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CD4 Count and Opportunistic Infections in HIV Positive Patients with Neurological Manifestations

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ABSTRACT

Introduction: CD4 count is having special predictive value in occurrence of opportunistic infection. Opportunistic infection mostly occurs when CD4 count goes below 250 cells/microL.

Methodology: This was a cross sectional study, done in 50 HIV positive patients attending medicine OPD and admitted patients in SMIMER, a tertiary care hospital in Surat, Gujarat, India. All HIV positive patients above 18 years presenting with neurological manifestations and ready to give informed written consent to participate were included. Complete clinical assessment and laboratory investigations were performed in all cases.

Results: Mean CD-4 count in TBM was 140, in Cryptococcal meningitis was 52, in Toxoplasmosis was 170 and in AIDP was 281. The difference in the mean CD4 count is statistically significant (p-Value<0.001). Thus AIDP can occur at CD4 level as high as 281 cells/microL.

Conclusion: Most common primary neurological illness was DSPN and secondary neurological illness was TBM. AIDP can occur at CD4 level as high as 281 cells/microL. Whereas other OIs can occur after CD4 count goes below 200 cells/microL.

Keywords: TB Meningitis (TBM), CD4 count, HIV, Neurological Manifestations

INTRODUCTION

India has a population of 1.2 billion people, around half of whom are adults in the sexually active age group. The first AIDS case in India was detected in 1986 and since then HIV infection has been reported in all states and union territories.[1]The highest estimated adult HIV prevalence is found in Manipur (0.78%), followed by Andhra Pradesh (0.76%), Karnataka (0.69%) and Nagaland (0.66%).[2]

The current CDC classification system for HIV-infected adolescents and adults categorizes persons on the basis of clinical conditions associated with HIV infection and CD4+ T lymphocyte counts. The system is based on three ranges of CD4+ T lymphocyte counts and three clinical categories and is represented by a matrix of nine mutually exclusive categories. Using this system, any HIV-infected individual with a CD4+ T cell count of <200/L has AIDS by definition, regardless of the presence of symptoms or opportunistic diseases. Once individuals have had a clinical condition in category B, their disease classification cannot be reverted back to category A, even if the condition resolves; the same holds true for category C in relation to category B.[3]

Follow-up and monitoring is essential in patients initiated on ART to track clinical progress and wellbeing. Among patients with HIV infection, CD4+ T lymphocyte counts continue to be the best validated predictors of the likelihood of an opportunistic infection. Although plasma viral levels independently provide important prognostic information with regard to AIDS, the risk of specific opportunistic infection has not yet been adequately related to plasma viral levels. The current guide-

lines for initiating prophylaxis do not include criteria based on plasma viral levels.[4]

A variety of monocyte-derived cytokines can contribute directly or indirectly to the neurotoxic effects in HIV infection; these include TNF-α, IL-1, IL-6, TGF-β,IFN- γ, platelet-activating factor, and endothelin. In addition, infection and/or activation of monocyte-lineage cells can result in increased production of eicosanoids, nitric oxide, and quinolinic acid, which may contribute to neurotoxicity. As reported, HIV-infected individuals with the E4 allele for apolipoprotein E (apo E) are at increased risk for AIDS encephalopathy and peripheral neuropathy. CD4 count is having special predictive value in occurrence of opportunistic infection. Opportunistic infection mostly occurs when CD4 count goes below 250 cells/microL. Common neurological manifestations are TB Meningitis (TBM), Cryptococcal meningitis (CCM), Progressive Multifocal Leuko-encephalopathy (PMLE), AIDS Dementia Complex (ADC), Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Distal Sensory Polyneuropathy (DSPN) etc.

The likelihood that HIV or its products are involved in neuro-pathogenesis is supported by the observation that neuropsychiatric abnormalities may undergo remarkable and rapid improvement upon the initiation of antiretroviral therapy, particularly in HIV-infected children.[3]

The present study was aimed to determined relation between CD4 count and opportunistic infections in HIV positive patients with neurological manifestations.

