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Idiopathic Bronchiolitis Obliterans Organizing Pneumonia: Case Review

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ABSTRACT

Background: Bronchiolitis obliterans organizing pneumonia (BOOP) is characterized clinically by a subacute or chronic respiratory illness. The purpose of this study was to describe clinical and radiologic features of Idiopathic (cryptogenic) bronchiolitis obliterans organizing pneumonia.

Materials and Methods: We retrospectively reviewed 11 patients with biopsy proven BOOP at Masih Daneshvari Hospital, for whom well documented clinical and radiographic data were available. The final diagnosis of BOOP was validated if the followings were present:

- 1) Negative sputum or bronchoalveolar lavage (BAL) analysis for *Mycobacterium tuberculosis*
- 2) Open lung biopsy (OLB) or trans-bronchial lung biopsy (TBLB) findings characteristic of BOOP
- 3) Negative findings for systemic disorders or associated primary pulmonary lesions such as cancer
- 4) Prompt response to steroid therapy.

Results: The mean age of patients with BOOP in this case series was 46.3±24.6 yrs.(range 32-70); the male/female ratio was 7/4. The clinical pattern in BOOP presentation was more similar to classic sub-acute infectious process: dyspnea in 9 patients (81.8%), fever in 5 (45.4%), and cough in 6 (54.5%). The symptoms were usually mild. Physical examination showed sparse crackles in 5 patients (45.4%) and wheezing in 7 (63.6%). The most frequent radiologic patterns were ground glass appearances (63.6%) and diffuse infiltration associated with reticular pattern (27.2%). In 6 patients chest images showed bilateral distribution. The clinical and radiological manifestation of BOOP in our patients did not differ from other reports.

Conclusion: BOOP cases may present a distinct entity like pneumonia. Physicians in charge of these patients were all surprised of BOOP diagnosis by tissue examination. Trans- bronchial lung biopsy specimens along with strongly suggestive clinical and radiologic findings in many cases were adequate for making the diagnosis. We suggest that the diagnosis of BOOP must be considered in any immunocompetent patient with pneumonia with poor or no response to antibiotic therapy.

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Key words: Bronchiolitis obliterans organizing pneumonia, Idiopathic, Diagnosis

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INTRODUCTION

Organizing pneumonia is characterized by the presence of granulation tissue in the distal air spaces.

When these characterizations are associated with granulation tissue in the bronchiolar lumen, organizing pneumonia is qualified by the term of bronchiolitis obliterans (BO). Hence, the term bronchiolitis obliterans organizing pneumonia (BOOP) is used. BOOP is characterized clinically by a sub-acute or chronic respiratory illness. Plain radiographic and CT findings are not specific in BOOP and may be seen in a variety of pulmonary infections, inflammatory processes and neoplastic diseases (1-4). Bronchoalveolar carcinoma may mimic BOOP. A pattern of organizing pneumonia adjacent to bronchogenic carcinoma is also a common pathologic finding (5). Histologically, trans-bronchial lung biopsy obtained during a fiberoptic procedure appears to be an effective method for initial investigation of BOOP that presents with patchy radiographic shadows strongly suggestive of clinical diagnosis (6, 7). Approximately one half of BOOP cases are idiopathic (1). A variety of conditions such as infections, drugs and neoplasms are associated with BOOP (8-11).

The purpose of this study was to describe the clinical and radiologic features of Idiopathic (cryptogenic) BOOP.

MATERIALS AND METHODS

We retrospectively reviewed 11 patients with biopsy proven BOOP, for whom well documented clinical and radiographic data were available at Masih Daneshvari Hospital, a large referral pulmonary center in Tehran during a six-year-period.. Initial findings were obtained from patients' medical records. Chest radiographs and pathology specimens of patients were reviewed for this study. The biopsy specimens were obtained by various methods, such as open lung (n=7) /or fiberoptic trans-bronchial lung biopsy (n=4). Given the fact that the presence of necrosis, acute inflammation, micro-abscess formation, and vasculitis are strong

evidences against the diagnosis of BOOP, pathologic diagnosis of BOOP was made if the histological features were the patchy lesions such as small buds of fibromyxoid tissue in the small bronchiole, alveolar ducts, and alveoli (Fig. 1).

