Two Cases of Bronchiolitis Obliterans with Organizing Pneumonia (BOOP)

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Abstract

Two cases diagnosed as Bronchiolitis Obliterans with Organizing Pneumonia (BOOP) by open lung biopsy are reported. The first was a 56-year-old man with cough, fever and hemoptesy for 7 months; while the second was a 60-year-old woman with cough, weakness and weight loss for 2 months which were not responding to the previous treatments. In P.A. chest roentgenograms, there were non-homogenic increases in density in bilateral middle bottom areas in both of the cases. While pneumonia treatment was given to the first case and tuberculosis treatment was given to the other, detailed investigations were done. And finally by open lung biopsy, both cases were diagnosed as BOOP and steroid treatment was given. The complaints of the second case relapsed, therefore the treatment was repeated. Two years after the treatment, a complete clinical-radiologic recovery was stabilized.

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Key words: *Bronchiolitis Obliterans with Organizing Pneumonia, Open Lung Biopsy*

Introduction

Bronchiolitis, as proliferative bronchiolitis and constrictive bronchiolitis, is the term used in describing many inflammatory small airway diseases. While organised connective tissue in bronchi lumen is dominant in proliferative type, scatricial appearance, where alveolar ducts are preserved and fibrosis and scar tissues are dominant, becomes very important (1).

Bronchiolitis obliterans with organizing pneumonia is the most frequent form of proliferative bronchiolitis. It was described in 1901 by Lange. It was called "BOOP" in 1985 by Epler and popularised cryptogenic organised pneumonia. Term was firstly used by Davidson in 1983. Now it is used as the BOOP forms in which the cause is unknown (2,3,4,5).

Case I

A 56-years-old man (SD. Protocol No: 138143). The patient has been coughing since 7 months, had fever, dyspnea,and hemoptysis. The patient was diagnosed as having bronchiolitis and antibiotherapy was given in the hospital. Several different antibiotics given by the patient's special physician were being used. He was sent to our hospital by VSD. He has been smoking three packets of cigarettes per day for 30 years.

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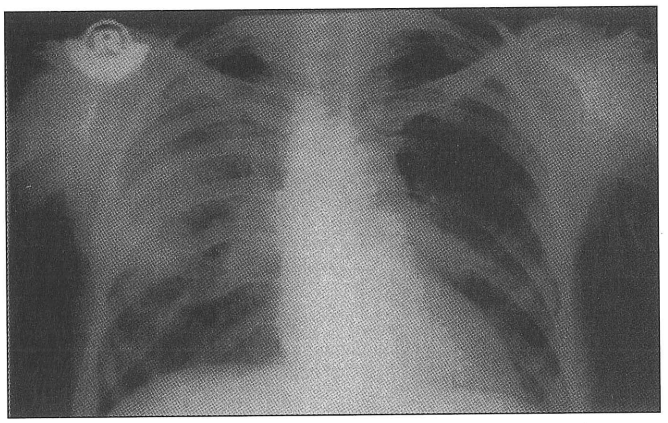

Fig. 1. Chest radiograph shows bilaterally infiltrations

When he was hospitalized in our hospital, dyspnea and cough and hemoptysis were continuing. He did not have fever. Physical examination revealed dullness in the lower area of the right lung by percussion and there was end inspiratory rhonchi in auscultation.

On PA Lung x-ray, there was increase in the density bilaterally the middle and lower area of the right lung especially in hilar region.

Sedimentation increased markedly (145 mm/hr) Leucocyte: 1350 Hct: 38%. Other findings were normal. Acid resistant basil (ARB) in sputum was negative (three times).

Respiratory Function Tests: VC: 4.10(96%), FVC: 2.23 (53%)

FEV_1: 2.10 (65%) FEV_1/FVC: 94%
Arterial Blood Gas: PO2 98%, PCO2: 36.5%, pH: 7,4 was measured.

Lung CT: In the lower lobe of superior and posterior base segment of the left lung, peri-bronchial thickening was seen. Massy lesion in solid density, which was beginning from upper lobe posterior segment and extending to posterior segment of lower lobe, with irregular frontiers and which in some places contained air bronchogram, was observed.

