



Study on Clinical Spectrum of Neurological Manifestations in HIV Positive Patients from a Tertiary Health Care Unit

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Abstract

Background: *Human Immunodeficiency Virus – 1 (HIV – 1) causing Acquired Immuno Deficiency Syndrome (AIDS) is not a rare disease anymore. Involvement of the nervous system was not recognized in the early years. Neuraxis involvement at various levels is now recognized in atleast one third of patients with advanced HIV infection and neurological symptoms might be the first sign of development of AIDS in 10% of the cases. Neurological manifestations of HIV include CNS disorders caused by HIV directly which include cognitive disorders and other CNS diseases like myelopathy and demyelinating neuropathy, and the secondary disorders caused by opportunistic infections, cerebrovascular events, neoplasm and medications^{1,2,3}. Taking into consideration of the versatile neurological manifestations in patients infected with HIV, the neurological manifestations were analysed in this group of patients.*

Aim of the Study: *To study the spectrum of neurological manifestations at various levels in HIV infected patients.*

Materials and Methods: *Study was conducted in the Department of General Medicine, Maharajah's Institute of Medical Sciences (MIMS), Vizianagaram for a period of 15 months (January 2019 to March 2020) which included 100 patients who were admitted in medical wards and ICU*

Conclusion: *CNS manifestations were more common in men than in women. Headache and altered sensorium were the two common symptoms observed in this study. Tuberculous meningitis was the most common opportunistic infection in our study.*

Keywords: *Human immunodeficiency virus ,Anti retroviral therapy, Neurological manifestations, Headache, TB Meningitis.*

Introduction

- Human Immunodeficiency Virus – 1 (HIV – 1) causing Acquired Immuno Deficiency

Syndrome (AIDS) is not a rare disease anymore.

- Involvement of the nervous system was not recognized in the early years.
- Neuraxis involvement at various levels is now recognized in atleast one third of patients with advanced HIV infection and neurological symptoms might be the first sign of development of AIDS in 10% of the cases.
- Neurological manifestations of HIV include CNS disorders caused by HIV directly which include cognitive disorders and other CNS diseases like myelopathy and demyelinating neuropathy, and the secondary disorders caused by opportunistic infections, cerebrovascular events, neoplasm and medications^(1,2,3).
- Taking into consideration the versatile neurological manifestations in patients infected with HIV, the neurological manifestations were analysed in this group of patients.

Aim of the Study

To study the spectrum of neurological manifestations at various levels in HIV infected patients.

Materials and Methods

Study was conducted in the Department of General Medicine, Maharajah's Institute of Medical Sciences (MIMS), Vizianagaram for a period of 15 months (January 2019 to March 2020) which included 100 patients who were admitted in medical wards and ICU.

Inclusion Criteria

- HIV positive patients admitted in medical wards and ICU were included in the study.

Exclusion Criteria

- Patients with immuno-compromised state due to any other cause were excluded from the study.

Overview and Data Collection

- Data regarding history and clinical examination findings were collected using proforma.

- HIV testing was done according to NACO guidelines.
- Other blood investigations and neurological investigations like CSF analysis and Brain Imaging were also done as per the requirement of the patient.
- Tests were done by the same person in the same laboratory to avoid interpersonal errors.

Results and Analysis

Incidence

- 31 patients had neurological manifestations among the 100 HIV patients studied (Incidence=31%).

Sex Distribution

- Out of 100 patients- 80 were males and 20 were females in our study.
- 28 among the 80 males and 3 among the 20 females had neurological symptoms.

Age Distribution

- Majority of the patients in our study were between 31-40 years of age.
- Out of which 19 cases (i.e.; 31.6%) had neurological symptoms

Mode of Transmission

- Mode of transmission in all patients in this study group was due to heterosexual behaviour.

Pre – Existing Infections

- Among the 31 patients who had neurological symptoms, 4 patients had Pulmonary TB as co-infection.

Clinical Presentation

Clinical Presentation	Frequency	Percentage
1. Headache	22	71%
2. Altered Sensorium	14	45%
3. Seizures	18	25%
4. Paraparesis	4	13%
5. Hemiplegia	3	9%
6. Quadriparesis	2	6.5%
7. Paraesthesias	2	6.5%
8. Cerebellar Syndrome	1	3.25%

- 22 patients had headache - associated with TB Meningitis(11), Pyogenic Meningitis (2), Seizure disorder(2), Cerebrovascular accident(2), AIDS Dementia Complex(1), Cerebellar Syndrome(1), Cryptococcal Meningitis(1), Toxoplasmosis(1) and Meningoencephalitis(1).
- 14 patients had altered sensorium- associated with TB Meningitis(8), Pyogenic Meningitis(2), AIDS Dementia Complex(1), Cryptococcal Meningitis(1), Meningoencephalitis(1) and Seizure Disorder(1).
- 8 patients had convulsions- associated with TB Meningitis(5), Seizure Disorder(2) and Toxoplasmosis(1).
- Disease pattern- TB Meningitis(11), Cerebrovascular accident(3), Peripheral Neuropathy(2), Seizure disorder(2), Pyogenic Meningitis(2), Cryptococcal Meningitis(1), AIDS Dementia Complex(1), Acute Flaccid Paralysis(1), Cerebellar Syndrome(1), Toxoplasmosis(1), Guillian Barre Syndrome(1), HIV Myelopathy(1), Meningoencephalitis(cause not determined)(1), Multiple Granuloma(1), Myopathy(1) and Tuberculoma(1).

