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E- CASE REPORT

Mucocutaneous Manifestations of Infection by *Histoplasma capsulatum* in HIV-Negative Immunosuppressed Patients[☆]

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KEYWORDS

Disseminated histoplasmosis;
Cutaneous histoplasmosis;
Immunosuppression;
Itraconazole

Abstract Histoplasmosis is a systemic mycosis caused by the dimorphous fungus *Histoplasma capsulatum* (*H. capsulatum*). The fungus enters the body through the respiratory tract in the form of microconidia, which are transformed into intracellular yeast-like structures in the lungs before disseminating hematogenously. Primary infection is usually asymptomatic and self-resolving. Some patients develop severe disease with acute or chronic respiratory involvement. Immunosuppressed patients, mainly those with altered cellular immunity, may have disseminated disease with variable mucocutaneous involvement characterized by papules, nodules, gummas, or ulcers with a granulomatous base. We report the case of 3 HIV-negative patients infected by *H. capsulatum* in whom diagnosis based on the skin lesions proved essential for early initiation of treatment.

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PALABRAS CLAVE

Histoplasmosis diseminada;
Histoplasmosis cutánea;
Inmunosupresión;
Itraconazol

Manifestaciones mucocutáneas de la infección por *Histoplasma capsulatum* en pacientes inmunosuprimidos

Resumen La histoplasmosis es una micosis sistémica causada por el hongo dimorfo *Histoplasma capsulatum* (*H. capsulatum*). Este entra en el organismo a través del tracto respiratorio en forma de microconidias, que a nivel pulmonar se transforman en elementos levaduriformes intracelulares, y luego se diseminan por vía hematógena. La primoinfección suele ser asintomática y autorresolutiva. Algunos pacientes desarrollan una enfermedad grave con

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compromiso respiratorio agudo o crónico. Los pacientes inmunosuprimidos, principalmente aquellos con alteración de la inmunidad celular, pueden presentar una enfermedad diseminada con compromiso mucocutáneo proteiforme, con pápulas, nódulos, gomas o úlceras de fondo granulomatoso. Se comunican 3 casos clínicos de pacientes inmunosuprimidos no VIH, con infección por *H. capsulatum*, en quienes el diagnóstico a partir de las lesiones cutáneas resultó fundamental para el inicio precoz del tratamiento.

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Introduction

Histoplasmosis is a systemic mycosis caused by the dimorphic fungus *Histoplasma capsulatum*, which enters the body upon inhalation of microconidia. Phagocytosis of these microconidia by alveolar macrophages transforms them into yeast-like structures, which are then disseminated in the bloodstream. Cell-mediated adaptive immunity promotes the activation of macrophages and the formation of epithelioid granulomas to control the infection.^{1,2} This response is absent in immunocompromised patients, and the infection spreads to multiple organs. We describe 3 cases of *H capsulatum* infection in patients with compromised immunity unrelated to human immunodeficiency virus (HIV) infection. In all cases, diagnosis based on skin lesions was fundamental to allow early initiation of treatment.

Case Descriptions

Case 1

A 54-year-old man reported fever, asthenia, dyspnea on moderate effort, and mucocutaneous lesions that had appeared 3 months earlier. The patient had an erythematous plaque with a tough, elastic-like consistency and diffuse borders that covered the nasal dorsum and left malar region, and on which sat a painful, rounded ulcer with a fibrinous base (Fig. 1). On the patient's soft palate was an ulcer 2 cm in diameter with clearly defined borders and a granulomatous base (Fig. 2). The results of laboratory tests were as follows: hemoglobin, 14g/dL; white blood-cell count, 5540/mm³; CD4⁺ T-cell count, low (78 cells/L); platelet count, 234 900/mm³. Liver and kidney function were normal, and the results of the tuberculin test, blood tests for HIV and hepatitis C and B, and the venereal disease research laboratory test were negative. The patient's protein profile was normal and the results of tests for antibodies (immunoglobulin M) against the Epstein-Barr virus, herpes 6 virus, cytomegalovirus, parvovirus B19, and human T-cell leukemia virus type 1 were negative. Computed tomography (CT) of the thorax, abdomen, and pelvis revealed a bilateral micronodular pulmonary infiltrate, mediastinal adenopathy, and bilateral adrenal gland hyperplasia. Direct microscopic examination of the lesions with Giemsa stain revealed intracytoplasmic yeast-like structures, with a predominantly polar staining pattern. Histology showed histiocytes and multinucleated Langhans giant cells in the dermis, with intrahistiocytic yeast-like structures. Skin cultures were

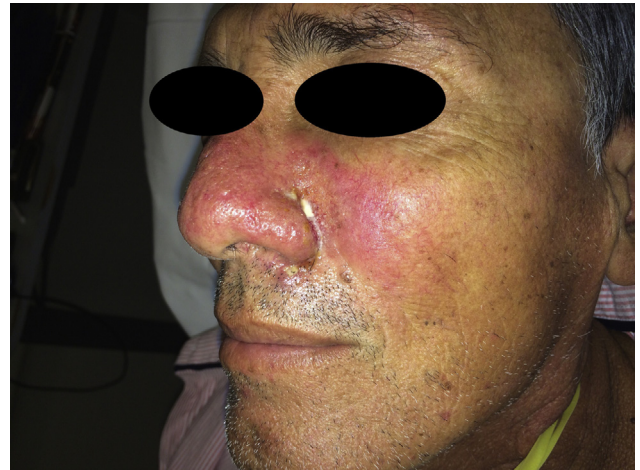


Figure 1 Hard, elastic, erythematous plaque with diffuse borders located on the nasal dorsum and the left malar region. Overlying this lesion is a rounded ulcer 5 mm in diameter with a completely fibrinous base.



Figure 2 Rounded ulcer 2 cm in diameter on the soft palate. The ulcer has well defined borders and a granulomatous base.

positive for *H capsulatum*. The patient was treated with liposomal amphotericin (3 mg/kg/d) for 10 days. Continued outpatient treatment with itraconazole (400 mg/d) for 1 year resulted in resolution of the clinical signs. Serial blood tests ruled out HIV infection. Autoantibody analyses and serial blood tests revealed no immunological or

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