Fiberoptic bronchoscopy was done to the patient who was taking non-specific therapy. In superior segment mucous of right lung, hyperemia and stenotic area was found. Bronchial lavage and bronchi mucous biopsy was done from the inferior lobe of the superior segment. Biopsy showed that there was chronic bronchiolitis in bronchi mucous. There were many polimorph leucocytes, hiystocytes and other inflammatory elements and fibrin in bronchial lavage. ARB was searched in lavage and found negative.

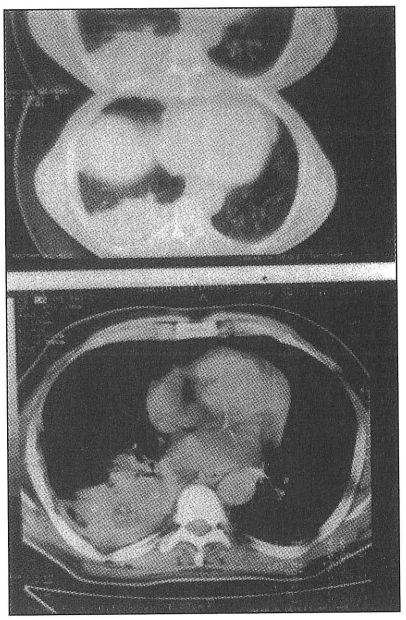

Fig. 2. Chest CT on the left lower lobe massy lesion and air bronchogram

Transthorasic fine needle aspiration biopsy was made. Alveolar histyocytes were seen in the blood cells.

The patient had still hemoptysis. Thoracic surgery was decided to be performed with open lung biopsy in order to reach a diagnosis.

The pathologic report showed that alveoli walls were structured generally as fibrosis and there were fibrinous nectonic and organised plaque in the lumen. In some alveoli, epithelial proliferations were found. There were hystiocytes and erythrocytes in alveoli lumen. There was no malignancy. Diagnosis was bronchiolitis obliterans with organizing pneumonia.

The patient did not want to take the therapy and was discharged. However, after 4 months, cough and hemoptysis started again and drug therapy was given to the patient. Transamin, codein, amoxicilin, amino glicosid therapy stabilised the patient. Then 64 mg/day (1mg/kg) prednol therapy was given for a month. Many symptoms of the patient decreased. PA Chest roentgenograms became normal. Prednol dosage was decreased 10 mg each month and the therapy continued for 6 months. In the control x-ray, lesions were completely resolved.

Case II

A 60-year-old woman (Protocol No: 142013). The patient had cough, fatigue, weight loss (5 kg/2months) Various therapies was given to her with the diagnosis of bronchiolitis. She had not smoked cigarettes. Antituberculosis therapy was given to her twenty years ago.

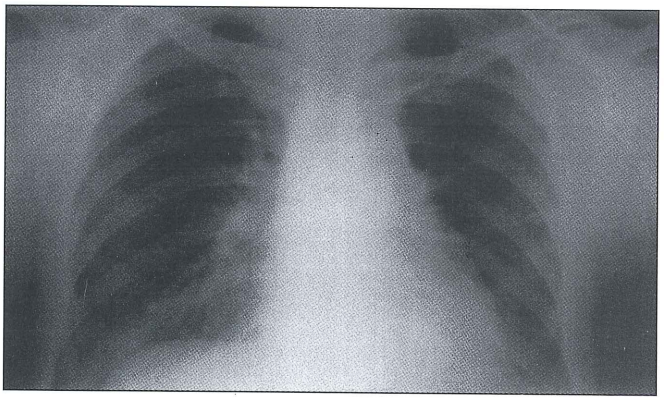

Fig. 3. Control Chest radiograph after steroid treatment: lesions are comletely cured

