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Case Report

A case of primary Sjögren's syndrome with polyserositis

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Abstract. Sjögren's syndrome (SS) is an autoimmune disease with glandular and extraglandular manifestations. In terms of pulmonary and cardiac involvement, pleural and pericardial effusion are rare. Moreover, pleural effusion accompanied by pericardial effusion is very rare. We report a case of primary SS (pSS) presenting as pleural effusion, pericardial effusion and ascites. A 58-year-old woman was admitted to our hospital with a 2-week history of dyspnea. Bilateral pleural effusion, pericardial effusion and ascites were detected. Primary SS was diagnosed, based on xerophthalmia, xerostomia, positive results for the Shirmer test and anti-SS-A antibody, and abnormal salivary gland sialography. Pleural and pericardial effusions were attributed to autoimmunological inflammation and ascites was thought to be due to hyperinflammation-induced severe hypoalbuminemia. Treatment with high-dose corticosteroid was proved successful.

Key words: Sjögren's syndrome, pleural effusion, pericardial effusion, ascites, polyserositis

1. Introduction

Sjögren's syndrome (SS) can cause many organic changes. Regarding pulmonary involvement in SS, xerotrachea, bronchial sicca, obstructive small airway disease, interstitial lung diseases, lymph-proliferative lung diseases, and pulmonary hypertension (PH) are known, along with other findings such as pleuritis, pleural effusion, and thickened pleura (1). Regarding cardiac involvement, pericarditis, pericardial effusion and atrioventricular conduction block have been reported (2). Pleural and pericardial effusions in association with SS are rare. Similarly, ascites is rare and it can occur in SS when combined with primary biliary cirrhosis (PBC) (3). We report herein the case of a 58-year-old woman with primary SS (pSS) presenting with pleural effusion, pericardial effusion and ascites. And we investigate the etiologies of these three morbid conditions.

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2. Case report

A 58-year-old woman was admitted to our hospital with a 2-week history of dyspnea. She had no history of diseases. But since around 1 year, she had experienced ocular and oral symptoms of xerophtalmia and xerostomia, respectively. Physical examination revealed weak chest sounds on the right side. Neither skin rash nor swollen joints were evident. Laboratory findings were as follows: white blood cell count (WBC), 7.340/μL; aspartate aminotransferase, 30 IU/L; alanine aminotransferase, 28 IU/L; blood urea nitrogen, 17.5 mg/dL; creatinine, 0.68 mg/dL; total protein, 6.9 g/dL (γ-globulin, 26.2%); albumin (Alb), 2.1 g/dL; C-reactive protein (CRP), 13.90 mg/dL. Serological tests showed: immunoglobulin (Ig)G, 1.997 mg/dL; IgM, 86 g/dL; IgA, 213 mg/dL; rheumatoid factor, 30 IU/L (normal <15.0 IU/L); C_3, 133 mg/dL; and C_4, 35 mg/dL. Hepatitis B surface antigen and anti-hepatitis C antibody were negative. No immune complex (IC) was detected by the C_{1q}-binding assay. Anti-nuclear antibody (ANA) titer was ×1280 with a speckled pattern and anti-SS-A antibody was positive. Negative results were obtained for all other autoimmune antibodies, including anti-SS-B, anti-DNA, anti-RNP, anti-Sm, anti-cardiolipin (CL), anti-centromere, anti-topoisomerase, and anti-mitochondrial antibodies. Negative results were

also obtained for myeloperoxidase and proteinase-3 anti-neutrophil cytoplasmic antibodies. Urinalysis revealed neither proteinuria nor hematuria. Chest roentgenography showed consolidation in the middle and lower bilateral lung fields. Enhanced chest computed tomography (CT) showed bilateral pleural effusions with atelectasis in the lower right lung field and pericardial effusion (Figure 1a). However, interstitial opacity was not apparent (Figure 1b). On ophthalmological examination, positive result was obtained for the Schimer test. Sialography of the left parotid gland revealed punctuate sialectasia with<1 mm in size. Pleural effusion was turbid and positive for the Rivalta test. TP was 3.5 g/dL, sugar was 89 mg/dL, adenosine deaminase (ADA) level was normal and no IC was detected. Pleural effusion was thus considered exudative. Smear tests for *Mycobacterium tuberculosis* and bacterial culture yielded negative results. No malignant cells could be detected in the pleural effusion, but lymphocytes and mesothelial cells were present. We therefore diagnosed pSS with pleuritis and pericarditis.

