Research Paper

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A Study of Clinical Profile of Neurological Manifestations in HIV Positive Patients With Reference to CD4 Cell Count

Medical Science

KEYWORDS : PLHIV, CNS manifestation, CD4 lymphocyte count.

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ABSTRACT

HIV infection affects millions of people around the world and many patients progress to AIDS with profound immunosuppression. HIV can affect central nervous system by direct infection as well as through opportunistic infections. Neurological manifestations are responsible for increased morbidity and mortality amongst HIV positive patients. These neurological manifestations have a definite correlation with CD4 lymphocyte cell count. Certain neurological manifestations occur only with CD4 cell count less than 200. Thus CD4 cell count can help guide the monitoring and treatment of HIV positive patients with neurological manifestations.

INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) is caused by Human Immunodeficiency Virus (HIV). It is a serious disorder of immune system in which normal defense of body breaks against infection leading to life threatening conditions.

After the detection of Acquired lmmunodeficiency Syndrome (AIDS) cases in summer of 1981 among Homosexuals in USA, the numbers of Human Immunodeficiency Virus (HIV) positive individuals and AIDS cases have increased explosively.

The central nervous system is among the frequent and serious target of HIV infection and it is more commonly occurring in patients with severe immunosuprresson. HIV affects all levels of the nervous system. Virtually all patients with HIV infection have some degree of nervous system involvement with the virus. This is evident by the fact that CSF findings are abnormal in ~90% of patients, even during asymptomatic phase of HIV infection. CSF abnormalities include intrathecal synthesis of anti HIV antibody (90%), detectable viral RNA (~75%), pleocytosis (50-60%), and evidence of elevated CSF protein (35%).

The neurological problems that occur in HIV infected individual may be either primary to pathological process of HIV infection or secondary to opportunistic infections or neoplasm. Neurological problems directly attributable to HIV occur throughout the course of infection and may be inflammatory, demyelinating, or degenerative in nature.

The neurological complication in HIV may be primary to the pathogenic process of HIV infection or secondary to opportunistic infections or neoplasms.

Primary Illnesses (Result of HIV infection due to inflammatory, demyelinating, and degenerative process)
HNCI (HIV associated neurocognitive impairment): this include minor cognitive impairment to most severe HIV encephalopathy;

Myelopathy, Peripheral neuropathy, Myopathy & Aseptic meningitis.

Secondary illnesses: (due to opportunistic infections)
Mycobacterium tuberculosis, Toxoplasmosis, Cryptococcosis, Progressive multifocal leukoencephalopathy (JC virus infection), Cytomegalovirus, Syphilis, HTLV-1 infection, Pneumocystis jiroveci (p.carini) infection, Atypical mycobacterium infection, Amoebiasis, & T.cruzi infection.

Neoplasm
Primary CNS lymphoma, Kaposi's sarcoma, Small noncleaved cell lymphoma burkitt type & Immunoblastic lymphoma body cavity type.

India appears to be fertile soil for HIV infection because of poverty, illiteracy, malnutrition, lack of sex education and high prevalence of STDs. In India HIV patient has more chances to manifest full blown AIDS because of poverty and illiteracy. Patient either doesn't take ART or become ART defaulter, and due to malnutrition, there are more chances of acquiring co- infection like TB.

Considering these facts we have decided to study the incidence and clinical profile of various neurological manifestations in HIV patients.

In assessment of neurological symptoms, it should always be kept in mind that (1) Multiple HIV associated disorders may coexist in a patient simultaneously. (2) Even in absence of specific complaints careful neurological examination frequently reveals evidence of CNS or PNS dysfunction.

AIMS AND OBJECTIVES

1. To study the clinical profile of PLHIV patients with neurological manifestations.
2. To correlate various neurological manifestations with the CD4 cell count of the patients.
3. To study the outcome of various neurological conditions in PLHIV patients.

MATERIALS AND METHODS

We studied HIV infected patients showing clinical evidence of nervous system involvement and admitted in or taking outpatient basis treatment from our hospital.

The study was conducted after obtaining prior permission from the **Institutional ethics committee** and State AIDS Control Society. The identity of the patients was not revealed in any manner.

All the patients were treated according to their opportunistic infections and indicated patients received ART also.

Patients were followed up regularly for change in the clinical condition and change in value of CD4.

