CASE REPORT

Cutaneous histoplasmosis disclosing an HIV-infection*

Histoplasmose cutânea reveladora de infecção pelo HIV

Silvio Alencar Marques[1]
Maria Regina Cavariani Silvares[2]
Rosangela Maria Pires de Camargo[3]
Mariangela Esther Alencar Marques[4]

DOI = Digital Object Indentifier = http://dx.doi.org/10.1590/abd1806-4841.20131812

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/mm^3. The treatment was performed with amphotericin B, a 2065 mg total dose followed by itraconazole 200mg/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 unnoted HIV-infection.
Keywords: Acquired immunodeficiency syndrome; Amphotericin B; Histoplasmosis

Resumo: Histoplasmose é infecção sistêmica endêmica em extensas áreas do continente Americano. Os autores relatam caso de paciente do sexo masculino, de zona urbana com lesões cutâneas e mucosas incomuns de histoplasmose. Investigação adicional posterior revelou infecção subjacente pelo HIV com contagem de células CD4 de 7/mm^3. O tratamento foi realizado com anfotericina B, dose total de 2065 mg, seguido por itraconazol 200 mg/dia associado à terapêutica antirretroviral com cura aparente do quadro. Histoplasmose é enfermidade oportunística definidora da síndrome de imunodeficiência adquirida, portanto, diagnóstico clinico de histoplasmose implica em investigação laboratorial de infecção subjacente pelo HIV.
Palavras-chave: Anfotericina B; Histoplasmose; Síndrome de imunodeficiência adquirida

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.

Received on 12.04.2012.
Approved by the Advisory Board and accepted for publication on 18.06.2012.
* Study carried out at the Department of Dermatology and Radiotherapy, Botucatu Medical School, São Paulo State University (Departamento de Dermatologia e Radioterapia - Faculdade de Medicina de Botucatu – Universidade Estadual Paulista "Júlio de Mesquita Filho" - FMB-UNESP) – Botucatu (SP), Brazil.
Conflict of interest: None
Financial funding: None

[1] Full Professor – Department of Dermatology and Radiotherapy. Botucatu Medical School, São Paulo State University (Unesp) – Sao Paulo (SP), Brazil.
[2] Assistant Professor - Department of Dermatology and Radiotherapy. Botucatu Medical School, São Paulo State University (Unesp) – Sao Paulo (SP), Brazil.
[3] Biologist - laboratory of Mycology - Department of Dermatology and Radiotherapy. Botucatu Medical School, São Paulo State University (Unesp) – Sao Paulo (SP), Brazil.
[4] Lecturer - Associate Professor - Department of Pathology. Botucatu Medical School, São Paulo State University (Unesp) – Sao Paulo (SP), Brazil.

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

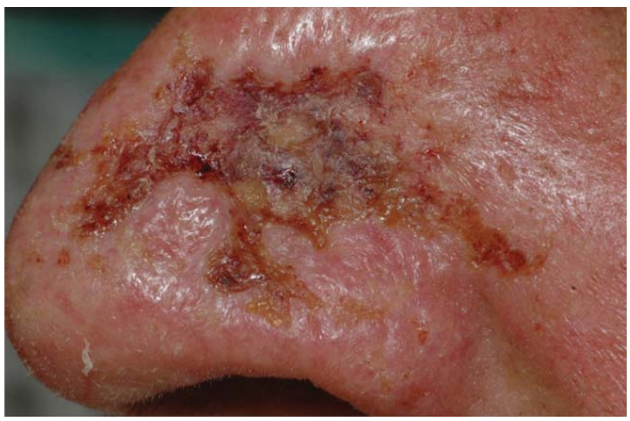

Figure 1: Histoplasmosis: shallow ulcer with irregularly shaped limits with haematic and meliceric crusts localized on the nose

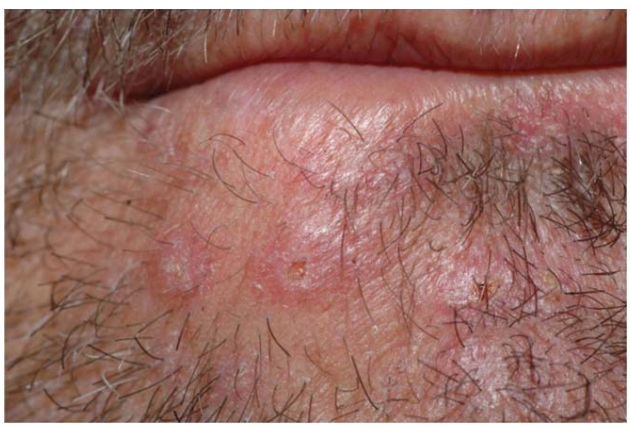

Figure 2: Histoplasmosis: erythematous papule and nodules with discrete central ulceration on the chin

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).

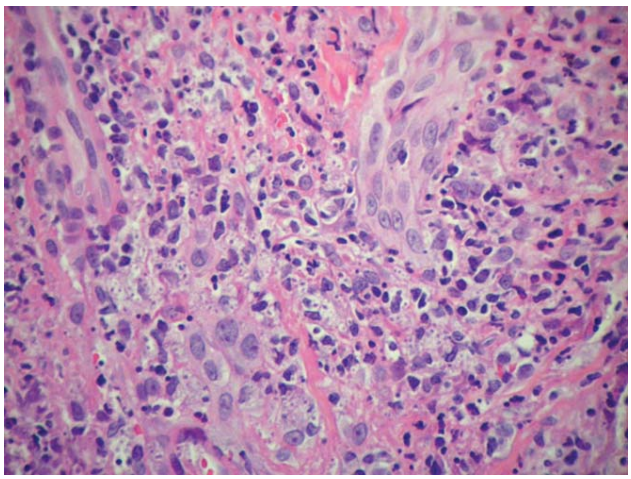

Figure 3: Histoplasmosis: histopathological examination showing lymphohistiocytic inflammatory infiltration with fungi in the cytoplasm of histiocytes. (HE 400 X)

