

Hospital-based study of Neurological manifestations in the Naive HIV patients with Neuro infection at Tertiary Care Hospital in Southern India.

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Abstract

Background and Objectives: HIV has posed many unprecedented challenges causing a large spectrum of disease manifestation. Approximately 60% of the AIDS patients have neurological symptoms and 80% are found to have Neuropathological abnormality at biopsy. The pattern of neurological manifestations in HIV in India is different from the Western countries and hence this study was undertaken to 1) Study the Neurological manifestations in the Naive HIV patients with special reference to neuro infections 2) To correlate the neurological manifestation with CD4 count

Methods: This retrospective analysis was conducted in a tertiary care teaching hospital between January 2019 to June 2020 with symptoms referring to the nervous system were screened and confirmed to have HIV

infection and were enrolled if they met the inclusion criteria.

Results: The total number of patients with human immunodeficiency virus (HIV) and AIDS with neurological manifestations was 79 among which there were 56 male patients and 23 female patients in the study with a male: female ratio of 2.4:1, with the mean age being 35 years and 33 years respectively. Most common clinical presentation in the study being fever (75%) altered sensorium (62%), headache (58%) and convulsions (29%). Tubercular Meningitis (58%) was the most common neurological manifestation in our study followed by Cerebrovascular accident (11%), cryptococcal meningitis (9%), and bacterial meningitis (5%). Also, 5 patients had an intracranial space-occupying lesion in the form of tuberculoma, 4 patients

had Myelopathy, 2 patients presented with Guillain-Barre syndrome, and 1 case of Bell's palsy and Toxoplasmosis each were also found in our study. CD4 counts less than 200 were seen in 47% of patients, others above 200. Hence, there is a robust association between the development of opportunistic infection and CD4 count.

Conclusion: Tubercular meningitis is the most common neurological manifestation in our study reflecting the high burden of tuberculosis in the country, hence the opportunity and the responsibility of identifying the same lies on the treating physician.

Keywords: TB meningitis, Neuro infection, Naïve HIV, Cryptococcal meningitis, CD4, opportunistic infection

Introduction

HIV in India came into public view in 1986 with the detection of the primary case of HIV in Chennai, Tamilnadu, and the first AIDS case in Mumbai in 1987[1]. To date, HIV/AIDS has challenged medical science by its unique pathogenesis, and also the real magnitude of the disease is under-evaluated just like the iceberg phenomena. In the year 2017, about 2.1 million people were living with HIV in India [2]. Though the incidence of the human immunodeficiency virus (HIV) is decreasing in India due to Anti Retro Viral therapy, the central nervous system (CNS) manifestations of the disease are being seen more frequently[3]. The pattern of presentation in India appears to differ from the world literature in that TB meningitis leads to the list of opportunistic neurological infections [4]. Neurological manifestations, natural course, and outcome of HIV disease might be different in India from other countries due to prevailing endemic infections, poverty, lack of awareness, and inability to take highly active antiretroviral therapy (HAART).

Materials and Methods

This retrospective study was conducted at a teaching hospital over 18 months from January 2019 to June 2020. The diagnosis of AIDS and AIDS-related Opportunistic infections was made using World Health Organization (WHO) guidelines.[5] Detailed demographic, clinical, laboratory and radiological data were obtained and information on the laboratory investigations including hemogram, renal, and liver parameters were obtained. Findings of the chest radiogram and cerebral imaging using computed tomography or magnetic resonance imaging were documented. Cerebrospinal fluid (CSF) analysis was performed based on clinical and radiological findings. CSF evaluation included India ink preparation, fungal culture, estimation of adenosine deaminase (ADA), Venereal Disease Research Laboratory (VDRL), toxoplasma serology, Gram's stain, and bacteriological culture.

Inclusion Criteria

1. Naive HIV patients
2. Age 18-65 years

Exclusion Criteria

1. Patients with pre-existing neurological disease, psychiatric patients, children, and pregnant women
2. Patients with other Neurological problems unrelated to HIV (neurodegenerative diseases, neuro dystrophies)
3. Patients on ART
4. Diabetes Mellitus
5. Severe Renal and Hepatic dysfunction

Results

In the present study, 79 patients fulfilled the inclusion criteria during the study period from January 2019 to June 2020. The mean age of males and females were 35 and 33 years respectively with the Female: Male ratio being 2.4:1, majority of the patients falling in the

economically productive age group of 20-45 yrs. The low figure of female infection rate is due to the admission pattern in most hospitals and social pattern (lifestyle) in our society where females are limited to household activities and socialize less compared to males.

Fever (75%) and altered sensorium was the commonest symptom (62%), followed by headache (58.2%), Focal Neurological Deficit (35.4%), and convulsion in (29%) of the patients. Signs of meningeal irritation were present in 29 patients (36.7%), out of these, 22 patients had CNS Tuberculosis (tubercular meningitis or Tuberculoma) and 3 patients had Cryptococci positive in CSF and 4 patients had bacterial meningitis. Four patients presented with a definite sensory level with bowel and bladder involvement and an MRI of the spinal cord showed demyelination. Cranial nerve involvement was seen in 8 patients, 4 were associated with tubercular meningitis, 3 with CVA, and 1 with bell's palsy, and all these patients had VII cranial nerve involvement.

The lowest CD4 count in the study was 34 cells/microliter and the highest 458 cells/microliter with the mean being 208 cells/microliter. Cryptococcal meningitis was associated with the average count of 147 cells / microliter and in CNS TB the average count was 213 cells/microliter. Cryptococcal meningitis was associated with advanced immunosuppression.

