



Original Research Article

Cutaneous Cryptococcosis in an Immunocompetent Host

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ABSTRACT

The author presents a case of a 56 year-old immunocompetent adult male who developed inflammatory skin lesions with nodules and ulcerations on the forehead and ala of nose after an injury. Histopathological examination of the lesions showed granulomatous processes with yeasts similar to *Cryptococcus neoformans*. Tissue fragments yielded yeasts when cultured that were identified as *Cryptococcus neoformans*. India ink preparation, Gram stain, Periodic acid Schiff, Mayer's muciramine staining, Hematoxylin and eosin, Gomori's methenamine silver stain, growth on SDA of excision biopsy material and positive urease test, confirmed the diagnosis in the present case. No evidence of systemic involvement or any underlying immunosuppressive diseases were identified, which supported the diagnosis of primary cutaneous cryptococcosis. The skin lesions of the patient showed regression after being treated with systemic Amphotericin B and oral fluconazole. The cutaneous form of cryptococcosis is rare and early diagnosis and treatment is essential in view of possible dissemination and variable non specific clinical manifestations.

Keywords

Cutaneous
Cryptococcosis,
*Cryptococcus
neoformans*,
Amphotericin B
and oral
fluconazole

Introduction

Cryptococcosis also known as torulosis, Busse-Buschke's disease and European blastomycosis is a cosmopolitan illness, with opportunist behavior (Joshi *et al.*, 2004)

It is a fungal systemic infection caused by *Cryptococcus neoformans*, characterized as a species of encapsulated yeasts which, based on the capsule structure, were grouped into two varieties that included five serotypes. *C. neoformans* var. *neoformans*

including serotypes A, D and AD, and *C. neoformans* var. *gatti* contained strains with serotypes B and C. Based on DNA genotyping methods, several changes have been proposed. According to that, serotype A would be classified as a separate variety, *C. neoformans*, var. *grubii*. In AIDS patients, the vast majority of isolates are serotype A (Lacaz *et al.*, 2002).

Cryptococcus spp. are ubiquitous in nature and may be isolated from decaying wood,

tree hollows, fruits, vegetables, grass, hay, soil, dust, and bird droppings, especially from *Columba livia*. Infection by *Cryptococcus* spp. occurs through the respiratory tract and the symptoms depend on the inoculum, the host immune status and the strain virulence. The central nervous system is commonly involved, and serotype A (VNI genotype), which has the most widespread distribution worldwide, accounts for more than 90% of the cases in immunocompromised patients (Meyer *et al.*, 2003). The skin is the most common extraneural site of infection, affecting 10-20% of those with systemic involvement. *Cryptococcus neoformans* serotype D has been more commonly isolated from these skin lesions, which could be related to dermatotropism (Martinez *et al.*, 2001) Many cases described are associated to the immunosuppression, due to lymphoma, chronic leukemia, transplants of organs, use of corticosteroid, immunosuppressive drugs, systemic lupus erythematosus, diabetes mellitus, Cushing's syndrome and with acquired immunodeficiency syndrome (Sandra Lopes Mattos e dinato *et al.*, 2006). Cutaneous Cryptococcosis lesions vary greatly in morphology and mimic other dermatological entities and are often the first presenting symptom of systemic disease. Literature has reported very few cases of Cutaneous cryptococcosis and this case is one of the eye openers in the differential diagnosis of cutaneous nodules.

Case report

A 56 year old male patient came with the chief complaints of two dark colored raised nodules on forehead (Figure 1) and ala of nose (Figure 2). He had no history of tuberculosis, diabetes mellitus asthma, use of corticosteroids, other immune-suppressants or prolonged antibiotic therapy. Histopathological examination of the skin

biopsy material with Periodic acid Schiff, Mayer's muciramine staining, Hematoxylin and eosin, Gomori's methenamine silver stain and India ink stain revealed plenty of budding yeast cells measuring 5–10µm in size and surrounded by a polysaccharide capsule. On Sabouraud dextrose agar (SDA); creamy, flat, shiny, mucoid colonies were grown with smooth edges within 4 days at 37°C and room temperature. Colonies were then subcultured on chocolate agar and SDA. Christensen's urease medium were inoculated which gave a positive urease test thus confirming the diagnosis of *Cryptococcosis neoformans*. The fungus was identified as *Cryptococcus neoformans* and confirmed by Department of Medical Mycology, PGIMER, Chandigarh. Hematological parameters were not suggestive of inflammatory pathology. Laboratory values were notable for haemoglobin of 10 gm%. The white blood cell count was 14000/cmm with 66% segmented neutrophils, 26% lymphocytes, 7% monocytes, 1% eosinophils and no basophils. CT scan and USG abdomen showed no abnormalities. Kidney function test and liver function tests were normal. Urine did not show any protein or glucose and culture did not show any growth. Blood culture was sterile. Chest X-ray was normal. The patient was presumed to be immunocompetent as the patient was not reactive for HIV and had no diabetes mellitus, neutropenia, evidence of hematologic or any other malignancy in the body, or any concurrent infections. The skin lesions of the patient showed regression after being treated with systemic Amphotericin B and oral fluconazole.

