

RISING PREVALENCE OF OPPORTUNISTIC INFECTIONS

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INTRODUCTION

Cryptococcus neoformans, a type of yeast found worldwide, can cause pulmonary and central nervous system (CNS) infections that can potentially spread to other areas of the body. This infection is called cryptococcosis. HIV/AIDS patients are especially vulnerable to developing the infection.

Cryptococcosis is an infection of the central nervous system mainly caused by *Cryptococcus neoformans*. The fungus is acquired by inhalation and causes the initial lesion in the lungs, though the pulmonary stage of infection is usually asymptomatic. The fungus disseminates in debilitated patients, usually involving the meninges. Cryptococcosis is one of the most common infections in AIDS and disseminated cryptococcosis occurs in about one-third of AIDS patients.(1)

C. neoformans is distributed worldwide. An ubiquitous environmental saphrophyte, it is found in soil contaminated with pigeon droppings and has also been isolated from the heartwood of several tree species in South America (2) and India (3), and from the homes of African HIV-seropositive patients (4,5). The current epidemic of acquired immune deficiency syndrome (AIDS) is one of the most destructive in recorded history, being associated with the death of more than 25 million people since the syndrome was recognized in 1981. Despite increasing global efforts to curb this menace, an estimated 39.5 million people now have the human immunodeficiency virus (HIV). (6) AIDS associated cryptococcal meningitis (CM), caused by *Cryptococcus neoformans*, is a severe opportunistic infection with a high mortality, even in developed countries. (7) Early mortality rates of 11% to 45% have been reported among cohorts from the United States. (8) In Africa, CM is responsible for 13% to 42% of all deaths among HIV-infected people. (9) CM is the AIDS-defining illness in 25% to 30% and 64% to 91% of cases in South-East Asia and sub-Saharan Africa, (10, 11) respectively.

In HIV-seropositive patients, most episodes of cryptococcal meningitis probably represent reactivation of latent infection, which may have been acquired many years earlier. HIV-associated cryptococcal meningitis usually presents as a subacute meningo-encephalitis in profoundly immunosuppressed patients (CD4 cell counts < 100 cells/ μ l), with malaise, headache, fever and, later, visual disturbance and altered mental status. We carried out a study with a view to determine the incidence of *Cryptococcus* species and the antifungal susceptibility pattern of the cryptococcal isolates in AIDS patients.

MATERIAL AND METHODS

Data Collection

A total of 20 AIDS patients with suspected meningitis, admitted to the different wards of Hospital and Research Centre were studied. The detailed clinical history of the patients regarding age, sex, clinical diagnosis, factors predisposing to fungal infections, drug therapy etc were recorded.

Sample Collection and Processing

A total of 15 CSF specimens were obtained from the 20 AIDS patients. 2ml of CSF was collected in the wards with sterile and with aseptic precautions and sent immediately to the laboratory for

processing. The wet film preparations were screened microscopically for the presence of cryptococci or other fungi using KOH and India ink

Culture and Identification

The CSF specimens were cultured on Sabouraud agar with chloramphenicol and brain heart infusion agar supplemented with blood. The specimens were inoculated in duplicate. One set was incubated at room temperature (25-30°C) and the other at 37°C. The media were incubated and observed for a month before discarding as no growth. The yeast colonies obtained after incubation were identified based on the colony characteristics, carbohydrate assimilation and fermentation reactions and the urease test.(12). Isolates of *Cryptococcus neoformans* obtained from CSF specimens were tested for their sensitivity to amphotericin B, fluconazole and itraconazole.

Antifungal Sensitivity Testing

The isolated cultures were tested for their sensitivity to 3 antifungal drugs namely amphotericin B, fluconazole and itraconazole. Method described by the National Centre for Clinical Laboratory Standards (NCCLS) was used to determine the minimum inhibitory concentrations (MIC) of the drugs.(13)

RESULTS

In the study group out of 20 patients there were 3 (15%) patients who presented with cryptococcal infection. Out of the patients 2 were male and 1 was female. The patients were predominantly in the age group of 26-40 years with cryptococcal meningitis occurring as a complication of AIDS all these patients presented with symptoms of headache, fever and vomiting. Neck stiffness was present in two and one of them was in altered sensorium. Gram's staining showed - gram positive capsulated budding yeast cells. All the specimens tested were culture positive for *Cryptococcus neoformans*. All the cultures were encapsulated yeasts which were urease positive. Antifungal susceptibility testing results showed that all the isolates were sensitive to amphotericin B, fluconazole and itraconazole.

DISCUSSION

The present study was conducted in the Department of Microbiology at Adesh Institute of Medical Sciences & Research, Bathinda, with an aim to evaluate the opportunistic infection in HIV patients presenting to a teaching hospital in Punjab. The study was carried out over a period of three years starting from May, 2008 to May, 2011. All HIV positive individuals who met the inclusion criteria were included. Detailed history, clinical examination and investigative work up was done. In the present study there were 3 (15%) patients who presented with cryptococcal infection. Both of these patients presented with symptoms of headache, fever and vomitings. Zuger A, et al (14) observed that meningitis was the most common initial manifestation affecting 72% to 90% of patients with cryptococcosis. Neck stiffness was seen in both patients and one patient was in altered sensorium as shown in table 4. The prevalence of fungal meningitis was 15% in the present study while 7-8% of AIDS patients in United States (15) manifest cryptococcal meningitis and cryptococcal meningitis is reported to be as high as 30% in AIDS cases in Africa.(16)

Male predominance among cryptococcal cases of meningitis has been documented in many studies [17] In the present study as well, 2 of the 3 cases of meningitis among AIDS patients were males as shown in table 2. However, among HIV positive adult subjects, 17 males and 3 females were noted. The increased males with fungal meningitis among AIDS cases could be due to overall male predominance among AIDS cases as shown in table 1.

The patients were predominantly in the age group of 26-40 years as shown in table 3 and this is the most productive age group and majority of HIV positive patients are also in this age group only.

Once the infection has been diagnosed the next step is prompt and appropriate treatment. We carried out the susceptibility testing in order to study the pattern of sensitivity of the local isolates. All the isolates of *Cryptococcus neoformans* were found to be susceptible to the three antifungal drugs tested namely amphotericin B, fluconazole and itraconazole. Similar results have been reported in literature.[18,19] With the high incidence of cryptococcal meningitis in AIDS it is important to examine all CSF specimens from HIV infected persons with meningitis for cryptococci.

Table 1: Sex predisposition in HIV positive patients

	No.	% Age
Male	17	
Female	3	

Table 2: Sex predisposition in cases of cryptococcal meningitis

	No.	% Age
Male	2	
Female	1	

Table 3: Age wise distribution of cases

Age group	HIV Patients	CM Patients
10-20	1	0
20-30	8	2
30-40	10	1
40-50	1	0

Table 4: Clinical features

Clinical features	No.	% Age
Headache	3	
Vomiting	3	
Fever	3	
Alter sensorium	1	
Neck stiffness	2	

CONCLUSION

Although CM is a treatable cause of death in AIDS, it is often undiagnosed in most resource-poor settings with improved human, laboratory and research capacity is critical to effective management of this infection. Also the availability of cheap and effective antifungal drugs cannot be overemphasized. So, there is also the urgent and crucial need to scale up efforts to make ART drugs universally available, accessible and affordable.

Hence, the presence study is only the basic but will serves as background for epidemiologist to know the trend of CM in HIV patients.

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