

Pulmonary mucosa-associated lymphoid tissue lymphoma presenting with a diffuse micronodular pattern in an HIV-infected patient

Linfoma do tecido linfoide associado à mucosa no pulmão com padrão micronodular difuso em paciente HIV positivo

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To the Editor:

Mucosa-associated lymphoid tissue (MALT) lymphoma is an extranodal B-cell lymphoma seen in various types of epithelial tissues, such as those of the stomach, salivary glands, lungs, and small intestine.⁽¹⁾ Although pulmonary MALT lymphoma—also known as bronchial-associated lymphoid tissue (BALT) lymphoma—is a rare disease, it is the most common form of primary low-grade pulmonary lymphoma.⁽²⁾ Some reports have associated pulmonary MALT lymphoma with Sjögren's syndrome and other immunological diseases.⁽³⁾ Case reports of pulmonary MALT lymphoma in HIV-infected patients are rare.⁽⁴⁾ Here, we report the case of an HIV-positive patient with pulmonary MALT lymphoma presenting with a diffuse micronodular pattern on chest X-rays and CT scans.

A 38-year-old single Black male sought treatment at a tertiary-care hospital in the city of Rio de Janeiro, Brazil. He was a native of the city and was employed as a cook. He had been HIV-positive since 2001 and was being followed at an outpatient clinic for infectious and parasitic diseases. He was not on antiretroviral therapy. The most recent CD4 count, performed in November of 2008, was 565 cells/mm³.

The onset of pulmonary manifestations, including fever, cough, and intermittent episodes of mild hemoptysis, occurred in December of 2008. The patient sought treatment at a teaching received antibiotic therapy with amoxicillin (500 mg every 8 h for 7 days). Although the fever subsided and the hemoptysis lessened, the dry cough persisted. He denied other symptoms, such as weight loss, night sweats, and worsening of the overall health status. The patient was referred to the pulmonology department of the hospital for further investigation. Physical examination revealed no significant changes. A chest X-ray

revealed mild, diffuse micronodular infiltrate (Figure 1a), which was better characterized by a HRCT scan of the chest (Figure 1b).

The principal diagnostic hypotheses were miliary tuberculosis and histoplasmosis. Tuberculin skin test results were negative, smear microscopy of induced sputum was negative for AFB, and serology for *Histoplasma capsulatum*

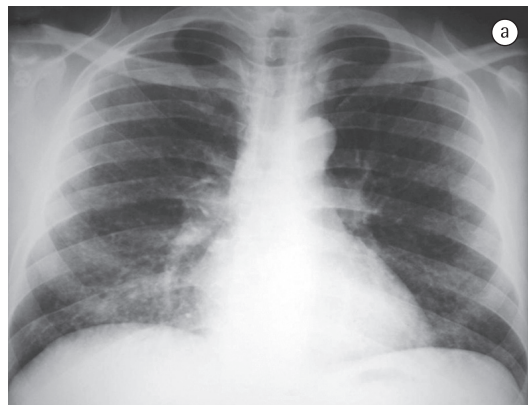


Figure 1 - In a, anteroposterior chest X-ray showing mild, diffuse micronodular interstitial infiltrate, predominantly in the lung bases. In b, HRCT slice at the level of the bronchial bifurcation showing small nodules sparsely distributed throughout the lungs.

was negative. Subsequently, the patient underwent BAL and transbronchial biopsy through bronchoscopy. The bronchoscopy findings were normal. The BAL fluid was negative for AFB and fungi, and BAL fluid cytology was negative. Although the transbronchial biopsy findings were suggestive of lymphoproliferative disease, it was impossible to establish a definitive diagnosis. The patient subsequently underwent lung biopsy through thoracotomy. The histopathological findings revealed pulmonary MALT lymphoma, which was subsequently confirmed by immunohistochemistry (Figure 2). After the diagnosis had been confirmed, the patient was referred to the hematology department. Because pulmonary MALT lymphoma is an indolent disease and the patient was clinically stable, we decided that clinical observation was the best therapeutic approach. At this writing (one year after having been treated at our hospital), the patient was under outpatient follow-up treatment and clinically stable, presenting with no relevant CT findings.

