CASE REPORTS

Bronchioloalveolar Adenoma Associated With Bronchiolitis Obliterans and Leishmaniasis With Lung Involvement in Acquired Immunodeficiency Syndrome

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Visceral leishmaniasis is not unusual in patients with acquired immunodeficiency syndrome (AIDS), but lung infiltration is uncommon. Leishmaniasis involving the lung often manifests as interstitial pneumonitis. We report a case in which the discovery of amastigotes in the transbronchial biopsy led to a diagnosis of leishmaniasis. However, the findings from x-rays and study of the bronchoalveolar lavage fluid were consistent with bronchiolitis obliterans, possibly caused by the AIDS virus. In addition, the transbronchial biopsy findings were consistent with a diagnosis of bronchioloalveolar adenoma with radiographic evidence of multiple nodules.

Key words: *Acquired immunodeficiency syndrome. Bronchiolitis obliterans. Leishmaniasis with lung involvement. Bronchioloalveolar adenoma.*

Adenoma bronquioloalveolar asociado a bronquiolitis obliterante y leishmaniasis pulmonar en el sida

La leishmaniasis visceral no es inusual en pacientes con síndrome de inmunodeficiencia adquirida (sida), pero su afectación pulmonar es infrecuente. La leishmaniasis pulmonar a menudo se presenta como neumonitis intersticial.

Describimos un caso en el cual el hallazgo de amastigotes en la biopsia transbronquial permitió el diagnóstico de leishmaniasis pulmonar. Sin embargo, los hallazgos radiológicos y del lavado broncoalveolar eran compatibles con una bronquiolitis obliterante que podría deberse al virus del sida. Además, la biopsia transbronquial permitió diagnosticar un adenoma bronquioloalveolar con la presencia radiológica de múltiples nódulos.

Palabras clave: *Síndrome de inmunodeficiencia adquirida. Bronquiolitis obliterante. Leishmaniasis pulmonar. Adenoma bronquioloalveolar.*

Introduction

Although visceral leishmaniasis has often manifested with coughing, *Leishmania* amastigotes are rarely isolated in the human lung. Bronchioloalveolar adenoma (BAA) is classified histologically as a highly differentiated adenocarcinoma or a benign tumor that could potentially become malignant. Similar lesions under different names have been reported, many of them associated with lung cancer or interstitial pneumonia. We report an unusual case of BAA associated with bronchiolitis obliterans and lung leishmaniasis in a patient with acquired immune deficiency syndrome (AIDS).

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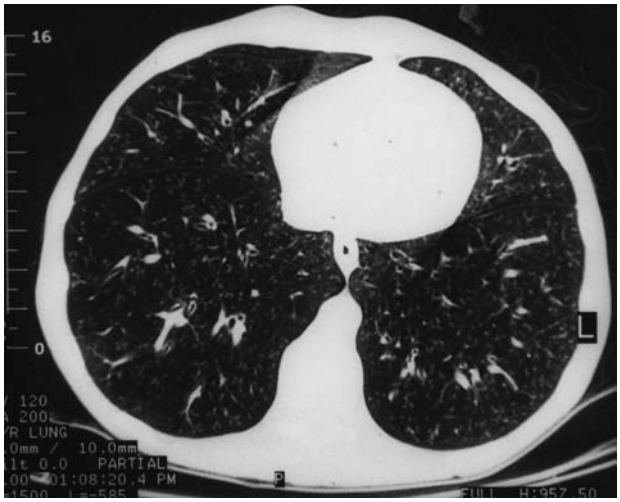
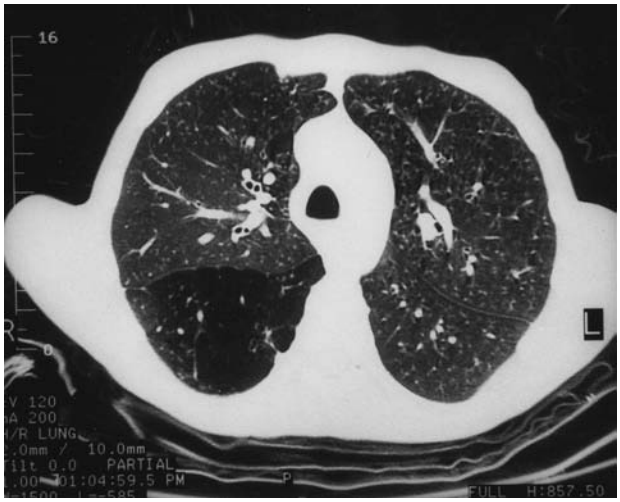
Clinical Description

