

Disseminated cutaneous histoplasmosis in elderly patients. An uncommon presentation



Histoplasmosis cutánea diseminada en un paciente mayor. Una presentación poco común

Histoplasmosis is a systemic mycosis caused by *Histoplasma capsulatum*. The disseminated form is more commonly a result of reactivation of quiescent foci in immunosuppressed patients, more frequently HIV-infected.^{6,7,9} Disseminated histoplasmosis in immunocompetent individuals is rare. Among 107 cases of disseminated histoplasmosis reported from a University Hospital in Brazil only one case was observed in an immunocompetent patient.³ In a large series of 123 cases of histoplasmosis in HIV-negative immunocompetent patients, 32 (26%) were reported as subacute/chronic disseminated form, half of them associated with other systemic disease.² In these cases the picture was lung and mucosal involvement associated with lymphadenomegaly or hepatomegaly and the skin was affected in only two patients (6.2%).² On the other hand, disseminated form of histoplasmosis in HIV-infected patients shows skin lesions in up to 85% of cases.^{1,8}

We report the case of a 73-year-old male patient with a 3-month history of genital lesion associated with weight loss and general complaints. The patient denied alcohol or tobacco consumption, and systemic hypertension was the only reported co-morbidity. On examination there were rare papules on the face, genital ulcers on the glans, foreskin and scrotum (Fig. 1), and two ulcerative lesions on the legs. A diffuse reticulonodular infiltrate was observed on the lungs on computed tomography. No visceromegaly or lymphadenomegaly were detected on abdomen investigation. Laboratory workout showed 12.7 g/dl of hemoglobin as lone alteration. Albumin and globulins were in the normal range, as well as the CD4+ and CD8+ lymphocytes subpopulations. Serological tests for HIV, HBV and HBC were negative. Two skin biopsies from the genital area and from the leg showed a similar picture: ulcerative epidermis plus a lymphohistiocytic cell infiltration on the dermis with the cytoplasm of histiocytes plenty of microorganisms encircled by a clear halo. The Grocott-Gomori stain revealed fungal cells of small diameter on the cytoplasm, suggestive of *Histoplasma capsulatum* (Fig. 2). Despite the negative serologic results for histoplasmosis (double immunodiffusion), the hypothesis was confirmed through culture on Mycosel® and by thermal dimorphism. The patient was treated with itraconazol 400 mg/day for two months followed by 200 mg/day for additional two months, interrupted due to intolerance, with sustained clinical resolution after 18 months of follow-up.

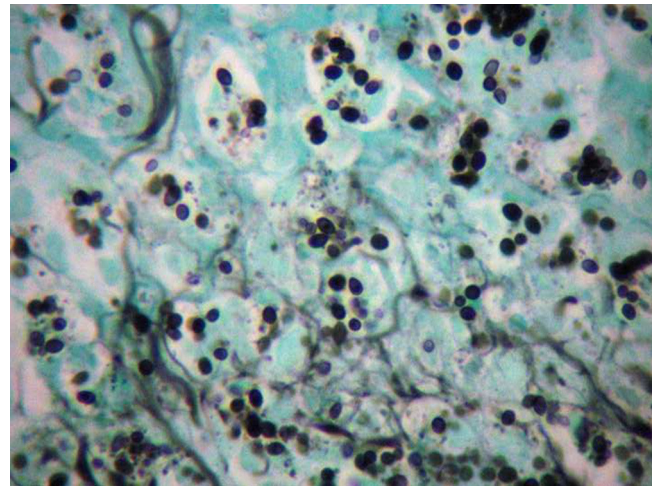


Fig. 2.

Disseminated histoplasmosis is usually associated with immunosuppression, mostly caused by HIV infection.^{6,8} Patients under chemotherapy, following solid transplants or taking corticosteroids may also be affected. There are many differences between disseminated histoplasmosis if occurring in immunosuppressed patient or, in contrast, in immunocompetent individual. Immunosuppressed patients are more commonly male, and present co-morbidities, skin lesions, positive direct examination and positive culture, and less commonly positive serology.¹⁰ The clinical profile of our patient looked quite similar to the one observed among immunosuppressed patients. As there were no co-morbidities or poor nutritional status as an associated risk factor in this case, the patient's age could be considered as a predisposing factor by itself. Immunosenescence impairs the immune system of aged individuals leading to susceptibility to infections and reduced vaccine responses.^{4,5} The effects observed on immune system includes changes in CD4 T cells, CD8 T cells, regulatory T cells, reduced intracellular signaling capacities, reduced cell replicative ability and lower antibody production.^{4,5} These alterations are closely related to the increased mortality and morbidity rates observed in the elderly. *Histoplasma capsulatum* is an intracellular microorganism whose control depends on cell-mediated immunity and satisfactory macrophages functions. This very uncommon case seems to represent an additional example of possible immunosenescence leading to severe cutaneous-systemic fungal infection.

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Fig. 1.

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Silvio Alencar Marques*, Juliana Hortense, Camila Bueno Requena, Rosângela Maria Pires de Camargo, Mariângela Esther Alencar Marques

Departamento de Dermatologia, Faculdade de Medicina, Botucatu, Brazil

* Corresponding author.