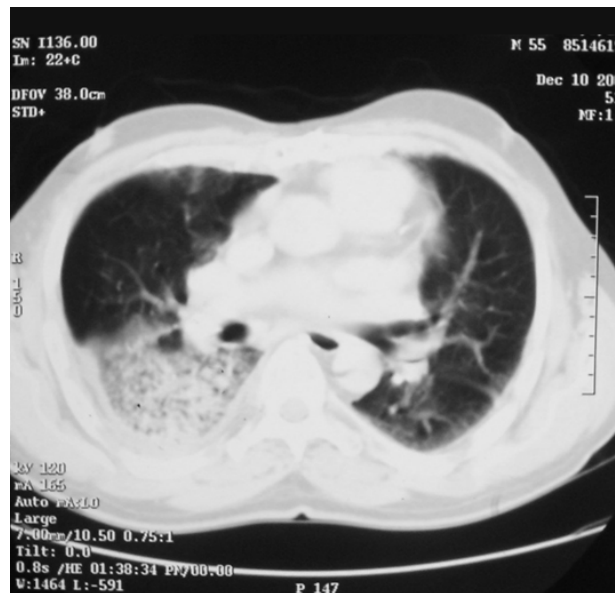


Figure 1. Chest CT-scan of a 57-year old woman with pneumonia – like illness, shows bilateral patchy alveolar infiltration, predominantly in the right lower lobe of the lung.

The extension of involvement of various small conducting airways differed from case to case. Terminal bronchioles commonly had a cellular infiltration in the wall that was predominantly composed of mononuclear cells, sometimes with neutrophils in the lumen. In some cases, presence of acute inflammatory cells and fibrinous exudates in or near the buds was suggestive that the process was still active. The intra-luminal buds frequently had central collection of inflammatory cells, including histiocytes, lymphocytes, and plasma cells, which tended to be in cluster form in the center of the buds. Away from the involvement of lung tissue, the alveoli appeared in normal or minimally affected form; with slight septa thickening adding to mild inflammatory infiltration and slight predominance of type II cells.

Clinical data were collected retrospectively from the patients' medical records with a special

questionnaire compiled for data collection and were reviewed by a single investigator and confirmed by another one independently, who were unaware of the pathologic data. All patients enrolled in this study were required to have the following criteria:

- 1) Negative sputum or BAL analysis for *Mycobacterium tuberculosis*
- 2) OLB or TBLB findings characteristic of BOOP
- 3) Negative findings for systemic disorders or an associated primary pulmonary lesion such as cancer
- 4) Prompt response to steroid therapy

RESULTS

The mean age of patients with BOOP was 46.3 ± 24.6 ; the male/female ratio was 7/4. The clinical presentation of BOOP was more similar to classic sub-acute infectious process and we detected dyspnea in 9 patients (81%), fever in 5 (45%) and cough in 6 (54%). The symptoms were usually mild. Physical examination showed sparse crackles in 5 patients (45%) and wheezing in 7 (63%). The most frequent radiological pattern was ground glass appearances in 7 (63%), and diffuse infiltration in 3 that was associated with reticular pattern (27%). In 6 (54%) patients chest images showed bilateral distribution. The physiologic and dynamic parameters and also radiologic and clinical characteristics are demonstrated in Tables 1 and 2.

Table 1. Pulmonary physiologic and dynamic parameters in 11 patients with idiopathic BOOP

Parameter	Values
PaO ₂ (mmHg)	88.2 ± 14 (n : 7)
FVC	85 ± 7.2 (n : 11)
FEV1	78 ± 8.2 (n : 11)
DLCO	75 ± 6.3 (n : 5)
WBC > 10.000/ml	10/11 (90.9%)
ESR > 50 mm/h	9/11 (81.8%)
Positive CRP > 2plus	8/11 (72.7%)

* Values are expressed as mean \pm standard deviation

** Values are expressed as percentage of predicted

Table 2. Radiological and clinical characteristics of patients with BOOP

	Characteristics	N (%)
Clinical	Dyspnea	9 (81.8%)
	Fever	5 (45.4%)
	Cough	6 (54.5%)
	Sparse Crackle	5 (45.4%)
	Wheezing	7 (63.6%)
Radiological*	Ground-glass attenuation	7 (63.6%)
	Linear and reticular opacities	3 (27.2%)
	Mixed pattern	1 (9%)

* Bilateral distribution was seen in 6 (54.5%) patients.

DISCUSSION

Clinical and radiological manifestations of BOOP in our patients did not differ from other reports (12-15). BOOP cases may present a distinct entity like pneumonia. Physicians in charge of these patients were surprised of BOOP diagnosis by tissue examination. Trans-bronchial lung biopsy specimens along with strongly suggestive clinical and radiological findings in many cases were adequate for making the diagnosis. (16-18)

BOOP is characterized by patchy interstitial inflammation and organizing granulation tissue in airspaces and small airways. BOOP has been classified as primary or cryptogenic and secondary which is associated with connective tissue diseases, hematological disorders, drugs, organ transplantation, radiotherapy, inflammatory bowel disease, AIDS, melanoma, and other mesenchymal lesions (19-21).

