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<tr>
<td>Citation</td>
<td>Acta medica Nagasakiensia. 1993, 38(2-4), p.45-48</td>
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<tr>
<td>Issue Date</td>
<td>1993-12-25</td>
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<td>URL</td>
<td><a href="http://hdl.handle.net/10069/15905">http://hdl.handle.net/10069/15905</a></td>
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Bronchiolitis Obliterans Organizing Pneumonia: Case Report and Review of Literature

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A 69-year-old female complaining of fever, cough and dyspnea was admitted to our hospital. Chest X-ray examination showed bilateral infiltration shadows that increased in spite of antibiotics therapy. Broncho-alveolar lavage fluid analysis demonstrated an increased lymphocytes with an inverted CD4/CD8 ratio. Histopathology of lung biopsy specimens showed organizing granulation tissue in the lumens of bronchioles, alveolar ducts, and alveoli, along with mononuclear cell infiltration in the interstitium. A diagnosis of bronchiolitis obliterans organizing pneumonia (BOOP) was thus made. The patient completely recovered by corticosteroid therapy, and is now without any indication of disease.

Introduction

In 1983, Epler and Colby proposed the following clinical classification for bronchiolitis obliterans: toxic-fume bronchiolitis obliterans, postinfectious bronchiolitis obliterans, bronchiolitis obliterans associated with connective tissue disease, localized lesion with bronchiolitis obliterans, and idiopathic bronchiolitis obliterans with organizing pneumonia (BOOP). In 1985, they stressed the importance of the diagnostic distinction of idiopathic BOOP from idiopathic pulmonary fibrosis (IPF) or usual interstitial pneumonia (UIP), in consideration of the favorable prognosis and response to corticosteroid therapy. This paper presents a case of idiopathic BOOP diagnosed by transbronchial lung biopsy and open lung biopsy.

Case Report

A 69-year-old female was admitted to a hospital on May 10, 1991 for complaints of fever, cough and dyspnea. Chest X-ray film (Fig. 1) indicated infiltration shadows in the right lung, which were considered bronchopneumonia. She was treated with several different antibiotics, but without satisfactory effect. Chest X-ray examination showed enlargement of the shadows, and other infiltration in the left lung. She was subsequently transferred to our hospital on May 28, 1991 for further evaluation and treatment. On admission, peripheral blood examination disclosed WBC 11,500/mm³ with neutrophils 72%, lymphocytes 15%, eosinophils 7%, RBC 3.44 × 10⁶/mm³ and erythrocyte sedimentation rate (ESR) 106mm/h. Serum total protein was 5.9g/dl, albumin 2.7g/dl, LDH 438IU/l, CRP 10.57mg/dl, and RA (2+). Arterial blood gas analysis indicated PaO₂ 48mmHg, PaCO₂ 35mmHg, AaDO₂ 60mmHg. Though bacterial infection was suspected, no significant microbe could be found in the sputum or blood, and antibody titers in pair sera for Legionella pneumophilia, Mycoplasma pneumoniae, Clamydia psittaci, C. trachomatis failed to show significant elevation. Chest X-ray (Fig. 2) and CT (Fig. 3) showed homogeneous alveolar opacities with an air bronchogram in both lungs. Microscopic findings (Fig. 4) of the transbronchial lung biopsy specimen showed polyoid granulation tissue in alveolar lumens, and mononuclear cell infiltration in alveolar walls. Broncho-alveolar lavage fluid (BALF) analysis demonstrated increased total cells 21.2 × 10⁴/ml, with lymphocytes 71%, alveolar macrophages 23%, neutrophils 5%, and eosinophils 1.3%. The CD4/CD8 ratio was 0.5. Based on these data,
idiopathic BOOP was suspected as most probable and consequently open lung biopsy was performed. Histopathologic findings (Fig. 5) showed organizing granulation tissue involving bronchioles, alveolar ducts and alveoli with infiltration of mononuclear cells and foamy macrophages. Mononuclear cell infiltration was also observed in the walls of alveoli and bronchioles. Thus, the diagnosis of idiopathic BOOP was made. Pulse therapy with methylprednisolone followed by maintenance therapy with prednisolone resulted in dramatic response. Steroid therapy was continued for four months, and BALF reexamination showed normal total cell and lymphocyte number, with normal CD4/CD8 ratio. Marked improvement was noted by chest X-ray reexamination (Fig. 6). The patient recovered completely with no indication of disease.
Fig. 6. Chest X-ray film after steroid therapy showing marked improvement.

