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PREVALENCE OF PULMONARY CRYPTOCOCCOSIS IN HIV/AIDS PATIENTS

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Abstract

Cryptococcus neoformans causes both pulmonary and meninges infection in healthy and immunocompromised hosts. The objective of this study was to determine the prevalence of pulmonary cryptococcosis in HIV/AIDS patients and assess the clinical presentations due to the infection. The subjects recruited for this study were confirmed HIV/AIDS patients, presenting with pneumonia complications. The demographic and clinical features were abstracted from the medical records and administered questionnaire. Early morning sputum samples were collected from the patients and examined by bacteriological methods. The isolated *Cryptococcus neoformans* were sub-cultured onto thistle bird seed agar and the identity was confirmed with API 20C Kit. Out of 250 patients investigated, 47 (18.8%) had pulmonary cryptococcosis. The *C.neoformans* isolates were more in females, 26 (10.4%) than the males, 21 (8.4%), while the age group of 20-40 years old had 39 (15.6%) isolates. The clinical features that were associated with the pulmonary cryptococcosis were the production of purulent and bloody sputum, and fever. The patients with prolonged duration of HIV/AIDS and are not on HAART regimens had higher *C.neoformans* isolates. The isolation of *C.neoformans* from HIV/AIDS patients is a major public health concern, since it complicates the severity of the disease. There is a need for routine check of pulmonary cryptococcosis, especially, in those who do not avail themselves for antiretroviral therapy.

Keywords: *Cryptococcus neoformans*, Cryptoccosis, HIV/AIDS, HAART, Thistle bird seed agar.

Introduction

Infections due to *Cryptococcus neoformans* occurs world wide without any specific endemic areas. The fungus is an ubiquitous pathogenic encapsulated yeast, classified as

Basichomy cota (Levitz, 1991). Human diseases caused by the fungus range from asymptomatic pulmonary colonization to life threatening meningitis and overwhelming cryptococcemia (Levitz, 1991; Duperval et al, 1977; Perfect et al, 1983). The mode of entry into a new host is through the respiratory tract.

Cryptococcosis occurs in healthy hosts, but majority has significant underlying predisposing factors especially in advanced HIV disease and transplant related immunosuppression. (Thomas et al, 1998; Aberg et al; Pappas et al, 2001; Dismukes, 1998) In immunocompromised patients, cryptococcosis can be severe and rapidly progressive; requiring prolonged systemic antifungal therapy (Dismukes, 1993; Saag et al, 2000). The infection is the most common life-threatening disease in HIV patients, and extra- pulmonary cryptococcosis is an AIDS- defining illness. The clinical presentation includes disseminated meningo-encephalitis, which is rapidly fatal in the absence of therapy (Mwaba et al, 2001; Dupont et al, 2000; Heyderman et al, 1998). Cryptococcosis in HIV/AIDS patients varies from <1.0 to 10% in western countries (Knight et al, 1993; Burckhardt et al,1999) to more than 33% in sub-Saharan Africa and South east Asia (Mwaba et al, 2001; Hakim et al, 2000). This presents with high morbidity in HIV/AIDS patients in sub-Saharan Africa. The majority of society affected by cryptococcsis is socio-economically low and is often responsible for the support and care of others (Quinn, 1996). In this region, prospective studies on cryptococal pulmonary infections are needed so that appropriate therapy can be initiated, thus reducing the incidence of opportunistic infections.

The goal of this study was to determine the prevalence of pulmonary cryptococcsis, and define clinical presentations in HIV/AIDS patients in Jos city, Nigeria. We showed that cryptococcsis is a major pulmonary marker in HIV/AIDS patients, presenting with systemic pneumonia.

Materials and Methods

Study Population

Human immunodeficiency Virus/Acquired immunodefiency syndrome (HIV/AIDS) patients were recruited for this study. The patients were attending Faith Alive Foundation Clinic, Jos, for support, care and highly active antiretroviral therapy (HAART). The study was in accordance with Helsinki declaration.