Three radiologic patterns have been described for BOOP: multiple alveolar patchy opacities (the most typical form), diffuse bilateral asymmetric infiltrative pattern, and a solitary focal lesion resembling tumors(22).The chest high resolution CT-scan shows bilateral areas of consolidation and ground glass opacities, usually with a peripheral distribution similar to chest radiographic findings(18)(Fig. 2).



Figure 2. High-resolution chest CT-scan shows areas of alveolar infiltration and consolidation with ground glass appearance

Large lung biopsy samples should be obtained to establish a diagnosis of idiopathic BOOP and to rule out other possibilities with certainty. The procedures used for BOOP diagnosis have been lung biopsy by mini-thoracotomy or video-assisted thoracoscopy and trans-bronchial lung biopsy. Biopsy specimens should be analyzed by two experienced pathologists (18, 22).

Trans-bronchial lung biopsy specimens may show organizing pneumonia in many cases (21-25). Poletti and colleagues reported that TBLB for cryptogenic BOOP had a sensitivity of 64% and a specificity of 86% (25). TBLB specimens were considered positive for BOOP if they showed buds of granulation tissue within the centrilobular air spaces, infiltration of alveolar walls with chronic inflammatory cells, and preservation of alveolar architecture, but these findings do not exclude associated lesions or disclose clues to causes of the process. (16,26,27). Therefore, diagnosis of organizing pneumonia by transbronchial biopsy may be accepted only in typical cases and requires careful patient follow up to prompt a surgical biopsy if the initial diagnosis has to be reconsidered because the

evolution of the illness is unusual. Most cases require a surgical lung biopsy specimen to be taken before starting the treatment. (18, 28) The use of transthoracic needle biopsy for diagnosing focal BOOP is controversial, because BOOP may exist adjacent to a malignant neoplasm. (28,29)

The diagnosis of BOOP without a biopsy is seldom justified. It may be considered in patients who are critically ill (particularly older patients) or if the clinical diagnosis is considered as highly probable by an experienced physician. Particular careful follow up would be necessary in such patients and lack of improvement with corticosteroids or relapses despite prescription of high doses of corticosteroids (over 25 mg per day) should lead the clinician to suspect other diagnoses, particularly lymphomas (30).

Although BOOP pattern is a common finding of coexisting pathology in association with bacterial, viral and fungal infections, idiopathic BOOP can mimic pneumonia in clinical field. Multifocal bilateral consolidations in patches on chest x ray and CT-scan with flu like signs and symptoms are usually attributed to infectious process. Thus, lack of response to antibiotic therapy and/or migration or relapse of opacities in x-ray images should lead the clinician to suspect other diagnoses such as BOOP or lymphoma. Main pathologic features and not merely an accessory to other well defined lesions such as vasculitis, eosinophilic pneumonia, hypersensitivity pneumonitis or nonspecific interstitial pneumonia disclose clues for diagnosis of BOOP (31-34).

Despite some forms of BOOP described with a fulminating and life-threatening variant (35, 36), in our series there was not any aggressive presentation.

In addition, two points need clarification with regard to cryptogenic variant of BOOP. First, except pulmonary infiltrates, no additional cardinal features characteristic of other diseases such as infectious, inflammatory or neoplasm process were seen in clinical, radiological or biopsy findings. Secondly,

patient's response to steroids after adequate antibiotic therapy had failed (37,38).

There were limitations in the interpretation of our clinical data, because the cases were collected retrospectively. Even though we used special data collecting questionnaires, some data were missing. Protocols of clinical therapy and follow-up planning were not uniform. Second, some of our cases were diagnosed on the basis of a pathologic specimen obtained via trans-bronchial biopsy. From an academic point of view, the pathologic diagnosis of BOOP should be made on the basis of a large specimen obtained via surgical biopsy. However, as Colby stated in a review (27), when the clinician is fully cognizant of the limitations of trans-bronchial biopsy and in the appropriate clinical setting, a clinicopathologic diagnosis of BOOP can be made using trans-bronchial biopsy.

In conclusion, we suggest that the diagnosis of BOOP must be considered in any immunocompetent patient with pneumonia with no or poor response to antibiotic therapy. The most common manifestation in high-resolution CT was bilateral ground glass opacities. In spite of few articles that explained nodular, linear or reticular opacities (38, 39), in this case series, these stigmata were not seen.

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