METHODOLOGY

The present study was done among 50 patients Living with HIV/AIDS (PLHA) attending medicine OPD and admitted patients in Surat Municipal Institute of Medical Education and Research (SMIMER), a tertiary care hospital in Surat, Gujarat, India.

This was a cross sectional study done from July 2013 to June 2014, in which all HIV positive patients attending medicine OPD above 18 years of age presenting with neurological manifestations and ready to give informed written consent to participate in the study were included in the study. Neurological manifestations considered were TB Meningitis (TBM), Cryptococcal meningitis (CCM), Progressive Multifocal Leukoencephalopathy (PMLE), AIDS Dementia Complex (ADC), Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Distal Sensory Polyneuropathy (DSPN) and toxoplasmosis.

Permission of Ethical Committee of Institute was obtained before conducting study. There were total 50 HIV infected patients included in the study showing clinical evidence of nervous system involvement who were ready to give consent to participate. Confidentiality of data at all level of project was maintained.

Semi structured questionnaire with case report form was developed after extensive review of literature and consulting subject expert. Detailed clinical history with special emphasis on consciousness, convulsions and headache was recorded in the questionnaire. Thorough clinical evaluations included sensory, motor, cranial nerves and mini mental status examination (MMSE).

Apart from routine investigations, CD4 count was measured using standard flow cytometry. Diagnostic investigations like MRI brain with contrast, cerebrospinal fluid (CSF) examination and electromyography-nerve conduction study (EMG-NCS) were done as and when required. Data was entered and analysed in Microsoft Excel.

RESULTS

There were total 50 HIV infected patients fulfilling all the inclusion criteria and found eligible for the study. There were total 15 (30%) patients diagnosed with primary neurological illness and 35 (70%) patients were diagnosed as Secondary Neurological Illness. Most common primary neurological illness was DSPN. Most common secondary neurological illness was TBM.

Table 1: Relation between CD4 Count and Opportunistic Infection

CD4 (cells/microL)	TBM (%)	CCM (%)	Toxoplasmosis (%)	PMLE (%)	ADC (%)	AIDP (%)	DSPN (%)
50	4 (22.2)	4 (50)	1 (20)	0 (0)	1 (50)	0 (0)	1 (9)
51-100	3 (16.7)	3 (37.5)	0 (0)	1 (25)	0 (0)	0 (0)	1 (9)
101-150	3 (16.7)	1 (12.5)	0 (0)	2 (50)	1 (50)	0 (0)	2 (18)
151-200	2 (11.1)	0 (0)	3 (60)	1 (25)	0 (0)	1 (50)	3 (27)
201-250	3 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)
251-300	3 (16.7)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	2 (18)
>300	0 (0)	0 (0)	0 (0)	0 (0)	(0)	1 (50)	1 (9)
Total	18 (100)	8 (100)	5 (100)	4 (100)	2 (100)	2 (100)	11 (100)

* **TBM-** TB Meningitis; **CCM-** Cryptococcal meningitis **PMLE**- Progressive Multifocal Leukoencephalopathy; **ADC**- AIDS Dementia Complex; **AIDP**- Acute Inflammatory Demyelinating Polyneuropathy; **DSPN**- Distal Sensory Polyneuropathy

Table 2: Mean CD4 count in various illness

Disease	Number	Mean CD4 Level (cells/microL)
CCM	8	52±3.02
ADC	2	93±8.12
PMLE	4	125±12.6
TBM	18	140±9.72
Toxoplasmosis	5	170±14.3
DSPN	11	191±6.2
AIDP	2	281±7.23

p-Value <0.0001

* **TBM-** TB Meningitis; **CCM-** Cryptococcal meningitis; **PMLE**-Progressive Multifocal Leukoencephalopathy; **ADC**- AIDS Dementia Complex; **AIDP**- Acute Inflammatory Demyelinating Polyneuropathy; **DSPN**- Distal Sensory Polyneuropathy

Table 1 shows that in Cryptococcal meningitis all patients had CD4 count less than 150. Although more than 70% patients of TBM had the CD4 count less than 200 it is distributed widely which indicates that TBM can occur at any CD-4 count. Table also shows that AIDP occur at higher CD-4 level (because AIDP is autoimmune phenomena). All PML patients had CD-4 less than 200. In DSPN more than 70% cases have CD-4 less than 200 but it is distributed widely.