RESULTS

- Maximum number of patient were in age group 21-40 years (82%) with Male: Female ratio of 3.2:1.
- HIV induced primary neurological illness was present in 24% cases, while secondary neurological illness was present in 76% cases.
- Most common neurological illness in HIV is TBM which is present in 58% HIV positive patients presenting with neurological manifestation, followed by Cryptococcal meningitis (20%) and Toxoplasmosis (8%).
- Amongst the primary neurological manifestations, ADC (8%), PML (4%) and primary CNS lymphoma (2%) were noted.
- The most common presenting symptom on admission is fever (64%), followed by headache (62%), altered consciousness (48%) and convulsion (44%)

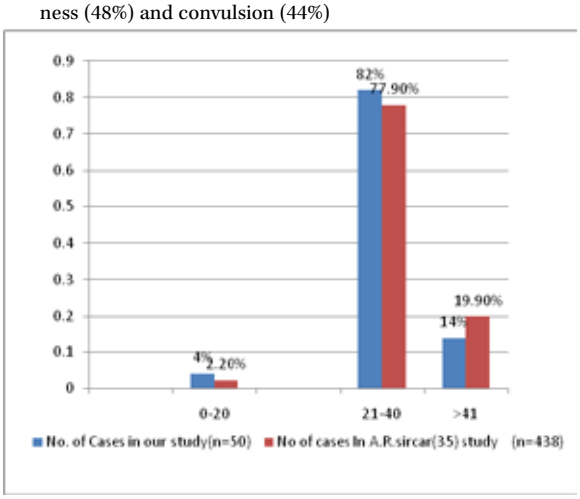

CHART 1: Age distribution in our study as compared to A.R.Sircar et al study

- On general examination most common finding was pallor (48%) followed by oral thrush (34%), lymphadenopathy (20%), and herpes zoster in (10%).
- Most common neurological sign was signs of meningeal irritation (50%), followed by altered consciousness (48%) and hemiparesis (16%).
- Commonest cause of altered consciousness is TBM (66.67%), followed by cryptococcal meningitis (25%) and toxoplasmosis (11%).
- Most common cause of headache was TBM (61.3%) followed by cryptococcal meningitis (19.4%) and toxoplasmosis (12.9%).
- TBM was the most commonly detected underlying cause of convulsions (50%), followed by cryptococcal meningitis (27.3%) and toxoplasmosis (13.6%).
- Most common cause of focal neurological deficit was TBM in 75% of cases which presented with fever (95.6%) followed by headache (82.6%), altered consciousness (66.67%) and convulsion (47.8%).
- Type of the neurological manifestation was associated with the CD4 T lymphocyte count of the HIV patients.
- Namely, in the patients with HIV related dementia mean CD4 T lymphocyte count was 75.75 cells/mm^3, in the patients with CNS toxoplasmosis mean CD4 count was 122.75 cells/mm^3, in the patients with Cryptococcal meningitis mean CD4 T lymphocyte count was 80.25 cells/mm^3, in the patients with TBM mean CD4 T lymphocyte count was 137.91 cells/mm^3, in the patients with Primary CNS Lymphoma mean CD4 T lymphocyte count was 34 cells/mm^3, in patients with PML mean CD4 T lymphocyte count was 97 cells/mm^3 and in the patients with CMV encephalitis mean CD4 T lymphocyte count was 26 cells/mm^3.
- Some neurological disorders such as TB meningitis can occur at any CD4 level.
- ADC, PMLE and Primary CNS Lymphoma were the conditions most frequently associated with CD4 count<100 cells/mm^3.
- Most common findings on neuroimaging in HIV positive patients presented with neurological manifestations were meningeal enhancement and meningeal enhancement with tuberculoma (23.5%) cases followed by meningeal enhancement with infarct, multiple ring enhancing lesions and cerebral cortical atrophy in (11.8%).
- Mortality was noted in 46% PLHIV patients with neurological manifestations as 23 out of 50 patients succumbed.

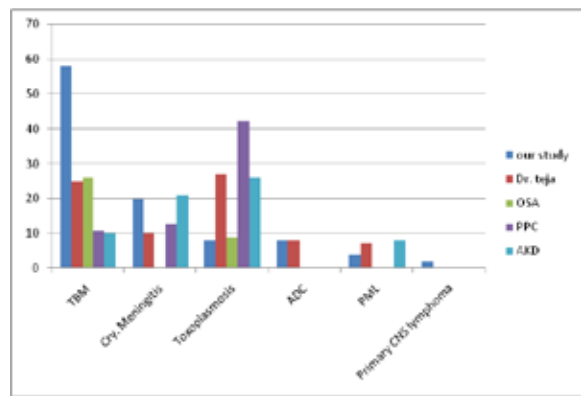

CHART 2 : Comparision of number of neurological illnesses in different studies

DISCUSSION

In our study incidence of neurological manifestations was highest in age group 21-40 years which is 82%, which correlates with study done by Sircar AR[35] in which maximum incidence (77.9%) was found in age group 21-40 years. This is the sexually active age group and hence increased prevalence of HIV and its neurological manifestation were found in this age group. This is a social danger as it is the most productive group of society.

