

Original Research Article

Clinical features and etiologies affecting nervous system in HIV patients

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Abstract

Background: The first reported case of AIDS was in United States in 1981. **Objective:** To study the clinical features and etiologies affecting nervous system in HIV patients. **Methodology:** The study was conducted at VIMS hospital, Ballari Patients who were HIV positive attending outpatient and inpatient services at VIMS, who fulfill the criteria for this study, were included. The study duration was from October 2017 to September 2018. **Results:** Patient's age ranged from 18 years to 58 years with female: male ratio – 1: 1.5. Meningitis was the commonest neurological presentation in HIV infection in this study around 62%. Tuberculosis was the single most common organism affecting CNS (46 %). Headache, fever and altered sensorium were commonest symptoms in HIV patients. Cryptococcal meningitis was present in 20% of the cases of HIV infection in this study. Headache and fever were commonest symptoms. It occurred in HIV infection as indicated mean CD4 count of 85.6/ cumm. 2 cases of Guillain-Barre syndrome were noted. **Conclusion:** Meningitis was the commonest manifestation (62%) comprising of 18 cases of tubercular meningitis, 10 cases of cryptococcal meningitis and 3 cases of bacterial meningitis. Tuberculosis was the commonest disease affecting nervous system (23/50) with 5 of these patients having intracranial space occupying lesion (tuberculoma) and the rest were meningitis.

Keywords: Nervous system, HIV patients, Meningitis, Tuberculosis

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Introduction

First case was recognized by the US centre for disease control and prevention (CDC) in five previously healthy homosexual men in Los Angeles with unexplained P cariniipneumonia and of Kaposi's sarcoma (KS) with or without P.cariniipneumonia in 26 previously healthy homosexual men in New York and Los Angeles. [1]

The First Indian case of HIV was reported from Chennai, Tamil Nadu in female sex workers by Dr.Suniti Solomon and her student Dr. Sellappan Nirmala in 1986. [2]

HIV 1 was identified as the causative organism in AIDS soon after the first recognition of the patients infected from USA.[3] HIV-2 was first recognized in Africa in 1985a nd is very different from HIV-1.[4]

The prevalence of HIV has increased globally since its discovery and has now spread across the globe, despite significant achievements made in the field of anti retroviral therapy. In developing countries, there is significant morbidity and mortality due to infections associated with HIV because of food insecurity and malnutrition. [5] There is wide variation in presentation of HIV/ AIDS. Neurological complication of HIV infection cause considerable morbidity and are often associated with high mortality. [6]

Estimated 60 percent of patients of AIDS have neurological symptoms and 80 to 90 percent were found to have neuropathological abnormalities at autopsy.[7] Current scenario in India is different from other countries in terms of prevalence of neurological complications where in neurotuberculosis is the leading

cause. [7] So the present study was conducted to study the clinical features and etiologies affecting nervous system in HIV patients.

Materials and Methods

The study was conducted at VIMS hospital, Ballari Patients who were HIV positive attending outpatient and inpatient services at VIMS, who fulfill the criteria for this study, were included. The study duration was from October 2017 to September 2018.

Inclusion criteria

Patients who are known or newly diagnosed HIV positive status presenting with new onset neurological signs and symptoms

Exclusion criteria

No consent to study , Patients less than 15 years, Patients with other coexisting immunodeficiency conditions like diabetes and malignancies and Patients with preexisting neurological illness like epilepsy, cerebrovascular accident will be excluded. Patients who are drug and substance abusers

Sample size of estimation

50 patients were selected for study using purposive sampling technique.

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.

Investigation

- CD4 count
- Trispot test, Trilene test, Dot immunoassay
- CSF analysis (where not contraindicated) – Protein, Glucose, cell count and type, AFB, Gram stain, ADA, India Ink preparation, VDRL and serology to detect specific infection.
- Neuroimaging (CT/MRI) where required.
- Chest Roentgenogram (X-ray) and sputum examination.

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➤ Serology to detect antibody to Toxoplasma, CMV and other opportunistic infection.

Statistical methods

Once data was collected and tabulated using MS Office Excel, the tabulated data was then analyzed. Descriptive Analysis was done using frequency Percentages, by using unpaired T-tests.

Results

Fifty patients were included in the study. Patient's age ranged from 18 years to 58 years. Out of 50 patients, 30 (60%) cases were male

and 20 (40%) cases were female. Male to female ratio was 1.5: 1. I. This indicates the high prevalence of HIV in economically productive age group, and burden on the economy. More than 50% of the patients presented late in the disease process indicating the ignorance and social stigma attached to this sensitive subject. Predominantly the route of transmission was heterosexual accounting for 20 cases (40%) followed by multiple routes 19 cases (38%). 33 patients (66%) were diagnosed to have HIV at the time of presentation (neurological). Table 1

Table 1: Distribution of the study subjects based on neurological symptoms (n=50)

Symptoms	Frequency	Percent
Altered sensorium	39	78.0
FND	15	30.0
Convulsions	24	48.0
Cranial nerve abnormality	8	16.0
Sensory abnormality	10	20.0
Behavioral abnormality	17	34.0
Headache	38	76.0

17 (34%) were known case of HIV positive before the onset of neurological deficits. Altered sensorium was the most common presentation in 39 cases followed by headache in 38 cases, convulsions in 24 cases (48%) and FND in 30 cases (60%) respectively. The commonest neurological complications in our study

was Tuberculosis in 23 cases of whom 18 cases were TB meningitis and 5 were intracranial tuberculomas. Table 2 History of pulmonary tuberculosis in 8 patients was present. Radiological abnormality was noted in chest radiogram in the form of one old lesion of PTB and eight new lesions of PTB.

