Multiple ulcers in an immunocompromised patient

A 60-year-old male presented to the dermatology outpatient department of the Postgraduate Medical Institute of Medical Education and Research, Chandigarh with multiple, crusted, ulcerative lesions of 2 months duration on the face. He had undergone renal transplantation 1 year ago for end-stage renal disease secondary to diabetic nephropathy, and was on oral prednisolone and tacrolimus. He had no other systemic complaints. No history of trauma or exposure to bird droppings was recalled. On cutaneous examination, there were four ulcers with rolled edges ranging in size from 1 × 1 cm to 1.5 × 1.5 cm, with overlying yellowish-brown to hemorrhagic crusting on the glabella, dorsum of nose and left cheek [Figure 1]. A punch biopsy from the ulcer margin was obtained and submitted for histopathological examination and culture (fungal and bacterial) [Figure 2a-c].

Question

What is the diagnosis?

Figure 1: Ulcers with rolled edges with overlying yellowish-brown to hemorrhagic crusting on the glabella, dorsum of nose and left cheek

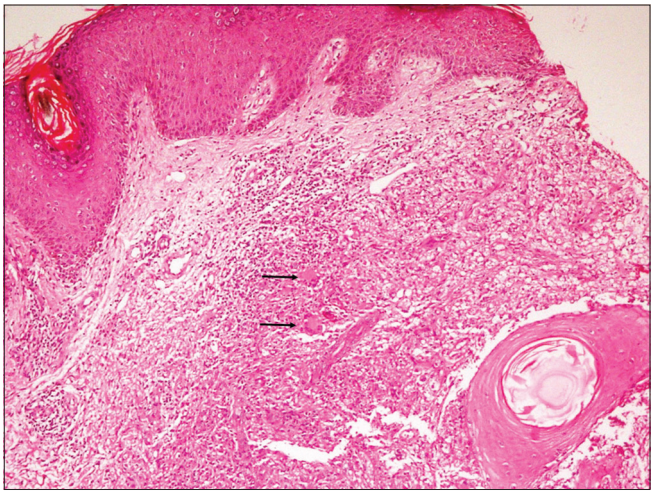

Figure 2a: Skin biopsy showing acanthosis and histiocytic infiltration in the dermis with presence of few multinucleated giant cells (shown by black arrows) (H and E, ×100)

Access this article online	
Quick Response Code:	Website: www.ijdvl.com
	DOI: 10.4103/ijdvl.IJDVL_538_17

How to cite this article: Bhattacharjee R, Chatterjee D, Narang T. Multiple ulcers in an immunocompromised patient. Indian J Dermatol Venereol Leprol 2020;86:394-7.

Received: September, 2017. **Accepted:** July, 2018.

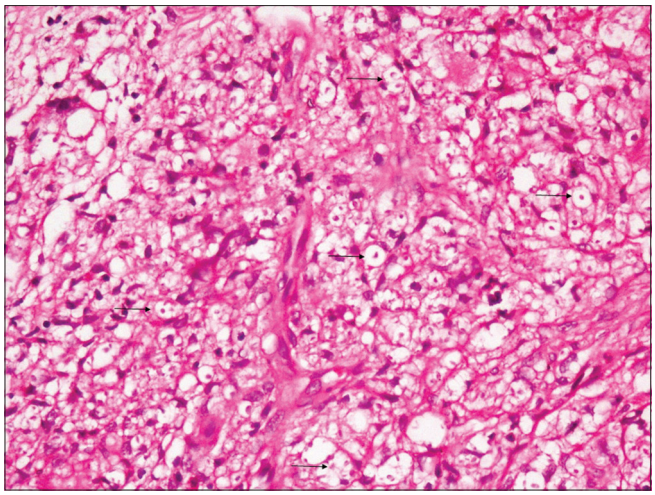

Figure 2b: Dermis showing numerous fungal profiles with yeast forms ranging from 5 to 15 μ (some are shown by black arrows) (H and E, ×400)

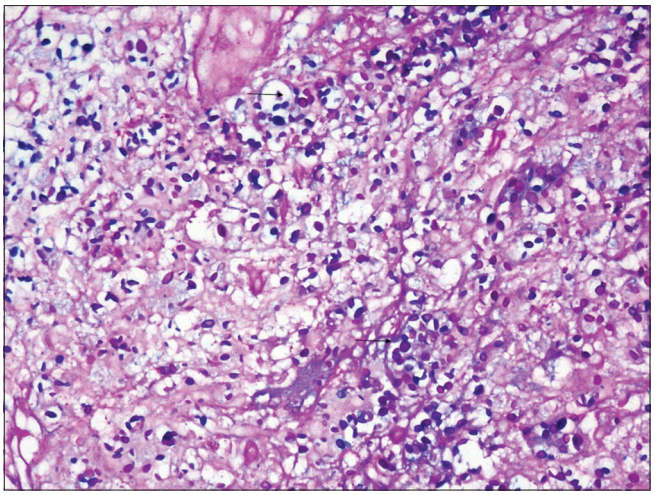

Figure 2c: The fungal yeast forms are better highlighted by Alcian blue-periodic acid-Schiff stain with few showing narrow neck budding (black arrows showing budding) (Alcian blue-periodic acid Schiff, ×400)

Figure 3: Almost complete resolution of the ulcers with minimal residual induration and atrophy

Answer

Cutaneous cryptococcosis in a post-renal transplant patient.

