



CLINICAL SPECTRUM OF MOVEMENT DISORDERS IN HIV PATIENTS.

General Medicine

Dr. Sawan Nitish Jivan*

Senior Resident, Department Of General Medicine, All India Institute Of Medical Sciences, Nagpur(MH). *Corresponding Author

Dr. Basavaraj Anita

Professor And Head, Department Of General Medicine, Government Medical College, Miraj(MH).

ABSTRACT

Movement disorders have been reported in 2-3% of patients with human immunodeficiency virus (HIV) infection¹. The movement disorders include: chorea, hemiballism, myoclonus, tics, dystonia and tremors². In some of the reported cases, a specific pathology, such as toxoplasmosis involving the basal ganglia has been identified and in the cases where no such pathology was demonstrable, the movement disorder was attributed to HIV infection related pathology. Recognizing the movement disorder is important, because it may be the presenting manifestation of HIV infection³.

Methods: A cross sectional observational study was conducted at a tertiary care institute in 50 HIV ELISA positive patients more than 12 years of age presenting with involuntary movements.

Results: Movement disorders were more common in the age group of 31-40 years, more common in males and in the WHO stage 3 and 4. Most common movement disorder was tremor followed by chorea and myoclonus. The most common neuro-imaging abnormality found was HIV related encephalopathy followed by central nervous system tuberculosis (CNS TB), toxoplasmosis and progressive multifocal leucoencephalopathy (PML). Most common opportunistic infection was CNS TB.

Conclusions: Only 50 patients presented with movement disorders in the 18 month study period making it an uncommon presentation. But movement disorders can be an initial presentation of HIV and early evaluation is needed to find out the treatable cause.

KEYWORDS

HIV, CD4, PML, CNS TB

INTRODUCTION

HIV / AIDS (Acquired Immunodeficiency Syndrome) is a chronic, potentially life threatening disease affecting millions of people across the world, including in India. AIDS is the most advanced stage of HIV infection. HIV attacks and destroys the backbone i.e. CD4 cells of the immune system. Loss of these cells makes it difficult for the body to fight infections and certain cancers. Without treatment, HIV gradually destroys the immune system and advances to AIDS. Unprotected sexual intercourse or sharing contaminated drug injection equipment (such as needles and syringes) with HIV infected persons are the most common ways HIV is transmitted⁴. Mother-to-child transmission is the most common mode through which children become infected with HIV. In India HIV / AIDS is now two and half decade old since the first case of AIDS was reported in 1986 from Mumbai in Maharashtra. In India, Maharashtra state is one of the five states with highest number of HIV infected individuals. As a result of HAART (Highly Active Antiretroviral Therapy), HIV has metamorphosed from an acute life threatening illness to a chronic but manageable illness.

Movement disorders in HIV are very rare occurring in 2-3% of the patients¹. The various movement disorders that have been reported include chorea, hemiballism, dystonia, myoclonus, tics and tremors. They can be the initial presentation of the HIV infection or occur late in the disease course. Various opportunistic infections have been identified as the underlying cause of the movement disorders making it important to recognize such treatable infections. In other patients, movement disorders were attributed to HIV infection itself.

The reported incidence of tremor in AIDS patients has ranged from 5.5 to 44% of patients with HAD (HIV associated dementia)⁵. As HAD is a late-stage manifestation of HIV infection, this may suggest an increased incidence of tremor with increasing immunosuppression⁶. Holmes tremor may occur as a result of opportunistic lesions in the midbrain such as tuberculosis or toxoplasmosis. Drug-induced tremor may be observed as part of an extrapyramidal syndrome seen in AIDS patients exposed to dopamine receptor antagonists such as neuroleptics or anti-emetics or it may be seen as an unusual complication of TMP-SMX (Trimethoprim- Sulphamethoxazole) used for treatment of PCP (Pneumocystis carini pneumonia) in such patients.

