

## CASE STUDY

# Bronchiolitis obliterans organizing pneumonia in an AIDS patient

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**ABSTRACT:** We present a case of bronchiolitis obliterans organizing pneumonia in a patient with acquired immune deficiency syndrome. Only three cases have previously been reported in patients infected with human immunodeficiency virus.

In these four cases, bronchiolitis obliterans organizing pneumonia was similar in presentation, radiographic features and clinical course to that occurring in patients not infected with human immunodeficiency virus.

*Eur Respir J., 1995, 8, 1021-1024.*

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Keywords: Acquired immune deficiency syndrome, bronchiolitis obliterans organizing pneumonia, human immunodeficiency virus

Received: August 4 1994

Accepted after revision February 6 1995

Patients with human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS) develop a variety of respiratory disorders, particularly infections, both opportunistic and nonopportunistic, malignancies, lymphocytic interstitial pneumonitis and non-specific interstitial pneumonitis [1-3]. Bronchiolitis obliterans organizing pneumonia (BOOP), a well-recognized clinicopathological entity, usually characterized by fever, cough, dyspnoea, various pulmonary infiltrates, unique histological features, and responsiveness to corticosteroids [4], is not generally associated with HIV disease. To our knowledge, only three cases of BOOP have been described in patients with HIV/AIDS [5-7]. We report a case of BOOP in an AIDS patient with two unusual features, unilateral focal infiltrates and a neutrophilic alveolitis.

### Case report

A 47 year old white male with AIDS presented with a chronic cough and an abnormal chest radiograph. He complained of a dry, nonproductive cough of approximately 11 months duration, occasional fever, sweats and wheezing. An 18 kg weight loss occurred during the 6 months prior to presentation. As an out-patient, the patient was prescribed ciprofloxacin for 5 days, with minimal symptomatic relief. A chest radiograph revealed consolidation in the anterior segment of the right upper lobe (fig. 1). A computed tomography (CT) scan of the chest demonstrated two mass lesions in the anterior segment of the right upper lobe (fig. 2). The patient was therefore admitted to the hospital for evaluation.

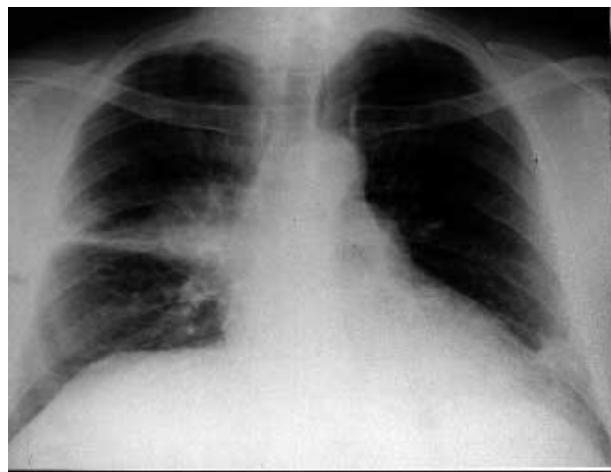


Fig. 1. - Chest radiograph showing right upper lobe consolidation



Fig. 2. - Computed tomography of the chest demonstrating two mass lesions in the anterior segment of the right upper lobe.

Table 1. – Summary of the clinical, radiographic, and treatment response in the reported cases of BOOP in HIV-infected patients

First authors [Ref.]	CDC Stage of AIDS	CD4 cells $\times 10^9\cdot L^{-1}$	CD4/CD8 ratio	Signs/symptoms	Radiographic finding	BAL %	Steroid administered	Steroid response
ALLEN <i>et al.</i> [5]	A?	NS	0.1	Fever Dyspnoea Cough Crackles	Bilateral alveolar infiltrates	45 lymph 40 macro 5 neutro	YES	2 months with resolution
LIOTE <i>et al.</i> [7]	C3	0.054	NS	Fever Dyspnoea Cough Crackles	Bilateral alveolar infiltrates	53 lymph 27 macro 20 neutro	NO	Resolution without treatment
LAGUNA DEL ESTAL <i>et al.</i> [6]	B?	NS	0.03	Fever Dyspnoea Cough Crackles	Bilateral alveolar infiltrates	NS	YES	11 months* with resolution
SANITO <i>et al.</i> (this study)	C3	0.018	0.03	Fever Dyspnoea Cough Crackles	Unilateral nodular infiltrates	100 neutro	YES	15 months with resolution

\*: this patient developed cytomegalovirus retinitis which required discontinuation of steroid treatment. ?: indicates that numerical stage was not given because CD4 count was not stated. NS: not stated; lymph: lymphocyte; macro: macrophage; neutro: neutrophils; CDC: Center for Disease Control; AIDS: acquired immune deficiency syndrome; BOOP: bronchiolitis obliterans organizing pneumonia; HIV: human immunodeficiency virus; BAL: bronchoalveolar lavage.

