Persistent eyelid ulceration in an immunocompromised host: A cutaneous sign with the potential for early diagnosis and intervention in disseminated cryptococcosis

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INTRODUCTION

Cryptococcosis is an infection caused by the ubiquitous encapsulated yeast of the genus *Cryptococcus*.[1] It is an opportunistic pathogen that may manifest systemically in immunocompromised individuals, primarily as pneumonia, meningitis, and disseminated cutaneous lesions.[2] Skin involvement occurs in 10% to 20% of cases.[3] Although primary direct inoculation of the skin may be seen, cutaneous lesions typically manifest secondarily via hematogenous spread in immunocompromised patients with severe systemic disease.[4] We present a case of disseminated cryptococcosis manifesting as a solitary ulcer on the eyelid of an immunocompromised patient.

CASE REPORT

A 67-year-old man with a medical history significant for renal transplant presented to the emergency department with 5 days of intermittent fevers, generalized malaise, nausea, vomiting, and diarrhea. He additionally reported a history of *Pneumocystis jiroveci* pneumonia and multidrug-resistant urinary tract infections related to the chronic use of systemic tacrolimus, mycophenolate mofetil, and prednisone. He was given a diagnosis of enteroaggressive *Escherichia coli* colitis, Carbapenem-resistant Enterobacteriaceae *Klebsiella* pneumonia, and an *Enterococcus faecalis* urinary tract infection.

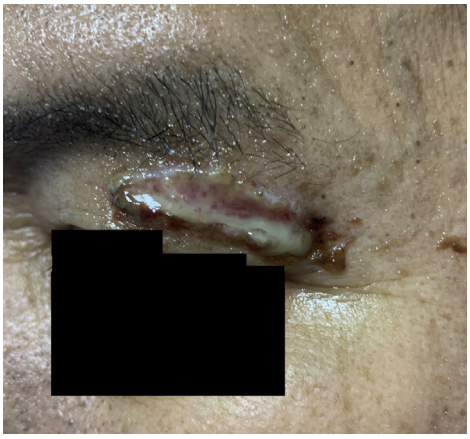

Fig 1. Cutaneous cryptococcosis. Clinical presentation shows a 3-cm deep, ovoid ulcer with heaped up borders, overlying purulence, and honey-colored crust on the left lateral upper eyelid.

Because of his altered mental status, a lumbar puncture was also performed, with cerebrospinal fluid polymerase chain reaction testing positive for cryptococcal antigen.

Incidentally, the patient was noted to have an ulcer on the left eyelid, which he attributed to a pimple that he picked repeatedly for the last 2 months. The dermatology department was consulted, and initial examination found a 3-cm tender, deep, ovoid ulcer on the lateral left upper eyelid with

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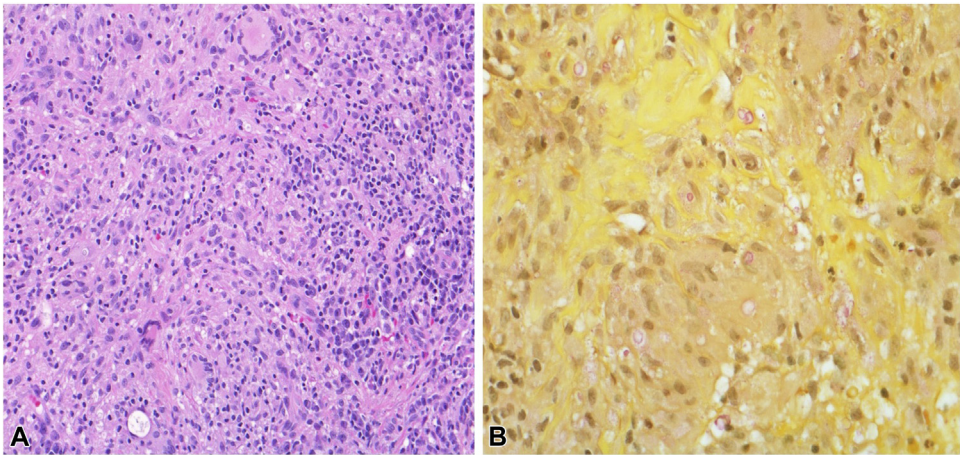

Fig 2. Histopathologic evaluation of punch biopsy specimen from the left lateral upper eyelid. **A**, Hematoxylin-eosin stain; original magnification: ×20. **B**, Positive mucicarmine stain supporting the diagnosis of cutaneous cryptococcosis. (Original magnification: ×40).

heaped up borders, overlying purulence, and honey-colored crust (Fig 1). The differential diagnosis included a localized herpes simplex virus infection and nonmelanoma skin cancer as well as cutaneous cryptococcosis, blastomycosis, and coccidioidomycosis. Wound culture and polymerase chain reaction tests for herpesviruses were negative. A tangential biopsy found granulomatous inflammation associated with refractile yeast compatible with cryptococcosis, and a positive mucicarmine stain corroborated the diagnosis (Fig 2). Treatment with amphotericin B and flucytosine resulted in complete resolution of the cutaneous lesion as well as central nervous system involvement.

DISCUSSION

Cryptococcosis affects 2.8% of all solid organ transplant patients and accounts for 8% of invasive fungal infections in this population.[1] Disease-specific mortality rates range from 17% to 37% with initial infection to 100% for relapsed systemic disease.[5] Cutaneous involvement is not uncommon and can be the presenting sign of infection, heralding symptoms of systemic disease by up to 8 months. However, with no archetypal lesion, this diagnosis is easily missed, especially as the various clinical presentations habitually mimic more common skin diseases that are treated empirically without histopathologic workup.[4] This delay in diagnosis may allow for progression of the underlying systemic infection as well as the severity of its consequences.

As such, cryptococcosis should be considered a diagnostic possibility in the immunocompromised patient with any cellulitis-, molluscum-, or herpes simplex–like lesions; however, clinicians must additionally be aware of the vast spectrum of alternative primary lesion morphologies, which includes acneiform lesions, purpura, vesicles, nodules, abscesses, ulcers, granulomas, pustules, and draining sinus tracts.[4] This expansive range of possible cutaneous manifestations emphasizes the crucial role dermatologists play in making this challenging diagnosis and facilitating timely intervention, as a solitary, innocuous-appearing lesion can be the heralding sentinel for a severely morbid underlying systemic disease.

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