Correspondence

Accurate Diagnosis of Infection with *Histoplasma capsulatum* var. *duboisii*

Sir—Although the image of the skin biopsy specimen in the recent photo quiz by Hasse and Kronenberg [1] may represent infection with *Histoplasma capsulatum* var. *duboisii,* it does not prove the diagnosis. The fungus was apparently not cultured, and the photomicrograph of the organisms shows nothing specifically diagnostic of *H. capsulatum* var. *duboisii.* The photomicrograph of the skin specimen stained with periodic acid-Schiff stain reveals clusters of yeast that appear more round than oval and do not show the "hour-glass" or "figure eight" budding forms typical of *H. capsulatum* var. *duboisii* [2]. Chain formation and bud scars are 2 other features of this organism (figure 1); neither is demonstrated in the image provided by Hasse and Kronenberg [1].

Cryptococcus neoformans may vary in size by as much as 20 microns, and the capsular-deficient form can appear similar to the image seen in the figure provided by Hasse and Kronenberg [1]; a positive reaction with mucicarmine stain would be diagnostic. *Blastomyces dermatitis* is a similar size and also has a thick cell wall; diagnosis requires identification of broad-based buds and/or multiple nuclei. Blastomycosis is not likely in a patient from Africa or Europe.

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1. Hasse B, Kronenberg A. African immigrant with weight loss and disseminated skin lesions [photo quiz]. Clin Infect Dis **2003**; 37:692–3,726–7.
2. Chandler FW, Watts JC. *Histoplasmosis duboisii.* In: Pathologic diagnosis of fungal infections. Chicago: American Society of Clinical Pathologists Press, **1987**:141–7.

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Reply

Sir—We appreciate the comments of Klassen et al. [1]. We agree that the findings of histologic examination of the skin biopsy specimen alone are congruent with but do not prove the diagnosis of infection

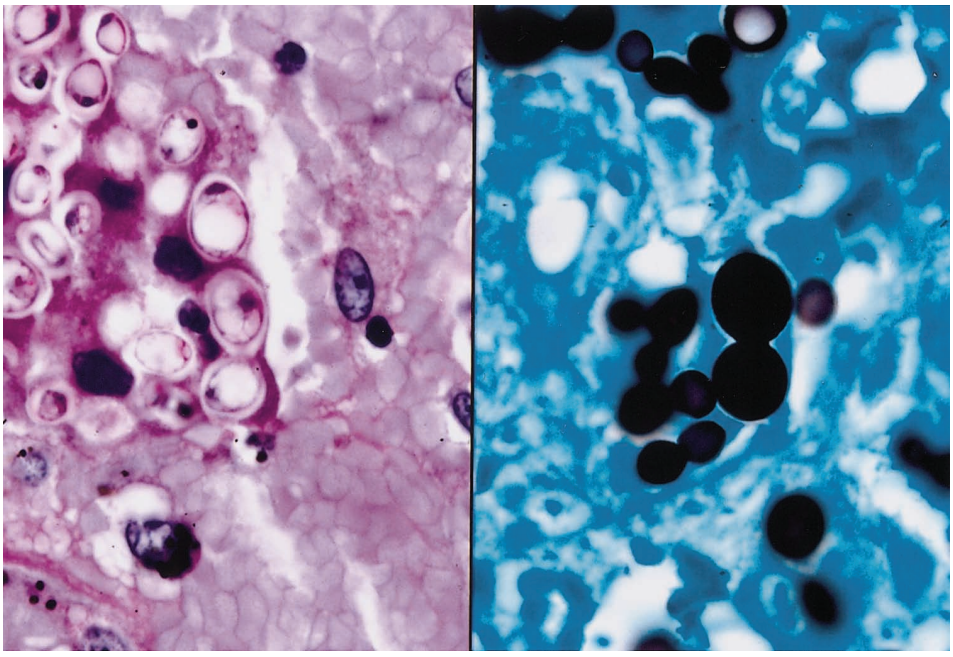

Figure 1. Photomicrographs of specimens from a lytic lesion of the right tibia demonstrating *Histoplasma capsulatum* var. *duboisii. Left,* periodic acid-Schiff staining reveals a thick cell wall, vacuolated cytoplasm, and narrow-based bud. *Right,* Grocott methenamine silver staining demonstrates the classic "hour-glass" shape of *H. capsulatum* var. *duboisii;* the parent and daughter cells are of equal size and joined by a narrow base.

with *Histoplasma capsulatum* var. *duboisii*. However, as we mentioned in the case description, we were able to cultivate *H. capsulatum* var. *duboisii* from a specimen of a relapsing skin lesion obtained 2 months after the patient had stopped taking his medication by his own decision. Furthermore, the clinical presentation was very typical for African histoplasmosis. As you mention, *Blastomyces dermatitis* infection is unlikely in an African patient. *Cryptococcus neoformans* infection could be excluded if a crytpococcal antigen test yielded a negative result.