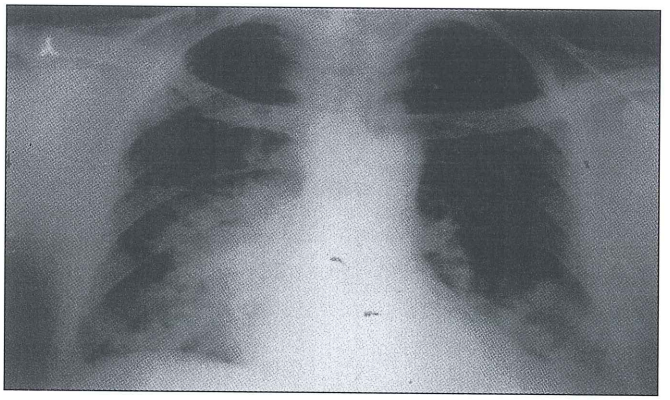

Fig. 4. P.A.Chest X-ray on admission. Infiltration on the right upper and middle zone, and enlargement of right hilar density

In auscultation, there were end inspiratory rhonchi. On PA chest x-rays, superior and middle part of the right lung density increased and an enlargement of the right hilar region was seen.

Sedimentation 132 mm/Hr; Leucocyte: 6800 mm^3; Htc: 36,5%; FVC: 1,53 (49%)

FEV_1:1,22(46.7%) FEV_1/FVC:79.7%
Macrolide antibiotic was given to the patient. On the computer tomography there were retractile linear consolidation in the left fissure and interstitial type pneumonic consolidation area in the left lower lobe of superior segment.

Fiberoptic bronchoscopy was peformed. All of the lobes and segments were open, the mucous on the right side was pale and secretion was coming from the middle lobe of the right lung and bronchoalveolar lavage were taken from this area. In BAL, 6 million/mm^3 cells that were 75% macrophages, 35% lymphocytes and 8% polymorphonuclear leucocytes.

On the 10th day of the therapy, there was no change in the clinical and radiological findings. Acid resistant bacteria were not seen in sputum smear, but due to the tomographic and the clinical results, antituberculosis treatment was started. INH300 mg, RMP 600 mg, MPZ2000 mg, EMB1500 mg was given.

On control PA chest roentgenograms, the lesion in the right lung had decreased and in the middle of the left lung, a new lesion had appeared as a non-homogenic density increase.

However, as there was the existence of ARB (-) in the repeated sputum culture and the treatment failed to result as expected in a short term. We decided to perform an open lung biopsy after consulting the thoracic surgery department.

Open lung biopsy result: In lung parenchymal tissues, fibrinous specimen, fibrocytes and mononuclear inflammatory cells and hystiocytes.

There were localized plaques in alveolar lumens. They were fully obliterated. And there was hyalinization in the perivascular area. Some alveolar spaces were full of erythocytes and there was thickening of alveolar septum that did not show any malignancy. The diagnosis was BOOP.

Treatment with 40 mg (0.8 mg/kg) prednol was started to the patient with the BOOP diagnosis. Prednol was decreased to 32 mg after 15 days. Steroid treatment has continued for 6 months and the patient's complaints were completely over.

However, after a year, there was recurrence. Clinical and radiological findings were the same as the year before. 48 mg/kg prednol treatment was started again. It was decreased 10 mg/day each month. At the last two months 8 mg prednol treatment was given and the therapy was stopped at 6th month. In control, total cure was obtained.

Discussion

The clinical findings of BOOP were defined when 94 patients who had bronchial obliterance were diagnosed by their lung biopsy samples. This disease is seen with the same incidence among males and females between ages 20 and 70. There was no correlation with smoking (6,7,8). Our cases were in the 5th-6th decade and were not smoking any cigarettes. Usually there were fever, fatigue, dyspnea, non-productive cough in these

