Original Research Article

A clinical study of neurological manifestations in HIV positive patients in a tertiary care hospital of Telangana, India

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Abstract

Background: Human Immunodeficiency Virus (HIV) infection is a global pandemic, India has second largest burden of HIV illness. Nervous system is most frequent and serious target of HIV infection.

Aim: The main aim of our study was to evaluate the occurrence of various neurological manifestations in HIV positive patients and to correlate them with CD4 count at the time of presentation.

Materials and methods: This prospective study was carried out for a period of 2 years from January 2014 to December 2016 in the Department of Neurology, Gandhi Hospital, Hyderabad, India. Those patients, who satisfied the inclusion criteria (>18 year of age; HIV positive; any gender) were included in our study. Patients who were HIV positive but having non neurological medical conditions were excluded. Those with various neurological symptoms were subjected to thorough neurological examination, whenever indicated neuroimaging, CSF analysis, NCS, Toxoplasma serology were done. CD4 count was done in all patients.

Results: Our study enrolled a total of 1011 HIV positive patients, out of them 354(35%) patients had neurological manifestations. Among them, 239 (67.51%) were male and115 (32.48%) were female. We analyzed patients presented with various neurological symptoms, 187(52%) patients presented with parasthesias. CD4 count was done to all patients. Out of 354 patients, 188 (39.4%) patients had low CD4 count (<200µL). NCS was abnormal in 182 (51.4%) patients. Axonal sensory neuropathy was the most common abnormality found in 82 (45.0%) patients. The most common neurological manifestation was peripheral neuropathy, seen in 166 (46.8%) patients.

Conclusion: HIV infection can affect all levels of the neuronal axis. Neurological manifestations are common in 4th decade of life and males affect more than females. Peripheral neuropathy was the most common neurological manifestation and Tuberculosis was the prominent infectious etiology. Neurological manifestations are seen with low CD4 count and there is a significant correlation between them hence can be stated that, these are the manifestations of the late stage of the disease.

Key words

HIV positive patients, Neurological manifestations, CD4 count, Peripheral neuropathy, Tuberculosis.

Introduction

Human Immunodeficiency Virus (HIV) infection is a global pandemic, India has second largest burden of HIV illness. Nervous system is most frequent and serious target of HIV infection, not only secondary to immune dysfunction but also to more primary effects of retrovirus.

Materials and methods

The present study of neurological manifestations in HIV Positive Patients was carried out for a period of 2 years from January 2014 to December 2016 in the Department of Neurology, Gandhi Hospital, Hyderabad, Telangana, India. All HIV Positive Patients, who were presented to Departments of Neurology, Medicine and ART Center of our hospital during this period were observed. Those patients who satisfied the inclusion criteria (>18 year of age; HIV positive; any gender) were included in our study. Patients who were HIV positive but having non neurological medical conditions were excluded from the study. HIV infection was confirmed by a combination of ELISA and Western Blot. Those with various neurological symptoms were subjected to thorough neurological examination, whenever indicated neuroimaging, CSF analysis, NCS, Nerve/muscle biopsy, Toxoplasma serology were done for that particular case's diagnosis and management.CD4 count was done in all patients.CD4 estimation was carried out by flow cytometer using Syflow counter in our ART Center. This study has approval from the parent Institute as well as Dr. NTR University of Health Sciences. Informed Consent was taken from the patients and their attendants, when patient was unable to give a valid consent.

Results

The presents study enrolled a total of 1011 HIV positive patients, out of them 354(35%) patients had neurological manifestations. In this, 239 (67.51%) were male and 115 (32.48%) were female. Male to female ratio was 2.07: 1.Youngest was 19 and oldest was 73 years, the mean age was 34.3 ± 7.8 years. Most common age group was 4thdecade (31 to 40 year), we found 178 patients (50.28 %) in this age group.

Neurological symptoms at presentation

We analyzed patients presented with various neurological symptoms. Sensory symptoms was the most common presentation, we found 187(52%) patients presented with parasthesias. The next common symptom was headache, which was seen in 107(30.2%) patients. We found motor symptoms in 90(25.4%) patients, among them 45(50%) patients presented with hemiparesis, flaccid quadriparesis in 13 (14%) patients and spastic quadriparesis in 4 (4.4%) patients. Other symptoms were fever in 82(23.86%) patients, seizures in 70(19.7%)

patients, altered sensorium in 55(15.53%) patients, vomiting in 36(10.16%) patients, visual symptoms in 20(5.6%) patients, aphasia in 7(1.97%) patients.

Investigations

HIV infection was confirmed by a combination of ELISA and Western Blot. All patients were subjected to routine laboratory investigations, whenever indicated neuroimaging, CSF analysis, NCS, Nerve/muscle biopsy, Toxoplasma serology were done for that particular case's diagnosis and management. CD4 count was done in all patients. CD4 estimation was carried out by flow cytometer using Syflow counter in our ART Center.

