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Study of central nervous system manifestation in HIV/AIDS patient

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Abstract
The neurological problem is either primary to infection of HIV itself or secondary to opportunistic infection, or neoplasm Neurological problem is due to inflammatory, demyelinating or degenerative nature. Among opportunistic infection tuberculosis, toxoplasmosis, CMV, varicella zoster, viral encephalitis, cryptococcosis, progressive multifocal leucoencephalopathy, primary CNS lymphoma are common. Response to the treatment was assessed by noting improvement in signs and symptoms, general wellbeing, increase in weight and changes in the cerebrospinal fluid. Lumbar puncture was done whenever indicated and were followed up regularly during their stay in the hospital Repeat CT scan was performed for mass lesions to know the extent of resolution of treatment. Neurolgoical deficits were noticed in 15 cases (30%). Among focal neurological deficits hemiplagia/hemiparisis with UMN facial nerve palsy were in 9(60%). Abducent nerve in 2(13%) of cases, probably as false localizing sign. 4(27%) cases presented as paraplegia/paraparesis.

Keywords: HIV/AIDS, neurological deficits, opportunistic infection

Introduction
India has second largest burden of HIV related disease. HIV affects all system. Predominant route of transmission is sexual. Neurological complication can occur at any stage of disease. Neurological complications as initial AIDS defining condition found in 9-39% of AIDS patients. Neuropathological examinations detects abnormal neurological conditions in over 90% of autopsies of AIDS patient [1].

The neurological problem is either primary to infection of HIV itself or secondary to opportunistic infection, or neoplasm Neurological problem is due to inflammatory, demyelinating or degenerative nature. Among opportunistic infection tuberculosis, toxoplasmosis, CMV, varicella zoster, viral encephalitis, cryptococcosis, progressive multifocal leucoencephalopathy, primary CNS lymphoma are common [2].

Any part of CNS can be affected as no part is immune to virus. HIV is also associated with toxic metabolic complications Wernicke's encephalopathy and B12 deficiency. ART is also associated with neurological complications. HIV is associated with increased cerebrovascular accidents due to procoagulent tendency. Recently it is recognized that ART treatment with recovery of CD4 counts showed to detoriate clinically even with lowering of viral load. This is attributed to immune reconstitution inflammatory syndrome. This is more common with opportunistic infection in which case the inflammation is targeted to the site of infection [3]. Neurological complications associated with profound immunosuppression in advanced disease. Hence knowledge of CD4 is of paramount importance. With CD4 count ≤ 200 cell/mm^3 morethan 90% of focal lesion in CNS is due to Toxoplasmosis.

Since many of conditions are amende able to treatment proper diagnosis and treatment decreases morbidity. Some opportunistic neurological infections are a result of latent or persistent infection requiring lifelong secondary prophylaxis [4].

HIV infection is commonest cause of Dementia in people under age of 50 years in developed world. TB is seen resurgence following outbreak of AIDS. TB meningitis is commonest infection in patient with HIV infected individual leading to increased morbidity and mortality. Cryptococcal meningitis is opportunistic fungal infection in patients with HIV is seen to be under diagnosed in India. Neurotuberculosis is more common in Indian AIDS patient. CSF examination and clinical finding cannot be relied to distinguish tubercular meningitis from cryptococcal meningitis [5].

Routine mycolocal surveillance is essential in every case. Approximately 10% HIV infected individual develop cryptococcal meningitis and morbidity over 60%.

Hence, extensive study has been made in central nervous system infection in HIV positive individual. In particular tubercular meningitis and cryptococcal meningitis which account for increased morbidity and some opportunistic infection are debilitating and do not respond to conventional treatment until the immune defect central to syndrome is rectified. The duration of survival and quality of life of patient can be influenced by predominantly by early diagnosis and effective treatment and long term supportive therapy for opportunistic infection [6].

