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A Study of Clinical Profile of Cryptococcal Meningitis in HIV Patients

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ABSTRACT

Introduction: Cryptococcus neoformans is a pervasive encapsulated yeast that mostly causes infections in immune-compromised individuals. Cryptococcal meningitis is a complication of advanced HIV infection. Hydrocephalus, infarction, or cryptococcoma may be identified on a CT or MRI scan of the brain. In cryptococcal meningitis, elevated intracranial pressure (ICP) and hydrocephalus are common. Fungal CSF culture is the gold standard. **Aims and Objectives:** The study was designed to study HIV positive patients with cryptococcal meningitis for their presentation, laboratory findings and response to treatment. **Material and Methods:** 20 patients of Cryptococcal meningitis who were HIV positive were studied retrospectively at Pt. B.D. Sharma, Postgraduate Institute of Medical Sciences, Rohtak over a period of 1 year. **Results:** Cryptococcal meningitis was more prevalent in males, with the majority of patients being between the ages of 20 and 40. The most common presenting symptoms included headache, vomiting, and fever. CSF India Ink was positive in 80% of the patients only while cryptococcal antigen was positive in 100% of the patients. Most of the patients had a CD4 count of <100/µl. Mortality was as high as 80 percent and all survivors were later started on HAART.

Keywords: Cryptococcal meningitis, Amphotericin, HIV

INTRODUCTION

Cryptococcus neoformans is a pervasive encapsulated yeast that mostly causes infections in immune-compromised individuals, with HIV infection accounting for 80% to 90% of all cases[1,2]. Central nervous system (CNS) and lungs are the common sites of infection. After HIV infection, immunosuppressive medications, solid-organ transplantation, chronic organ dysfunction (renal and liver), hematologic malignancy, chronic lung disease, and rheumatologic diseases are those diseases that increase the risk of infection [3].

Cryptococcal meningitis is a complication of advanced HIV infection (CD4+ counts usually <100/mL) that causes headache, fever, stiff neck and photophobia. On the other hand, meningeal symptoms and signs can be mild or absent in more than half of thecases, and can manifest as malaise, personality changes, cognitive impairment, cranial neuropathy, altered mentation, and a variety of other symptoms such as coma[4].

Hydrocephalus, infarction, or cryptococcoma may be identified on a CT or MRI scan of the brain. Neuroimaging also shows cerebral atrophy associated with advanced HIV disease. In cryptococcal meningitis, elevated intracranial pressure (ICP) and hydrocephalus are common. The CSF image can range from elevated proteins with lymphocytic pleocytosis and hypoglycorrhachia to normal glucose to minor anomalies that overlap with HIV infection alone. Fungal CSF culture is the gold standard, but incubation takes weeks. India ink preparations for cryptocoocus are extremely sensitive and precise for cryptococcal antigen testing of CSF, or serum if CSF cannot be obtained [5].

Amphotericin B (AmB) deoxycholate (AmBd; 0.7–1.0 mg/kg per day intravenously [IV]) and

flucytosine (100 mg/kg per day orally in 4 divided doses for at least 2 weeks, followed by fluconazole (400 mg [6 mg/kg] per day orally) for at least 8 weeks is being used to treat cryptococcal meningitis in HIV positive patients. AmBd (0.7 mg/kg per day IV) plus fluconazole (800 mg per day orally) for 2 weeks, supplemented by fluconazole (800 mg per day orally) for a minimum of 8 weeks, is an alternate regimen[15].

AIMS AND OBJECTIVES:

The series was designed to study HIV positive patients with cryptococcal meningitis under following subsets:

1) Clinical features
2) Laboratory findings:
    - CD4 count
    - CSF picture
    - Radiological findings
3) Response to treatment

MATERIAL AND METHODS: -

SOURCE OF DATA: 20 patients of Cryptococcal meningitis who were HIV positive were studied retrospectively at Pt. B.D. Sharma, Postgraduate Institute of Medical Sciences, Rohtak. The study was done over a period of 1 year (2015-2016).

Inclusion criteria: All the HIV positive patients with features suggestive of meningitis were initially screened for cryptococcal meningitis based on CSF demonstration of Cryptococcus neoformans by India ink preparation or positivity for cryptococcal antigen in CSF were included.

INVESTIGATIONS DONE:

ELISA test for HIV

CD4 count was determined by BD FACS Count system.

CSF analysis for

1. Proteins and sugar
2. Cell count and cell type
3. India ink smear
4. Cryptococcal antigen

NCCT/CECT Brain

OBSERVATIONS: -

AGE: In the present study the mean age of patients was 38.4 years, with 40% of patients being between the ages of 41 and 60 and 60% being between the ages of 20 and 40. This is in accordance with the study done by Imwidthaya P et al [6] where the mean age of patients was 32.1years.

TABLE 1: AGE DISTRIBUTION

AGE INTERVAL	Number of patients(percentage)
20-30	2(10%)
31-40	10(50%)
41-50	8(40%)

SEX: In the present study, the number of males was more as compared to the number of females (19 vs. 1). In the study done by Imwidthaya P et al [6] 80.46% of the patients were males.