The case reported here highlights a rare manifestation of an uncommon disease. Although low-grade B-cell non-Hodgkin's lymphomas account for a very small proportion of all lung neoplasms, they account for 58-87% of the cases of primary pulmonary lymphoma.⁽⁵⁾ Approximately 90% of low-grade B-cell non-Hodgkin's lymphomas are of the MALT lymphoma type.⁽⁶⁾

It has been estimated that the risk of developing a lymphoma, especially a marginal zone lymphoma, is higher in patients with Sjögren's syndrome than in the general

population.⁽⁷⁾ A study published in 2009 demonstrated the presence of autoimmune disease in 10 of 63 cases of pulmonary MALT lymphoma analyzed.⁽⁸⁾ The association between HIV infection and pulmonary MALT lymphoma is unclear, few cases having been reported.⁽⁴⁾

The diagnosis is usually difficult and time-consuming because most individuals are asymptomatic, being diagnosed on the basis of incidental findings on chest X-rays. The time elapsed between the first clinical or radiological changes and the diagnosis of the disease can range from 5 months to 8 years.⁽²⁾ When present, clinical manifestations are usually nonspecific, including mild dyspnea, cough, chest pain, and, occasionally, hemoptysis, as in the case reported here.

The most common radiological finding is alveolar opacity with air bronchogram.⁽¹⁾ Studies based on CT scans have reported the presence of nodular opacities, ground-glass opacities, and small nodules with centrilobular distribution, as well as of the tree-in-bud pattern, findings that are suggestive of a wide range of diseases.⁽²⁾

Pulmonary MALT lymphoma typically has an indolent course and a good prognosis, although systemic dissemination and transformation into high-grade B-cell lymphoma can occur. A recent study reported a five-year survival rate of 90% and a ten-year survival rate of 72%.⁽⁸⁾ The most effective treatment has yet to be defined. Various therapeutic regimens have been proposed, including radiotherapy, surgery, chemotherapy, and clinical observation. Currently, chemotherapy with chlorambucil seems to be the best treatment option in cases of

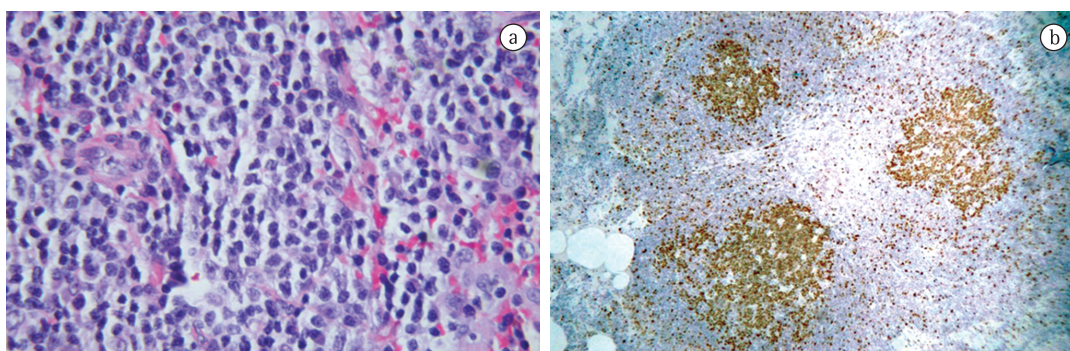


Figure 2 - Histopathology. In a, lung fragment showing lymphoepithelial lesion characterized by small lymphocytes distributed throughout the lung parenchyma (H&E; magnification, $\times 40$). In b, immunohistochemistry with the Ki-67 marker, showing the activated germinal center, as well as the expanded mantle and marginal zones. Note also that the lymphoma is not highly proliferative, indicating the indolent nature of the disease.

disseminated disease.⁽⁹⁾ The approach to the case reported here was close observation, a decision that was based on the fact that the patient was clinically stable and was HIV-positive.

As previously stated, pulmonary MALT lymphoma is a rare disease, although it is the most common form of primary pulmonary lymphoma. The progression of pulmonary MALT lymphoma is generally indolent, and the disease can be accompanied by autoimmune diseases. We reported an atypical case of an HIV-infected patient who presented with clinical symptoms of cough and mild hemoptysis, as well as with a CT finding of diffuse micronodular infiltrate, which is common to many other diseases. The diagnosis of pulmonary MALT lymphoma was established after lung biopsy by thoracotomy.

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