CASE REPORT

PRIMARY CUTANEOUS CRYPTOCOCCOSIS DUE TO Cryptococcus neoformans var. gattii
SEROTYPE B, IN AN IMMUNOCOMPETENT PATIENT

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SUMMARY

The authors report a male patient, a seller with no detected immunosuppression, with an extensive ulcerated skin lesion localized on the left forearm, caused by *Cryptococcus neoformans* var. *gattii* serotype B. Oral treatment with fluconazole was successful.

A review of the literature showed the rarity of this localization in HIV-negative patients. In contrast, skin lesions frequently occur in HIV-positive patients, with *Cryptococcus neoformans* var. *neoformans* serotype A predominating as the etiological agent.

In this paper, the pathogenicity of *C. neoformans* to skin lesions in patients immunocompromised or not, is discussed, showing the efficacy of fluconazole for the treatment of these processes.

KEYWORDS: *Cryptococcus neoformans* var. *gattii*; Serotype B; Immunocompetent patient; Cutaneous cryptococcosis.

INTRODUCTION

Cryptococcosis is a fungal infection caused by two varieties of *Cryptococcus neoformans*, with five serotypes. We traditionally consider the varieties *C. neoformans* var. *neoformans* (serotypes A, D and AD) and *C. neoformans* var. *gattii* (serotypes B and C) (LACAZ et al., 1991)12. According to some researchers, *C. neoformans* var. *grubii* represents strains of serotype A, var. *neoformans* (serotypes D and AD) and var. *gattii* (serotypes B and C) (FRANZOT et al., 1999)7. Based on sequential analysis of intergenic rDNA spaces, DIAZ et al., (2001)9 consider two pathogenic varieties: *C. neoformans* (serotypes A, D and AD) and *C. bacillispora* (serotypes B and C), the latter corresponding to *C. neoformans* var. *gattii*.

The sexual states of *C. neoformans* are assigned to Filobasidiella, with the species *neoformans* and *bacillispora*. A heterothallic yeast, *C. neoformans* presents two types of conjugating hyphae: α and α (KWON-CHUNG & BENNETT, 1992; TAKEO et al. 1993)18,25.

A capsulated yeast, *C. neoformans* (SANFELICE, 1894) Vuillemin, 1901 can be isolated in a relatively easy manner, making possible the study of its sexuality and of its antigenic and genetic structure.

Current research has been mainly directed at the study of the genome of *C. neoformans*, its life cycle and ecological niche (LAZERA et al., 2000; MONTENEGRO & PAULA, 2000)13,17.

*C. neoformans* var. *gattii* has been isolated in Brazil by several investigators, mainly from hollow trees (LAZERA et al., 2000)14 but also from soil and plant detritus (LAZERA et al., 1998)15.

BARRETO DE OLIVEIRA (2001)2 observed that 40 of 58 serotyped strains (70%) were serotype A, 10 (17%) serotype B, 5 (8%) serotype D, 2 (3%) serotype C, and 1 (2%) serotype AD. *C. neoformans* var. *neoformans* serotype A predominates in Brazil, followed by the variety *gattii*, serotype B at lower frequency.

Cryptococcosis has been reported to be associated with AIDS in most cases, or with other immunodeficiencies, being rarely observed in immunocompetent patients (KWON-CHUNG & BENNETT, 1992; SPEED & DUNT, 1995)18,24. According to SEVERO et al. (1999)23, cryptococcosis induced by *C. neoformans* var. *neoformans* usually occurs in immunocompromised patients and *C. neoformans* var. *gattii* occurs in immunocompetent subjects.

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In a study on immunosuppressed Wistar rats, ALMEIDA FILHO (2001) observed that *C. neoformans* var. *neoformans*, serotype A, is more virulent to these animals than var. *gattii*, serotype B. MITCHELL & PERFECT (1995), in a review of cryptococcosis during the AIDS era, reported that this fungal infection is causing great suffering to mankind.

**CASE REPORT**

T.U, patient attended in the Faculty of Medicine of ABC, Santo André, São Paulo, 65 years old, a male seller borned in Japan and living in São Bernardo do Campo, presented an extensive ulceration with erythematous borders and irregular infiltrates on the left forearm starting 50 days before his consultation (Fig. 1). According to the patient, the lesion had started with a macula that progressed to ulceration.

The culture of the lesion was positive for *Cryptococcus neoformans* var. *gattii,* serotype B (Fig. 2). Histopathological examination was positive for *C. neoformans* (mucicarmin method) (Fig. 3). A chest X-ray was normal. A search for anti-HIV antibodies was negative. Blood count and cerebrospinal fluid were normal. A latex test applied to serum for the detection of circulating *Cryptococcus neoformans* antigen was positive. Skull tomography showed no alterations and digestive tomography revealed mild erosive gastritis. Glucose: 70 mg/dL; Creatinine: 0.8 mg/dL. Treatment with fluconazole, 150 mg/3 capsules a day, led to a complete cure within 45 days (Fig. 4).