The patient was initially treated with prednisolone (PSL) at 30 mg/day for 1 week. CRP levels decreased from 13.90 g/dL to 8.25 g/dL by 5 days after starting this treatment. But one week after starting the treatment, right pleural effusion was exacerbated (Figure 2a) and ascites appeared (Figure 2b) accompanied by edema of the lower extremities. But pericardial effusion remained unchanged (Figure 2a). At this stage, CRP levels increased again to 8.84 g/dL. Ascites was translucent and negative for the Rivalta test. TP was 2.1 g/dL, sugar was 79 mg/dL, ADA level was normal and no IC was detected. Ascites was therefore considered transudative. Smear tests showed negative results for *Mycobacterium tuberculosis* and bacterial culture. No malignant cells could be detected. At the time, cardiothoracic ratio was normal and abnormal chest sound, such as coarse crackle, was not audible. So ascites was not attributed to congestive heart failure. Because ascites appeared

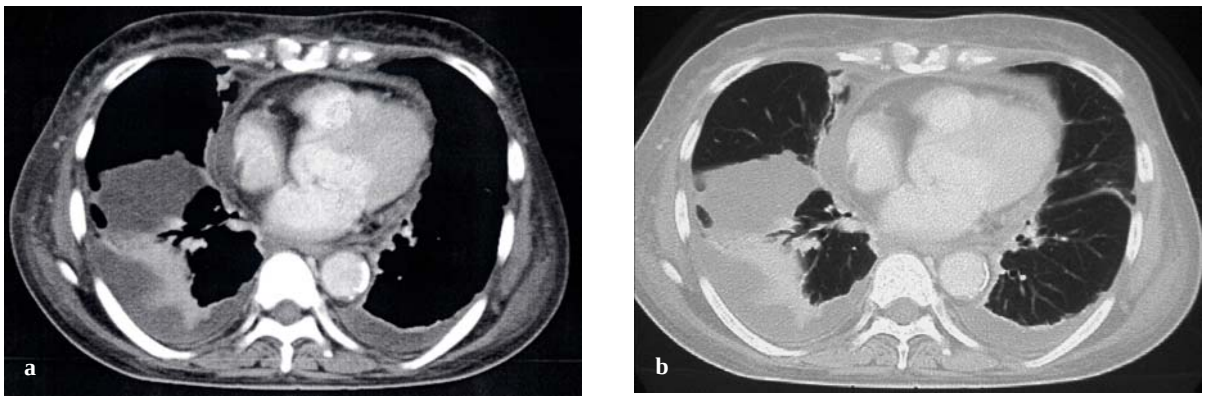

Fig. 1a) Enhanced chest computed tomography (CT) showed bilateral pleural effusions with atelectasis in the lower right lung field and pericardial effusion at the time of admission, b) Chest CT showed no interstitial opacity.

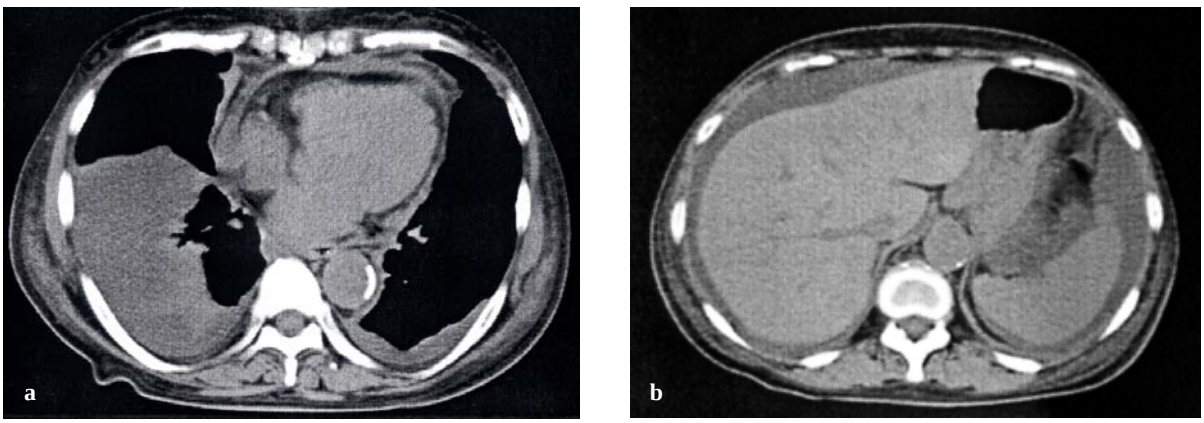

Fig. 2a) Chest CT showed the exacerbation of right pleural effusion 1 week after starting prednisolone (PSL) (30 mg/day) treatment, b) Abdominal CT showed ascites.

