Two Cases of Sjögren’s Syndrome with Multiple Bullae

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Abstract

Here, we report two rare female cases of Sjögren’s syndrome with multiple bullae, involving a 66- and a 51-year-old. Neither had any obvious pulmonary complaint. Chest radiographs and high-resolution CT (HRCT) scans showed interstitial linear and nodular opacities and multiple bullae. In the first case spirometry indicated an obstructive change judged by FEV1.0 and V50/V25. In both cases, histologic examination of the lung revealed thickening of alveolar septa and interstitial mononuclear cell infiltration. In the first case the bullae decreased in size with corticosteroid treatment. Airway narrowing due to peribronchiolar mononuclear cell infiltration causes a check-valve mechanism, which may lead to bullae formation. Although a rare occurrence, it is important to recognize that cystic or bullous lung disease can accompany Sjögren’s syndrome.

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Key words: cystic lung disease, lymphocyte infiltration, check-valve mechanism

Introduction

Sjögren’s syndrome is a chronic autoimmune exocrinopathy characterized by lymphocytic infiltration of glandular and extraglandular organs (1). The diagnostic criteria for Sjögren’s syndrome includes keratoconjunctivitis sicca and xerostomia. In addition, different types of pulmonary manifestations have been described in Sjögren’s syndrome, including interstitial lung disease, desiccation of the tracheobronchial tree, follicular lymphocytic bronchitis and bronchiolitis, and diffuse or focal nodular infiltrates (pseudolymphoma, malignant lymphoma, amyloidosis) (2). This case report describes two cases of Sjögren’s syndrome with multiple bullae, which is a very rare occurrence, and reviews the literature describing other relevant cases.

Case Report

Case 1

A 66-year-old woman who had Sjögren’s syndrome was admitted to our hospital in October 1997 because of morning stiffness and worsening of interstitial opacities on a chest radiograph. She complained of dry eyes and dry mouth ten years previously, and keratoconjunctivitis sicca and xerostomia were confirmed by the Schirmer test (right; 9 mm, left; 10 mm) and a positive reaction to the Rose-Bengal test, and a sialography showing apple-tree pattern, respectively. She had no obvious pulmonary symptoms. Laboratory data on admission were as follows: ESR, 59 mm/h; CRP, 0.11 mg/dl; WBC, 2,800/mm3, (Neu 63%, Lym 27%, Mono 7%, Eos 2%, Baso 1%); TP, 8.1 g/dl; γ-globulin, 26.1%; IgG, 3,080 mg/dl; IgA, 343 mg/dl; IgM, 161 mg/dl; RF, 242 IU/ml; antinuclear antibody, 135; anti SS-A/Ro, >256; anti SS-B/La, 1. As analyzed by enzyme-linked immunosorbent assay (ELISA), the normal ranges of antinuclear antibody, anti SS-A/Ro and anti SS-B/La were <12.0, <7.0, and <10.0, respectively. Arterial blood gas analysis revealed a PaO2 of 76.2 mmHg, PaCO2 of 41.6 mmHg, and pH of 7.41. Pulmonary function tests showed obstructive ventilatory dysfunction (VC, 2.05 l; %VC 94.0%; FEV1.0, 1.36 l; FEV1.0 %, 67.3%; V50/V25, 4.68; %DLco, 114.3%). The total cell number in bronchoalveolar lavage fluids (BALF) was 6.3x104/ml and the percentage of lymphocytes was significantly increased (lymphocytes 34%). The CD4/CD8 ratio was 2.15. A chest radiograph showed linear and small nodular shadows, and high-resolution CT (HRCT) scans showed peribronchovascular nodules and multiple bullae (Fig. 1A, B). These abnormal shadows were increased compared with radiographs taken five years ago. Histologic examination of the lung revealed thickening of alveolar septa and interstitial mononuclear cell infiltration (Fig. 2). Administration of prednisolone (40 mg/day) did not improve Sjögren’s syndrome, however, resulted in a decrease in peribronchovascular nodules and bullae (Fig. 1C), and the FEV1.0 and V50/V25 improved from 1.36 l to 1.75 l and 4.68 to 3.97, respectively (Fig. 1D–E).

Case 2

A 51 year-old woman with Sjögren’s syndrome was admitted to our hospital in July 1998 because of observation of mul-
Sjögren’s Syndrome with Multiple Bullae

Figure 1. (A) A chest radiograph showing linear and small nodular shadows, and (B) HRCT scans showing peribronchovascular nodules and multiple bullae. (C) Administration of prednisolone decreased peribronchovascular nodules and bullae, and (D–E) the FEV₁₀ and V₅₀/V₂₅ improved from 1.36 l to 1.75 l and 4.68 to 3.97, respectively. (D, before treatment; E, after treatment)
Sjögren’s syndrome has been characterized as an autoimmune exocrinopathy and more recently as an autoimmune epithelitis (1, 3). The syndrome pathologically accompanies lymphoproliferation and lymphocytic infiltration of glandular and extraglandular tissues. In most patients, lymphocyte infiltration is confined to the salivary and lacrimal glands; however, extraglandular infiltration of the lungs, pancreas, gastrointestinal tract, hepatobiliary system, kidneys, skin, and bone marrow has been identified in 5 to 10% of affected patients (4).

