# Extensive Primary Cutaneous Cryptococcosis in a Patient with HIV: A Rare Case

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**Cryptococcosis is an infection caused by encapsulated yeast Cryptococcus neoformans. It primarily affects the lungs before manifesting in the skin. Direct skin infection or primary cutaneous cryptococcosis can occur, but is rare. We report here a rare case of primary cutaneous cryptococcosis in a patient with HIV with extensive skin lesions, who showed improvement after receiving fluconazole monotherapy.**

Keywords: primary cutaneous cryptococcosis; human Immunodeficiency virus, fluconazole monotherapy.

## Introduction

Cryptococcosis is an opportunistic infection caused by *Cryptococcus neoformans*, which is found in the environment, including in soil, dust, and bird droppings. *C. neoformans* can be found in tropical areas of the world (1). The main infection route is through inhalation; thus lung infection is the primary infection site (2, 3). Cryptococcus is usually disseminated from the lungs; however, direct infection to the skin is possible and is called primary cutaneous cryptococcosis. Cryptococcosis is a rare infection, with an estimated prevalence in the general population of 1 in 2.4 million, while the corresponding figure in patients with HIV is approximately 3–12% (4). It is classified into pulmonary cryptococcosis, central nervous system (CNS) cryptococcosis, and disseminated cryptococcosis. Among these types of cryptococcosis, cutaneous cryptococcosis is one of the rarest, with a prevalence of 0.5–13% in patients with HIV (5). Du et al. (6) found that cutaneous cryptococcosis occurs mostly in men, with a male:female ratio of 17:4. Lesions varied in morphology and may resemble molluscum contagiosum, histoplasmosis, and *Penicillium marneffei*. Other clinical features were papules, pustules, tumours, plaques, abscesses, cellulitis, purpura, fistula, ulcers, bullae, subcutaneous swelling, herpetiform, purplish lichenoid, nodular, and Kaposi-like cryptococcosis sarcoma (3, 7).

## Case Report

A 35-year-old man reported painful nodules over almost his entire body during the past month. The nodules first appeared on his right hand and then enlarged, ruptured, secreted yellow liquid, and eventually spread to his entire body. He had intermittent fever. The patient had been diagnosed with HIV infection and pulmonary tuberculosis (TB) one year previously in primary healthcare. A diagnosis of pulmonary TB had been made based on acid-fast bacillus testing from sputum. He had been treated with antiretroviral therapy for one year, but this was stopped one month prior to admission. He had received a multidrug treatment regimen for TB for 3 months, but then discontinued his medication. He is heterosexual, with no history of headache, seizures, decreased consciousness, or weakness of the extremities. His neighbour kept pet doves.

Dermatological examination revealed extensive multiple umbilicated papules and nodules with some lesions covered with red crusts (Fig. 1). There were no lesions on the palms, feet, mucosa of the mouth, or genitals. There was no cervical or axillary lymphadenopathy, a sign of meningeal irritation, or neck stiffness. Blood tests showed low haemoglobin (Hb) level, 9 g/dl (normal value: 13–17 g/dl), low CD4 1 cell/µl (normal value: 470–1,298 cell/µl), IgM anti-cytomegalovirus (CMV) 0.21 COI (cut-off index) (non-reactive <0.7 COI; indeterminate 0.7–<1.0 COI; reactive ≥11.0 COI), IgG anti-CMV 66 U/ml (non-reactive 0.5 U/ml; indeterminate 0.5–<1.0 U/ml; reactive ≥ 1.0 U/ml), IgM anti-Rubella 0.16 COI (non-reactive < 0.8 COI; indeterminate 0.8–<1.0 COI; reactive ≥ 1.0 COI), IgG anti-Rubella 71 IU/ml (non-reactive <10 IU/ml; reactive ≥ 10 IU/ml). Chest X-ray showed no abnormalities in the lungs and no further investigations were performed.

