CASE REPORT

Cutaneous histoplasmosis disclosing an HIV-infection*

Histoplasmosis cutânea reveladora de infecção pelo HIV

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Abstract: Histoplasmosis is a systemic mycosis endemic in extensive areas of the Americas. The authors report on an urban adult male patient with uncommon oral-cutaneous lesions proven to be histoplasmosis. Additional investigation revealed unnoticed HIV infection with CD4+ cell count of 7/mm³. The treatment was performed with amphotericin B, a 2065 mg total dose followed by itraconazole 200 mg/daily plus antiretroviral therapy with apparent cure. Histoplasmosis is an AIDS-defining opportunistic disease process; therefore, its clinical diagnosis must drive full laboratory investigation looking for unnoticed HIV-infection.

Keywords: Acquired immunodeficiency syndrome; Amphotericin B; Histoplasmosis

INTRODUCTION

Histoplasmosis is a systemic mycosis caused by Histoplasma capsulatum, a thermo-dimorphic fungus and a soil saprophyte. It is endemic in the central southern region of the United States of America (USA) and in Central and South America. Infection with H. capsulatum is caused by the inhalation of conidia from nature in endemic areas.1

The majority of infected people have either no symptoms or a very mild clinical presentation. Individuals who develop acute pulmonary histoplasmosis are usually those exposed to heavy infection.1 Some of them may present chronic cavitary pulmonary histoplasmosis, granulomatous mediastinitis or mediastinal fibrosis later in their lives. Dissemination of the disease is a possible event following acute infection or a later event due to the reactivation of quiescent foci.1 It is important to consider that even with the development of cell-mediated immunity against H. capsulatum patients may have persistent foci of viable fungi in various organs in equilibrium with the immune response, similarly to the situation observed in paracoccidioidomycosis, coccidioidomycosis and tuberculosis.2 The most important risk factor for dissemination of the disease has been HIV-induced immunosuppression and, therefore, the diagnosis of cutaneous histoplasmosis must drive attention to possible subjacent unnoticed HIV-infection.3,4

The authors present an atypical case of histoplasmosis associated with unnoticed HIV-infection, which was later confirmed.

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CASE REPORT

An urban 57-year-old male patient reported a cutaneous lesion on his nose. The lesion had been initially noticed three months before. General complaints included a 3-kg weight loss, sporadic fever and malaise. Dermatologic examination showed a crusted ulcerated lesion surrounded by an erythematous halo on the nose and few erythematous papular nodules on his mentum (Figures 1 and 2). Oral examination revealed a sublingual atypical ulcerated lesion suggesting a traumatic etiology. Clinical examination was unremarkable. Microscopic examination of representative cutaneous lesions and of the oral lesion showed chronic lymphohistiocytic inflammation with granuloma formation on the dermis. Multiple intracellular structures were observed in the cytoplasm of histiocytes and giant cells, which were better observed and demonstrated on especial staining, such as Grocott-Gomori (Figures 3 and 4). Culture from biopsy material in Sabouraud dextrose-agar and Mycosel® was positive for *Histoplasma capsulatum* (Figure 5).
Additional investigation revealed interstitial infiltration and nodules on both lungs which were suggestive of pulmonary histoplasmosis. Serology tests were positive for HIV infection, at that point unknown to the patient and negative for HBV and HCV. Blood CD4+ cell count was 7/mm³; CD8+ cell count was 236/mm³ and HIV RNA measurement performed on plasma revealed a viral load of 241,265 copies and a log of 5.383.

The patient was treated with amphotericin B deoxycholate, 2065 mg of total dose, followed by itraconazole 200mg/daily as a maintenance treatment, with clinical resolution of all lesions and improvement of general conditions. Anti-retroviral therapy and nutritional support were added to treatment as well.

DISCUSSION

Histoplasmosis is one of the most common systemic mycosis in AIDS patients worldwide, and it is particularly important as an opportunistic co-infection where it is endemic. Skin lesions are referred as uncommon in patients diagnosed in the USA, occurring in less than 10% of cases. On the other hand, among cases from Latin America, skin lesions are reported to occur in 38% to 85% of patients with histoplasmosis and AIDS. These differences were thought to be a consequence basically of reporting bias or delayed diagnosis in cases reported from Latin America, but evidence of molecular differences in strains of H. capsulatum prevalent in the United States and South America has recently been provided as an additional explanation for such data, suggesting tropism of the fungus to the skin in strains from South America. Cutaneous lesions as a primary manifestation of HIV-related diseases are not rare, and in histoplasmosis, they are particularly evident. The cutaneous manifestations of histoplasmosis vary from acneiform papules to plaques, ulcers and vegetating lesions, usually in large numbers, as a consequence of the hematogenous dissemination of the fungus. However, cutaneous lesions in histoplasmosis are not diagnostic by themselves in the immunosuppressed patient as many other infectious and non-infectious diseases share a similar morphological pattern. Therefore, physicians must value systemic signals and symptoms to narrow the spectrum of hypotheses. In this reported case, the mucosal lesion did not present the granulation or hemorrhagic points usually observed in paracoccidioidomycosis, and this favored the hypothesis of histoplasmosis. Disseminated histoplasmosis occurs in HIV-infected patients with a CD4+ cell count of < 50/mm³ as found in most studies. Our patient presented with a CD4+ cell count of 7/mm³ and an expressve viral load, but besides non-specific clinical symptoms, his HIV-status was unnoticed until the histoplasmosis diagnosis.

Treatment guidelines for disseminated histoplasmosis suggest amphotericin B deoxycholate or liposomal amphotericin B for moderate to severe disease. As a second option, itraconazole 600mg/daily for three days followed by 400 mg/daily for 12 months. The treatment schedule used in the present case showed to be very effective, and the patient remains well in an outpatient follow-up basis. It is noteworthy that maintenance therapy with itraconazole may be required for life if immunosuppression cannot be reversed.

The present case report, once again, emphasizes the role of cutaneous lesions as a sentinel of severe systemic diseases and subjacent immunosuppression.
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