Several pulmonary complications have been described in patients with Sjögren’s syndrome, including interstitial lung disease, airway disease, and diffuse or focal nodular infiltrates (2). In this report, we present cases of Sjögren’s syndrome with multiple bullae. Among various kinds of pulmonary manifestations with Sjögren’s syndrome, cystic or bullous lung disease is very rarely associated with the syndrome. From a review of the literature, 8 cases (5–12) were found; these cases together with the two cases presented here are shown in Table 1. All patients were middle-aged females, and pathological findings of the lung included one case of lymphocytic interstitial pneumonia (LIP) (11) and the remainder consisting of peribronchiolar and/or interstitial lymphoplasmacytic infiltrates in association with cystic changes (5–10, 12). In both cases, bullae formation was thought to be due to a check-valve mechanism caused by lymphoplasmacytic infiltrates of the bronchial wall. In addition, four cases other than the present two cases were accompanied by nodular amyloidosis (5, 6, 8, 12).

Pulmonary function tests have shown that lung involvement in primary Sjögren’s syndrome is particularly related to the small airways (13, 14). In addition, Sjögren’s syndrome is accompanied by lymphocyte infiltration (particularly CD4-positive T lymphocytes) of the bronchial mucosa (15). Furthermore, air trapping on expiratory HRCT has been shown in primary Sjögren’s syndrome (16). These findings suggest that lymphocyte infiltration of the small airways in Sjögren’s syndrome causes air trapping on expiration.

Interestingly, Ichikawa et al reported multiple pulmonary cyst formation in two patients with LIP (17). In those cases, the chest CT showed nodular and cystic lesions around the bronchovascular bundles and areas of increased attenuation. Pathologically, lung biopsy specimens revealed stenosis and/or obstruction of several bronchioles by peribronchiolar lymphocyte infiltration. Taken together with that report, bullae formation of Sjögren’s syndrome appears to be caused by air trapping and/or a check-valve mechanism by peribronchiolar lymphoplasmacytic infiltrates.

Cystic abnormalities of the lung include pulmonary histiocytosis X, lymphangioleiomyomatosis, different types of emphysema, and airway diseases, such as bronchiectasis and bronchiolitis obliterans. In addition, honeycomb cysts in idiopathic pulmonary fibrosis and thin- or thick-walled cysts in Pneumocystis carinii pneumonia are also included in cystic lung diseases. Therefore, one should distinguish the cystic lesions accompanying Sjögren’s syndrome from other cystic lung diseases and evaluate them together with clinical symptoms, laboratory data and representative features on the HRCT.

The prognosis of Sjögren’s syndrome with multiple bullae,
Figure 3. (A) A chest radiograph showing reticulo-nodular shadows, and (B) HRCT scans showing multiple bullae.

Figure 4. A trans-bronchial lung biopsy specimen showing thickening of alveolar septa and interstitial mononuclear cell infiltration (HE stain, ×100).

In the 8 cases found in the literature and the two described here, was as follows: three improved with corticosteroid treatment, two showed no significant change with corticosteroid treatment, one showed no change without therapy, one deteriorated despite corticosteroid treatment, one deteriorated despite immunosuppressant therapy, one deteriorated without therapy, and the outcome of one case is unknown. Thus, since the prognosis of this disease varies, clinicians should carefully...
Table 1. Reported Cases of Sjögren’s Syndrome with Multiple Bullae

<table>
<thead>
<tr>
<th>Reporter</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Lung biopsy</th>
<th>Pathological findings</th>
<th>Complications</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonner (5)</td>
<td>1973</td>
<td>59</td>
<td>F</td>
<td>OLB</td>
<td>lymphocyte infiltration around the bronchioles</td>
<td>nodular amyloidosis</td>
<td>improved with CS</td>
</tr>
<tr>
<td>Kobayashi (6)</td>
<td>1988</td>
<td>53</td>
<td>F</td>
<td>OLB</td>
<td>lymphocyte and plasma cell infiltration of the bronchial wall</td>
<td>nodular amyloidosis</td>
<td>NC with CS</td>
</tr>
<tr>
<td>Inase (7)</td>
<td>1990</td>
<td>52</td>
<td>F</td>
<td>TBLB</td>
<td>lymphocyte infiltration around the bronchial gland</td>
<td></td>
<td>deteriorated</td>
</tr>
<tr>
<td>Schlegel (8)</td>
<td>1992</td>
<td>66</td>
<td>F</td>
<td>TTNB</td>
<td>lymphocyte and plasma cell infiltration</td>
<td>nodular amyloidosis</td>
<td>unknown</td>
</tr>
<tr>
<td>Hachiya (9)</td>
<td>1996</td>
<td>58</td>
<td>F</td>
<td>OLB</td>
<td>cellular interstitial pneumonia with lymphoid follicles</td>
<td></td>
<td>improved with CS</td>
</tr>
<tr>
<td>Meyer (10)</td>
<td>1997</td>
<td>42</td>
<td>F</td>
<td>OLB</td>
<td>interstitial and peribronchiolar lymphoplasmacyte infiltration and lymphoid follicles</td>
<td></td>
<td>deteriorated despite IS</td>
</tr>
<tr>
<td>Hayasaka (11)</td>
<td>1999</td>
<td>64</td>
<td>F</td>
<td>TLB</td>
<td>lymphocytic interstitial pneumonia</td>
<td></td>
<td>NC</td>
</tr>
<tr>
<td>Teruuchi (12)</td>
<td>2000</td>
<td>62</td>
<td>F</td>
<td>OLB</td>
<td>peribronchiolar lymphoplasmacyte infiltration</td>
<td>nodular amyloidosis</td>
<td>deteriorated despite CS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66</td>
<td>F</td>
<td>OLB</td>
<td>interstitial mononuclear cell infiltration</td>
<td></td>
<td>improved with CS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51</td>
<td>F</td>
<td>TBLB</td>
<td>interstitial mononuclear cell infiltration</td>
<td></td>
<td>NC</td>
</tr>
</tbody>
</table>


pursue the clinical course of each case and initiate appropriate therapeutic intervention.

References