Discussion

Epler et al.6,7 proposed the clinicopathological entity of bronchiolitis obliterans organizing pneumonia (BOOP), though, this is not a new disease. Idiopathic BOOP is similar to bronchiolitis interstitial pneumonia (BIP),8 organizing pneumonia-like process,9 chronic organizing pneumonia (pneumonitis) of unknown cause,9 and cryptogenic organizing pneumonitis.10 This category is sometimes confused with idiopathic pulmonary fibrosis (IPF) or usual interstitial pneumonia (UIP).2,9,10 It is important to distinguish BOOP from IPF or UIP, since the former can be effectively treated with corticosteroid.

Clinical and radiologic findings vary, and thus pathologic conditions are considered as response to various types of injury to the lung, and not specific to only one disease. Cordier et al.11 distinguish three characteristic clinical and imaging profiles in patients with idiopathic BOOP: group 1 with multiple patchy migratory pulmonary involvement of the pneumonia type, group 2 with solitary pulmonary involvement of the pneumonia type, and group 3 with diffuse pulmonary involvement of the interstitial lung disease type. The clinical course of group 1 is subacute, with cough, fever, weight loss, mild dyspnea, and increased ESR; that of group 2 is similar to group 1. Chest X-rays show several patchy alveolar opacities with an air bronchogram, and these opacities are often migratory, or other patchy opacities appear during the course of the disease. Lung function tests show rather mild restrictive defects, but with no airflow obstruction. In group 3, there is a more progressive onset of more severe dyspnea, crackles, and interstitial opacities with or without alveolar opacities on chest imaging. In Japan, Yamamoto et al.12 also classified BOOP as wandering type, non-wandering type, and unclassified type.

It is sometimes difficult to differentiate chronic eosinophilic pneumonia from multiple patchy migratory pneumonia type BOOP, and IPF or UIP from diffuse pulmonary involvement of the interstitial lung disease type BOOP. The present case showed multiple patchy opacities on chest X-ray film, but not increased eosinophils in BALF or lung biopsy specimens. A diagnosis of BOOP group 1 was thus made according to Cordier et al.

Epler et al.7 emphasize that plugs of granulation tissue involving bronchioles and alveolar ducts (bronchiolitis obliterans) together with extension of organization from distal alveolar ducts into alveoli, with variable degrees of interstitial infiltration by mononuclear cells (organizing pneumonia) are distinct histological features. This is their reason for calling the disease bronchiolitis obliterans organizing pneumonia (BOOP). Cordier et al.13 mention that plugs were more conspicuous in alveolar than bronchiolar lumens and extended from one alveolus to another through the pores of Kohn, but intra-alveolar fibrosis did not disorganize structures of preexisting lung parenchyma, and interstitial inflammatory cell infiltration and interstitial fibrosis were present in all cases. In this study, interstitial pneumonia with organizing granulation tissue in the airspaces of alveolar ducts and alveoli were predominant findings. Granulation tissue was found in the lumens of membranous bronchioles, but in small amounts.

Physiologic studies show restriction with reduced vital capacity, as well as impaired gas exchange, and obstructive patterns are uncommon. Interstitial pneumonia is thus a more significant feature than bronchiolitis obliterans. Kitagawa12 suggests that BOOP is not an independent disease entity, and the nomenclature does not express this histopathologic category correctly. He considers this category to be allergic interstitial pneumonia that includes chronic eosinophilic pneumonia.

BALF analysis in the present case showed increased lymphocytes, and decreased CD4/CD8 ratio. These features should facilitate differentiating idiopathic BOOP from UIP.13 There also appears to be the possibility of an immunologic disorder in consideration of the dramatic response to corticosteroid therapy. An unidentified infectious agent or unusual immune pneumonitis may possibly be the most likely cause for this.

References


T. Tashiro et al.: Bronchiolitis Obliterans Organizing Pneumonia