Methodology

Each case was studied in detail and the results of various findings were worked out according to the proforma analysed. The diagnostic criteria adopted were

1. Detailed History
2. Signs of Meningeal irritation
3. Cerebrospinal fluid analysis including CSF HIV 1&2

Lumbar puncture was done on admission and was subsequently repeated whenever indicated to assess the course of the disease. CSF analysis was done including routine fungal work up, grams stain, cell type, cell count, Antitoxoplasma antibody, VDRL, Zeihl Neelson staining and biochemical analysis. Chest X-ray was routinely taken to rule out opportunistic infection computed tomography brain was not performed in all patients, it was done only in those patients who had focal neurological deficits and signs of raised intra cranial tension.

Treatment with Zidovudine 100mg every fourth hourly as monotherapy was started in patients who had lymphocyte count in the range of 1000-2000 cells/mm^3

- Phenobarbitone was used to control convulsion and restlessness when present
- Supportive therapy in the form of
- Vitamins
- Other nutrients
- Control of temperature
- Intra venous fluids when necessary was given.
- Ryle's tube feeding was done in unconscious patients.

Response to the treatment was assessed by noting improvement in signs and symptoms, general wellbeing, increase in weight and changes in the cerebrospinal fluid.

Lumbar puncture was done whenever indicated and were followed up regularly during their stay in the hospital Repeat CT scan was performed for mass lesions to know the extent of resolution of treatment.

Diagnostic methods adopted

Routine investigation like hemoglobin, Blood counts and ESR were done including biochemical investigations like

- Fasting blood sugar
- Blood urea
- Serum creatinine
- Serum electrolytes.
- CD4 counts

1. **CSF Analysis**

(a) CSF HIV 1&2
(b) Macroscopic appearance
(c) Cell count and type of cells using
(d) Neubars counting chamber
(e) India ink preparation
(f) VDRL
(g) Anti toxoplasma Antibody in CSF
(h) Biochemical Analysis

(i) Protein - By Turbidity method (20-40mg)
(ii) Sugar - By Folin wu method (50-80mg)

Bacteriological examination
Direct ZN staining of CSF
(ii) Grams staining
Culture - Fungal on saborauds agar

2. Radiology Chest x-ray was taken in all cases CT scan brain was done in patients who had focal neurological deficits/Raised intra cranial tension.

Sputum for AFB - using Z-N stain

Blood sugar and renal function tests - Blood sugar was done in all cases to assess the ratio of blood sugar and CSF sugar. Renal function tests and serum electrolytes were monitered closely during treatment, in particular with systemic antifungal agents.

Lymphnode biopsy - If any patients presented to us with significant lymphadenopathy.

Results

Table 1: Sensorial disturbances (n=50)

Sensorial disturbances	No. of cases	Percentage
Conscious	18	36
Drowsy	20	40
Unconscious	12	24
Total	50	100

Around 36% were conscious at the time of presentation, 40% were drowsy and remaining 24% were unconscious. In few cases the level of consciousness deteriorated as the disease progressed.

Table 2: Focal neurological deficits (n=15)

Paralytic lesion	No. of cases	Percentage
Hemiplegia/ Hemiparesis with Facial palsy (UMN)	9	60
Paraplegia/ Paraparesis	4	27
Occulomotor nerve dysfunction	0	0
Abducent nerve dysfunction	2	13

Neurolgoical deficits were noticed in 15 cases (30%). Among focal neurological deficits hemiplagia/hemiparisis with UMN facial nerve palsy were in 9(60%). Abducent nerve in 2(13%) of cases, probably as false localizing sign. 4(27%) cases presented as paraplegia/paraparesis. Presence of neurological deficit indicated severe form of central nervous system disorder.

Table 3: Fundal picture

Fundal changes	No. of cases	Percentage
Papilloedema	8	16
Optic atrophy	0	0

Fundal changes were present in 8 cases (16%), all comprised of papilloedema.

Table 4: CD4 count

Features	Mean cell count
Candidiasis	90
Cryptococcus neo formins	52
Tuberculous meningitis	52

Table 5: Computed tomography/MRI scan (BRAIN)(n=28)

Features	No. of cases	Percentage
Normal	17	60
Infarct	9	32
Transverse myelitis	2	8

CT/MRI scan was not performed in all cases, it was reserved only for those patient who presented with unconsciousness, focal neurological deficits (28 cases). Infract was found 32% of the patients and transverse myelitis in 8% of cases. 60% of the cases showed normal imaging.