Investigations and Follow-up

Biopsy from the lesion showed scattered, foreign body giant cells and dense collection of foamy macrophages in the dermis. Many of the macrophages showed the yeast form of fungal element measuring 5–20 μ in diameter, and were positive on periodic acid-Schiff staining [Figure 2c]. Fungal culture from the biopsy tissue specimen grew *Cryptococcus neoformans var grubii*. High-resolution computed tomography of the chest and CD4 counts were normal. Cerebrospinal fluid examination for cryptococcal antigen and human immunodeficiency virus serology was negative. Blood and urine cultures were negative for fungus.

The patient was treated with oral itraconazole 200 mg daily, and within 1 month, there was significant improvement in the lesions with marked decrease in crusting and induration. At 12 weeks follow-up, the ulcers had healed almost completely. Itraconazole was stopped by 16 weeks. At the 10-month follow-up, he continues to be lesion free without any evidence of cutaneous or systemic infection [Figure 3].

Discussion

Cryptococcus neoformans, an encapsulated yeast, is a common opportunistic human pathogen, especially in immunocompromised hosts. Inhalation by the respiratory route is the most common mode of acquiring infection, disseminating via the hematogenous route.

Cryptococcosis is a serious complication in the post transplant period, occurring in approximately 2.8% of the patients undergoing solid organ transplant, with mortality ranging from 33% to 42%.[1] Skin involvement may be isolated, that is, primary cutaneous cryptococcosis, (31%) or associated with systemic infection (69%).[1]

It mainly affects men of around 40 years of age. Skin lesions occur more commonly on the extremities in the form of maculopapule, nodule, ulcer, pustule, abscess or cellulitis. Necrotizing fasciitis, eschar, bone or joint involvement and cellulitis with necrotizing vasculitis have also been reported.[2,3] Clinically, the lesions may resemble leishmaniasis, which was another differential diagnosis considered in our case. The morphology of the lesions and the immunocompromised status of the patient also led us to consider multiple basal cell carcinomas as a differential diagnosis. Histological examination with demonstration of fungal profile using special stains is usually diagnostic, as in our case. However, at low power magnification, histology can mimic xanthogranuloma or lepromatous leprosy if the fungal load is low.

Most cases of cutaneous cryptococcosis in solid organ transplant recipients have had disseminated disease. Hence, a diagnosis of cutaneous cryptococcosis should prompt a thorough investigation of cerebrospinal fluid, blood and the lungs to look for systemic involvement. In our patient, no signs of other sites of skin or other organ involvement were found during the 10-month follow-up.

Although no test is currently sensitive enough to rule out dissemination in cutaneous cryptococcosis, a positive antigenemia could be predictive of systemic dissemination (e.g., meningitis); however, a negative result does not exclude the diagnosis.[3]

The choice of treatment for cryptococcosis depends on the anatomic site of infection and the host immune status. Several antifungal agents have been used for the treatment of cutaneous cryptococcosis, with fluconazole and itraconazole being preferentially used, especially in cases localized exclusively to the skin. A report on the practice guideline for the management of cryptococcal infection recommended use of azoles for non-central nervous system cryptococcal infections, including cutaneous disease.[4] Most patients with primary cutaneous cryptococcosis respond favourably to short-term monotherapy. Patients should be evaluated at frequent intervals for at least one year, as relapse after that is rare.[5]

Our case highlights a typical presentation of localized cutaneous cryptococcosis in a renal transplant patient. Awareness and high index of suspicion is needed for early diagnosis and treatment, especially to pick up disseminated disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Rajsmita Bhattacharjee, Debajyoti Chatterjee[1], Tarun Narang

Departments of Dermatology, Venereology and Leprology and [1]Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Correspondence: Dr. Tarun Narang, Department of Dermatology, Venereology, and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh, India.
E-mail: narangtarun@yahoo.co.in

References

1. Sun HY, Alexander BD, Lortholary O, Dromer F, Forrest GN, Lyon GM, *et al.* Cutaneous cryptococcosis in solid organ transplant recipients. Med Mycol 2010;48:785-91.
2. Biancheri D, Kanitakis J, Bienvenu AL, Picot S, Morelon E, Faure M, *et al.* Cutaneous cryptococcosis in solid organ transplant recipients: Epidemiological, clinical, diagnostic and therapeutic features. Eur J Dermatol 2012;22:651-7.
3. Lanternier F, Chandesris MO, Poirée S, Bougnoux ME, Mechai F, Mamzer-Bruneel MF, *et al.* Cellulitis revealing a cryptococcosis-related immune reconstitution inflammatory syndrome in a renal allograft recipient. Am J Transplant 2007;7:2826-8.
4. Saag MS, Graybill RJ, Larsen RA, Pappas PG, Perfect JR, Powderly WG, *et al.* Practice guidelines for the management of cryptococcal disease. Infectious Diseases Society of America. Clin Infect Dis 2000;30:710-8.
5. Zorman JV, Zupanc TL, Parac Z, Cucek I. Primary cutaneous cryptococcosis in a renal transplant recipient: Case report. Mycoses 2010;53:535-7.