Polymyositis and Sjögren’s Syndrome Associated with Bronchiolitis Obliterans Organizing Pneumonia

Takao Imasaki, Akio Yoshii, Sumiaki Tanaka*, Tateo Ogura*, Akira Ishikawa and Tadao Takahashi

Bronchiolitis obliterans organizing pneumonia (BOOP) occurred in a 53-year-old woman with well-documented Sjögren’s syndrome (SjS) and polymyositis (PM). BOOP has often been reported as a pulmonary manifestation of collagen vascular diseases, mainly rheumatoid arthritis (RA), but the association of BOOP and PM has rarely been documented. A search of the literature showed only 16 case reports of BOOP associated with polymyositis-dermatomyositis (PM-DM). It is interesting that BOOP occurred prior to PM-DM, while it is commonly believed to occur after RA. (Internal Medicine 35: 231-235, 1996)

Key words: interstitial lung disease, polymyositis-dermatomyositis (PM-DM), rheumatoid arthritis (RA)

Introduction

Bronchiolitis obliterans organizing pneumonia (BOOP) was first described as an independent disease entity by Epler et al in 1985 (1). Since then, it has been reported by many authors and is believed to be either idiopathic or associated with various factors such as collagen diseases, infections and inhalation of poisonous gas. Among patients with collagen diseases, it most often occurs as a pulmonary manifestation of rheumatoid arthritis (RA) (2–9), and only a few cases of BOOP associated with polymyositis (PM) or Sjögren’s syndrome (SjS) have been reported. Here, we describe a case of BOOP associated with PM and SjS with reference to the literature.

Case Report

A 53-year-old woman visited us on September 6, 1993 complaining of fever and dyspnea. There was nothing in particular in her past or family history. Although the presence of goiter was pointed out at about the age of 30, she was told that her thyroid function was normal. Dry eyes occurred around June 1993, followed by fever (37–38°C) and malaise in late August. She visited a nearby doctor after coughing and expectoration occurred in September. No improvement was seen despite medication. She visited us on September 6, because dyspnea occurred as well. She was admitted on September 10 when chest X-rays showed interstitial shadows in the left and right lower lung fields.

Upon admission, her body temperature was 37.6°C, and fine crackles were heard in the left and right lower lung fields. The thyroid was slightly swollen and soft. No tenderness was noted. The cervical flexor muscles showed slight weakness. Peripheral white blood cell count (WBC) was 8,860/mm³ and neutrophils 82% in laboratory tests conducted upon admission. Biochemical data showed: aspartate aminotransferase (AST), 71 IU/l; alanine aminotransferase (ALT), 55 IU/l; lactate dehydrogenase (LDH), 899 IU/l; creatine kinase (CK), 787 IU/l; aldolase, 22.4 IU/l; myoglobin, ≥500 ng/ml; C-reactive protein (CRP), 4.4 mg/dl; the erythrocyte sedimentation rate (ESR), 73 mm/h; C₃, 78 mg/dl; C₄, 34 mg/dl; CH50, 36.5 U/ml; IgG, 2,154 mg/dl; IgA, 227 mg/dl; IgM, 419 mg/dl; rheumatoid factor (RF), 12 U/ml; thyroid stimulating hormone (TSH), 11 U/ml; free thyroxine (FT₃), 2.4 pg/ml; and free triiodothyronine (FT₄), 0.74 ng/dl. Mycoplasma, antinuclear, anti-DNA, anti-RNP, anti-Sm, anti-SS-A, anti-SS-B, and anti-Jo-1 antibodies were negative. The thyroid test was negative but the microsome test was 1,600. Arterial blood gas analysis showed pH 7.471, PaCO₂ 30.7 mmHg, PaO₂ 55.8 mmHg, and HCO₃ 22.1 mmol/l. Results of respiratory function tests were %VC 76.5%, %FEV₁ 84.7%, DLCO/CO 4.62 ml/min/mmHg, and %DLco 64.6%. Electrolymographic examinations revealed generalized myopathic changes, especially in the proximal muscles. Motor unit potentials were brief in duration and reduced in amplitude, and there was no spontaneous activity such as fibrillation potential.

From the Department of Internal Medicine, Isehara Kyodo Hospital, Isehara and *the Department of Internal Medicine, Kitasato University, School of Medicine, Sagamihara

Received for publication December 26, 1994; Accepted for publication October 23, 1995

Reprint requests should be addressed to Dr. Takao Imasaki, the Department of Internal Medicine, Kitasato University School of Medicine, 1-15-1 Kitasato, Sagamihara, Kanagawa, 228

Internal Medicine Vol. 35, No. 3 (March 1996)
or positive sharp wave. Chest X-rays taken upon admission showed interstitial shadows in the left and right lower lung fields (Fig. 1), while chest computed tomography (CT) revealed light infiltration shadows with relatively well-defined margins and infiltration shadows with elevated areas of markedly high absorption associated with air bronchograms on the margins, mainly in the left and right lower lung fields (Fig. 2). Transbronchial lung biopsy was conducted through the left

**Figure 1.** Chest X-ray taken at admission shows interstitial shadows in lower fields of both lungs.

**Figure 2.** Chest CT obtained at admission shows strong dorsal alveolar filling centered in S10 of lower fields of both lungs.