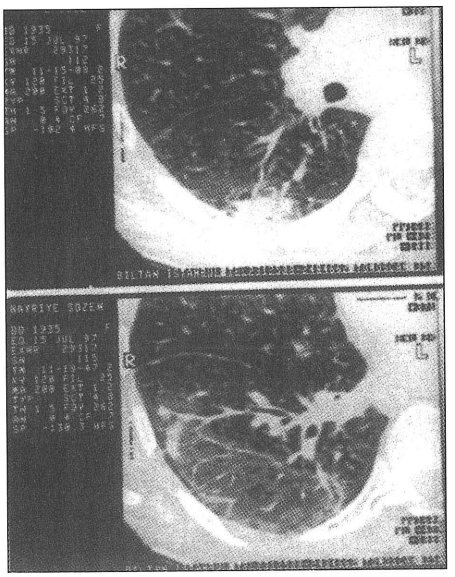

Fig. 5. Chest CT of patient: Interstitial type pneumonic consolidation on the left lower lobe

patients and the symptoms were manifested in 2 months and weight loss was also seen frequently (9). Hemoptisy seen in case I, occurs rarely. End inspiratory rhonchi which we obtained in both cases (I and II) was the most frequently seen auscultation finding. Clubbing was seen in less than 5% of the cases (9).

Routine labaratory examination was non-specific (10,11,12). Leucocytosis were seen in half of the patients. Increase in sedimentation (>100mm/hr) that we obtained in both cases was frequently seen in BOOP. CRP was positive in 70-80% of the patients (9,13). Auto antibodies were usually negative or were positive only in few cases (13).

Restrictive type ventilation defect was frequent in respiratory functions. Obstructive type defect (FEV_1/FVC70%) was seen only in 20% of the patients and those were the smokers. We found restrictive type defect in both cases. Furthermore, diffusion capacity in BOOP was limited to the 72% of the patients (14).

In PA chest x-rays, non-segmental patchy type consolidation was seen frequently on one side or asymmetrically on both sides (8,15,16,17). Recurrent or migratory pulmonary opacities were common (18). In some cases, small nodules and irregular linear opacities were also seen. Some cases which contained pleural effusion, thickening of pleura, cavities were reported (19). The degree of abnormalities in radiology was related to the histological involvement of the respiratory bronchioles and alveolar ducts in the case.

Although a specific finding was not seen on the computer tomography of BOOP, the related studies are rare. The most common findings on CT were consolidation area that were located in lower lobes and peripheral and small nodular opacities (1-10 mm radius). In the pathology cross sections, these nodules were shown to represent organised pneumonia spaces around abnormal bronchiolitis (20,21,22).

Broncho alveolar lavage (BAL) plays an important role both in the diagnosis and the differential diagnosis. Although BAL results of BOOP patients' macrophage ratio were lower than healthy volunteers, lymphocyte, neutrophily and eosonophile were high. CD4/CD8 ratio had decreased, but Leu-7 lymphocyte ratio was normal contrary to extrinsic allergic alveolitis. CD57 and NK ratio was normal and activated T lymphocytes had increased. Foamy degeneration was seen in macrophages (23,24,25).

Usually transbronchial biopsy cannot provide sufficient samples for diagnosis of BOOP (26).

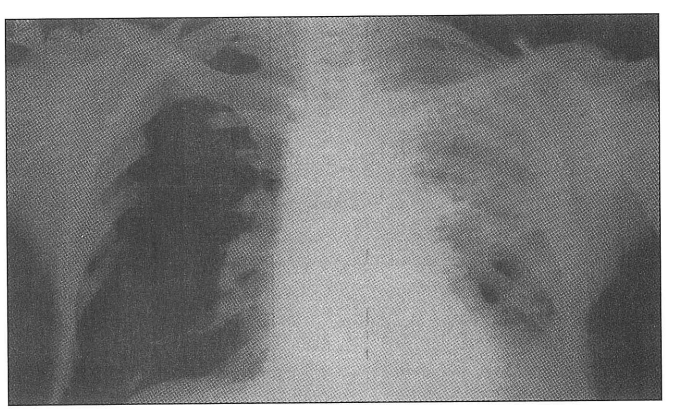

Fig. 6. Control P.A. Chest radiograph: new infiltration appeared on the left middle zone.

