

Manifestations of Opportunistic Infections of Central Nervous System in HIV/Aids

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Abstract: Background: CNS is the second most commonly affected organ in HIV/AIDS. The most frequent opportunistic infections of CNS in HIV/AIDS are toxoplasmosis, progressive multifocal leucoencephalopathy (PML), cryptococcosis and cytomegalovirus infection.

Methods: This study, conducted at Regional Institute of Medical Sciences (RIMS) Imphal, Manipur between July 2016 and August 2018 aims to evaluate the prevalence and manifestations of CNS opportunistic infections and other CNS conditions in HIV/AIDS cases and to find out correlation between CD4 count and type of CNS manifestation in this population.

Results: A total of 50 cases of AIDS with CNS opportunistic infections and 25 cases with other CNS manifestations were studied during the period from July 2016 to August 2018. In both the groups, maximum cases were in the age group of 31-41 years (36% and 40% respectively). 39 cases (79%) were females in first group. Major route of infection was by IVDUs in both groups (58% and 56% respectively). Commonest OI in the first group was TB meningitis (23 cases-46%) whereas Aseptic meningitis was the most common CNS manifestation in second group (9 cases-36%). Definite correlation with CD4 count was also observed with various infections in both the groups.

Conclusion: Most prevalent CNS OI in HIV/AIDS patients is TB meningitis and most frequent CNS manifestation is aseptic meningitis. Adults between 31-40 years are mostly affected. Level of CD4 count can be correlated with type CNS infection.

Key Words: HIV, Manipur, tubercular meningitis, neurological manifestation, cryptococcal meningitis

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I. Introduction

Acquired Immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus. It was first recognized in the US in 1981. Since the introduction of highly active anti-retroviral therapy (HAART), the morbidity and mortality associated with HIV has significantly decreased and AIDS has become a chronic and manageable disorder.^[1] However, neuropathological manifestations associated with AIDS are still present in approximately 70% of patients and can be due to HIV itself or of associated opportunistic infections. AIDS epidemic in India is in an alarming phase, with patient doubling time seen in just one year.^[2]

There are only few studies published regarding the neurological manifestations of AIDS in India. This is the first study examining the impact of neurological manifestations of HIV/AIDS in Manipur.

II. Material and Methods

This was a retrospective observational study conducted at department of medicine RIMS, Imphal in collaboration with Microbiology and Radiology departments. 50 cases of AIDS with CNS opportunistic infections and 25 cases of AIDS with other CNS manifestations from medicine OPD and ward were included in the study.

A detailed history was noted in each patient with special emphasis on history of multiple sexual partners, drug abuse, penile ulcer, blood transfusions or a history of STD. Clinical examination was performed including detailed neurological examination like higher function, cranial nerves, motor and sensory system etc.

Fundoscopy was done in each patient. Routine haematological, biochemical and bacteriological investigations including CSF examination, chest x-ray, special staining studies, serum and CSF antigen tests were performed along with computed tomography (CT) of the brain and magnetic resonance imaging (MRI) of the brain.

III. Results

Age and sex distribution

Out of 50 cases of AIDS with opportunistic infections, 39 cases (78%) were male and 11 cases (22%) were female. Maximum cases were in the age group of 31-40 years (36%).

Out of 25 cases of AIDS with other CNS manifestations 19 cases (76%) were male and 6 cases (24%) were female. Maximum cases were in the age group of 31-40 years (40%).

Clinical Manifestations

In the first group, fever and weight loss were the commonest symptoms (80%). Oral thrush (74%), head ache (70%) was also common in this group. Head ache (76%) was the commonest symptom in the second group followed by fever and weight loss (64% each).

Table No.1A: Symptoms and signs in AIDS cases with opportunistic infections (n=50)

Signs and symptoms	No. of cases	Percentage
Fever	40	80%
Weight loss	40	80%
Neck stiffness	37	74%
Headache	35	70%
Oral thrush	36	52%
Altered sensorium	24	48%
Lymphadenopathy	10	20%
Convulsion	9	18%
Hemiplegia	6	12%
Cranial nerve palsy	4	8%
Unsteady gait	2	4%

Table No.1B: Signs and symptoms of CNS manifestations other than OI in AIDS cases (n=25)

Signs and symptoms	No. of cases	Percentage
Fever	16	64%
Weight loss	16	64%
Neck stiffness	12	48%
Headache	19	76%
Oral thrush	12	16%
Altered sensorium	14	56%
Hemiplegia	10	40%
Dysarthria	1	4%
Unsteady gait	4	16%

Route of Infection

IVDU is the commonest route of infection in both the groups (58% and 56% respectively) followed by heterosexual route (36% and 32% respectively).