**Figure 3.** Histological preparation of TBLB. Polyp-shaped fibrotic changes are seen protruding in the alveolar spaces, and there is also a complication of organizing pneumonia with inflammatory cells and foam cells (HE stain, ×66).

**Figure 4.** Histological preparation of muscle biopsy. Focal inflammatory cell infiltration of the tissues is seen (HE stain, ×100).

B10b and B8b in order to diagnose lung lesions. The diagnosis of BOOP was established based on pathological and roentgenological findings (Fig. 3). In addition, biopsy samples were taken from the musculus biceps brachii in order to examine muscular lesions (Fig. 4). The result of the Schirmer test, conducted to closely evaluate eye dryness, was positive. Sialography revealed slight ductular dilatation. Subsequent labial biopsy revealed lymphocyte infiltration in the salivary glands.

We established the diagnosis of PM and SjS associated with BOOP based on these findings and initiated treatment with 60 mg/day of prednisolone. Subjective symptoms, chest X-rays and laboratory findings improved in about 2 months (Fig. 5). Although Hashimoto’s disease was suspected due to goiter, the increases in TSH and the positive result of the microsome test, thyroid biopsy was not conducted.
PM, SjS, with BOOP

<table>
<thead>
<tr>
<th>1993</th>
<th>1994</th>
</tr>
</thead>
<tbody>
<tr>
<td>muscle weakness</td>
<td>cough</td>
</tr>
<tr>
<td>CK(IU/l)</td>
<td>787</td>
</tr>
<tr>
<td>LDH(IU/l)</td>
<td>899</td>
</tr>
<tr>
<td>PaO2 (torr)</td>
<td>55.8</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Figure 5. Clinical course of the patient after hospitalization. CK: creatine kinase, LDH: lactic dehydrogenase, CRP: C-reactive protein.

Discussion

A diagnosis of BOOP associated with PM and SjS was made in the present patient based on symptoms such as fever, cough, expectoration and dyspnea, and the presence of interstitial shadows on chest X-rays and interstitial shadows and air bronchograms on chest CT. According to Yamamoto et al (10), chest X-ray findings from patients with BOOP can be classified into three categories: type 1, bilateral, multiple, macular shadows which migrate with time; type 2, fine granular shadows in the base of the left and right lungs; and other unclassifiable types. According to Nishimura et al (11), major chest CT characteristics of BOOP include the presence of the following: 1) areas of markedly increased lung field density which show laminar distribution or form nodular lesions; and 2) extensive areas of slightly increased lung field density. [In the case of the former, internal blood vessel shadows cannot be traced and the bronchi form air bronchograms in central adjacent areas.] Chest X-rays obtained from the present patient were classified as type 2 as proposed by Yamamoto et al (10) and were consistent with CT findings reported by Nishimura et al (11).

Pathological findings of BOOP include the trias of obliterative bronchiolitis, organizing pneumonia, and alveolitis. According to Epler et al (1), open-chest lung biopsy is essential to establish the diagnosis of BOOP, because transbronchial lung biopsy (TBLB) can provide evidence of alveolitis and organized pneumonia but not of bronchiolitis obliterans. However, Barter et al (12) reported that the diagnosis of BOOP could be clinically made based on TBLB findings alone. We made the diagnosis of BOOP using TBLB alone, but were able to obtain evidence of both organized pneumonia (presence of inflammatory cells and foam cells in alveoli) and alveolitis. Polyp-like fibrosis protruding into alveoli, evidence of bronchiolitis obliterans, was also observed. We made the diagnosis of BOOP since all these pathological findings are consistent with this disease.

BOOP is associated with various diseases, especially collagen disease. We therefore retrieved reports of BOOP associated with PM-DM from the literature (Table 1). Our search revealed a total of 16 cases of BOOP associated with PM or DM, 4 in Japan and 12 in other countries, reported since Schwarz reported 3 cases of PM-DM associated with organizing pneumonia in 1976 (13–20). Of these 16 patients, mostly females, 9 had PM and 7 DM. The age at which the disease occurred varied considerably, although it was between 40 and 50 years in most patients.

