



Study on Neurological Manifestations in Patients with HIV Infection

Authors

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Abstract

Introduction: HIV/AIDS has posed many unprecedented challenges. Further, the visible manifestation of HIV occurs only at the last stage. As a result, there is a visible lack of realization of the problem in the society. Neurological complications of HIV infection cause considerable morbidity and are often associated with high mortality.

Aim: To study neurological manifestations in patients with HIV infection admitted in Government general hospital from December 2017 to November 2019, Kakinada.

Results: In the present study, 58 patients fulfilled the inclusion criteria from about 400 patients admitted during the study with prevalence of 14% reflects the high prevalence of neurological manifestation in HIV patients. Altered sensorium was the commonest symptoms seen in 35 patients (60.3%) followed by headache (53.4%), convulsions and focal neurological deficit shared equally (29.3%). Most common neurological sign is meningeal irritation (51.7%). Most common illness are secondary infections among them Tuberculosis ranks first (60.3%) followed by cryptococcal meningitis. Neurological manifestations have been reported at all stages of HIV infection but detected especially in advanced HIV disease. The opportunistic infections remain the leading cause of neurological manifestations in HIV. Prevalence of neurological manifestation was highest in the young adult. High index of suspicion of neurological involvement in HIV patients in all stages helps in early diagnosis and timely institution of specific therapeutic treatment, which may considerably reduce the morbidity and mortality due to the disease.

Keywords: HIV/AIDS, Neurological manifestations, TB Meningitis.

Introduction

AIDS was first recognized in the United States in 1981, when the U.S. Centers for Disease Control and Prevention (CDC) reported the unexplained occurrence of *Pneumocystis jiroveci* (formerly *P. carinii*) pneumonia. The HIV/AIDS has posed many unprecedented challenges.

Further, owing to the insidious and covert nature of the disease, the problem is compounded by a

prevailing attitude of denial or resistance of complacency at all levels. The visible manifestation of HIV occurs only at the last stage. As a result, there is a visible lack of realization of the problem in the society.

HIV and AIDS cause a wide spectrum of diseases and manifestation. Approximately 60 percent of patient of AIDS have neurological symptoms and 80 to 90 percent for found to have neuro

pathological abnormalities at autopsy. Neurological complication of HIV infection cause considerable morbidity and are often associated with high mortality.

Materials and Methods

To study neurological manifestations in patients with HIV infection admitted in Government general hospital, Kakinada.

To note the differences in neurological manifestations of HIV infected patients in this study with various studies that carried in western countries.

Inclusion Criteria: Patients presenting with neurological manifestations and diagnosed to be HIV seropositive by ICTC

Exclusion Criteria: Patient having pre existing neurological disorders. Patients with age less than 20 years.

Method of Collection: Data was collected in a pretested proforma by meeting the objective of the study. A detailed history, physical findings with thorough neurological examination and necessary investigation were recorded. Treatment and outcome were not included in this study.

Investigations:

Complete haemogram, CSF analysis, Neuroimaging (CT/MRI) where required, Chest X-ray and sputum examination, Serology to detect antibody to Toxoplasma, CMV and other opportunistic infection. Nerve conduction studies and EMG where required, CD4 count wherever possible.

Results

400 seropositive HIV patients were admitted in Government general hospital, Kakinada between December 2016 and November 2018.

58 patients with neurological manifestations were enrolled in this study

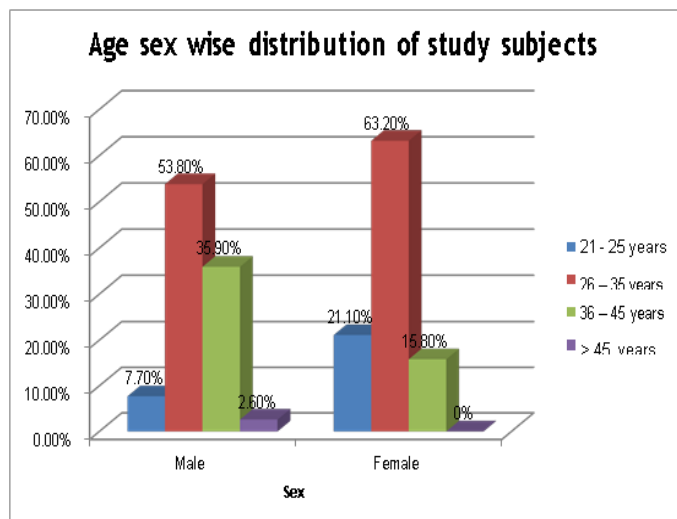


Figure 1- Age sex distribution

Table 1: Distribution of study subjects based on Neurological symptoms

Symptoms	Frequency	Percentage
Altered sensorium	35	60.3%
Convulsions	17	29.3%
Vertigo	04	06.8%
FND	17	29.3%
Cranial abnormality	05	08.6%
Sensory	03	05.1%
Behavioral abnormality	03	05.1%
Headache	31	53.4%

