

## Disseminated cryptococcosis presenting as cellulitis

Sir,

Cryptococcosis is commonly associated with immunosuppression and the primary site of infection is usually lungs; however, a cutaneous form of infection is seen in about 6–10% of patients. The cutaneous lesions develop as a result of dissemination or rarely, through direct inoculation. Major cutaneous findings include umbilicated or acneiform papules, pustules progressing to crusted plaques, or nodules.<sup>1,2</sup> Cryptococcal cellulitis is not commonly considered as a differential diagnosis in a patient without acquired immunodeficiency syndrome (AIDS) or history of undergoing organ transplant. We report cryptococcal infection presenting as cellulitis in a patient with renal failure, undergoing oral steroid therapy.

A 63-year-old man was referred for skin lesions over the left forearm accompanied by high fever, for three weeks. He had chronic kidney disease for the past 20 years for which he was undergoing continuous ambulatory peritoneal dialysis. He had developed recurrent episodes of spontaneous bacterial peritonitis during the treatment and encapsulating peritoneal sclerosis, probably secondary to the peritonitis. Bacterial culture from the ascitic fluid confirmed *Klebsiella pneumoniae* infection. The patient was treated with intravenous cefotaxime and ciprofloxacin for bacterial peritonitis and peritonectomy was carried out as treatment for peritoneal sclerosis. He had also been prescribed oral prednisolone as part of the treatment protocol for peritoneal sclerosis, which he was taking in a dose of 10–45 mg per day for 5 months. The patient had previously undergone a procedure for autologous arteriovenous fistula (AVF) 4 years ago, in preparation for hemodialysis. He did not recall any history of exposure to bird droppings or other local injury.

Local examination revealed tender, erythematous, indurated erosive patches with blistering, ulceration and oozing at the site of previous surgery on the left forearm [Figure 1]. The clinical features were similar to bacterial cellulitis, therefore, intravenous vancomycin was administered for 4 days without significant improvement. Laboratory tests showed only a mild leukocytosis (13,200/ $\mu$ L) with an absolute neutrophil count of 12,764/ $\mu$ L. Serum HIV antigen and antibody



**Figure 1: Tender swollen eroded patches on the left forearm (whitish material overlying the skin lesion is the remnant of topical preparation applied by the patient)**

testing were negative. Chest X-ray did not reveal any remarkable abnormalities. Punch biopsy was performed from the skin lesion. Periodic acid-Schiff (PAS) and Grocott's methenamine silver (GMS) stains on the histopathology sections revealed numerous positively stained fungal spores [Figure 2a and b]. Blood cultures were done along with pus cultures from the affected site, using Sabouraud agar media. *Cryptococcus neoformans* infection was confirmed in both studies. Based on these findings, the patient was diagnosed with disseminated cryptococcosis, presenting as cellulitis. Echocardiography and spinal fluid tap were also carried out but there was no significant abnormality.

To minimize the risk of nephrotoxicity, the patient was treated with intravenous liposomal amphotericin B, 4 mg/kg/day for 4 weeks as induction therapy. The skin lesions showed gradual improvement with disappearance of blisters and erosions during the treatment period [Figure 3]. Oral fluconazole, 400 mg/day was prescribed for 8 weeks, as consolidation therapy at the time of discharge. Oral fluconazole was further continued in a dose of 200 mg/day after the consolidation period for maintenance. The patient was allowed to continue oral prednisolone (30 mg per day) during antifungal treatment. The skin lesions had completely resolved at the follow-up appointment after 9 months, with no signs of recurrence. The arterio-venous fistula is intact and hemodialysis is being continued until now.