Table No. 2A: Routes of infection of AIDS cases with CNS opportunistic infections (n=50)

Route of Infection	No. of cases		Percentage
	Male	Female	
IVDUs	28	1	58%
Heterosexual	9	9	36%
Homosexual	1	0	2%
Blood transfusion	1	0	2%
Parent to child	1	0	2%

Table No. 2B: Distribution of routes of infection of AIDS cases with other CNS manifestations

Route of Infection	No. of cases		Percentage
	Male	Female	
IVDUs	28	1	58%
Heterosexual	9	9	36%
Homosexual	1	0	2%
Blood transfusion	1	0	2%
Parent to child	1	0	2%

Disease Spectrum

Commonest CNS opportunistic infection in first group was TB meningitis-23 cases (46%) followed by cryptococcosis which was detected in CSF by India ink method. Toxoplasmosis was detected in 7 cases (14%). PML was seen in 2 cases and CMV Ab was seen only in 1 case (2%).

Aseptic meningitis was the commonest CNS manifestation in the second group (9 cases-36%) followed by cerebral Infarct (5 cases-20%) and CNS lymphoma (3 cases-12%).

Table NO. 3A: Distribution of CNS Opportunistic Infections

Diseases	No. of cases	Percentage
Tubercular meningitis	23	46%
Cryptococcal meningitis	17	34%
Toxoplasmosis	7	14%
Progressive multifocal leucoencephalopathy	2	4%
CMV antibody	1	2%

Table No. 3B: Distribution of other CNS Manifestations

Diseases	No. of cases	Percentage
Aseptic meningitis	9	36%
CNS lymphoma	3	12%
Cerebral Infarct	5	20%
Intracerebral haemorrhage	3	12%
Myelopathy	2	12%
Dementia complex	1	8%

Correlation with CD4 Count

In first group, out of 23 cases of TB meningitis, 17 cases (73%) had CD4 count <100. All 17 cases (100%) of cryptococcal meningitis had CD4 <200. 100% of toxoplasmosis (7 cases) and PML (2 cases) had CD4 <100. One case of CMV was having a CD4 count <50.

In the second group, all 9 cases of aseptic meningitis had CD4 <100 and all 3 cases of CNS lymphoma had a CD4 <50.

Table No. 4A: Distribution of AIDS cases with CNS opportunistic infections in relation with CD4 count

Level of CD4 count	TB meningitis	Cryptococcal meningitis	Toxoplasmosis	PML	CMV Ab
>300	0	0	0	0	0
200-299	1	0	0	0	0
100-199	5	2	0	0	0
50-99	7	3	4	1	0
0-49	10	12	3	1	1

Table No. 4B: Distribution of AIDS cases with other CNS opportunistic manifestations in relation with CD4 count

Level of CD4 count	Aseptic meningitis	Cerebral infarct	Intra cerebral hemorrhage	CNS lymphoma	Myelopathy	Dementia complex
>300	0	0	0	0	0	0
200-299	0	1	1	1	0	0
100-199	0	2	1	0	2	0
50-99	4	1	1	0	0	1
0-49	5	1	0	3	1	1

IV. Discussion

It has been well established that CNS is extensively involved in patients with HIV/AIDS with no part of the neuraxis immune from the virus.^[3] The neurological manifestations that occur in AIDS patients may be due to the disease itself or from subsequent opportunistic infections. Damage to the CNS may be secondary to release of neurotoxins and cytokines such as IL-1, TNF alpha and IL-6.^[4]

Manipur with hardly 0.2% of India's population contributes nearly 8% of India's HIV positive cases. Estimated cases of HIV positives among general population are around 40,000. To the best of our knowledge, this study is the first of its kind to assess the CNS manifestations of opportunistic infections and other conditions in HIV/AIDS patients in Manipur. Incidence of neurological manifestation was highest in the age group of 31-40 years. This constitutes a highly productive section of the society which might affect favourable growth of the nation and future generations.^[1] IVDUs was the commonest route of disease transmission, in contrast to western studies where homosexual transmission is more prevalent.