Table 6: Cerebral fluid analysis CSF clarity (n=36)

Colour	No. of cases	Percentage
Clear	34	94
Opalescent	2	6
Total	36	100

CSF analysis was done in 36 cases. In some patients because of massive cerebral edema and patients attend, not willing for analysis it was done. CSF was clear in majority of cases in around 94% and opalescent in 6%.

Discussion

Neurological diseases are common in HIV infection. More than 50% of HIV infected persons develop symptomatic neurologic diseases. Neurological complication may occur at any stage of HIV infection, with predilection for certain syndrome to occur in relation to falling CD4 count. In 10-20% cases, neurologic disease heralds AIDS, and pathological involvement of nervous system is seen in 80% of the cases at autopsy. Any part of the neuraxis may be involved and more than one disease may co-exist in the same individual. In our study there were co-existing diseases. As it has already been quoted that NEUROAIDS does not follow the law of parsimony, i.e., a single entity may not be responsible for the entire constellation of signs and symptoms. Cryptococcosis is the commonest infection affecting central nervous system in HIV sero positive individuals as reported by C.P DAS, sawhney. In our study Tubercular meningitis + pulmonary Koch's and TB spine comprised 62% and the next culprit was Candidiasis and cryptococcal menigitis. Aquinas *et al.* [7] reported a case of co-existence of cryptococal with tubercular meningitis which was strongly suspected as there was evidence of dissemination of Tubercular infection elsewhere in the body. In our study though rare there was no case of co-existence of CNS diseases. There should be a high index of suspicion of coexisting infection whenever there is evidence of dissemination of infection elsewhere in the body, particularly in developing country like ours. Cerebral abscess, toxoplasmosis and neurosyphilis were found in rarity.

In our study Tubercular meningitis comprised about 62% of all chronic meningitis cases which was studied over a period of one and half years. It has recently been included as an AIDS defining illness in the criteria laid by NACO (National AIDS control organization). In Uganda 66% of hospitalized patients are tested HIV positive. For the individuals infected with mycobacterium Tuberculosis and then with HIV, the risk of developing tuberculosis is 5-10% per year. Conversely tuberculosis develops in as many as 50% of HIV positive patients who develop primary infection with mycobacterium tuberculosis. The corresponding statistics in Indian population is sparse, Gupta *et al*., 1993 reported 58.8% association of neuro tuberculosis in neuro AIDS. Though neuro tuberculosis can occur at any stage of HIV infection, it occurs typically when CD4 count are below (<350). However tuberculosis precedes other AIDS defining illness, as reported by selwin *et al*., 1989. Berenguer *et al.* [8] reported 59% tuber culous meningitis in their series Wadia *et al.* [9] reported 91.2% tuberculous meningitis cases. In our study we reported 62% of tuberculous meningitis.

In our study all Tubercular meningitis had acquired HIV infection through heterosexual contact. In Bishburg *et al.* [10] group 90% were intra venous drug abusers. Headache and fever was the predominant presenting symptoms found in all our cases. This is consistent with the study conducted by Wadia *et al*., [9] Bishburg *et al.* [10], who studied 10 cases of HIV over a period of 2 years 50%, presented with seizures as the presenting symptoms, followed by headache and vomiting.

In our study cryptococcal meningitis comprised 14% of all the chronic meningitis cases. Cryptococcal meningitis comprised 12.5% of cases conducted by Aquinas *et al.* [7] This implies that cryptococcal meningits is also one of the commonest opportunistic infections next to tuberculous meningits in immunocompromised individuals especially in developing countries as established in our study.

Conclusion

- CSF was normal or showed marginal pleocytosis in quite a good number of cases (84%) and hence one should have a high index of suspicion in recognizing these cases. Full work up for all chronic meningities is mandatory in all HIV seropositive individuals presenting with fever, with headache, even if CSF is acellular
- In majority of patients CD4 count is less than 200/cumm.

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