CD4 Count

CD4 count was done to all patients in our study. Out of 354 patients with neurological manifestations, 188 (39.4%) patients had low CD4 count (< 200µL), 156(32.5%) patients had CD4 count in the range of 201 to 499 µL and 10(18.5%) patients had CD4 count more than 500 µL (**Figure - 1**,**Table - 1**). This was shown that patients with low CD4 counts were more prone to develop neurological manifestations (P value - 0.0026).

Figure – 1: Distribution of patients according to CD4 count (n = 354).

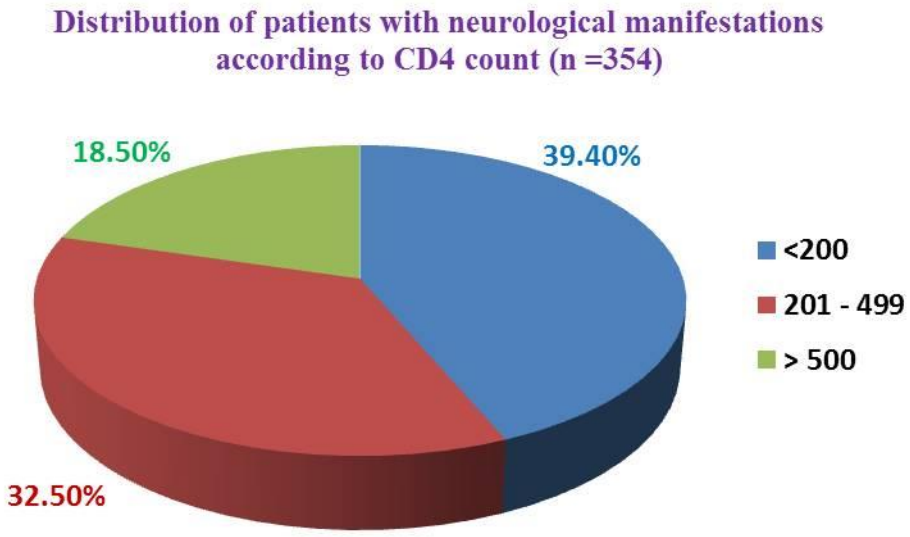

Table – 1: Distribution of patients according to CD4 count (n = 1011).

CD4 count	No of patients with neurological manifestations	%	No. of patients without manifestations	%	Total	%	P value
<200	188	39.4%	289	60.6%	477	47.2%	0.0026
201 – 499	156	32.5%	324	67.5%	480	47.4%	
> 500	10	18.5%	44	81.5%	54	5.4%	

(Chi- square – 11.85; degree of freedom-2)

CSF analysis

Clinical diagnosis of meningitis was confirmed with CSF analysis. In our study, 42(11.8 %) patients had tuberculous meningitis and 6(1.69%) patients had cryptococcal meningitis. Albumino cytological dissociation was not found in our AIDP patients.

Nerve conduction study

Nerve conduction studies were done in all except 5 patients. NCS was abnormal in 182 (51.4%) patients. Axonal sensory neuropathy was the most common abnormality found, which was seen in 82 (45.0%) patients. Other abnormalities found were axonal sensory motor neuropathy in 80 (43.9%) patients, demyelinating and axonal motor, sensory neuropathy in 13 (7.14%) patients. Facial nerve axonopathy was found in 4(2.19%) patients.

MRI Brain/ CT Brain

MRI brain/CT brain with/ without contrast was done in our patients who were suspecting intra cranial pathology. ICSOL was found in 62 (17.5%) patients, among them most common ICSOLs were tuberculoma, which was seen in 40(64%) patients. Other ICSOLs were TB abscess which was seen in 6 (9.6%) patients, bacterial abscess in 9 (14.5%) patients, toxoplasmosis in 5 (8.06%) patients and neurocysticercosis was seen in 2(3.2%) patients. Cerebrovascular diseases were found in 28 (7.9%) patients, those were confirmed with CT/ MRI Brain.

Diagnosis

In our study, most common neurological diagnosis we made was peripheral neuropathy, found in 166 (46.8%) patients (**Table - 2**).

CNS infections were seen in 131(37%) patients. Most common infectious etiology was tuberculosis, which was seen in 88 (67%) patients. We found TB Meningitis in 42 (11.86%), tuberculoma in 40 (11.29%), TB abscess in 6 (1.69%) patients, TBM with hydrocephalus in 5 (1.41%) patients. Cryptococcal meningitis was found in 6 (1.69%) patients. Bacterial abscess in 9 (2.54%) patients, PML (Progressive Multi focal Leucoencephalopathy) was found in 2(0.5%) patients, Toxoplasmosis was found in 5(1.41%) patients. Neurocysticercosis was found in 2 (0.5%) patients, CMV infection in 2 patients (0.5%), viral encephalitis was seen in 10 (2.82%) patients, HIV myelitis was found in 7 (1.97%) patients. Other manifestations we found were, AIDP in 7 (1.9%) patients, CIDP in 4(1.12%) patients, cranial neuropathy in 8(2.25%) patients among them Bell's palsy in four patients.