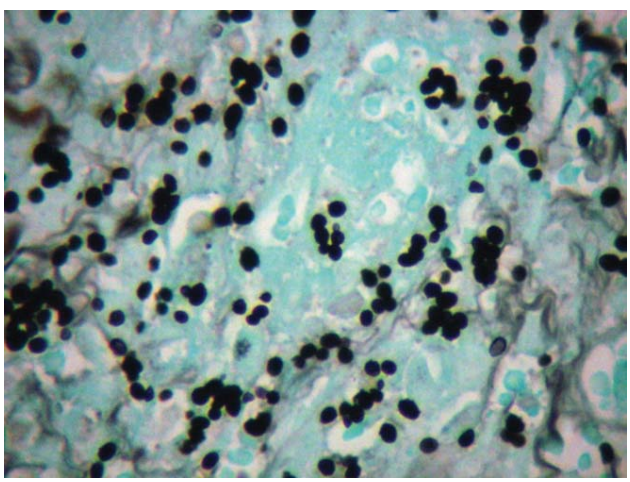

Figure 4: Histoplasmosis: histopathological examination showing multiple small size yeast-like cells. (Grocott-Gomori 1000 X)

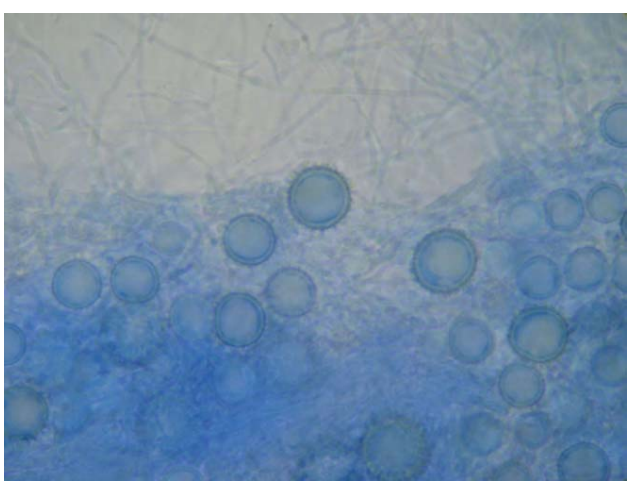

Figure 5: Histoplasma capsulatum: macroconidia with stalagmospores. (Cotton-blue 1000 X)

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 $7/mm^3$; $CD8^+$ cell count was $236/mm^3$ 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.[4] Skin lesions are refereed as uncommon in patients diagnosed in the USA, occurring in less than 10% of cases.[1,4] 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.[1,5] 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.[6] Cutaneous lesions a`s 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.[7] 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.[8,9] Disseminated histoplasmosis occurs in HIV-infected patients with a $CD4^+$ cell count of $< 50/mm^3$, as found in most studies.[1,4] Our patient presented with a $CD4^+$ cell count of $7/mm^3$ and an expressive viral load, but besides nonspecific 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.[10] 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. ❑

REFERENCES

1. Kauffman CA. Histoplasmosis: a clinical and laboratory up-date. Clin Microbiol Rev. 2007;20:115-32.
2. Nosanchuk JD, Gacser A. Histoplasma capsulatum at the host-pathogen interface. Microbes Infect. 2008;10:973-7.
3. Control for Disease Control. (CDC). Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. Council of State and Territorial Epidemiologists; AIDS Program, Center for Infectious Diseases. MMWR. 1987;36:1s-15s.
4. Wheat L. Histoplasmosis in the acquired immunodeficiency syndrome. Curr Top Med Mycol. 1996;7:7-18.
5. Cunha VS, Zampese MS, Aquino VR, Cestari TF, Goldani LZ. Mucocutaneous manifestations of disseminated histoplasmosis in patients with acquired immunodeficiency syndrome: particular aspects in a Latin-American population. Clin Dermatol. 2009;32:250-5.
6. Goldani LZ, Aquino VR, Lunardi LW, Cunha RV, Santos RP. Two specific strains of Histoplasma capsulatum causing mucocutaneous manifestations of histoplasmosis: preliminary analysis of a frequent manifestation of histoplasmosis in southern Brazil. Mycopathologia. 2009;167:181-6.
7. Orsi AT, Nogueira L, Chrusciak-Talhari A, Santos M, Ferreira LCL, Talhari S, et al. Histoplasmosis and AIDS co-infection. An Bras Dermatol. 2011;86:1025-6.
8. Marques SA. Fungal infections of the mucous membrane. Dermatol Ther. 2010;23: 244-50.
9. Marques SA, Lastoria JC, Marques MEA. Paracoccidioidomycosis in a patient with cervical cancer. An Bras Dermatol. 2011;86:587-8.
10. Wheat LJ, Freifeld AG, Kleiman MB, Baddley JW, McKinsey DS, Loyd JE, et al. Clinical practice guidelines for management of patients with histoplasmosis: 2007 update by the Infectious Disease Society of America. Clin Infect Dis. 2007;45:807-725

MAILING ADDRESS:
Silvio Alencar Marques
Distrito de Rubião Junior S/N
18618-970 - Botucatu - SP
Brazil
E-mail: smarques@fmb.unesp.br

How to cite this article: Marques SA, Silvares MRC, Camargo RMP, Marques MEA. Cutaneous histoplasmosis disclosing an HIV-infection. An Bras Dermatol. 2013;88(3):420-3.