Sample collection: Early morning sputum was collected from each patient, after due counseling and instructions (Beneke and Rogers, 1996; Robinson and Pachye, 1988). The consistency and cellular make-up of the sputum was used to determine the quality of the samples ensuring that the specimens were expectorated from deep within the lungs.

Cultural methods: The sputum was routinely plated onto thistle Baird seed agar, sheep blood agar, Brainheart infusion both, brainheart infusion agar and Sabouraud dextrose agar. All cryptococcal isolates were sub-cultured onto Sabouraud dextrose agar and thistle Baird seed agar, and their identity was confirmed with API 20C kits (Biomereux, France).

Study Definitions

The patients were classified as either having pulmonary cryptococcosis or disseminated *C. neoformans.* The criteria used for pulmonary cryptoccosis in this report are: (1) Certainty of diagnosis; the isolation of *C. neoformans* from the sputum samples, with radiographic evidence of disease and clinical symptoms; (2) Colonization, was identified on the basis of isolation of *C. neoformans* in respiratory specimen with either a normal chest radiograph or asymptomatic State with abnormal radiograph. The sites of involvement were classified as pulmonary because only the lungs and/or pleura were the sites involved.

Results

Two hundred and fifty patients with HIV/AIDS infection, and proven evidence of lung abnormality were enrolled for this study. Respiratory specimens were not collected from the patients that did not meet-up the study criteria, after reviewing the medical records. Out of 250 patients who met the study criteria, 47(18.8%) had pulmonary colonization with *C. neoformans*, (pulmonary cryptococcosis); 15 (6.0%) had possible disease while 188 (75.2%) either had growth or no *C. neoformans* was isolated.

Demographic characteristics

The subjects were made–up of 102 (40.8%) males and 148 (59.2%) females. Pulmonary cryptococcosis was confirmed in 21 (8.4%) males and 26 (10.4%) females. The age group of 20-40 years old was 209 (83.6%), with 39 (15.6%) isolates of *C. neoformans* only 8(3.2%) isolates were from the elderly patients. The duration of HIV/AIDS infection showed that those with prolonged AIDS has more yield of *C. neoformans* (13.6% Vs 5.2%) (Table 1**).**

The clinical signs and symptoms attributable to cryptococcosis and observed in the patients at the time of diagnosis varied from one patient to another (Table 2). Overall the patients with purulent and bloody sputum production has 43% yield of pulmonary colonization while those with fever has 36% yields. Those without any specific clinical symptoms had 26% of pulmonary cryptococosis.

The patients on therapy options were analyzed. Those on HAART regimens had lower yields, while those who has not started HAART regimens, but may have abused antibiotics in treating opportunistic infections and those who experimented the use of local herbs for cure yielded higher isolates of *C neoformans*, (26% Vs 40%) The patients, who had not started therapy, gave a yield of 23%. These are group of patients from rural communities who came for treatment of pneumonia and were diagnosed of HIV infection, in the patients stuttering from other opportunistic infections (Data not shown), 87% of *C. neoformans* were isolated, while those that have no other opportunistic infections had 13% of isolates of *C neoformans*.

Table 1: Demographic characteristics of 250 patients suspected of pulmonary cryptoccoial infections.

Characteristics	N = 250	Positive isolates (%)
Sex:		
Male	102 (40.8)	21 (8.4)
Female	148 (59.2)	26 (10.4)
AGE < 20	 5	 0 (0)
20 –40	209	39 (15.6)
> 40	36	8 (3.2)
Duration of HIV infection (years)		
1 – 5	121	13 (5.2)
6 – 10	104	20 (8.0)
11+	25	14 (5.6)

Table 2: Presenting clinical characteristics of 47 isolated pulmonary cryptococcosis.