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TABLE 2: SEX DISTRIBUTION

GENDER	Number of patients (percentage)
Male	19(80%)
Female	1(20%)

DURATION OF HIV SEROPOSITIVE STATUS AND TREATMENT:

In about 40% of patients, cryptococcal meningitis was the first manifestation of AIDS. This finding is similar to the study done by Chuck SL et al [7]. They found that cryptococcal meningitis was the defining illness in 45.28% of patients with AIDS. 8 of the 20 patients (40%) had their first presentation and were not on ART.

TABLE 3: DURATION OF HIV POSITIVE STATUS

HIV status since	Number of patients (percentage)
Newly diagnosed	8(40%)
Less than 12 months	3(15%)
More than 12 months	9(45%)

PRESENTING SYMPTOMS: In the present series headache, vomiting and fever were the most common presenting symptoms. Fever and headchae were the most common presenting symptoms in the study by Woldemanuel Y et al [8].

TABLE 4: PRESENTING SYMPTOMS

PRESENTING SYMPTOMS	Chuck SL et al [7] (n=106)	Kalra SP et al [9] (n=15)	PRESENT STUDY(n=20)
Headache	73%	80%	90%
Vomiting	42%	-	75%
Altered sensorium	28%	26.6%	65%
Fever	45%	86.6%	75%
Seizures	-	-	35%
Neurological deficit	-	-	10%

TABLE 5: DURATION OF NEUROLOGICAL SYMPTOMS

DURATION	Number of patients (percentage)
Less than 10 days	5(25%)
10 days to 20 days	9(45%)
20 days to 30 days	5(25%)
More than 30 days	1(5%)

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TABLE 6: LEVEL OF CONSCIOUSNESS

GLASSGOW COMA SCALE	Number of Patients (percentage)
GCS 15/15	7(35%)
GCS 7-15	3(15%)
GCS <7	10(50%)

TABLE 7: SEIZURES

	Number of Patients(percentage)
+	7(35%)
-	13(65%)

TABLE 8: HEADACHE

	Number of Patients(percentage)
+	18(90%)
-	2(10%)

TABLE 9: FEVER

	Number of Patients(percentage)
+	15(75%)
-	5(25%)

TABLE 10: VOMITING

	Number of Patients(percentage)
+	15(75%)
-	5(25%)

TABLE 11: NEUROLOGICAL DEFICIT

Slurring of Speech	Number of Patients(percentage)
+	2(10%)
Weakness of Any Limb	**Number of Patients(percentage)**
+	1(5%)

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CSF POSITIVITY FOR CRYPTOCOCCAL ANTIGEN/INDIA INK POSITIVE:

India Ink preparation was positive in 80% of patients and CSF cryptococcal antigen was positive in 100% of the patients.

TABLE 12: POSTIVITY OF CSF

	Darras-Joly C et al [10] (n=65)	Khanna N et al [11] (n=87)	Present study (n=20)
CSF Cryptococcal antigen positivity	92%	98.81%	100%
CSF India ink preparation	87%	87.36%	80%

CSF PROTEIN: The mean CSF protein in this study was 141.5. CSF proteins of >50mg/dl were found in 90% of the patients. Findings correlated with the study done by Hakim et al[12] where 80.6% of the patients had a CSF protein level of >40mg/dl. Mildly raised CSF proteins are found commonly in patients with cryptococcal meningitis.

TABLE 13: CSF PROTEINS

CSF Proteins	Number of Patients(percentage)
<50	2(10%)
50-100	9(45%)
101-150	4(20%)
>200	5(25%)

CSF SUGAR: The mean sugar levels in CSF were 40.15mg/dl in the present study. Kumar S. et al conducted a study with findings of mean CSF glucose of 45.63mg/dl.[13]

TABLE 14: CSF SUGAR

CSF Sugar	Number of Patients(percentage)
<30	2(10%)
31-40	7(35%)
41-50	9(45%)
>50	2(10%)

CD4 COUNT: Mean CD4 count was found to be 80.3.50% of patients had CD4 count < 50, 25% of patients with CD4 count between 51-100 and 25% having >100. This finding is similar to study conducted by Kumar S. et al in which 56.66% of the patients had a CD4 count of <50. [13]

MORTALITY: In the present study mortality was 80%. Mortality was 100% in the study done by P Mwaba et al [14] Mortality in cryptococcal meningitis is high and mainly due to the immunodeficiency seen in the patients and complications of the treatment

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SUMMARY: The aim of this study was to examine the Clinical features, Laboratory findings and outcome in HIV seropositive patients with Cryptococcal meningitis. For this, a retrospective study was conducted on 20 HIV positive patients with cryptococcal meningitis.The salient features of this study include-

1. Cryptococcal meningitis was more prevalent in males, with the majority of patients being between the ages of 20 and 40.
2. The majority of patients presented with an acute to subacute symptoms, with cryptococcal meningitis being the first manifestation of AIDS in 40 percent of cases. The most common presenting symptoms included headache, vomiting, and fever.
3. CSF India Ink was positive in 80% of the patients only while cryptococcal antigen was positive in 100% of the patients.
4. Most of the patients had a CD4 count of <100/µl.
5. Mortality was as high as 80 percent and all survivors were later started on HAART.

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