Outcome

- 11 out of 31 patients who had neurological manifestations in our study group expired (35.6 %) and the remaining 20 patients improved clinically.

CSF Analysis

- 20 patients were subjected to CSF analysis in this study
- 11 patients had elevated proteins and predominant lymphocytosis
- 4 patients had normal CSF analysis
- 2 patients had elevated proteins and acellular smear
- 2 patients had predominant neutrophils
- 1 patient had elevated proteins and occasional lymphocytes and was positive for cryptococcus in India Ink preparation.

CT Brain

- CT Brain was performed on 24 patients
- Out of which 3 patients had middle cerebral arterial territory infarct
- 1 patient had hypodense lesion in the cerebellar area
- And 1 patient had multiple calcified granuloma.

MRI Brain

- MRI Brain was done for 4 patients
- 1 patient had multiple ring enhancing lesions and was diagnosed to have tuberculoma and the other patients had features suggestive of normal pressure hydrocephalus.

Discussion

Incidence

- 31 out of 100 seropositive patients in our study group had neurological manifestations (incidence = 31%).
- The incidence of neurological manifestations in HIV seropositive patients according to levy et al⁽²⁾ was 39% and snider et al⁽¹⁾ was 31%.
- In India, according to Gupta et al⁽⁴⁾, the incidence was 25.75% in his study.

Age

- In this study, majority of the patients were in the age group 31-40yrs (61.3 %).
- The mean age of the patients with neurological manifestations in this study was 36.8 years.
- According to the data of a study in university of California and Sanfransisco , the mean age of patients with neurological manifestations was 37.3 years⁽⁵⁾.

Sex

- Neurological manifestations were more common in male patients (90.32 %) when compared with females(9.68 %).
- Male : Female ratio was 9 : 1 approximately.

Pre-Existing Infections

- 4 out of 11 patients with tuberculous meningitis had pre - existing pulmonary TB.

Headache

- Headache was the most common presenting symptom in this study. 22 out of 31 patients with neurological manifestations presented with headache (70.96 %).
- 16 out of these 22 patients(72.7%) had opportunistic infections like tuberculous meningitis, pyogenic and cryptococcal meningitis.
- 6 of the remaining patients had HIV dementia and multiple granuloma as the cause.
- Headache is a very common symptom in HIV infected patients due to the frequency of intracranial infection and mass lesions.
- C B Graham et al⁽⁶⁾ described headache as a common symptom in HIV infection frequently.

Altered Sensorium

- 14 out of 31 patients had altered sensorium (45.16 %) in this study.
- Meningeal infection was the primary cause altered sensorium in this study. Tuberculous meningitis was the most common etiological cause followed by pyogenic and cryptococcal meningitis.
- None of the patients in this study had CNS lymphoma.
- University of California and Sanfransisco data showed altered sensorium as a manifestation in secondary viral infection, progressive multifocal leucoencephalopathy, toxoplasmosis , cryptococcosis, HIV dementia and lymphoma⁽⁵⁾.

Seizures

- Tuberculous meningitis was the most common cause for seizures in our study.
- 8 patients had seizures out of the 31 patients.
- 2 patients had normal CT Brain and CSF analysis was normal and definite identifiable disease of the brain was detected in these HIV

infected patients and cerebral infection seems to be the likely cause of seizures, as reported by Holtzman et al⁽⁷⁾ study which described HIV encephalopathy as the cause of seizures in 24% of the patients.

Paraparesis

- 4 out of 31 patients had paraparesis as clinical presentation in our study (12.9 %).
- Guillian-Barre syndrome in 1 case and HIV myelopathy in 3 cases were the etiological causes.
- A. I Bhigjee et al⁽⁸⁾, in their study described HTLV-1(Human T cell Lymphotropic Virus-1), tuberculosis, herpes zoster and syphilis as the causes for paraparesis.

Paraesthesias

- 2 out of 31 patients had paraesthesias in both lower limbs (6.45 %).
- 1 patient was on ART (which included zidovudine) and the other was not on ART.
- Both the patients improved with amitryptilline and nutritional support.
- Incidence of peripheral neuropathy was 8.82 % in a study done by Gupta et al⁽⁴⁾ .

Cerebellar Syndrome

- 1 patient had features of cerebellar syndrome (3.25 %).
- On CT Brain(plain), hypodense lesion in the cerebellar area was detected.
- Gait disturbances and clumsiness was reported in 45% patients with HIV dementia in a study by Mc Arthur et al⁽⁹⁾ .
- Our patient with cerebellar syndrome did not have associated dementia.