Histopathological examination revealed epidermis with irregular psoriasiform hyperplasia and micro-ulceration. There was no proliferation of blood vessels in the dermis, but there was an infiltration of lymphocytes, histiocytes, and dense neutrophils (Figs 2A–C). Periodic acid-Schiff staining revealed large rounded capsular spores (Fig. 2D). Creamy coloured fungal colony mucus was seen in Saboraud dextrose agar. Indian ink staining showed globular white capsuled yeast, which

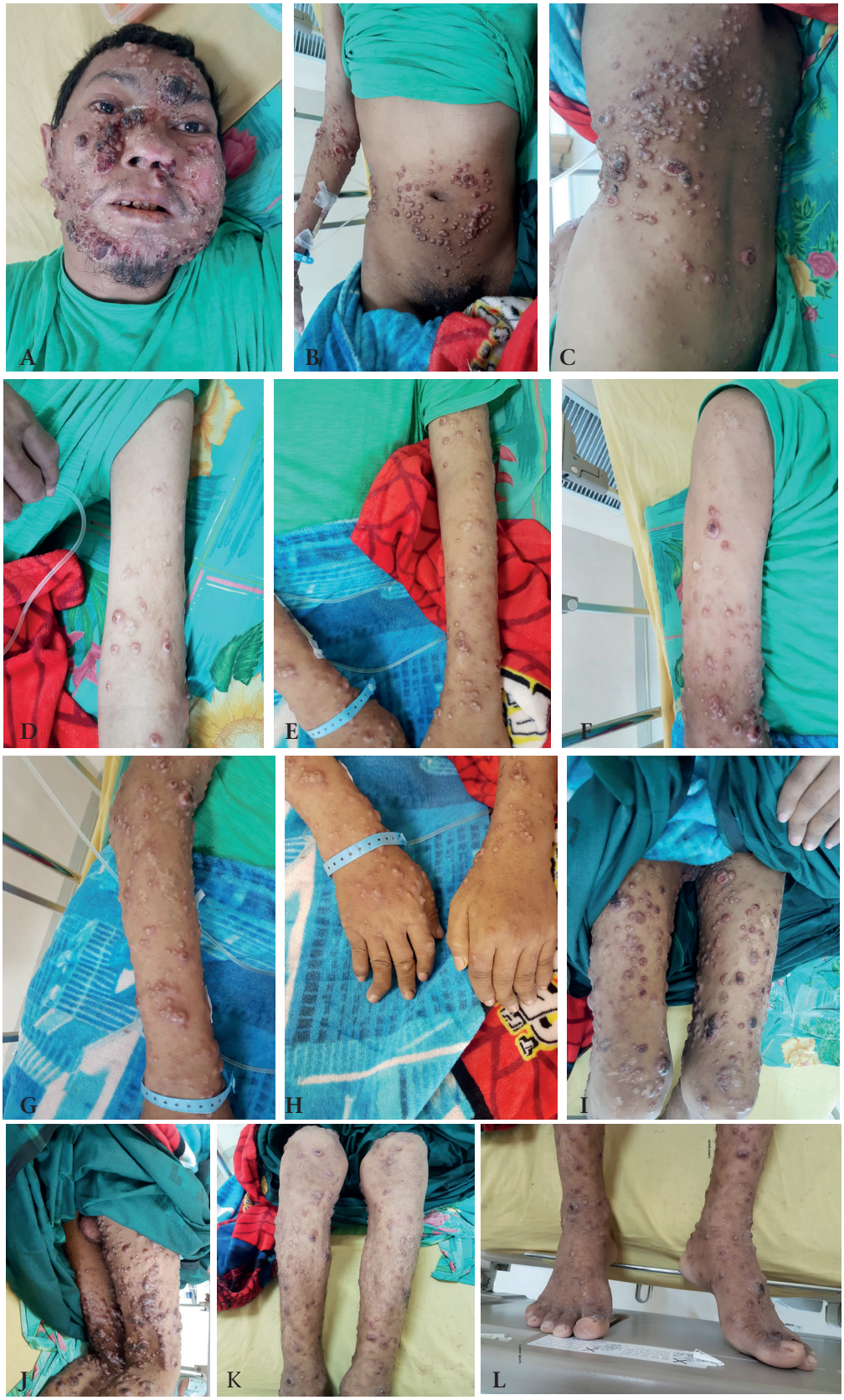


*Fig. 1A–L.* Multiple papules and nodules in almost the entire body.