While some studies have reported hemichorea- hemiballism as the most common movement disorder in HIV positive patients^{7,8,9}, other reports describe them as the second most frequent movement disorder after parkinsonism^{10,11}. Interestingly, hemichorea-hemiballismus is

one of the rarest of all movement disorders in patients without HIV infection¹². A subthalamic toxoplasmic abscess is the most common cause of hemichorea-hemiballism in AIDS patients^{13,14}. Generalized chorea may be the result of bilateral toxoplasmosis abscesses but may also be associated with HAD^{15,16,17}. More rarely, other aetiologies have been described, including cryptococcus⁸, progressive multifocal leucoencephalopathy and iatrogenic⁹.

Myoclonus is a rarely reported movement disorder in AIDS patients. Both segmental and generalized myoclonus have been described in AIDS patients. No clear correlation was observed between the clinical signs and lesions observed on brain imaging studies. However, cerebral toxoplasmosis, progressive tuberculous radiculomyelopathy and HAD have been described as the potential etiologies. Myoclonic ataxia has been described as an initial presentation of PML in HIV patients¹⁸.

Dystonia has rarely been reported in patients with AIDS. However, generalized, segmental, and focal dystonia have been described in AIDS patients. Dystonia of arm has been associated with the involvement of basal ganglia by toxoplasmosis¹⁹. Spasmodic torticollis was found to be associated with thrombosis of internal jugular vein which resolved with the anticoagulation treatment²⁰. AIDS patients treated with dopamine receptor-antagonists appear to be particularly susceptible to developing an acute onset medication-induced dystonia (and/or parkinsonism)^{21,22}.

Paroxysmal dyskinesias, a rare movement disorder which presents with dystonic or choreoathetotic movements that occur suddenly and transiently, with complete recovery between attacks, have been described in two case reports of AIDS patients. It is hypothesized that infection of the basal ganglia by HIV may lead to calcium metabolism dysregulation, causing paroxysmal dyskinesias^{23,24}.

METHODS

- A cross sectional observational study carried out at a single tertiary care institute.
- Fifty cases of more than 12 years age were selected from ART clinic and wards who presented with involuntary movements.
- A descriptive observational study was performed.
- A written informed consent was taken from each selected case.

Once the patients were selected, a detailed history with respect to their demographic features and general examination was done according to

a standardized proforma with due importance to the HIV disease, symptomatology, clinical presentation, investigations and treatment of all the patients.

Demographic Features Of The Study Group:

This included the basic information like age, gender, baseline CD4, current CD4, clinical stage of HIV infection were collected through the proforma.

Symptomatology:

A detailed history of all patients was taken regarding the involuntary movements as-tremors, chorea, hemiballism, myoclonus, dystonia and paroxysmal dyskinesias. The onset, duration and progress of the involuntary movements was noted as well as its relation to rest and activity was also noted. The history regarding any other associated neurological complaints was also recorded with special reference to cognitive function.

Examination Findings :

Thorough clinical examination was performed and the findings were documented in the case proforma. Detailed examination was done in all patients for general and systemic features with special regard to central nervous system.

REVIEW OF RECORDS:

Records of all patients included in the study were reviewed to obtain the following data:

- a) Year of diagnosis
- b) CD4 count at the time of diagnosis
- c) Duration of HAART
- d) Switch / Substitution of HAART drugs with reason
- e) Adherence and compliance to drugs
- f) Any opportunistic infection in past

Investigations Done:

Radiological neuro-imaging was done in all the patients with CT/MRI scans.

RESULTS

Demography and WHO clinical stage- In this study, 8 patients were less than 20 years of age, 8 patients belonged to age group of 21-30 years, 20 patients belonged to age group 31-40 years, 10 patients were from the age group 41-50 years and 4 patients were above 50 years of age. Of the 50 patients, 34 were males and 16 were females with male to female ratio being 2.12:1. In terms of WHO clinical stage, 28 patients were in WHO HIV stage 3, 22 patients were in WHO HIV stage 4 and no patients were found in WHO stage 1 and 2.