Totally 73 cranial CTs and 4 MRIs were done. 42 Cranial CT's were normal. The most common abnormality was cerebral oedema 14%; inflammatory exudates 2.5%, hypodense lesion 12.7% -suggestive of an infarct, single lesion and multiple lesions were found to be in three patients and one patient respectively. All mass /enhancing lesions were diagnosed to be tubercular granuloma supported by clinical, CSF

analysis and treatment response. 4 MRIs taken from suspected myelitis cases showed changes suggestive demyelination in the thoracic spinal cord.

Neurological manifestations in Naive HIV patients

A. INFECTIONS	This study (n=79)
Tubercular meningitis	58.22%
Cryptococcal meningitis	8.9%
Meningo encephalitis	-
Cerebellitis	-
Myelitis	5.1%
PML	-
Bacterial meningitis	5.1%
Guillain barre syndrome	1.3%
B. INTRACRANIAL MASS LESION	6.3%(Tuberculoma)
C. HIV ENCEPHALOPATHY	-
D. PRIMARY VASCULAR	12.7%
E. OTHERS	
Cranial Neuropathies	10.12%
Toxoplasmosis	1 case
Peripheral Neuropathy	-
Myopathy	-

CNS Tuberculosis

Presentation	This study(n=79)
Fever	94%
Headache	61%
Altered Sensorium	78%
Focal Neurological defect	23%
Convulsions	33%
Weight loss	25%
Lymphadenopathy	7%

Pulmonary Tuberculosis	15%
CSF Mean protein	160mg/dl
CSF Mean sugar	48mg/dl
CSF Mean cell count	188cells/mm ³
Meningeal enhancement(exudates)	3%
Tuberculoma	9%
Infarcts	-
Hydrocephalus	-
Mean CD4	213 cells/mm ³

The commonest neurological complication of HIV infection in this study was due to tubercular involvement of the nervous system. It was seen in 51 patients (64.55%). Of them, 46 patients had tubercular meningitis, 5 patients had intracranial tuberculomas. The Mean CD4 count in TB meningitis:213 cells/mm³ and P-value was 0.002, the relation between CD4 count which was statistically highly significant. Among the 5 patients who had tuberculoma, the mean CD4 count was 173 cells/mm³ and P-value was 0.001 which was statistically highly significant with a positive correlation between the occurrence of tuberculoma and CD4 count.

Comparison of Mean CD4 count

	CD4 Count(cells/mm ³)
TB Meningitis	234
CVA	263
Cryptococcal Meningitis	147
Toxoplasmosis	43
Tuberculoma	173
Bell's Palsy	124
Guillain barre syndrome	158
Myelopathy	138
PML	-
Bacterial Meningitis	116
Mean CD4	208

Discussion

Though there is a gradual decrease in the overall incidence and prevalence of HIV infection and occurrence of opportunistic infections due to HAART and increasing awareness of HIV/AIDS globally [6], neurological manifestations, natural course, and outcome of HIV disease might be different in India from other countries because of prevailing endemic infections, poverty, lack of awareness and inability to take HAART. The prevalence of HIV infection in India is estimated to be 0.26% amounting to about 2.1 million HIV patients making India the third-largest country for HIV infection [2]. HIV-infected individuals can experience a variety of neurological abnormalities due either to opportunistic infections and neoplasm or direct effects of HIV or its products. Opportunistic infections can occur at any time during the illness and a few may be AIDS-defining illnesses as well.

The commonly observed neurological manifestations globally are the neuro infections such as Tubercular and cryptococcal meningitis, space-occupying lesions due to tuberculoma, primary CNS lymphoma, toxoplasmosis, CMV infections, meningoencephalitis, JC virus causing Progressive Multifocal leukoencephalopathy[7]. Other commonly observed conditions are Cerebrovascular accident, Peripheral neuropathy, and AIDS Dementia complex [8].

In our study, the most common clinical presentation was fever with altered sensorium followed by

headache. Even in patients without overt focal brain dysfunction, headache can be presenting symptom of focal parenchymal diseases when they involve “non-eloquent” brain areas or are characterized by small multifocal lesions. However, when CNS dysfunction is truly absent, headache most commonly relates to either meningitis or a poorly understood condition sometimes referred to as HIV headache[9]. CSF analysis helped to differentiate types of meningitis, however, the same could not be done in six patients due to the presence of papilledema. In this study, we found that acute presentation was more common in tuberculosis and subacute to chronic presentation in patients with cryptococcal meningitis. Seizures and hemiparesis were common in tuberculosis compared with other groups similar to a previous study[10].

Cerebral imaging in HIV patients revealed features of cerebral oedema, exudates, and granulomata, symmetrical or asymmetrical white matter hyper intensities, infarction, cerebral atrophy, and space-occupying lesions. Contrast-enhanced cerebral imaging is essential in the diagnosis of opportunistic infections. In this study, the most common imaging abnormality revealed cerebral oedema in 11 patients, cerebral infarctions in 10 patients, granulomas in 4 patients, and 4 patients had transverse myelitis secondary to demyelination.

Studies from the western world reveal Cryptococcal meningitis as the most common neuro infection in HIV [11], however, in this study, Tubercular pathology was the most common etiology due to its high prevalence in the country.

Conclusion

More than 50% of the patients presented late in the disease process indicating the unawareness and social stigma attached to this sensitive subject. A wide array

of neurological manifestations were found in the study led by meningitis (72%), predominantly Tubercular meningitis with half of the study population having a CD4 count less than 200. Early initiation of ART with appropriate prophylaxis for opportunistic infections based on CD4 count can help to reduce the neurological and other syndromic manifestations thereby improving the quality of life and reduce mortality. Simple investigations like CD4 count may provide a clue to understand the degree of underlying immunosuppression and help in alerting the clinician to screen for opportunistic infection and treat them accordingly.

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