Table 2: Distribution of study subjects based on h/o TB

H/o TB	Frequency	Percentage
Present	07	12.0%
Absent	51	88.0%
Total	58	100%

Table 3: Distribution of study subjects based on candidiasis

Candid infection	Frequency	Percentage
Present	11	18.9%
Absent	47	81.1%
Total	58	100%

Table 4: Distribution of study group based on CNS Signs.

CNS signs	Frequency	Percentage
Meningismus	30	51.7%
HMF	26	44.8%
Motor system	15	25.8%
Cranial	07	12.0%
Abnormal fundus	11	18.9%
Gait	04	06.8%
Cerebellar	06	10.3%
Sensory	04	06.8%
Plantar	30	51.7%

Table- 5: Distribution of study subjects based on imaging (CT/MRI)

Imaging findings	Frequency	Percentage
Normal	30	58.8%
Edema	08	15.6%
Abnormal MRI	02	03.9%
Hydrocephalus	01	01.9%
Inflammatory exudates	03	05.8%
Multiple enhancing lesion	01	01.9%
Single enhancing lesion	01	01.9%
S/o hypo dense lesion	05	09.8%
Total	51	100%

Table 6: Distribution of study subjects based on Diagnosis

Diagnosis	Frequency	Percentage
TB Meningitis	35	60.3%
Cryptococcal Meningitis	09	15.1%
CVA	05	08.6%
Tuberculoma	02	03.4%
Bacterial Meningitis	03	05.1%
Myelopathy	02	03.4%
Bell's palsy	01	01.7%
Guillain-Barre syndrome	01	01.7%
Total	58	100%

Table 7: Comparison of meningitis

Features	Meningitis			P value*
	TBM (35)	CM (09)	BM (03)	
Symptoms				
Weight loss	11 (31.4%)	05 (55.5%)	01 (33.3%)	0.40
Headache	18 (51.4%)	08 (88.8%)	02 (66.6%)	0.12
Sensorium	26 (74.2%)	01 (11.1%)	03 (100%)	0.01
FND	06 (17.1%)	00	01(33.3%)	0.28
Convulsions	11 (31.4%)	02 (22.2%)	01(33.3%)	0.85
Fever	31(88.5%)	07(77.7%)	03(100%)	0.54
Vertigo	03(08.5%)	01 (11.1%)	00	0.83
Signs				
Pallor	21 (60.0%)	08 (88.8%)	01 (33.3%)	0.14
Candida	05 (14.2%)	04 (44.4%)	02(66.6%)	0.03
Lymphadenopathy	08 (22.8%)	02 (22.2%)	00	0.64
CNS				
Abnormal HMF	18 (51.4%)	02 (22.2%)	01 (33.3%)	0.26
Abnormal	03 (08.5%)	00	00	0.57
Cranial nerve				
Abnormal	08(22.8%)	00	01(33.3%)	0.24
Fundus				
Abnormal Motor	03 (08.5%)	01 (11.1%)	02(66.6%)	0.01
Meningismus	22(62.8%)	06 (66.6%)	01(33.3%)	0.56
CSF protein				
< 50	01 (02.8%)	01 (11.1%)	00	0.001
50 – 100	15 (42.8%)	03 (33.3%)	03 (100%)	
> 100	19 (54.4%)	05 (55.6%)	00	
CSF Sugar				
< 40	05 (14.4%)	03 (33.3%)	03 (100%)	0.02
40 – 60	23 (65.6%)	06 (66.7%)	00	
> 60	07 (20.0%)	00	00	
CSF cells				
<50	0	03 (33.3%)	00	0.01
>/=50	35 (100%)	06 (66.7%)	03(100%)	
CD4				
< 200	22 (62.8%)	07(77.7%)	03(100)	0.01
>/=200	13 (37.2%)	02(22.3%)	00	

Discussion

In the present study, prevalence of 14% reflects the high prevalence of neurological manifestation in HIV patients.

