Disseminated cryptococcosis with cutaneous manifestation

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Abstract
Cutaneous cryptococcosis is uncommon. It is usually a result of disseminated infection and can present with a wide variety of skin lesions. We report a case of disseminated cryptococcosis in a kidney transplant recipient who presented with nodular lesions in the forehead following a bout of acute cellular rejection.

Keywords
Cryptococcosis, cutaneous, kidney, transplant

1 | CASE

A 60-year-old male presented 2 years after kidney transplant with soft, fleshy, non-tender, nodular lesions on the forehead with central umbilication, ulceration, and necrosis (Figure 1). These lesions developed over a period of three weeks. He had no other skin lesions except human herpes simplex 2 (HSV 2)-related perirectal ulceration. About a month prior to this, he had been treated with methylprednisone followed by a prednisone taper for a bout of acute cellular rejection. At the time of presentation, he was on tacrolimus, mycophenolate, and prednisone 10 mg a day. He was alert and oriented. He did not have chest pain or dyspnea but endorsed intermittent fevers, minimal cough, and generalized weakness. The shave biopsy of the largest lesion in the forehead showed ulceration and necrosis, and a dermis laden with budding yeast cells ranging from 5 to 15 micrometer in diameter, with peripheral clearing consistent with a mucinous capsule, compatible with Cryptococcus species on hematoxylin and eosin stain (x400) (Figure 2).

The CT chest showed large pulmonary nodules consistent with cryptococcomas (Figure 3). Serum and cerebrospinal fluid (CSF) cryptococcal antigen titers were greater than 1:2560 and 1:2560, respectively. Both peripheral blood and CSF cultures grew Cryptococcus neoformans var grubii, confirming disseminated cryptococcosis involving the skin, lungs, and the central nervous system (CNS). The patient was treated with liposomal amphotericin B and 5-flucytosine for 21 days followed by fluconazole with a good response.

2 | DISCUSSION

Cryptococcosis is the third most common invasive fungal infection in solid organ transplant (SOT) recipients after candidiasis and aspergillosis. In a recent study from Canada, where Pneumocystis jiroveci was relatively common, cryptococcosis lost its place to the fourth position among the common invasive fungi in SOT. It usually occurs more than a year after transplant with a median time of onset of 575 days following transplant. Cutaneous manifestation of cryptococcosis is the third most common presentation (after CNS and pulmonary) but nonetheless remains uncommon. In a review of 146 SOT recipients with cryptococcosis, only 26 (18%) had cutaneous manifestation—half of which were kidney transplant recipients. The cutaneous lesions have a non-specific manifestation, and an affected individual may present with more than one type of lesion (eg, nodule and cellulitis presenting concurrently). In fact in the study by Sun et al, there were overlapping presentations with 35% of the lesions presenting as nodules or mass, 30% as maculopapular lesions, 30% as ulcers or pustules or abscess, 30% as cellulitis, and a few cases as vesicles, bullae, and hemorrhagic lesions. Two third of the lesions occurred in lower extremities with forehead and neck accounting for only 4% cases. Cutaneous manifestation is usually a part of disseminated disease as was seen in 70% cases in the study by Sun et al. Hence, a diagnosis of cutaneous cryptococcosis should lead to further investigation including lumbar puncture to rule out disseminated infection (especially infection in the lungs and the CNS). The diagnosis is usually made by culture (tissue and body fluids including CSF and blood), serum and CSF antigen tests, and histopathology of biopsy specimens. In SOT recipients, even cryptococcosis presenting solely as cutaneous lesions without evidence of infection elsewhere is likely a result of occult dissemination. Primary cutaneous cryptococcosis without disseminated disease is uncommon but can occur via traumatic skin inoculation and generally presents as a solitary lesion in exposed skin susceptible to trauma (usually upper extremities) in relatively immunocompetent people.
CONFLICTS OF INTEREST
None (all authors).

AUTHOR CONTRIBUTION
MMJ involved in interpretation of histopathology and critical review of the manuscript. KG involved in writing of the manuscript.

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