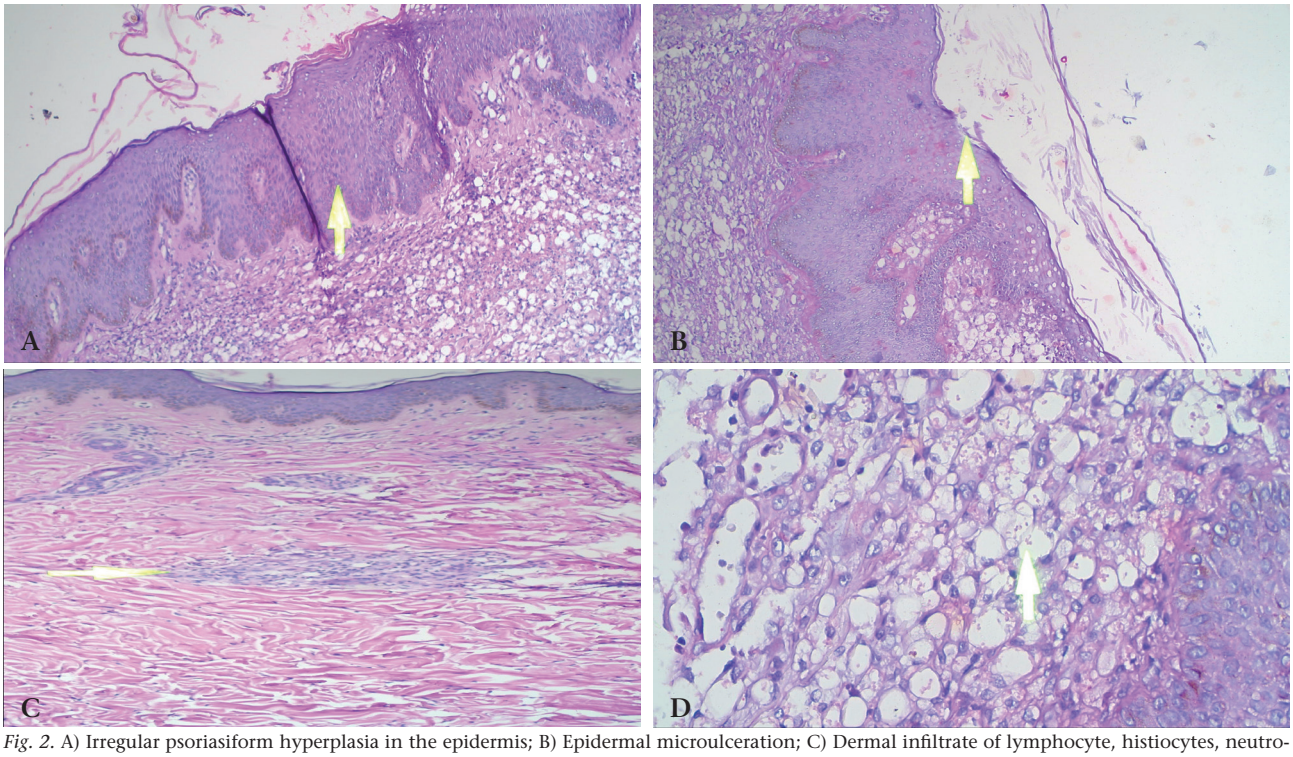


*Fig. 2.* A) Irregular psoriasiform hyperplasia in the epidermis; B) Epidermal microulceration; C) Dermal infiltrate of lymphocyte, histiocytes, neutrophile; and D) Spores of *C. neoformans* in PAS staining.

resembles Cryptococcus sp. (Fig. 3). Therefore, the patient was diagnosed with primary cutaneous cryptococcosis with past CMV and rubella infection. He was treated with 0.9% NaCl intravenous fluid, fluconazole 150 mg 2 times daily, 1 g intravenous paracetamol 3 times/day, lansoprazole 30 mg 4 times/day, ciprofloxacin intravenously 200 mg 2 times/day, and tenofovir/lamivudine/efavirenz 1 tablet 4 times/day.

## Discussion

The diagnosis of cutaneous cryptococcosis was established since there is no symptom and sign other than in his skin. Chest X-ray showed no lung abnormalities. The classic signs of CNS cryptococcosis, including meningism, headache, neuropathy, altered consciousness, mental changes, lethargy, memory disorders, cerebral palsy, and meningeal irritation