E-mail address: smarques@fmb.unesp.br (S.A. Marques).

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Onicomicosis por levaduras: agentes y estudio de sensibilidad en la región de Valparaíso, Chile



Onychomycosis due to yeasts: Agents and a sensitivity study in the Valparaíso region, Chile

Estimados Editores:

Las onicomicosis por levaduras son frecuentes en la población adulta. Entre los factores de riesgo se encuentran la diabetes mellitus, la inmunodepresión y el traumatismo ungüeal^{7,8}. Afectan principalmente a las uñas de las manos de mujeres, y *Candida albicans* y *Candida parapsilosis* son las especies aisladas con mayor frecuencia^{3,8}.

Se realizó un estudio con pacientes con onicomicosis de la región de Valparaíso, Chile, para identificar las especies implicadas y evaluar su sensibilidad a fluconazol, itraconazol y terbinafina. El estudio descriptivo y prospectivo de 117 pacientes con diagnóstico de onicomicosis por levaduras se realizó en la Cátedra de Micología de la Universidad de Valparaíso, entre los años 2011 y 2012. El examen directo fue realizado con NaOH al 40%, y los cultivos de las muestras, en agar Sabouraud y agar Lactrimel¹.

Para la identificación de las especies aisladas se utilizó agar Harina de Maíz¹, agar Clamidosporas (BBL-BDTM, EE. UU.), CHROMagar CandidaTM (CHROMagar Company Ltd., Francia), agar Sabouraud y la galería bioquímica API ID32C[®] (bioMérieux,

Francia). Las pruebas de sensibilidad se realizaron según la metodología de difusión en agar con tabletas Neo-SensitabsTM de fluconazol (25 µg), itraconazol (8 µg) y terbinafina (30 µg)¹¹. Para el análisis estadístico se emplearon los programas Excel y Stata 10. Para determinar la significación estadística se utilizó la prueba χ^2 y el test exacto de Fisher.

El 72% de los pacientes eran mujeres. Las especies aisladas con mayor frecuencia fueron *C. parapsilosis* (36,7%), *C. albicans* (26,5%) y *Candida famata* (10,2%), lo que concuerda con los resultados de otras series clínicas^{6,8,9}. *C. albicans* se aisló mayoritariamente de uñas de manos ($p = 0,001$), y *C. famata*, junto con *Trichosporon* spp., de uñas de pies ($p = 0,004$ y $p = 0,002$, respectivamente). En el 63% de las mujeres la onicomicosis estaba presente en las uñas de las manos, siendo este dato estadísticamente significativo ($p = 0,02$), en comparación con la presencia de onicomicosis en las uñas de los pies. La mayoría de los aislamientos fueron sensibles a fluconazol y a itraconazol, y resistentes a terbinafina. La [figura 1](#) y la [tabla 1](#) muestran, respectivamente, las especies aisladas y los resultados de las pruebas de sensibilidad a los antifúngicos.

Si bien el CLSI, a través del documento M44-A¹⁰, estandariza el método de sensibilidad por difusión con discos para *Candida* spp. solo para fluconazol y voriconazol, el empleo de esta metodología para otros antifúngicos con tabletas Neo-Sensitabs^{TM2-4} puede ser una alternativa en el laboratorio clínico. Esta prueba, si bien no es la de referencia, podría ser útil para orientar el tratamiento^{5,9}.

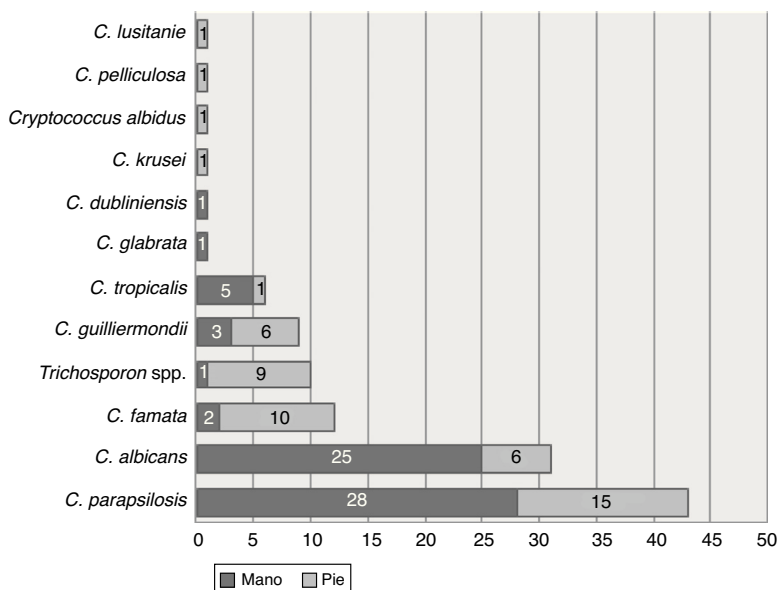


Figura 1. Frecuencia de las especies aisladas según la localización de la lesión ungüeal.