Table – 2: Neurological manifestations in HIV positive patients.

Neurological manifestations	No. of patients	%
Peripheral neuropathy	166	46.8
AIDP	7	1.9
CIDP	4	1.12
Cranial neuropathy	8	2.25
TB meningitis	42	11.86
Tuberculoma	40	11.29
TB Abscess	6	1.69
TBM with hydrocephalus	5	1.41
Cryptococcal meningitis	6	1.69
Bacterial abscess	9	2.54
PML	2	0.56
Toxoplasmosis	5	1.41
CMV Infection	2	0.56
Neurocysticercosis	2	0.56
HIV Myelitis	7	1.97
HAD	8	2.25
Viral Encephalitis	10	2.82
Strokes	28	7.9
Myopathy	2	0.5

Cerebrovascular diseases were found in 28 (7.9%) patients among them 24 patients presented with ischemic stroke, 3 patients with CSVT and one patient presented with hemorrhagic stroke. HAD (HIV Associated Dementia) was seen in 8 (2.25%) patients. Myopathy was seen in 2 patients (0.5%).

Correlation of Neurological manifestations with low CD4 Count

Out of 354 patients, 188 (39.4%) presented with low (<200µL) CD4 count. Sixty seven (40.36%) patients with Peripheral neuropathy, 14% patients with AIDP, 75% of patients with CIDP (3 out of 4 patients), 37.5% of patients with

cranial neuropathy (3 out of 8 patients) had low CD4 count. 52.38% of patients with TB meningitis (22 out of 42), 70 % of patients with tuberculoma (28 out of 40), 50 % of patients with TB abscess (3 out of 6) had low (<200) CD4 count.

All patients with cryptococcal meningitis, toxoplasmosis, PML, CMV infections, HAD, viral encephalitis and myopathy had low (<200)CD4 count. 66% of patients with bacterial abscess (6 out 9), 85.71% of patients with HIV myelitis (6 out of 7), 46.4% of patients with stroke (13 out of 28) had low CD4 count (**Table - 3**).

Table – 3: Distribution of patients with neurological manifestation with low CD 4 count (< 200 µL) (n = 188 cases).

Neurological manifestations	**No. of patients with CD4 count < 200 µL/Total No.of patients**	**%**
Peripheral neuropathy	67/166	40.36
AIDP	1/7	14
CIDP	¾	75
Cranial neuropathy	3/8	37.5
TB Meningitis	22/42	52.38
Tuberculoma	28/40	70
TB Abscess	3/6	50
Cryptococcal meningitis	6/6	100
Bacterial Abscess	6/9	66.66
PML	2/2	100
Toxoplasmosis	5/5	100
CMV infection	2/2	100
HIV Myelitis	6/7	85.71
HAD	8/8	100
Viral Encephalitis	10/10	100
Strokes	13/28	46.4
Myopathy	2/2	100

Discussion

Our study was enrolled a total of 1011 patients, out of them 354(35%) patients had neurological manifestations. A Pune based study, Wadia, et al. [1] reported neurological manifestation in 457 patients (29.9%) out of 1527 HIV reactive subjects. Sonkar, et al. [2] study reported that 40.9% of patients have neurological manifestation; our study is correlating with these studies.

Youngest age at presentation was 19 years and eldest was 73 years. The mean age was 34.3 ± 7.8 years. Most common age group in our study was 4th decade (31 to 40 years), we found 178 patients (50.28 %) in this age group. Teja, et al. [3] study and Singh, et al. [4] study reported that the maximum patients were seen in the age group of 31-40 years. Our study is correlating with these studies. Male to Female ratio in our study was 2.07:1, which was comparable to Singh et al[4] study in which, it was 1.83:1.

Patients presented with various neurological symptoms were observed in our study, sensory symptoms were the most common presentation, we found 187 (52%) patients presented with parasthesias. These were comparable to the study done by Simpson, et al. [5] in which sensory symptoms were the most common presentation seen in 53%. The next common symptom was headache which was seen in 107 (30.2%) patients, Sonkar, et al. [2]study also reported that 57.4% of patients had headache. We found motor manifestations in 90(25.4%) patients. Seizures were seen in 70(19.7%) patients, this was comparable to Sonkar, et al. [2] study, in which seizures were reported in 33%. Axonal sensory neuropathy was the most common (82 patients (45.0%)) abnormality we found. In similar to our study, Simpson, et al. [5] study reported that Axonal sensory neuropathy was the most common (52%) form of neuropathy. Most common neurological manifestation was peripheral neuropathy which was found in 166 (46.8%) patients. Evans, et al. [6] study reported that peripheral neuropathy was the most common neurological complication of HIV infection affecting of one third of patients. Our study was comparable to this study. Other manifestations we found were, AIDP in 7 (1.9%) patients, CIDP in 4(1.12%) patients, those were comparable to

Sonkar, et al. [2] study who reported AIDP and CIDP cases in 2.33% of each.