Type of movement disorder- Thirty six out of 50 patients were found to have tremors making it the most common movement disorder observed. It was followed by chorea and myoclonus seen in 6 patients each. Two patients had hemiballism while dystonia was not found in any of the patients.

Neuro-imaging Results- Neuro-imaging was done in all patients by either CT scan or MRI of brain. HIV encephalopathy was found in 10 patients, CNS TB in the form of either tuberculous meningitis or tuberculoma was found in 8 patients. Toxoplasmosis was found to be the cause of movement disorders in 4 patients while PML was seen in 4 patients. Imaging was normal in 12 patients while other non-specific findings were seen in 12 patients.



Image no. 1 - HIV-1 Encephalopathy And AIDS Dementia Complex. CT Scan Of The Brain Of A Patient With AIDS dementia complex (ADC) shows diffuse atrophy and ventricular enlargement and attenuation of periventricular white matter.

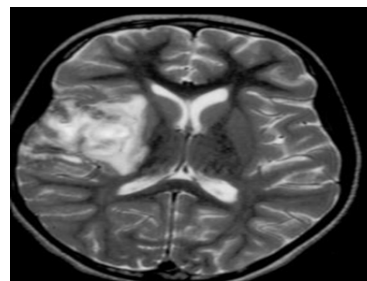


Image No. 2- T2-weighted magnetic resonance image of a right parietal tuberculoma. Note the low-signal-intensity rim of the lesion and the surrounding hyperintense vasogenic edema.

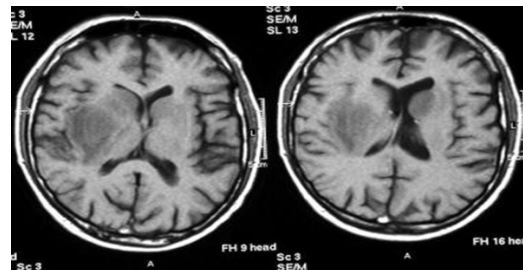


Image No. 3- Nonenhanced T1-weighted images in a patient infected HIV and cerebral toxoplasmosis. These images show hypointense, asymmetrical, bilateral periventricular/basal ganglial lesions.

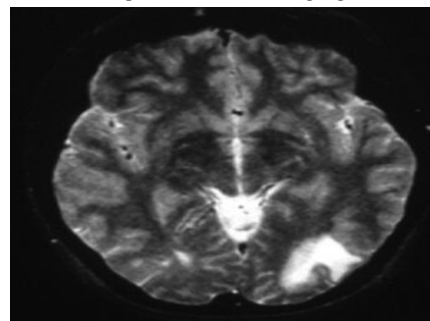


Image No. 4- T2-weighted MRI shows left occipital hyperintense white matter changes with the lesion margin reaching the cortex.

Out of 36 patients of tremors, a majority of patients i.e, 12 had normal imaging results while 6 patients had CNS TB, 4 had toxoplasmosis, 2 had HIV encephalopathy and 2 had PML. The remaining 10 patients had other non-specific imaging results like infarct, cerebral atrophy and dural lipoma. Out of 6 cases of chorea, 4 were having HIV encephalopathy and 2 were having CNS TB. Both the cases of hemiballism had HIV encephalopathy on imaging. Two cases of myoclonus showed HIV encephalopathy, 2 cases showed PML while the remaining 2 cases showed CVST out of the total 6 cases. Dystonia was not seen in any patient.

Table 1- Movement Disorders And Neuro-imaging Results

	HIV ENCEPH	CNS TB	PML	TOXO	OTHERS	NORMAL
TREMOR	2	6	2	4	10	12
CHOREA	4	2	0	0	0	0
MYOCLONUS	2	0	2	0	2	0
HEMIBALLISM	2	0	0	0	0	0
TOTAL	10	8	4	4	12	12

Neuro-imaging also gave us an idea about different opportunistic infections that might occur in such patients. The opportunistic infections documented were CNS tuberculosis, toxoplasmosis and PML, former one being the most common. As seen from the table above, 12 patients of tremors suffered from opportunistic infections. Six patients had CNS TB, 4 patients had toxoplasmosis, 2 patients had

PML. Only 2 patients with chorea had opportunistic infection, both being CNS TB. Two patients with myoclonus were suffering from PML and the rest 2 did not show any imaging findings suggestive of any opportunistic infection. Patients presenting with hemiballism did not show any evidence of opportunistic infections.

