, Kojima N, Yamauchi Y, et al. An autopsy case of primary biliary cirrhosis with severe interstitial pneumonia. Intern Med 2001; 40: 1104-8.
10. Swartz SL, Dluhy RG. Corticosteroids: clinical pharmacology and therapeutic use. Drugs 1978; 16: 238-55.
11. Deheinzelin D, Capelozzi VL, Kairalla RA, et al. Interstitial lung disease in primary Sjögren's syndrome: clinical-pathological evaluation and response to treatment. Am J Respir Crit Care Med 1996; 154: 794-9.
12. Fox PC, Datiles M, Atkinson JC, et al. Prednisone and piroxicam for treatment of primary Sjogren's syndrome. Clin Exp Rheumatol 1993; 11: 149-56.