**DISCUSSION**

Cutaneous cryptococcosis in its generalized forms, especially in patients with AIDS, presents multiple lesions, most of them simulating molluscum contagiosum. Acneiform, nodular, or herpetiform lesions, or cellulitis are frequently recorded (LACAZ et al., 1991; RICCHI et al., 1991; MANRIQUE et al., 1992). HECKER & WEINBERG (2001) recorded one case of cutaneous cryptococcosis simulating a cheloid in a man with AIDS.
In the case described here, a hypothesis that might be raised is that the site of entry of the fungus was by inhalation of small yeast propagula, probably its basidiospores, that were first installed in the lungs and were radiologically undetectable, followed by skin lesion (KWON-CHUNG & BENNETT, 1992). Direct examination of biopsy with a drop of India ink, showed yeast cells with capsules. The fungus isolated from the lesion was identified as C. neoformans var. gattii, serotype B.

The literature reports marked dermotropism of the so-called grubii variety of C. neoformans, serotype A (FRANZOT et al., 1999). We should point out the absence of trauma preceding the lesion and of any detected immunosuppression.

According to RODRIGUES et al. (1999), when the host is immunocompromised, C. neoformans cells try to escape the defenses of the organism by producing stidal acid, capsulated polysaccharides, melanin, mannitol and phospholipase. In contrast, in immunocompetent hosts the mechanisms of pathogenicity have not been carefully clarified. In cryptococcosis, melanin seems to interfere with the virulence of the yeast, with great tropism for the central nervous system, rich in catecholamines.

PAPPAS et al. (2001) conducted a review study in the United States involving 15 American Medical Centers from 1990 to 1996 and a total of 306 patients with cryptococcosis, all of them HIV negative. Of these, 109 presented pulmonary lesions, 157 central nervous system lesions, and 40 lesions located at other sites. Fluconazole was administered to approximately 2/3 of the patients, with therapeutic success in 74% of them.

BOHNE et al. (1996) reported an erysipela-like lesion induced by C. neoformans in a female patient with sarcoidosis after a traumatic injury, which was treated with corticoids. This patient was treated successfully with itraconazole.

HAMANN et al. (1997), in Australia, reported an immunocompetent patient with cellulitis induced by C. neoformans var. gattii.

PATEL et al. (2000) reported a case of cutaneous cryptococcosis involving an immunocompetent elderly woman (85 years of age) induced by C. neoformans which was cured with fluconazole.

VELEGRAKI et al. (2001), in Greece, reported two cases of cryptococcosis induced by C. neoformans var. gattii serotype B, one involving an HIV-positive patient and the other a patient with systemic lupus erythematosus.

SEVERO et al. (1999) in Rio Grande do Sul (Brazil), reported three cases of cryptococcosis induced by C. neoformans var. gattii, affecting HIV-positive patients. SEVERO et al. (2001) also reported a case of cutaneous cryptococcosis induced by C. neoformans var. gattii in an immunocompetent host.

In Teresina (PIAU), C. neoformans var. gattii is the causal agent of cryptococcosis in 91.2% of HIV-negative patients (CAVALCANTI, 1997). This variety has been found in Belém (Pará) as an agent of pediatric neurocryptococcosis (CORRÊA, 2001).

In Brazil, the serotypes of C. neoformans strains predominantly belong to A, followed by B (LACAZ & RODRIGUES, 1983). For the patient reported here, we emphasize the excellent therapeutic result obtained after 45 days of fluconazole treatment.

**RESUMO**

Criptococose cutânea primária causada por Cryptococcus neoformans var. gattii sorotipo B em paciente imunocomprometido

Os autores registram em paciente do sexo masculino, vendedor ambulante sem qualquer doença de base, lesão cutânea extensa, localizada no antebraço esquerdo, sob forma ulcerada, provocada pelo Cryptococcus neoformans var. gattii sorotipo B. Sucesso terapêutico com fluconazol, por via oral.

Revisão da literatura foi realizada, mostrando raridade de tal localização em pacientes HIV-negativos. Já em pacientes HIV-positivos, lesões cutâneas ocorrem com frequência, predominando como agente etiológico O Cryptococcus neoformans var. neoformans, sorotipo A.

A patogenicidade do C. neoformans nas lesões cutâneas é discutida em pacientes imunocomprometidos ou não, mostrando a eficácia do fluconazol no tratamento de tais processos.

**REFERÊNCIAS**