Characteristics	No (%)
General:	
Fever	17 (36)
Night sweats	11 (23)
Fatigue	2 (4)
Lack of appetite	3 (6)
Weight loss	6 (13)
Malaise	6 (13)
Headache	2 (4)
Pulmonary	
Cough	9 (19)
Chest pain	6 (13)
Sputum production	20 (43)
None	12 (26)
Patients on Therapy:	
HAART	5 (11)
Local herbs	12 (26)
Antibiotics	19 (40)
None	11 (23)
Presence of other opportunistic infection:	
Yes	41 (87)
No	6 (13)

Discussion

Cryptococcosis has emerged as defining feature for HIV/AIDS infection. The occurrence of pulmonary cryptococcosis can range from asymptomatic nodular disease to severe acute distress syndrome (ARDS) (Saag et al., 2000; Warkentine et al., 2000). The epidemiological trends of infection with *C. noefomans* can only be evaluated through surveillance studies (Dromer et al., 2004). This study was aimed to determine the prevalence of primary pulmonary cryptococcosis in AIDS patients with isolated cases of pulmonary pneumonia. All subjects enrolled in the study were confirmed HIV–positive and presenting with AIDS–defining-illness, and CD4+count $\leq 200/mm^2$ (CDC). Of 250 patients enrolled in this survey, 47 (18.8%) had primary lung infections due to *C neoformans*. Batungwanayo et al (1994) reported higher primary pulmonary cryptococcosis in Rwanda. In a study of 37 AIDS patients; 29 (78%) had pulmonary cryptococcosis. It is assumed that *C neoformans* generally gains access to the host by inhalation and the respiratory system is the usual portal of entry (Aberg et al., 1999). Therefore, colonization of the lungs is expected hence the high isolation of *C. neoformans* from HIV/AIDS patients. In the normal host, inhalation of organism is followed by localized immunologic response that contains the organism before symptoms or dissemination occurs (Warkentine et al., 2000). Since the AIDS patients are immunocompromised, dissemination of the disease will be a common characteristic.

The demographic characteristics indicate that the females were more infected than the males. This gender difference may be as result of certain factors such as; the patients not availing themselves for medical care on time or considering themselves not at risk for HIV-infection or in patients with poor access to care (Mirza et al., 2003). This is reflected in the duration of HIV/AIDS infection, as those with long-term infection AIDS had more isolates of *C neoformans* than those with shorter duration. It can be explained by the fact that *C*

neoformans infection may be initially asymptomatic but progresses as the patients CD4+ cell count declines.

C neoformans infection have high incidence and is the liter- threatening fungal pathogen most communally seen in AIDS patients (Dismukes, 1998). Cryptococcal pneumonia may present with or without evidence of dissemination. It is unclear if disseminated disease represents a progression or reactivation of pulmonary disease because many patients have no evidence of pulmonary involvement at the time of diagnosis of disseminated disease. Our study showed that those with fever, night sweats, weight loss and malaise gave higher isolates of *C. neoformans*. It was observed that patients with pulmonary cough, chest pain and produces bloody sputum had high yields of *C. neoformans.* The asymptomatic patients with an isolate of 26% indicate the clinical variable nature of the pulmonary cryptocccosis. The conditions of such AIDS patients are likely to worsen in absence of treatment. Taken together, dissemination of the disease to central nervous system due to cryptococcal invasion will be a common feature thereby causing crytococcal meningitis. There is high morbidity and mortality of such cryptococcal meningitis. This is illustrated in the study of Heyderman et al. (1998) in Zimbabwe, where anti-fungal therapy was not available. Their work showed that cryptococcal meningitis was the AIDS defining illness in 88% of the patients.

The management of HIV/AIDS disease is dependent on the suppression of viral replications and on the ability to preserve and restore immune function. Highly active antiretroviral therapy (HAART) results in longer term of virus load reduction (Hammer et al., 1997; Gulizk et al, 1997). The clinical benefit from HAART is increased CD4 lymphocyte and thus immune system restoration. This decreases the frequency of opportunistic infections. In this study, 11% isolates of *C. neoformans* were from the patients on HAART. Those on local herb mediations, self-prescribed antibiotics and those that are not on therapy have combined isolation rate of 89%. This indicates that cryptococcosis continues to occur, but primarily in patients availing themselves less to routine medical care and whereas those patients with higher *C. neoformans* isolates may have been as result of reticence and ignorance (Mirza et al, 2003).

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