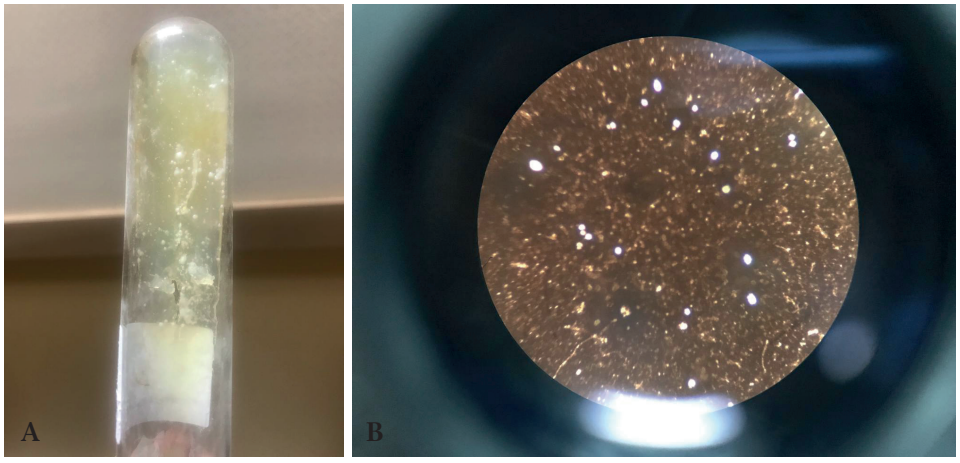


*Fig. 3.* A) The creamy mucoid appearance of *C. neoformans*; B) *C. neoformans* in Indian ink staining

signs (5), were absent. Fifty-four percent of cutaneous cryptococcosis present as papules or nodules with the colour as its surrounding area (8). Seventy-eight percent of the cases occurred in the head and neck (9). The primary cutaneous cryptococcosis lesions were mostly localized in the entry site through a minor injury to the skin. Interestingly, in this patient, primary cutaneous cryptococcosis was presented as extensive multiple ulcerated-umbilicated papules and nodules covered with red crusts in almost the entire body with an unknown injury site.

Cryptococcosis can be an acute, subacute, or chronic infection. This patient had experienced complaints for one month. The patient is a 35-year-old man; most patients are between 20–50 years old and it is rarely found in children (10). In Brazil, it was reported that 81.8% of the patients with cryptococcosis were men (11). This patient claimed the reason on his neighbour's pet doves. He suspected that he might had been infected from inhalation of the spores of *C. neoformans* brought by the dust of doves dropping.

Predisposing factors included immunodeficiency/AIDS, malignant lymphoma, sarcoidosis, collagen disease, carcinoma, immunosuppression due to systemic corticosteroid therapy or after kidney transplantation (12). Cryptococcosis is experienced in 5–10% of patients with AIDS. This patient had been categorized with AIDS with a CD4 level of only 1 cell/µl. His routine blood tests showed low Hb; 9 g/dl. Gao et al. (10) reported a decrease of Hb in 26.9% of cases of cryptococcosis. The pus investigation on Saboraud dextrose agar is consistent with the characteristics of *C. neoformans*, which are soft, cream or pale brown colonies and mucus growth (13). Indian ink staining finding (Fig. 3b) match with the presentation of *C. neoformans* as globular, capsulated yeast, with or without budding, 5–20 µm in diameter, and it has 80% sensitivity in HIV patients (3). A skin biopsy confirms the diagnosis of cutaneous cryptococcosis. Histopathological examination showed irregular psoriasiform hyperplasia of epidermis, microulceration, inflammation cell such as lymphocytes, histiocytes, dense neutrophils in the dermis, which is consistent with cutaneous cryptococcosis (8, 15). A definitive diagnosis can be established when we can find the fungi (15).

Treatment options for *C. neoformans* were determined by systemic involvement and host immune status. According to the Infectious Disease Society of America (IDSA) guideline recommendations for patients without CNS involvement and systemic symptoms, fluconazole 200–400 mg/day can be given for 6–12 months (16, 17). This patient received fluconazole monotherapy at a dose of 300 mg/day, and after 2 weeks he showed clinical improvement with deflated and dry lesions, and the pain disappeared. In 2015, Wang et al. (17) stated that the prognosis of primary cutaneous cryptococcosis was good; patients recovered in weeks to 10 months after antifungal therapy. Fluconazole monotherapy had been used in 17 cases since 2011. A French cryptococcosis study group treated 20 patients with fluconazole monotherapy, regardless of the immune status the median duration of therapy was 32 days, with improvement in 75% of the patients (16).

## Conclusion

Extensive primary cutaneous cryptococcosis is a rare opportunistic skin infection. Fluconazole monotherapy has shown clinical improvement in HIV patients.

*Patient consent and ethics approval*

The authors declare that patient consent has been obtained (including permission for publication of clinical photographs), and the local committee granted ethics clearance.

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