AIDS had been diagnosed 21 months prior to admission. At that time, the patient had documented *Pneumocystis carinii* pneumonia (PCP) and concurrent HIV seropositivity, oral candidiasis and shingles. Tuberculin skin testing was negative a year prior to admission. Blood transfusions and intravenous drug use were denied. Homosexual contacts had occurred.

On presentation, the patient's medications were zidovudine, ciprofloxacin, trimethoprim-sulphamethoxazole (TMP-SMX), fluconazole, cimetidine, cromolyn and albuterol inhalers.

Physical examination was unremarkable, except for a temperature of 38.7°C, and bibasilar crackles on auscultation of the chest. Significant laboratory data included: white blood cell count 7.800 cells $\times 10^9\cdot L^{-1}$ , platelet count 419 platelets $\times 10^9\cdot L^{-1}$ , CD4 lymphocyte count 0.018 cells $\times 10^9\cdot L^{-1}$  (31.5% of the total lymphocyte count), CD4:CD8 cell ratio 0.03, erythrocyte sedimentation rate 120 mm $\cdot h^{-1}$ , and arterial oxygen tension (Pa<sub>o2</sub>) 11.5 kPa (86 mmHg) whilst breathing room air.

Following admission, the patient was empirically treated with ceftriaxone and TMP-SMX (for 10 days) in addition to his routine medications. Fiberoptic bronchoscopy, with bronchoalveolar lavage (BAL) and transbronchial lung biopsy, was performed. BAL revealed a neutrophil alveolitis (table 1), and no evidence of *Pneumocystis carinii*. Cultures for bacterial, fungal, and acid-fast organisms were negative. Transbronchial lung biopsy was nondiagnostic, and the patient underwent thoracoscopy.

At thoracoscopy, two contiguous mass lesions in the anterior segment of the right upper lobe, adherent to the chest wall, were resected. Postoperatively, the patient continued to cough and developed worsening dyspnoea, hypoxaemia, and associated atelectasis; 2 days later mechanical ventilation was instituted. Ceftriaxone and

TMP-SMX were discontinued; methylprednisolone, imipenem and pentamidine were initiated. The pathological specimen showed diffuse areas of airspace consolidation with foamy macrophages, and intra-alveolar buds of granulation tissue containing inflammatory cells and myofibroblasts. Mild intra-alveolar and interstitial fibrosis was noted. A mixed lymphocytic and neutrophilic infiltrate was noted in the interstitium. Intraluminal buds of granulation tissue were also observed to involve the small airways (fig. 3). There was no evidence of granuloma formation, eosinophilic infiltration, or malignancy. Tissue cultures were negative for bacterial, fungal, mycobacterial and viral organisms. No pathological evidence of infection was noted by special staining methods. These biopsy findings were consistent with BOOP.

Antibiotics were withdrawn and steroids continued. Improvement in oxygenation allowed the patient to be weaned from mechanical ventilation after 9 days. The

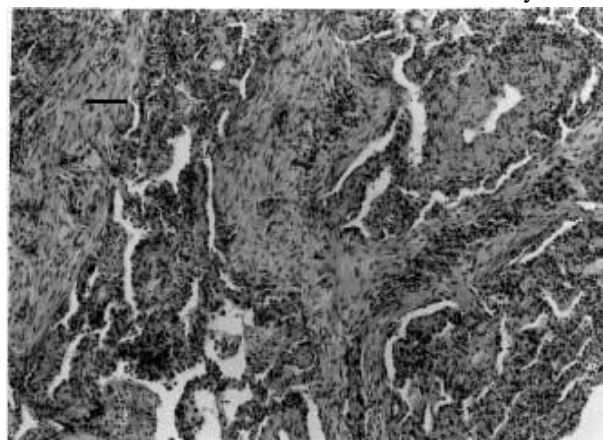


Fig. 3. – Histological section of the resected mass reveals bronchiolitis obliterans pneumonia, showing lumens of terminal bronchioles and alveoli filled and replaced with loose connective tissue (Bar: 100 $\mu m$ ).

chest radiograph cleared within 3 weeks. An unremarkable recovery led to his discharge from the hospital on a regimen of prednisone, 60 mg daily. The patient was maintained on 30 mg of prednisone daily for 15 months. He was subsequently weaned from prednisone, and is presently well, without steroid therapy.