Peripheral Neuropathy

- HIV associated sensory neuropathies include distal sensory polyneuropathy caused by both HIV infection and ART toxicity. It is difficult to differentiate between the two⁽¹⁰⁾ .
- 2 patients had peripheral neuropathy (6.45 %) in our study and both the patients had paraesthesias and foot drop.
- One was on ART and the other was not using ART.

- Both the patients improved with change in ART regimen, amitryptilline and nutritional support.

Myopathy

- One patient in our study had myopathy (3.25 %).
- The patient presented with proximal muscle weakness and myalgias.
- Creatinine kinase levels were elevated on investigation.
- Patient was on ART and even after stopping zidovudine the patient did not show improvement in symptoms in follow up.
- Studies have shown that zidovudine induced myopathy occurs only when there is an underlying HIV related inflammatory myopathy⁽¹¹⁾.

HIV Myelopathy

- 2 out of 31 patients had HIV related myelopathy(6.45%).
- Both the patients had lower limb weakness and urinary incontinence on presentation.
- MRI spine showed no abnormalities and CSF analysis was normal. Vitamin B12 levels were also normal.
- A study by Jerez.p et al⁽¹²⁾ showed 22% incidence of spinal lesions in AIDS. Leading cause of myelopathies described in association with HIV was vacuolar myelopathy.

Neurotuberculosis

- 12 of the 31 patients with neurological manifestations had tuberculous infection of the nervous system in our study.
- TB meningitis was diagnosed in 11 patients.
- CSF analysis showed elevated protein levels and lymphocyte predominance.
- Tuberculoma was diagnosed in 1 patient.
- Partial seizures in the right upper limb and headache was the presenting complaint in a patient diagnosed with tuberculoma. MRI Brain showed multiple ring enhancing lesions.

Pyogenic Meningitis

- 2 patients had features of pyogenic meningitis (6.5%)
- Presenting complaints were altered sensorium, fever and headache.
- CT Brain was normal and CSF analysis showed elevated protein levels and predominant neutrophils in cytology.
- Both the patients failed to improve and expired proving the point that pyogenic infection coexisting with HIV infection has a very high mortality rate.
- AIDS related CNS complication from bacterial pathogens have not been reported from western studies.
- Studies from Uganda, such as that of Baingana et al⁽¹³⁾ from Uganda reported 7% incidence of bacterial meningitis.

Cryptococcal Meningitis

- One patient had cryptococcal meningitis (3.25%) with signs of headache, altered sensorium and signs of meningeal irritation as the clinical presentation.
- Confirmed by CSF analysis which was positive for cryptococcus on India ink preparation.
- Bandyadhyay et al⁽¹⁴⁾, in his study showed 3.7% incidence of cryptococcal meningitis.

Cerebrovascular Accidents

- 3 patients had CVA (9.3%).
- All of them presented with hemiparesis. Middle cerebral arterial territory infarct was seen on CT Brain.
- One of the patient with poor GCS(7/15) expired on the same day of admission. Remaining 2 patients were evaluated for young stroke and showed no abnormalities.
- Gupta et al⁽⁴⁾ has reported 8.82% incidence of CVA in seropositive patients in his study.
- There is a broad spectrum of etiologies causing this scenario, but in many cases the pathogenesis is unclear.

- Cerebral granulomatous angitis due to HIV infection could result in vascular occlusivedisease⁽¹⁵⁾.

Guillian – Barre Syndrome

- One patient had GBS in our study.
- Patient presented with ascending paralysis and CSF analysis showed elevated protein levels with acellular cytology.
- HIV-GBS occurs in early and late stages of HIV infection, and may follow onset of AIDS.
- TH Brannagan et al⁽¹⁶⁾ had reviewed 10 patients with HIV-GBS between 1986 and 1999, in which GBS was the first symptom of the HIV infection in 3 patients.

Seizure Disorder

- Seizure disorder was seen in 2 out of 31 patients in our study (6.25%).
- 1 patient had focal seizure involving right upper limb with secondary generalization and the other patient had generalized tonic clonic seizures.
- CT Brain and C.S.F. analysis were normal in both the patients.
- Approximately half of HIV infected patients with seizures have no definite identifiable disease of the brain and cerebral HIV infection seems to be the most likely cause of the seizures.
- In the study by Holtzman et al⁽⁷⁾, HIV encephalopathy was responsible for seizures in 24% of the patients.

Mortality

- 20 out of 31 patients with neurological manifestations had improved outcome (64.52%) and 11 patients expired (35.48%).
- Morbidity and mortality in HIV/AIDS is well established. Co-existing neurological manifestations appear to significantly contribute to poor outcome.

Conclusion

- Incidence of neurological illness in HIV infection in our study was 31%.
- CNS manifestations were more common in men than in women.
- Headache and altered sensorium were the two common symptoms observed in this study.
- Tuberculous meningitis was the most common opportunistic infection in our study.
- Tuberculous meningitis was associated with good outcome and pyogenic meningitis had high mortality in our study.

Keywords

HIV (Human immunodeficiency virus)

ART (Anti retroviral therapy)

Neurological manifestations, Headache, TB Meningitis

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