The commonest CNS opportunistic infection in AIDS patients was TB meningitis i.e, 23 cases (46%). This is consistent with a previous study in a tertiary institute in north east.^[5] The most common CNS manifestation other than OI in AIDS patients, was aseptic meningitis i.e. 9 cases (36%).

Cryptococcal meningitis was the most common CNS fungal infection in HIV infected patients. In the United states, approximately 5–10% patients had AIDS with cryptococcal meningitis.^[6] In our study, 17 out of 50 (34%) patients with neuro-AIDS had cryptococcal meningitis. Cryptococcal meningitis occurred in the last stages of HIV illness, particularly with CD4 counts <100 μL .^[6] A high index of suspicion is the key to the diagnosis of cryptococcal meningitis.

PML (progressive multifocal leukoencephalopathy) results from infection with human polyoma virus (JC virus), developing in 4% of patients with AIDS, and this was the initial manifestation of AIDS in 29% of these cases.^[3] However, in the present study, only two patients have history, findings and MRI picture suggestive of PML.

HIV-associated neurocognitive impairment, myelopathy, peripheral neuropathy, myopathy, and aseptic meningitis are part of the primary illnesses. HIV infection characteristically generates a “subcortical” pattern of neuro-cognitive dysfunction with deficits predominantly affecting executive functions, speed of information processing, attention/working memory, motor speed, new learning, and retrieval of new information. It generally occurred when CD4 count was less than 100 cell/ μL .^[7] In our study, eight patients (32%) in second group were diagnosed to be having a cerebrovascular accident (CVA). Five of them had an infarct in the basal ganglia and other three had an intracerebral hemorrhage. The incidence of CVA in the present study is higher in contrast to that seen in other studies.^[8]

In the present study, the mean CD4 was and was found to be below 300 in both the groups. All cases were having CD4 less than 200 in first group except for one case of cerebral infarct. People living with HIV who have a CD4 cell count below 200 are at a significant risk of developing serious illnesses, which has been seen in this study too. Presence of neurological manifestations is associated with decreased CD4 counts. CD4 count can serve as a guide to assess the HIV status, assess the risk for the development of neurological manifestations in such patients and help in instituting timely intervention in the form of prophylaxis and treatment.^[9]

Our study shows that when signs and symptoms of CNS infection such as head ache, fever, altered sensorium hemiplegia etc. are presented by an adult in the age group of 31-40 years, proper investigations must be done to exclude HIV/AIDS with CNS manifestations.

V. CONCLUSION

Central nervous system is one of the major target organs for HIV virus. With the advent of effective anti-retroviral drugs, AIDS has transformed into a chronic disorder, leading to increased prevalence of neurological manifestations. It is of utmost importance to address the primary causal factors as initiation of therapy may dramatically improve the quality of life in these patients. Hence the importance of preventive measures and public education cannot be over emphasized.

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Conflicts of Interest

There are no conflicts of interest

References

- [1]. Patil VC, Patil HV. Neurological manifestations of HIV- AIDS at a tertiary care centre in western Maharashtra. *Int J Med Public Health* 2014;4:210- 17
- [2]. Sircar AR, Tripathi AK, Choudhary SK, Misra R. Clinical profile of AIDS: A study at a referral hospital. *J Assoc Physicians India* 1998;46:775- 8
- [3]. Das CP, Sawhney IMS. Neurological complications of HIV infection. *Neurol India* 1998;46:82- 93
- [4]. Fauci AS, Lane HC. Human immunodeficiency virus disease: Harrison's Principle of Internal Medicine. Vol 1. 17th ed. New York: Mcgraw Hill; 2008.pp. 1139- 83
- [5]. Sharma SR, Hussain M, Habung H. Neurological manifestations of HIV- AIDS at a tertiary care institute in North Eastern India. *Neurol India* 2017;65:64- 8.
- [6]. Kovacs JA, Kovacs AA, Polis M, Wright WC, Gill VJ, Tuazon CU. Cryptococcosis in acquired immunodeficiency syndrome. *Ann Intern Med* 1985;103:533- 8.
- [7]. Price RW, Brew BJ. The AIDS dementia complex. *J Infect Dis* 1988;158:1079- 83.
- [8]. Mc Arthur JC. Neurologic manifestations of AIDS. *Medicine* 1987;66:407- 37.
- [9]. Deshpande AK, Patnaik MM. Non- opportunistic neurologic manifestations of the Human immunodeficiency virus: An Indian Study. *J Int AIDS Soc* 2005;7:2.