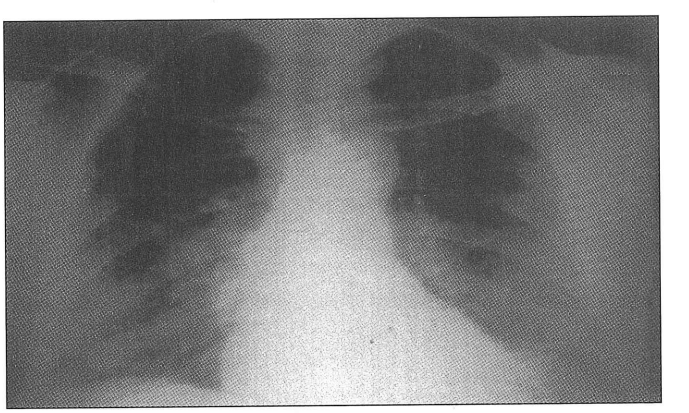

Fig. 7. Control P.A.Chest radiograph after steroid treatment

In both cases fiber optic bronchoscopy did not provide any evidence for the diagnosis. There was no response to antibiothic theraphy and clinical-radiological course in case II lead us to antituberculosis theraphy. However, when we have performed open lung biopsy, BOOP was diagnosed and steroid theraphy was started.

Open Lung Biopsy is very important in gaining sufficient lung tissue and having a definite pathologic result. Essential clinical information of the patient must be given to pathologist, to eliminate possible processes that can show similar pathologic findings, a detailed search is compulsory. Pathologic explanation of BOOP is granulation tissue plaques located in small airways lumen which may obliterate and stretch out to alveolar channels by alveola. Also, connective tissue proliferation that form intraluminal polyps, fibrinious exuda and foamy macrophages in alveoles and inflammation of alveolar wall can be seen (1).

Chronic eosinophilic pneumonia (CEP), extrinsic allergic alveolit (EAA), idiopathic pulmonary fibrosis (IPF), diffuse bronchiolitis must be also considered in the diagnosis (27).

Altough it seems like BOOP, from the point that in CEP, there were multiple alveolar opacities located peripheraly, lesions were seen at the upper zone and they differ by the dominance of eosinophilia in BAL (28,29).

EAA differs from BOOP by inhalation of organic dust anamnesis and obstructive type respiratory function defect in its beginning. Also in BOOP, contrary to EAA Leu-7 NK rate was normal in BAL (25).

In IPF, radiologic findings had honeycomb lung appearance besides bilateral alveoler opacities. And IPF had a fulminant course and did not respond perfectly to steroid theraphy. Symptom duration in BOOP was less than 3 months before the diagnosis, but this duration was longer in IPF (30,31).

In a study that was done by Costabel and et al., to differantiate CEP-EAA-IPF from BOOP, BAL results were taken as a base and consequently they determined that eosinophilia in the differentiation of BOOP and KEP, lymphocytes in the differentiation of IPF from BOOP and Leu-7 cell value in the differentiation of EAA from BOOP were the best indicators (24,25).

Obstructive type respiratory function defect, fulminant clinical findings, resistance to steroid theraphy and fibrosis that was not regenerated were the main differences of diffuse bronchiolitis from BOOP (32).

In the treatment of BOOP, corticosteroids were tested and very good results were expressed (32,33). Steroid treatment was started usually at 1mg/kg (max 100mg). By the follow up response to therapy, treatment was completed in 6 months by decreasing the dose. Response to repeated steroid therapy can be obtained if there is recurrence (34). In our second case, the same recurrence happened and illness could be treated by the repeated steroid therapy. High dose is tried in inhaler steroid therapy (35). As an alternative to steroids, erithromisin was also tested and the results were satisfactory (29). If the patient could not tolerate the steroid therapy, treatment by cytotoxic agents was also reported. Usually cyclophosphamide was used. However, generally, the response to steroid therapy was good and there was no need for an alternative therapy.

As it is seen in the representation of the cases that took place in many publications in our country in recent years, BOOP must be remembered in differential diagnosis of infiltrative lung lesions which do not respond to antibiotic therapy (32,36,37).

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