Discussion

Over the past 2 decades, almost 90 percent of cases of cryptococcosis have developed in patients in the late stages of HIV disease.

The widespread use of highly active antiretroviral therapy (HAART) has led to a marked reduction in the rate of cryptococcosis associated with HIV disease. Now, with the onset of drug resistance and longer life expectancy, cryptococcosis is returning as a significant cause of morbidity and mortality. Less frequently, the disease can be diagnosed in other immunosuppressed patients or in immunocompetent hosts exposed to pigeon droppings (Calista *et al.*, 1997). The prognosis of cryptococcosis depends on the degree of the patient's immunosuppression, the involvement of CNS, and time to onset of treatment (Sing and Ramdial, 2007).

Infection in humans is mainly the result of inhalation and occasionally penetration of the yeast through the skin. Primary pulmonary infection is usually asymptomatic. When symptomatic, the course of the disease may range from a mild, self-limited influenza-like illness to severe pneumonia (Van Griek, 2007). *Cryptococcus neoformans* may spread hematogenously to any organ of the human body producing life-threatening diseases such as meningoencephalitis, hepatitis, pericarditis, endocarditis, or prostatitis, endophthalmitis, and renal abscesses (Sarosi *et al.*, 1971). Cutaneous manifestations occur in about 15 percent of cases. Cutaneous lesions of cryptococcosis are usually characterised by multiple, discrete, flesh to red coloured papules varying in size from 1–6 mm and often slightly umbilicated, leading to differential diagnosis of molluscum contagiosum, penicilliosis and histoplasmosis. Less often, violaceous papules, vesicles, crusted plaques, or subcutaneous nodules appear, mimicking a variety of dermatological diseases such as Kaposi's sarcoma, basal cell carcinoma, cellulitis or acneiform lesions, or varicella (Murakawa *et al.*, 1996). It is often

necessary to take biopsy and culture the skin lesions to exclude the more serious condition of cryptococcosis. Skin lesions occur in 5% of patients with cryptococcal meningitis, and a higher frequency among liver transplant recipients who receive tacrolimus has been observed. This lesion may be the first clinical manifestation of disseminated infection, particularly in subjects with cell immunity deficits.

The case presented herein is instructive for its deceptive and unusual clinical presentation. India ink preparation, Gram stain, Periodic acid Schiff, Mayer's muciramine staining, Hematoxylin and eosin, Gomori's methenamine silver stain, growth on SDA of excision biopsy material and positive urease test, confirmed the diagnosis in the present case. According to our patient's history, he had suffered traumatic skin lesions which might have favored accidental fungal inoculation. Direct inoculation into the skin as a result of traumatic injury can cause the condition of primary cutaneous cryptococcosis.

This has occasionally been described in elderly individuals from rural areas who have histories of cutaneous injuries and activities predisposing to wounds or exposure to bird droppings. The skin lesion is usually solitary or confined to a limited and unclothed body area, and its clinical appearance can be in the form of whitlow, cellulitis, or ulceration, with or without regional lymphadenopathy (Christianson *et al.*, 2003). Our case report and the investigations correlate with those reported by the other authors. When added to the lack of evidence of systemic disease, this information supports the diagnostic hypothesis of primary cutaneous cryptococcosis in this immunocompetent patient.

Conclusion

The cutaneous form of Cryptococcosis is rare, and the differential diagnosis with the disseminated giant molluscum contagiosum is particularly important. Skin lesions are

significant in early diagnosis of Disseminated Cryptococcosis. Hence, a high index of suspicion is desired in view of possible dissemination and variable non specific clinical manifestations.

Figure.1 Cutaneous nodule on forehead



Figure.2 Cutaneous nodule on ala of nose



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