The patient was a 30-year old man, a smoker, diagnosed with AIDS 4 years earlier and largely noncompliant with treatment (his last monitoring had revealed a viral load of 560 000 copies and a CD4+ cell count of 72/μL). He came to our hospital complaining of progressive weight loss, shortness of breath, and a dry cough during the past 5 months. His medical history included hepatitis C, *Pneumocystis carinii* pneumonia, *Campylobacter* gastroenteritis, and condyloma acuminata. For several years he had experienced recurring episodes of visceral leishmaniasis resistant to antimonial compounds at the standard dosage, and as a result had received treatment with liposomal amphotericin B for 17 months.

Upon admittance, the patient's temperature was 36°C. No diseased lymph nodes were observed, and the lung auscultation revealed diffuse crackles. No splenomegalia, hepatomegalia, or abdominal masses were detected. The neurological examination was normal except for diffuse weakness. The white cell count was 2600/μL with 73% polymorphonuclear cells, 10% lymphocytes, and 17% monocytes. The viral load was 314 000 copies, and the CD4+





Figures 1 and 2. High resolution computed tomography scans in which multiple well-defined centrilobular nodules and linear opacities in tree-in-bud pattern are observed. Also evident is a localized area of air trapping in the right lower lobe in the expiratory scan.

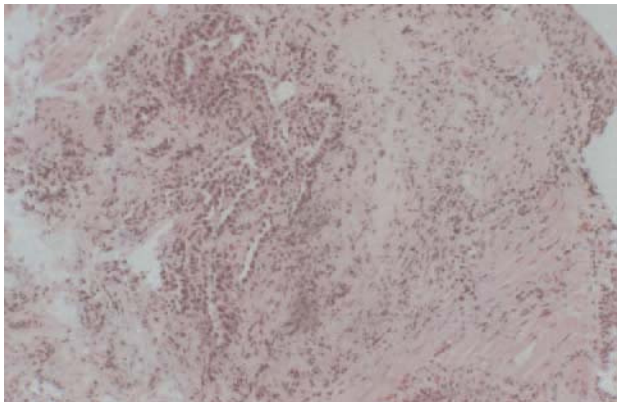


Figure 3. Transbronchial biopsy: bronchioloalveolar adenoma (endobronchial lesions with columnar epithelial cells without nuclear atypia.

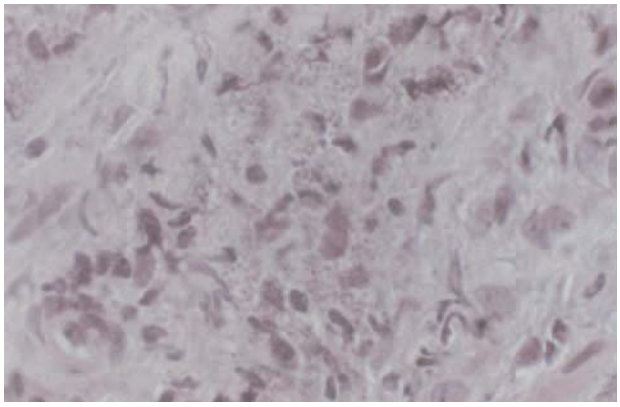


Figure 4. Transbronchial biopsy: bronchial submucosal histiocytes containing intracytoplasmic *Leishmania* amastigotes.

