An Exophytic Mass on the Mandible of an Immunocompromised Man

(See page 540 for the Photo Quiz.)

Diagnosis: Coexistent Cryptococcus neoformans and Kaposi sarcoma in a patient with AIDS.

Histopathologic examination revealed multiple budding yeast forms surrounded by a clear halo (Figure 1A). Grocott-methamine-silver and mucicarmine (Figure 1B) stains highlighted these organisms and their capsules, respectively. A proliferation of atypical spindle cells arranged in fascicles, associated with slit-like vascular spaces and extravasated red blood cells, was also identified (Figure 1A). Immunohistochemistry for human herpesvirus 8 demonstrated positive nuclear staining within these spindled cells (Figure 2). These findings were diagnostic for cutaneous Cryptococcus infection in the context of Kaposi sarcoma (KS).

The patient was treated with amphotericin B and flucytosine followed by fluconazole for his cryptococcal infection; emtricitabine, tenofovir, and raltegravir were initiated as therapy for AIDS. Doxorubicin therapy was initiated for probable multifocal KS. The patient’s cutaneous lesions have improved on this regimen, with concomitant resolution of his lower extremity swelling and improvement in breath sounds. His human immunodeficiency virus (HIV) load is currently undetectable.

Cutaneous disorders are estimated to affect approximately 64% of patients with HIV, with an increasing prevalence at lower CD4 counts [1]. These conditions include common infections and malignancies such as Staphylococcus aureus and squamous cell carcinoma, as well as a variety of inflammatory dermatoses that are often more severe than in immunocompetent patients [1]. Of particular concern are those opportunistic infections and neoplasms that are classified as AIDS-defining illnesses, including cryptococcosis and KS. Often these conditions have a protean presentation and may simulate one another [2, 3]. Nevertheless, the coexistence of Cryptococcus and KS in a single clinical lesion is an uncommon occurrence [4–8]. Colocalization of these infections may be the presenting sign of AIDS in patients with known HIV or those who had been previously undiagnosed; it has also been associated with paradoxical immune reconstitution inflammatory syndrome (IRIS) following initiation of highly active antiretroviral therapy (HAART) [5, 8]. The latter association is particularly noteworthy as significant morbidity and mortality are associated with KS-IRIS, particularly among patients with visceral KS [9].

Figure 1. Punch biopsy of the mandible. A, Hematoxylin-eosin stain. A proliferation of atypical spindle cells arranged in fascicles was present in the mid-to-deep dermis, consistent with a diagnosis of Kaposi sarcoma (arrow). Adjacent to these cells are budding yeast forms surrounded by clear halos, indicative of cutaneous cryptococcosis (arrowhead) (×100 magnification). B, Mucicarmine stain. The capsules of Cryptococcus organisms are highlighted (arrow) (×400 magnification).
KS-IRIS may be more difficult to treat than other forms of IRIS and has important prognostic implications [9]. Cutaneous biopsy with meticulous histologic evaluation is therefore suggested in all HIV-infected patients with new or unusual skin lesions, even in the context of previously treated or active skin disorders. This practice guards against misdiagnosis of alternative or coincident disease. Multiorgan evaluation for cutaneous and visceral KS may be especially prudent in those patients who have also recently initiated HAART.

Rarely, KS can present with other viral, mycobacterial, or opportunistic fungal infections in the same lesion. In addition to cryptococcosis, other coincident infections include cytomegalovirus, molluscum, Candida albicans, Mycobacterium tuberculosis, Histoplasma capsulatum, and Mycobacterium avium-intracellulare [4, 10, 11]. An instance of KS coexistent with both Cryptococcus and Mycobacterium avium-intracellulare has also been reported [4]. The etiology of this phenomenon is unknown, and may represent a chance occurrence. It has also been hypothesized that the vascular lesions of KS represent an ideal environment for the growth and protection of blood-borne opportunistic infections [4]. Conversely, cryptococcal infection may induce a local inflammatory milieu that is hospitable to the development of KS, a concept known as inflammatory oncotaxis [7, 12]. These suppositions remain speculative, however, and the pathophysiologic mechanisms underpinning this unusual occurrence remain to be formally elucidated.

Notes

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Drafting of the manuscript: H. G., M. D. B. Critical revision of the manuscript for important intellectual content: H. G., C. M., M. D. B. All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Figure 2. Punch biopsy of the mandible (human herpesvirus 8 stain). Nuclear staining of spindled cells arranged in fascicles within the dermis confirms the diagnosis of Kaposi sarcoma (>200 magnification).

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