In a study done by Millago et al^[8] 14% had neurological manifestation same as in this study. A study by Chouhan et al^[6] in north india among 200 patients, they found 28% patients has neurological manifestations which is far higher than this study .

Neurological symptoms

Altered sensorium was the commonest symptoms seen in this study which accounts for 35 patients (60.3%), which is mostly contributed by the TB meningitis (26 Patients) and 1 case by the cryptococcal meningitis. Second most common symptoms seen is headache (53.4%) followed by convulsions and focal neurological deficit shared equally (29.3%). Fever and weight loss were the common general symptomatic presentation in HIV patients. Even in patients without any focal neurological dysfunction, headache can be a presenting symptom of focal parenchymal disease when they involve non-equolent brain areas are characterised by small multifocal lesions. However, when truly CNS dysfunction is not seen headache is mostly contributes to meningismus. In Chouhan et al^[6] study altered sensorium is the most common neurological symptom seen. Contributes 68.2%, followed by convulsions (26.3%), headache (87.7%). In shripad et al^[5] study from Gujarat , fever was the most common general symptom (46%), headache was neurological symptom(38%). Sundararcharya et al^[4] study from south india also shows similar results like shripad et al. Among the other symptoms fever was present in 77.5% (45) patients that included 31 cases of tuberculosis and 7 cases of cryptococcal meningitis and significant weight loss seen in 18 patients (31%). Commonest cause of altered consciousness was tuberculous meningitis (74.2%), followed by cryptococcal meningitis and toxoplasmosis, whereas the commonest cause of altered consciousness in a study done by Mansuri ZH et al^[7] was also tuberculous meningitis (67%). Most common cause

of headache was tuberculous meningitis followed by cryptococcal meningitis. Most common cause of convulsions was tuberculous meningitis followed by cryptococcal meningitis.

Neurological signs: Most common neurological sign seen in this study is meningeal irritation (51.7%) followed by higher mental functions (44.8%). In Shripad et al^[5] study most common neurological sign was signs of meningeal irritation (46%), followed by altered consciousness (26%) and hemiparesis (12%). Similarly a study done by Mansuri ZH et al^[7] revealed that the most common neurological sign was meningeal irritation (50%). Most of altered sensorium was contributed by CNS tuberculosis (62.8%) and 6 had cryptococcal positive in CSF and 2 were bacterial meningitis. Two patients presented with paraparesis with definitive sensory loss with bowel and bladder involvement.

CD4 count comparison

In this study, the lowest CD4 count was 28 cells/microltr and highest was 452 cells/microltr with mean being 165 cells/microltr. Tubercular meningitis was associated with the average of 189 cells/microltr CD4 count and cryptococcal meningitis was associated with the average of 111 cells/microltr CD4 count. In Chouhan et al study^[6] Mean CD4 count was 181.44+83.50 in patients with TBM, 97.25+71.27 for cryptococcal meningitis, 110.75+57.62 for BM seen.

CSF Analysis

CSF analysis was helpful in differentiating types of meningitis. It was done in 54 patients and not done in 4 patients as it was contraindicated in them. Cells counts ranged from 2 to 1352 cells with mean of 191 cells/microltr. Most of the cases had predominantly lymphocytes. CSF Protein levels ranged from 26mg/dl to 450mg/dl with the mean of 127mg/dl. P-value for CSF protein in this study is statistically significant. Mean CSF sugar in TB meningitis in this study is 49.7+/-14 mg/dl and in cryptococcal meningitis is 40.6 mg/dl.

Neuroimaging

In this study 51 patients had undergone imaging, most of them are CT scans because of the cost effectiveness and the poor conditions of the patients does not permit for further imaging studies. Most of the imaging are Normal (58.8%), among the abnormal scans cerebral edema accounts for the majority (15.6%). Sundaracharya et al study^[4] shows 39.16% scans are normal, as seen in present study. Infarct seen in 17%, next commonly seen was Space occupying lesion 13.2%. Shripad et al study^[5] meningeal enhancement seen in 32.07% scans, infarct in 16.8% and ring enhancing lesion (11.8%).