lymphocyte count was 80/µL. The hematocrit was 34%, and the platelet count was 110 000/µL. Blood chemistry was normal except for aspartate aminotransferase (82 U/L), gamma glutamyl transpeptidase (193 U/L), and sodium (127 mEq/L) values. Arterial blood gas analysis (with a fraction of inspired oxygen of 21%) showed a PaO_2 of 58.5 mm Hg, pH of 7.36, and $PaCO_2$ of 24.4 mm Hg. The chest x-ray was normal. The high resolution computed tomography (HRCT) scan revealed multiple well-defined centrilobular nodules, linear opacities in tree-in-bud pattern, and the expiratory scan revealed a localized area of air trapping in the right lower lobe (Figures 1 and 2). Sputum analysis was negative for acid-alcohol fast bacilli, but *Mycobacterium tuberculosis* was detected by polymerase chain reaction. Treatment with isoniazid (300 mg/d), rifampicin (600 mg/d), and pyrazinamide (1500 mg/d) was initiated, but no clinical or radiographic evidence of improvement was noted. Fiberoptic bronchoscopy was inconclusive. The bronchial aspirate and bronchoalveolar lavage were negative for acid-alcohol fast bacilli, as was the Löwenstein-Jensen culture 60 days later. However, the polymerase chain reaction was positive for *M tuberculosis*. Analysis of bronchoalveolar lavage showed 33% alveolar macrophages, 2% lymphocytes, and 65% neutrophils. The transbronchial biopsy revealed a BAA (Figure 3) and bronchial submucosal histiocytes containing intracytoplasmic *Leishmania* amastigotes (Figure 4). Treatment of liposomal amphotericin was started but the patient died a month later. The patient's family refused an autopsy.

Discussion

The incidence of visceral leishmaniasis is increasing in immunocompromised populations, especially in patients with AIDS. In immunocompetent patients it presents with subacute or chronic symptoms and fever, hepatomegaly, massive splenomegaly, anemia, leukopenia, and progressive wasting. In healthy patients, organs can remain viable for extended periods, but when the individual is immunodepressed, disease can develop rapidly. Visceral leishmaniasis often manifests atypically in immunocompromised patients. An unusual finding in the case we report was the onset with respiratory symptoms. Isolation of *Leishmania* amastigotes in the lung is very rare, although such an

infestation has been reported in immunocompromised patients.[1,2] Most of the published cases of *Leishmania* isolation report patients with the recent onset of a persistent dry cough that remains constant while the patient is ill but that disappears with treatment. Such a cough is, presumably, a clinical sign of interstitial pneumonitis. These findings indicate that *Leishmania* species can give rise to respiratory disease in immunocompromised patients more often than was previously believed.

The clinical course of visceral leishmaniasis in AIDS patients is usually chronic and subject to recurrences. Treatment with pentavalent antimonial drugs, the standard treatment in immunocompetent patients, is often ineffective in AIDS patients. Such a response is not surprising given the importance of cellular immunity in the host's response to *Leishmania* species. Leishmaniasis should therefore be considered at the onset of unexplained lung symptoms in AIDS patients.

BAA is characterized by the proliferation, along the alveolar walls, of round cells with a variable degree of nuclear atypia. The majority of such findings have been associated with lung cancer or interstitial pneumonitis.[3] Many authors have suggested that such lesions may be consistent with early premalignant phases of a glandular neoplasm that may progress to carcinoma.[4] BAA has been discovered incidentally through biopsy of resected lung samples from patients in whom BAA had not been detected by chest radiography. HRCT images of BAA show small well-defined pulmonary nodules with ground-glass attenuation.[5]

The HRCT of our patient showed many such nodules that were widely distributed, presumably because of BAA, as well as findings consistent with bronchiolitis obliterans with areas of air trapping and tree-in-bud sign. The latter were probably secondary to the AIDS virus given that no other cause could be identified. The bronchiolitis diagnosis was based on radiographic examination as well as on bronchoalveolar lavage findings that revealed a neutrophil percentage exceeding 50% (65% in our patient) and on the worsening of respiratory symptoms.[6] However, there was no histological evidence of bronchiolitis obliterans in the transbronchial biopsy, perhaps because the sample obtained was small. Therefore, the final diagnosis of bronchiolitis obliterans was considered tentative despite the highly suggestive clinical, radiographic, and bronchoalveolar lavage findings not attributable to the previously diagnosed disease.[7]

Two different disease processes overlapped in our patient: on the one hand, lung infestation by *Leishmania* species, secondary to AIDS, may have caused the bronchiolitis obliterans, and on the other hand the respiratory condition of our patient was aggravated by BAA. BAA is a possible precursor to bronchioalveolar carcinoma, which might have developed later on the preexisting inflammatory lesions. While, in theory, no relation between respiratory infection and BAA was demonstrated, the hypothetical association between *Leishmania* infection and BAA cannot be ruled out because the cause of BAA in our patient is unknown and both diseases developed at the same time.

We conclude that pulmonary leishmaniasis should be suspected with the onset of unexplained respiratory symptoms in AIDS patients; furthermore, this disease may be associated with other lung diseases such as BAA and bronchiolitis obliterans.

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