Table 2: Distribution of the study subjects based on CNS findings

CNS signs	Frequency	Percent
Higher motor functions		
Drowsiness	24	48.0
Stuper	7	14.0
Aphasia	4	8.0
Comatose	3	6.0
Dysarthria	2	4.0
Delirium	1	2.0
Cranial nerves		
Abducens palsy	5	10.0
Facial palsy	3	6.0
Oculomotor palsy	2	4.0
Glossopharyngeal Nerve palsy	1	2.0

Meningitis was the commonest neurological presentation in HIV infection in this study around 62%. Table 3 Tuberculosis was the single most common organism affecting CNS (46 %). Headache, fever and altered sensorium were commonest symptoms in HIV patients. CD4 count less than 200 was seen in many of these patients (42%). CSF analysis was useful in diagnosing cryptococcal meningitis

and providing clue to tubercular pathology. As compared to western literature CNS TB was the commonest disease associated with HIV infections in our study. It was presenting pathology in 46% of the cases. It was associated with history of pulmonary TB (past and present) in 16% the cases. Table 4

Table 3: Distribution of the study subjects based on CNS findings-2

CNS signs	Frequency	Percent
Motor function		
Left CVA	1	2.0
Right CVA	7	14.0
Paraparesis	1	2.0
Quadripareisis	1	2.0
Normal	40	80.0
Reflexes		
Abnormal	38	76.0
Normal	12	24.0
Plantar reflex		
Extensor	48	96.0
Flexor	2	4.0

Table 4: Distribution of the study subjects based on CNS findings-3

CNS signs		Frequency	Percent
Cerebellar function			
	Abnormal	2	4.0
	Couldn't be assessed	41	82.0
	Normal	7	14.0
Gait			
	Abnormal	3	6.0
	Couldn't be assessed	42	84.0
	Normal	5	10.0
Meningism			
	No	17	34.0
	Yes	33	66.0
Fundus			
	Abnormal	2	4.0
	Normal	48	96.0

Cryptococcal meningitis was present in 20% of the cases of HIV infection in this study. Headache and fever were commonest symptoms. It occurred in HIV infection as indicated mean CD4 count of 85.6/ cumm. 2 cases of Guillain-Barre syndrome were noted. One

had abnormal CT in the form of old gliosis in left temporal lobe (Incidental detection). Table 5

Table 5: Comparison of clinical profile among cases with meningitis

Variable	Bacterial M (n=3)		Cryptococcal M (n=10)		Tubercular M (n=18)		P value
	N	%	N	%	N	%	
Symptoms							
Fever	3	100.0	9	90.0	18	100.0	0.338
Headache	3	100.0	9	90.0	16	88.9	0.833
Altered sensorium	3	100.0	9	90.0	17	94.4	0.803
FND	1	33.3	1	10.0	2	11.1	0.538
Convulsions	0	0.0	5	50.0	10	55.6	0.203
Abbehaviour	0	0.0	5	50.0	5	27.8	0.219
Signs							
Pallor	0	0.0	6	60.0	16	88.9	0.005
Lymphadenopathy	0	0.0	0	0.0	7	38.9	0.038
Candida	1	33.3	3	30.0	1	5.6	0.168
CNS							
Ab HMF	3	100.0	10	100.0	18	100.0	-
Ab Cranial N	0	0.0	3	30.0	2	11.1	0.562
Ab Fundus	0	0.0	0	0.0	1	5.6	0.689
Ab Motor	0	0.0	0	0.0	0	0.0	-
Meningeism	2	66.7	10	100.0	18	100.0	0.008

In this study two case of Peripheral neuropathy in the form of AIDP was detected. In studies from developed countries more number of peripheral neuropathy was detected which may be due to side effects of ART therapy. No case of toxoplasmosis was detected in this study although it is the commonest cause of space occupying intracranial lesions in western countries. CNS lymphoma was not detected in the study though tumor in the form of olfactory lobe meningioma was detected.