Neurological Illness

Most common illness in this study are secondary illness among them TB ranks first (60.3%) followed by cryptococcal meningitis. Similar results are seen in Shripad et al^[5], Sundaracharya et al^[4] studies. In CNS tuberculosis commonest presenting features in present study were fever, headache, altered sensorium, convulsions and less commonly was focal deficit. In Shripad et al^[5] study common presentation of CNS tubercular disease was headache (50%), followed by convulsions (45.5%), altered sensorium (30%). Mean CD4 count for tubercular meningitis in present study is 170 cells. In Chouhan et al study^[6] it was 181 cells. CSF analysis showed protein ranging from 45 to 450mg/dl with mean being 133 mg/dl. Csf cells ranging from 86 to 660 cells/cumm with mean count of 188 cells with lymphocyte predominance. Tuberculosis is widespread and rampant in our country, with a large segment of the population being constantly exposed to infection from open infected cases, irregular, incomplete therapy often results in partially treated and resistant cases. The poor hygiene and poor socio-economic states only compounds the problem. This accounts for the very high incidence of tubercular infection in HIV patients in our country. This is in contrast with the developed world where TB was almost eradicated and only the advent of HIV infection has seen the re-emergence of TB in the population.

Meningitis manifested in 75% of the cases in present study. Tubercular meningitis account for 74.4% next majority are cryptococcal meningitis account for 19.14% (9 cases). Shripad et al^[5] reported 7% cases. Cryptococcal meningitis is caused by cryptococcal neoformans. It is most common fungal infection of CNS in HIV patients. In this study 9 patients diagnosed with cryptococcal meningitis based on indian ink preparation. Most common presentation of Cryptococcal meningitis is headache followed by fever in present study. Common co infection seen with cryptococcal meningitis was candidiasis, seen in 4 patients.

In the present study no cases were detected as toxoplasmosis positive with serum antibody detection. Studies by Shripad et al^[5] reported the prevalence of toxoplasma to be far lower in India, when compared to tuberculosis.

Bacterial meningitis has 8- fold higher risk in HIV patients when compared to Non HIV patients. In present study 3 of them had bacterial meningitis (5.7) and all cases found to have Mean CD4 count less than 200cells/cumm. Mean CSF protein value is 74 mg/dl and sugar are 32.2mg/dl. (%). Chouhan et al^[6] reported 7% of bacterial meningitis cases. Sundaracharya et al^[4] reports 11.1% cases. Common presentation of bacterial meningitis in this study are fever and altered sensorium seen in 100% of patients, followed by headache (66%).

Cerebrovascular Accident / Stroke

In this study 5 cases presented with stroke and facial nerve was involved in 3 cases. CT brain of all 5 cases showed infract and no hemorrhage was noted.

Myelopathy / Myelitis

Spinal cord involvement in form of Myelitis was seen in two patients, both presenting with flaccid paraparesis with definite sensory level and sphincter disturbance of acute onset. In both cases MRI of the spine showed abnormal signal intensities in thoracic cord, suggestive of demyelination. Milligo et al^[8] reported 8% of Myelitis in his study.

Cranial neuropathies

7 patients in this study had cranial nerve palsy. It involved 7th nerve in all cases and causes was CNS TB (3), 3 due to CVA, one Bell's palsy.

Literature discusses that the prevalence of HIV encephalopathy as the most frequent cause of central nervous system damage in PLWHAs, is rising despite the wide administration of ART. This can be a result of worldwide emerging HIV drug resistance. Among the other neurological diseases, PML is one of the most common neurological manifestations among PLWHAs with advanced disease that can affect approximately 4%-8% of patients. Chouhan et al^[6] reported that 5.3% patients has PML in their study.

Recent times in western studies shows the increase in the prevalence of ART related neurological complication and decreasing in secondary neurological complications. It may due to increase in survival of the patients after introduction of C-ART and development of newer HIV drugs.

Conclusions

Neurological manifestations have been reported at all stages of HIV infection but detected especially in advanced HIV disease.

The opportunistic infections remain the leading cause of neurological manifestations in HIV.

Prevalence of neurological manifestation was highest in the young adult i.e. in economically productive age group with high male preponderance.

Most common presenting symptom on admission was fever and altered sensorium, whereas headache was a significant predictor of the occurrence of neurological complications and most common abnormal neurological finding was meningeal irritation while most common finding on neuroimaging was meningeal enhancement.

Most common cause of convulsion, headache and altered sensorium was tubercular meningitis.

High index of suspicion of neurological involvement in HIV patients in all stages helps in early diagnosis and timely institution of specific therapeutic treatment, which in turn may

considerably reduce the morbidity and mortality due to the disease.

Drawbacks

Due to cost constraints, opportunistic infections workup were done in limited number of patients and due to unavailability of PCR, stereotactic biopsy and other advanced investigating modalities all patients could not be investigated completely.

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