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Reference

1. Klassen-Fischer M, McEvoy P, Neafie RC, Nelson AM. Accurate diagnosis of infection with *Histoplasma capsulatum* var. *duboisii* [letter]. Clin Infect Dis 38:595 (in this issue)

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Hypothyroidism in HIV-Infected Patients Who Have or Have Not Received HAART

Sir—Beltran et al. [1] recently reported an increase in the prevalence of subclinical hypothyroidism among HIV-infected patients, compared with the general population. This difference was particularly relevant for male patients. Moreover, the authors reported a statistically significant relationship between subclinical hypothyroidism, receipt of therapy containing stavudine, and the degree of immunodeficiency of the patients [1].

To assess the prevalence of subclinical hypothyroidism among HIV-infected patients and to identify the associated risk factors, we performed a retrospective analysis of HIV-infected patients who were untreated or who were receiving highly active antiretroviral therapy (HAART). The patients had been observed at 6 departments of infectious diseases and had total thyroxine and thyroid-stimulating hormone levels measured during the period of January 2000 through December 2002. Thyroid function had generally been assessed during routine testing or as part of the screening examinations performed before treatment of hepatitis C virus (HCV) coinfection and chronic hepatitis. None of these patients had any symptoms of altered thyroid function.

We investigated 687 patients observed in 6 infectious diseases departments belonging to the Coordinamento Italiano Studio Allergia e Infezione da HIV group. A total of 446 patients (65%) were men, and the mean age ($\pm$SD) was 40.5 $\pm$ 8.5 years. The mean $CD4^+$ lymphocyte count ($\pm$SD) when the thyroid function was checked was 469 $\pm$ 267 cells/mm^3. Three hundred thirty-two patients (48.3%) tested positive for HCV antibody, none of whom were receiving IFN therapy at the time. Fifty-nine patients were naive to antiretroviral therapy, and 628 were receiving HAART.

In 51 patients (7.42%), we detected subclinical hypothyroidism; 5 (9.8%) of these patients were treatment naive, and 46 (90.2%) were receiving antiretroviral therapy. The frequency of this disease among male subjects was 7.11%, which was slightly lower than the frequency among female subjects (8.71%). The results of tests for antithyroglobulin antibody and thyroid antimicrosomes performed for 270 cases were negative.

To assess risk factors, we considered the following covariates: age, sex, stage and duration of infection, $CD4^+$ lymphocyte count when thyroid function was tested, positive results of tests for HCV antibody, and, in patients receiving HAART, total duration of HAART and of treatment with protease inhibitors. Statistical differences between general and clinical characteristics were analyzed using the χ^2 test, comparing observed and expected events. ORs, as estimators of relative risks, were computed using unconditional multiple logistic regression.

None of the variables considered were significantly related to the onset of subclinical hypothyroidism. In particular, we did not find a statistically significant relationship between subclinical hypothyroidism and any drug or the degree of immunodeficiency.

The results from our study confirm the data on the prevalence of subclinical hypothyroidism reported by Beltran et al. [1] and others [2, 3]. Our results also confirm that the prevalence of this condition is higher among male subjects, compared with men in the general population. In our cohort, we noted subclinical hypothyroidism in both treatment-naive and HAART-treated patients with a similar prevalence. In contrast with the findings of Beltran et al. [1], we found no clear risk factors in HAART-receiving subjects that were related to the occurrence of subclinical hypothyroidism.

Our data, if confirmed in a prospective study, might raise issues regarding the pathogenesis of subclinical hypothyroidism as it relates to HIV infection itself. However, it appears to be important to periodically assess thyroid function in HIV-infected patients, especially in view of the possibility that subclinical hypothyroidism might be a risk factor for cardiovascular disease [4].

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