Discussion: Majority of people were falling in 21-45 years. Mean age of presentation was 36.08 ± 10.93 . Epidemiological analysis of AIDS cases reported by NACO 2017 reveals that the disease is affecting mainly sexually active group (15-44 years). Mc Arthur et al studied 186 patients with ages between 18- 72 years with a mean age of 36 years in male and 38 years in female. [8] Snider et al reported 50 cases with age ranging from 16-69 years. Sircar et al [10] reported male to female ratio as 4.12: 1. [9]

The various routes in multiple transmission groups were blood transmission, surgery and contact with CSW in various combinations. Heterosexual route is the most common route as compatible with other studies reported from India (John et al, Bollinger et al). [10,11] This is in contrast to western studies where homosexual transmission is more common (Levy et al, MC Arthur et

al. [12, 8] This could be because of the cultural differences in between the societies and non acceptance of same sex relationships. Fever occurred in 36 cases (72%) and weight loss in 31 cases (62%) Fever and weight loss can occur without FND. The lesions if present in non eloquent brain areas or small multifocal area need not have FND. Headache most commonly relates to meningitis or another entity called HIV headache. Millogo et al reported 35% of patients among his study group to have FND. [13]

Commonest presenting symptom was fever, altered sensorium, and headache. Focal neurological deficit (FND) was the least common. CSF proteins were raised in TB meningitis with mean of 355 ± 143.95 . CSF glucose showed lowest values in TB meningitis 43.33 ± 14.5 CSF cells were raised that is >50 cells in all cases of TB meningitis which was lymphocyte predominant. Berenguer et al compared clinical features and course of culture proven TBM\with and without HIV infection and concluded the HIV infection did not alter the course of the tubercular illness and also response to treatment. [14] Bisburg et al reported 10 cases of CNS TB in patients with AIDS and their findings were similar to that of Berenguer et al. [14, 15] They advocate that TB should always be considered in the DD of CNS lesion in HIV infected individuals. 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.

Of the 31 cases with meningitis, 18 had tubercular, 10 had cryptococcal and 3 had bacterial meningitis respectively. Wadia et al reported meningitis in 17.88 percent of the 457 patients with cryptococcal meningitis in 67.44 % and tubercular in 18.60 %. [16]

Table 6: Comparison to other studies regarding presenting symptom

Symptoms	Current study	Jorge et al[17]	Chuck et al[18]	Millogo et al[13]	Jimenez et al[19]	P.Satishc-handra et al[20]
Fever	90%	42%	90%	33%	69%	86.5%
headache	90%	57%	87%	75%	77%	97.3%
Altered sensorium	90%	42%	50%	39%	77%	75.7%
Convulsion	50%	-	-	25%	-	29.7%
FND	10%	14%	50%	-	31%	-

Cryptococcal meningitis is caused by *Cryptococcus neoformans*, yeast like budding, capsulated fungus. It is the most common fungal CNS infection in HIV infected patients.

In this study 10 patients were diagnosed to have Cryptococcal meningitis. It was based on CSF India ink preparation. 9 had fever, 9 had headache and altered sensorium, 5 had convulsions Candidiasis was seen with 3 patients. Signs of meningeal irritation were present in 10 cases. CSF analysis showed cell count of >50 in 5 cases and <50 cells in 5 cases with mean 51.2 ± 34.84 , mean protein 102.2 ± 20.29 mg/dl and mean sugar of 63 ± 14.73 mg/dl. Cryptococcal antigen detection and culture was not carried out due to cost constraints and CSF India ink was the diagnostic criteria for all cases. Chuck et al found CSF India ink preparation for cryptococci positive in only 50-70% of cases while Fernandes et al showed Indian ink positivity in 55% of cases. Hence a number of patients with Cryptococcal meningitis may have been missed in this study. [18] Spinal cord involvement in form of myelitis was seen in one patient, presenting with flaccid paraparesis with definite sensory level and sphincter disturbance of acute onset. MRI of the spine showed abnormal signal intensities in thoracic-lumbar cord, suggestive of demyelination. Levy et al have reported a case of necrotizing ascending myelitis, which resulted in complete quadriplegia. [21] Culture of CSF in this patient yielded CMV. Millogo et al reported myelitis in 8% in his study from France. [13] In this study 9 cases presented with stroke of which 8 were Arterial and one was venous. 7 cases had right sided hemiparesis and their 1 had left sided hemiparesis. Facial nerve was involved in 8 cases. No hemorrhage was noted. Mc. Arthur et al reported 9(7%) cases of cerebrovascular accident. [8] Levy et al have reported 7(5.46%) cases of AIDS with cerebrovascular complications – 4 cases were infarct. [21]

Conclusion

Young adults were mainly affected with neurological complications among HIV patients. In the present study, Sexual activity with CSWs (Heterosexual) was the major mode of transmission. Meningitis was the commonest manifestation (62%) comprising of 18 cases of tubercular meningitis, 10 cases of cryptococcal meningitis and 3 cases of bacterial meningitis. Tuberculosis was the commonest disease affecting nervous system (23/50) with 5 of these patients having intracranial space occupying lesion (tuberculoma) and the rest were meningitis. Neuroimaging studies and CSF analysis are useful in diagnosing in opportunistic infections of the nervous system. A high degree of suspicion, a good history taking, early diagnosis and proper management reduces morbidity and mortality in HIV patients affected with neurological disorders.

Limitations

This is an observational study with 50 patients done at our centre. Considering the large burden of HIV, further studies are required to ascertain the spectrum of neurological manifestations of HIV.

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