DISCUSSION

In our study, maximum number of patients i.e, 20 belonged to the age group of 31-40 years followed by 10 patients in the age group of 41-50 years while only 4 patients were above 50 years of age. It gives us clear indication that movement disorders are common in young age group which is also the high risk group for HIV in the society. All of these patients had acquired HIV infection through the heterosexual route. It is noteworthy that 8 patients were under the age of 20 years. Six of them were diagnosed HIV positive since birth (vertical transmission) and 2 were diagnosed 2 years back with the history of opportunistic infections. Near about two-thirds i.e. patients in our study were males and 16 were females, male:female ratio being 2.12:1. In our study, 28 patients were in WHO stage 3 and 22 patients were in WHO stage 4 and no patient was found in WHO stages 1 and 2. It indicates that movements disorders are common in the advanced stages of HIV, may be correlating with the lower CD4 counts in the more advanced stage. The most common movement disorder found in our study was tremor seen in 36 patients followed by chorea and myoclonus found in 6 patients each. While dystonia was not seen in any patient, hemiballism was seen in 2 patients. In a study done by Dr. James P de Mattos at Clementino Fraga Filho University Hospital, Rio, Brazil(2002), the most common movement disorder seen was parkinsonism (presenting as tremors), followed by hemichorea/hemiballism out of 28 patients studied¹⁰.

Table 2- Comparison Of Etiologies Of Movement Disorders Between Mattos et Al And Our Study.

	Mattos et al(2002)	Our study
Tremors	HIV related-12 Atrophy-7 Toxo-1 Benedict's-1 Metoclopramide-1	Normal imaging-12 CNS TB-6 Toxo-4 HIV enceph-2 PML-2
Hemichorea/Hemiballism	Toxo-6	HIV enceph-6 CNS TB-2
Myoclonus	Toxo-1 HIV enceph-1 Radiculopathy-1 Herpes zoster-1	HIV enceph-2 PML-2 CVST-2

We compared the results of study done by Mattos et al with our study. In that study, out of 14 patients of parkinsonism(tremors), 12 were HIV related, 7 patients had cerebral atrophy, 1 had toxoplasmosis, 1 patient was a case of Benedict's syndrome and 1 patient had drug induced tremors(metoclopramide)¹⁰. Considerable overlapping was seen between patients with HIV related and cerebral atrophy. All 6 patients of hemiballism had toxoplasmosis on imaging. Out of 4 patients of myoclonus, 1 patient had toxoplasmosis, 1 patients had HIV encephalopathy, 1 patient had radiculopathy and 1 patient had herpes zoster.

The most common opportunistic infection seen in our study was CNS TB seen in 8 patients. This finding actually signifies the burden of tuberculosis in India as compared to western countries. Despite of continuous efforts to combat tuberculosis using highly effective regimens under national programmes, it remains a major health problem in the developing nations, especially in immunocompromised patients.

CONCLUSION

Movement disorders were more common in the age group of 31-40 years, more common in males and in the WHO stage 3 and 4. Most common movement disorder was tremor followed by chorea and myoclonus. Dystonia was not seen in any of the patients studied. Most common imaging abnormality found was HIV related encephalopathy followed by CNS TB, toxoplasmosis and PML. Most common opportunistic infection was CNS TB. Of approximately 35,000 HIV patients registered at tertiary hospital ART Centre and approximately 6000 patients on ART, only 50 presented with movement disorders in the 18 month study period making it an uncommon presentation. But movement disorders can be a presentation of HIV and early evaluation is needed to find out the treatable cause.

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