BOOP occurred prior to PM-DM in 10 of the 16 reported cases. It is difficult to determine when PM occurred in the
Table 1. Reported Cases of PM-DM Complicated by BOOP

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Disease</th>
<th>Time to BOOP Dx*</th>
<th>Treatment</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schwarz et al 1976</td>
<td>37</td>
<td>M</td>
<td>DM</td>
<td>-3M</td>
<td>PSL 60mg</td>
<td>A 6 yr</td>
</tr>
<tr>
<td></td>
<td>61</td>
<td>F</td>
<td>PM</td>
<td>-24M</td>
<td>PSL 60mg</td>
<td>D 4 yr</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>M</td>
<td>PM</td>
<td>-3M</td>
<td>PSL 40mg</td>
<td>D 1.5 yr</td>
</tr>
<tr>
<td>Imokawa et al 1992</td>
<td>58</td>
<td>F</td>
<td>PM</td>
<td>-5M</td>
<td>PSL 60mg</td>
<td>A</td>
</tr>
<tr>
<td>Mouri et al 1993</td>
<td>60</td>
<td>F</td>
<td>DM</td>
<td>-2M</td>
<td>steroid, pulus→ PSL 60mg+CY</td>
<td>A</td>
</tr>
<tr>
<td>Hsue et al 1993</td>
<td>36</td>
<td>F</td>
<td>PM</td>
<td>-10M</td>
<td>PSL 60mg+AZA</td>
<td>A 14 yr</td>
</tr>
<tr>
<td>Iwata et al 1991</td>
<td>57</td>
<td>F</td>
<td>PM</td>
<td>-3M</td>
<td>PSL 30mg</td>
<td>A</td>
</tr>
<tr>
<td>Schiavi et al 1984</td>
<td>42</td>
<td>F</td>
<td>DM</td>
<td>3M</td>
<td>PSL 60mg</td>
<td>A</td>
</tr>
<tr>
<td>Mahler 1992</td>
<td>24</td>
<td>F</td>
<td>DM</td>
<td>-4M</td>
<td>PSL 1mg/kg</td>
<td>A 1 yr</td>
</tr>
<tr>
<td>Tazelaar et al 1990</td>
<td>65</td>
<td>F</td>
<td>PM</td>
<td>0</td>
<td>PSL 60mg</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>47</td>
<td>F</td>
<td>PM</td>
<td>0</td>
<td>steroid</td>
<td>A 7 yr</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>F</td>
<td>DM</td>
<td>-1M</td>
<td>steroid</td>
<td>A 2 yr</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>M</td>
<td>PM</td>
<td>0</td>
<td>steroid</td>
<td>A 18 yr</td>
</tr>
<tr>
<td></td>
<td>32</td>
<td>F</td>
<td>DM</td>
<td>2M</td>
<td>steroid, MTX</td>
<td>D 4 weeks</td>
</tr>
<tr>
<td></td>
<td>73</td>
<td>M</td>
<td>PM</td>
<td>-6M</td>
<td>PSL</td>
<td>A 14M</td>
</tr>
</tbody>
</table>


The present patient, because she had few subjective symptoms of PM and had received no specific test before visiting us. Since myogenic enzyme levels were already elevated upon her initial visit, however, we thought that BOOP occurred at the same time as or after PM.

Four of the 16 reported cases died, 2 due to PM and another 2 due to DM. BOOP occurred first in 3 and later in the others. The general causes of death were reported to be adult respiratory distress syndrome (20), respiratory failure (13), air leak (20), and progression of pulmonary and muscle disease (13). As mentioned above, BOOP usually occurs before PM-DM. Therefore, patients need to be closely monitored for possible onset of PM-DM once the diagnosis of idiopathic BOOP is made.

The prognosis of idiopathic BOOP is generally believed to be good, so we evaluated the prognosis of BOOP associated with PM-DM in the literature. In 1990, Tazelaar et al (20) histologically examined lesions of interstitial pneumonia associated with PM-DM. Reporting death in 2 of 6 patients with BOOP, they mentioned that the prognosis of BOOP was generally good and histological examinations of pulmonary lesions were useful in predicting the prognosis of PM-DM. Our literature search, which revealed death in 4 of the 16 patients, is consistent with the report of Tazelaar et al. Other types of interstitial pneumonia associated with PM-DM include usual interstitial pneumonia (UIP) and diffuse alveolar damage (DAD). According to Tazelaar et al, mortality due to UIP and DAD was 3/5 and 3/3 patients. Therefore, the prognosis of BOOP associated with PM-DM seems better than that of other pulmonary diseases associated with PM-DM.

We also investigated the literature with respect to BOOP associated with other types of collagen disease. Yousem et al (8) conducted open-chest lung biopsy in 40 RA patients and found that 6 had BOOP as the primary lesion. This finding suggests that the incidence of BOOP is fairly high among RA patients. We then compared BOOP associated with RA to BOOP associated with PM-DM observed in our patient. As discussed by Ippolito et al (9), there is no report on the timing of onset of BOOP associated with RA in Western countries. According to the literature from Japan we found (2-7), BOOP occurred before RA in only 3 of 15 patients. This sequence of onset contrasts with that observed with respect to BOOP associated with PM-DM.

The present patient also had SjS, but our literature search showed that the combination of primary SjS and BOOP is very rare and that it has been reported in only 1 patient in Japan (21) and in 1 in another country (22).

There has been no extensive study on BOOP as a pulmonary disease associated with collagen disease, and our knowledge of it is very limited. Further studies are therefore warranted on BOOP associated with PM-DM, RA and other types of collagen disease.
PM, SjS, with BOOP
diseases.

References