with serum Alb level decreasing from 2.1 g/dL to 1.4 g/dL and edema, ascites was thought to be due to severe hypoalbuminemia. Neither proteinuria nor the deterioration in liver function and renal function which might cause hypoalbuminemia, were present. In the end, severe hypoalbuminemia was attributed to hyperinflammation. So she was treated with methylprednisolone (mPSL) at 500 mg for 3 days with Alb (50 g/day) and furosemide (20 mg/day) infusion for 7 days and subsequently PSL at 50 mg/day for 2 weeks. About 2 weeks after starting this treatment, negative results were obtained for CRP. And marked decreases in pleural effusion and pericardial effusion, and gradual decrease in ascites were observed. The PSL dose was gradually reduced from 50 mg/day to 20 mg/day over 2 months. Effusion was almost completely resolved by about 4 months after starting methyl-prednisolone (500 mg/day) and subsequently PSL treatment.

3. Discussion

Based on xerophthalmia, xerostomia, positive results for the Shirmer test and anti-SS-A antibody, and abnormal salivary gland sialography, SS was diagnosed, according to the criteria of the American-European Consensus Group (4). Systemic lupus erythematousus (SLE) and rheumatoid arthritis (RA) could have caused serositis. However, because skin eruptions such as erythema, arthritis, renal dysfunction, neurological symptoms, and immunological abnormalities such as positive results for anti-DNA, anti-Sm and anti-CL antibodies were not found, we could not diagnose SLE. Similarly, we could not diagnose RA because she had no clinical signs of RA such as morning stiffness, arthralgia and articular swellings. Finally, SS turned out to be pSS.

In the 522 pSS Chinese patients with CT, 221 cases (42.3%) developed pulmonary disease. Among a total of 221 cases, 30 patients (5.7%) were identified with pleural effusion (2). Papathanasiou et al. (5) reported that pleural effusion was observed in none of the cases with pSS and 2 of 26 cases of secondary SS. Pleural effusion associated with SS is rare. Only 8 reports of pSS with pleural effusion have been reported. In the present case, pleural effusion was exudative without infection and malignancy, and so attributed to autoimmunological inflammation associated with pSS.

In the 352 Chinese pSS patients, pericardial effusion was detected in 52 patients (14.8%) with ultrasonic echocardiography (2). Rajani et al. (6) reported the case of a 50-year-old woman with pSS who presented with severe PH and pericardial effusion. Vassiliou et al. (7) reported pSS patients with pericardial effusion associated with PBC. In the present case, we could not diagnose PH, because chest CT revealed pulmonary arteries of normal caliber. Similarly, we could not diagnose PBC, because liver function, IgM and anti-mitochondrial antibody levels were all normal. So, pericardial effusion was not associated with PH or PBC. In addition, when ascites appeared, pericardial effusion remained unchanged. So, pericardial effusion was thought not to be due to severe hypoalbuminemia, but to be due to pericardial inflammation, namely pericarditis.

There have been only two reports of pSS with pleural effusion accompanied by pericardial effusion (8, 9), so the present report was thought to be a very rare case.

No previous reports have described pSS with peritonitis due to autoimmunological inflammation. In the present case, ascites was transudative, and so was not thought to be due to peritonitis. Ascites can occur in SS when combined with PBC (3). However, PBC could not be diagnosed because of the reasons above, so ascites was thought to be due to severe hypoalbuminemia resulting from hyperinflammation.

The immunopathology of pleuritis and pericarditis found in autoimmune diseases remains unclear. Suzuki et al. (9) speculated that IC deposition occurs in the pleura and pericardium, resulting in an inflammatory response and effusion in pSS. In patients with SS, activated polyclonal B lymphocytes and autoantibodies, such as anti-SS-A antibody and anti-SS-B antibody are considered to cause systemic tissue damages, leading to pleuritis (10). In the present case, because IC was not detected in either pleural effusion or serum, but lymphocytes were present, mechanisms other than IC deposition, namely mechanisms associated with lymphocytes might cause effusion.

Corticosteroid therapy, namely PSL at a dose of 30 or 40 mg/day is a common treatment for pleuritis associated with SS, and good response is expected (11). However, in the present case, because PSL at 30 mg/day for 1 week was not entirely effective, the patient was successfully treated with mPSL at 500 mg/day for 3 days and subsequently 50 mg/day for 2 weeks. High-dose corticosteroid was thought to be needed because of the pleuritis accompanied by pericarditis. Suzuki et al. (9) also reported the case of a 53-year-old woman with pSS associated pleuritis and

pericarditis treating with high-dose corticosteroid and cyclophosphamide.

No evidence of recurrence has been seen in our patient, who has remained on treatment with PSL at 3 mg/day, but careful follow-up is warranted.

In conclusion, pleural or pericardial effusions associated with pSS are rare. But physicians should take notice that pSS may cause pleural effusion and pericardial effusion.

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