Cryptococcosis is a systemic infection caused by the encapsulated yeasts of *Cryptococcus* species. It is mainly encountered as a complication of AIDS, but also rarely observed in non-AIDS, non-organ

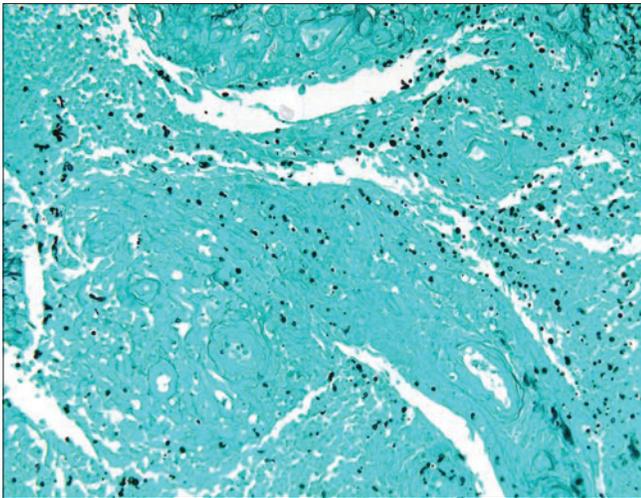


Figure 2a: Dark brown stained spores are observed (GMS, x200)

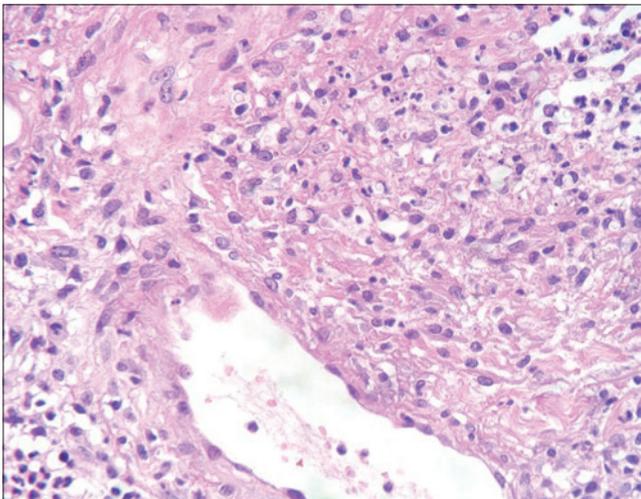


Figure 2b: Spores surrounded by wide capsules (H and E, x400)



Figure 3: Resolving lesions after intravenous amphotericin injections for a month

transplant recipient patients. *Cryptococcus* was grown in blood culture and seen on skin biopsy in our patient. This could be a result of dissemination due

to secondary hematologic spread from a cutaneous portal of entry but due to lack of evidence or definite history of this mode of spread, we preferred the label of disseminated cryptococcosis. Cutaneous infections are reported to be observed in only up to 10% of disseminated cryptococcosis and the lesions usually appear as painless papules which ulcerate at the summit. Ulcerated papules may become a plaque or could be covered by serosanguinous crust. Cellulitis-like presentation is considered as a relatively rare presentation of cryptococcal infection. There are several previous reports of cryptococcal cellulitis in non-AIDS, non-organ transplant recipient patients. These cases developed in patients taking systemic steroids for a long time period for underlying diseases such as myelodysplastic syndrome or nephrotic syndrome. The differential diagnoses considered for skin lesions should include herpes, histoplasmosis, tuberculosis, molluscum contagiosum and syphilis.<sup>3</sup> Diagnosis can be made by direct mycological examination with India-ink stain revealing large (5–15 µm) budding cells with capsules. Additional diagnostic tools include serological tests and biopsy with GMS and PAS staining positive for yeast form. The treatment of choice for cryptococcosis without central nervous system involvement is oral fluconazole, 400 mg daily for 6–12 months. However, in our case, considering the prolonged oral steroid therapy and kidney failure, the patient was treated and showed remission with intravenous liposomal amphotericin B, followed by consolidation and maintenance therapy with fluconazole.

Skin lesions may precede other systemic manifestations of cryptococcosis and some of them may be serious including meningitis. Therefore, careful evaluation is needed in those who present with skin lesions. Here, we report a rare case of cutaneous cryptococcal infection with an unusual presentation of cellulitis with fungemia. Furthermore, the fact that this case has uncommonly occurred in a non-HIV, non-organ transplant recipient highlights the importance of suspecting cutaneous cryptococcal cellulitis in antibiotic resistant cases, especially if they are on long-term steroids, given the high mortality rate of untreated cryptococcosis.<sup>4,5</sup>

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#### Conflicts of interest

There are no conflicts of interest.

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