Table 2 shows that mean CD-4 count in TBM was 140, in Cryptococcal meningitis was 52, in Toxoplasmosis was 170, in PML was 125, in AIDS dementia complex was 93, in DSPN was 191, and in AIDP was 281. The difference in the mean CD4 count is statistically significant (p-Value<0.001). Thus AIDP can occur at CD4 level as high as 281 cells/microL. Statistical test used to calculate p value was ANOVA (Analysis of Variance).

DISCUSSION

It has been well-recognized that the nervous system is extensively involved in patients with HIV-AIDS with no part of the neuraxis being immune from the virus.[5] Neurological manifestation that occurs in HIV patients may be either due to the primary pathological process of HIV infection or secondary to opportunistic infection or neoplasm. [6] Infected macrophages infiltrate the brain parenchyma resulting in slow neuro-degeneration, especially in the hippocampus, basal ganglia, prefrontal cortex, and white matter. Damage to the CNS may be secondary to the release of neurotoxins and cytokines such as IL-1, TNF-TNF, and IL-6.[7]

In the present study, the incidence of neurological involvement was found to be maximum in the age group of 18–60 years, which correlates with other studies. This constitutes a highly productive section of the society that is likely to affect the growth of the nation as well as future generations. [8]

There were total 50 HIV positive patients attending medicine OPD above 18 years presenting with neurological manifestations enrolled in the study. Out of these, total 15 (30%) patients were diagnosed with primary neurological illness and 35 (70%) patients were diagnosed as Secondary Neurological Illness. Most common primary neurological illness was DSPN. Most common secondary neurological illness was TBM.

With lowering of CD4 count accounts for more neurological manifestations in HIV patients. Although more than 70% patients of TBM and DSPN had the CD4 count less than 200 it is distributed widely which indicates that TBM and DSPN can occur at any CD-4 count. Table also shows that AIDP occur at higher CD-4 level (because AIDP is autoimmune phenomena). Sonkar, et al.[9]study reported that 64.7% of neurologically manifested patients had CD4 count less than 200. Only 67 (40.36%) patients with Peripheral neuropathy had low CD4 count. Robinson, et al.[10]study reported that peripheral neuropathy patients had higher CD4 count which was comparable to our study. In our study 70% of patients with TB meningitis had low CD4 count and this was comparable to Sonkar, et al.[9] study who reported that 55% of patients with TB meningitis patients had low CD4 count.

In present study, all patients with cryptococcal meningitis had low (<200µL) CD4 count which was comparable to Bolokadze, et al.[11]study who reported that 83% of patients with cryptococcal meningitis had low (<200µL) CD4 count. Cryptococcal meningitis occurred in the last stages of HIV illness, particularly with CD4 counts <100 µl. [12]

Except for cryptococcal meningitis, results of present study are comparable with results of Alka et al, [13] which shows mean CD4 count in TBM was 160, in cryptococcal meningitis was 114, in toxoplasmosis 150 and in PML w. In cryptococcal meningitis we had relatively low CD4 Count.

In India today, the only affordable methodology is the estimation of the CD4+ cell counts. It 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. [14] HIV patients having CD4 count less than 200 are at high risk of serious neurological illness.[16]

In the era of HAART and specific treatment that is available for opportunistic infections, mortality in patients with HIV with neurological illness has considerably decreased. [17]

CONCLUSION

Most common primary neurological illness was DSPN. Most common secondary neurological ill-

ness was TBM. All Cryptococcal meningitis patients had CD4 count less than 150. Although more than 70% patients of TBM had the CD4 count less than 200, it can occur with higher CD4 count also. AIDP can occur at CD4 level as high as 281 cells/microL. Whereas other OIs can occur after CD4 count goes below 200 cells/microL.

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