Tuberculous meningitis was found in 58% of cases, cryptococcal meningitis in 20%, toxoplasmosis in 8%, PMLE in 4% and Primary CNS Lymphoma was found in 2% cases which is comparable with Dr Teja et al study in which TBM was most common opportunistic infection,found in 25% of cases. Cryptococcal meningitis was present in 10% of cases, toxoplasmosis in 27%, and PML in 7%.

Out of 50 patients with neurological manifestations, 32 (64%) patients presented with history of fever. 31 (62%) patients presented with history of headache. 22 (44%) patients presented with history of convulsion. 24 (48%) patients presented with altered conciousness. Vomiting was found in 11 (22%) patients. 8 (16%) patients presented with focal deficit. 12(24%) patients had dementia. 12(24%) patients had speech disturbance. Bowel/bladder incontinence was found in 10 (20%) patients. Study done by Gettler JF et al(41) also concluded that most common symptoms in order of frequency were fever, headache, convulsion and altered consciousness.

In our study 31 patients presented with headache. The most common cause of headache was TBM which was seen in 19(61.3%) of patients, cryptococcal meningitis was responsible for 19.4% of cases. Toxoplasmosis is responsible for 12.9% cases. Cause of headache was undetermined in 6.4% cases; these data match with the results of Suresh Satya et al and R. B. Lipton et al which shows TBM as the most common cause of headache.

Out of 22 patients presented with convulsion 11 patients (50%) had Tuberculous meningitis, 6 patients (27.3%) had Cryptococ-

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cal meningitis. Toxoplasmosis was found in 3 (13.6%) patients. Other causes of convulsions are ADC and Primary CNS Lymphoma. These results correspond with P. Satishchandra et al study in which TBM was the cause in 44%, Toxoplasma in 35% and Cryptococcal meningitis in 25%.

Mean CD-4 count in TBM was 118.10, in Cryptococcal meningitis was 80, in Toxoplasmosis was 122.75, in PML was 97, in Primary CNS Lymphoma was 34, in AIDS dementia complex was 75.75. Except for cryptococcal meningitis our results are comparable with Alaka K. Despande et al study(AKD), which shows mean CD4 count in TBM was 160; in cryptococcal meningitis it is 114 and toxoplasma-150 and in PML 108. In cryptococcal meningitis we had relatively low CD-4 count. For ADC mean CD4 in our study was 75.75 which is comparable with NIMS study in which mean CD4 was 92. Results are also comparable with NIMS study for cryptococcal meningitis.

Mortality was noted in 46% PLHIV patients with neurological manifestations as 23 out of 50 patients succumbed.

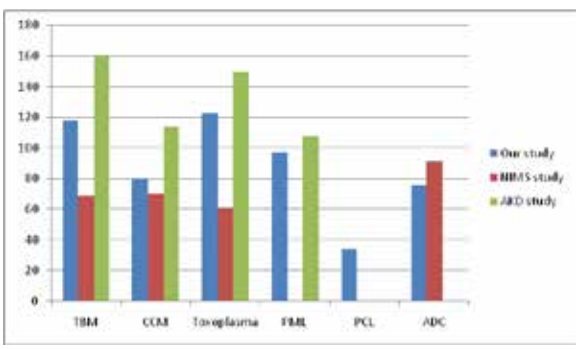

CHART 3 : Mean CD4 count in various diseases in present study as compared with NIMS study and AKD study.

CONCLUSION

1. Neurological manifestations can occur at any stage of HIV infection but frequently detected in advanced HIV disease.
2. Neurological abnormalities are sometime the first manifestation in symptomatic HIV patients. Because of immunosuppression in HIV, some patients of TBM and cryptococcal meningitis can have normal CSF, So High index of suspicion of neurological involvement in HIV patients at all stages helps in early diagnosis and early institution of specific therapeutic treatment which in turn considerably decreases morbidity and mortality.
3. There is definite correlation between CD4 T lymphocyte count and type of neurological manifestation and lower CD4 T lymphocyte counts are associated with higher morbidity and mortality. So the CD4 T lymphocyte counts can guide us for the early diagnosis and prompt management of the neurological manifestations preventing their fatal complications.

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