Singh, et al. [4] study has reported that CNS infections were found in 21.63% of HIV positive patients. Similarly in our study, CNS infections were seen in 131(37%) patients. Most common infectious etiology in our study was tuberculosis which was seen in 88 (67%) patients. In Mehta, et al. [7] study it was found that tuberculosis was most common (55%) infectious etiology, our study is comparable to this study. Cryptococcal meningitis was found in 6 (1.69%) patients. Singh, et al. [4] study showed that cryptococcal meningitis was seen in 6% patients. Shembhalkar, et al. [8] study documented that tubercular meningitis has been more common than cryptococcal meningitis in India, the present study also shown similar results.

Singh, et al. [4] study reported 1% of patients had PML, similarly in our study PML (Progressive Multifocal Leucoencephalopathy) was found in 2(0.5%) patients. Wadia, et al. [1] study reported that Toxoplasmosis was seen in 2.09% patients comparable to this in our study Toxoplasmosis was found in 5(1.41%) patients. HAD (HIV Associated Dementia) was seen in 8 (2.25%) patients. Levy, et al. [9] study shown that 6.5% of patients had HIV dementia and Oliveira, et al. [10] study showed that HIV Associated Dementia seen in 2.16% patients, our study was comparable to this study. Deshpande, et al. [11] study reported that strokes were seen in 7.6%, similarly in our study strokes were found in 28 (7.9%) patients. Myopathy was seen in 2(0.5%) patients this was comparable to Deshpande, et al. [11] study who reported myopathy in 0.33% of patients. Thorat, et al. [12] study reported that ICSOL was seen in 10.7% of patients, comparable to this our study shown ICSOL in 62 (17.5%) patients. Most common ICSOL in our patients were tuberculoma which was seen in 40(64%) patients. Other ICSOL we seen were, bacterial abscess in 9 (14.5%) patients, TB abscess in 6 (9.6%) patients, Toxoplasmosis in 5 (8.06%) patients and neurocysticercosis was seen in 2(3.2%) patients.

Correlation of patients Neurological manifestations with low CD4 Count

With lowering of CD4 count accounts for more neurological manifestations in HIV patients. Our study enrolled a total of 1011 patients, out of them 354(35%) patients had neurological manifestations. Among them, 188 (39.4%) presented with low (200µL) CD4 count, 156(32.5%) patients had CD4 count in the range of 201 to499 µL and 10(18.5%) patients had CD4 count more than 500.In our study it was proven that neurological manifestations were more common in patients, who are having low (200µL) CD4 count. P value is significant (P value – 0.0026) (Chi square-11.85, degree of freedom-2).

Similar to our results, Sonkar, et al. [2] study also 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. [13] study reported that peripheral neuropathy patients had higher CD4 count which was comparable to our study. In our study 52.38% of patients with TB meningitis (22 out of 42) had low CD4 count and this was comparable to Sonkar, et al. [2] study who reported that 55% of patients with TB meningitis patients had low CD4 count.70% of patients with tuberculoma (28 out of 40), 50% of patients with TB abscess (3 out of 6) had low (<200) CD4 count.

In our study, all patients with cryptococcal meningitis had low (<200µL) CD4 count which was comparable to Bolokadze, et al. [14] study who reported that 83% of patients with cryptococcal meningitis had low (<200µL) CD4 count. In our study all patients with Toxoplasmosis, PML, CMV infections, HAD and viral encephalitis had low (<200µL) CD4 count showing that those neurological manifestations were commonly present in late stages of illness.

Conclusion

Although the main and direct target of HIV infection are the cells of immune system, the nervous system is often damaged in course of infection, not only by the disease process that are secondary to immune dysfunction and its systemic manifestations but also by more fundamental effects of the retrovirus. HIV infection can affect all levels of the neuronal axis.Our study concluded that neurological manifestations are common in 4th decade of life and males affect more than females. Peripheral neuropathy is the most common neurological manifestation in our study. Tuberculosis is the prominent infectious etiology of all neurological disorders in HIV patients. Neurological manifestations are seen with low CD4 count in our study and there is a significant correlation between them hence can be stated that, these are the manifestations of the late stage of the disease, when the level of immunodeficiency has achieved a higher degree and which cloud result in high mortality. Hence their accurate and timely diagnosis is important for earlier therapeutic measures.

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