### Discussion

In 1985, EPLER *et al.* [4] reported idiopathic BOOP as a distinct entity. The clinical and radiographic findings, as well as the treatment responses of the reported cases of BOOP in HIV/AIDS patients are outlined in table 1 [5–7]. In all cases, the pathological specimens demonstrated the classical defining features of BOOP. Thus it appears that the presentation [4], radiographic features [4, 8, 9], and clinical course of BOOP [4] in non-HIV-infected patients is similar to that in HIV-infected patients (table 1).

The BAL findings of BOOP in non-HIV patients generally reveal a "mixed pattern", with increased levels of lymphocytes, neutrophils and eosinophils [10]. Neutrophils generally represent about 10% lavaged cells [8], although neutrophils have been reported in the 25–40% range [11–13]. The pronounced neutrophil predominance in our case is atypical, and may suggest an infectious origin of the process; however, this was not supported by microbiological findings.

Whether the pathogenesis of BOOP in HIV/AIDS patients is different from the non-HIV patient is unknown, as idiopathic BOOP has no known cause. It is tempting to speculate that infection is the major aetiological factor for BOOP in HIV-infected patients. In fact, all four of the HIV-infected patients with BOOP, reported in table 1, had evidence of immune suppression, as evidenced by a low CD4 cell count or a low CD4/CD8 ratio. However, only one patient [7] had evidence of *Pneumocystis carinii* infection at the time of diagnosis of BOOP. It therefore appears unlikely that infection is the sole cause of BOOP in HIV/AIDS patients. Although immunosuppression is not a characteristic feature of idiopathic BOOP, BOOP has been associated with other immunosuppressed states, such as common variable immunodeficiency syndrome [14], and lung transplant [10]. Furthermore, we cannot exclude the possibility that BOOP may be a direct pulmonary consequence of HIV infection.

Regarding the treatment of BOOP, corticosteroids are the therapy of choice, with a success rate exceeding 60% [4]. In three of the four HIV-infected cases who were treated with steroids, BOOP resolved, whilst the fourth patient improved without steroid treatment (table 1). One issue which remains unresolved is the safety of a prolonged course of steroids in an already immunosuppressed patient. Typically, BOOP is treated for a year before discontinuing corticosteroid therapy [4]. ALLEN and WEWERS [5] empirically stopped prednisone therapy after 2 months, for fear of the potential adverse effects with respect to opportunistic infection, and their patient did not experience a relapse. LAGUNA DEL ESTAL *et al.* [6]

kept their patient on prednisone for 11 months, until cytomegalovirus retinitis developed, requiring discontinuation of steroid therapy. Our patient experienced recurrence of symptoms when prednisone was decreased below 30 mg daily, and had to remain on this dosage for more than a year. He did not develop any opportunistic infections whilst on this regimen.

In summary, BOOP is similar in presentation, radiographic features and clinical course in HIV/AIDS patients to that occurring in the non-HIV population. The BAL patterns are variable and not suggestive of a specific illness. Although open lung biopsy is not often necessary for the diagnosis of opportunistic pneumonias in AIDS patients [15], in the reported cases transbronchial lung biopsy was nondiagnostic, and open lung biopsy (or thoracoscopic lung biopsy) was necessary. Occasional cases remit spontaneously, but corticosteroids remain the cornerstone of therapy. We therefore suggest that in the HIV/AIDS patient with pulmonary infiltrates which fail to respond to empirical antibiotic therapy or remain undiagnosed after bronchoscopic procedures, open lung biopsy should be strongly considered if the clinical status of the patient allows it. By this means, a disease such as bronchiolitis obliterans organizing pneumonia may be identified, and, more importantly, may be successfully treated.

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