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CASE REPORT

HIV Presenting as Cerebellar Ataxia

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ABSTRACT

Cerebellar disorders associated with HIV infection are typically the result of discrete cerebellar lesions resulting from opportunistic infections such as toxoplasmosis and progressive multifocal leukoencephalopathy or primary CNS lymphoma. Clinical symptoms and pathologic abnormalities related to the cerebellum may also be observed with HIV dementia. A primary cerebellar degeneration with HIV is rare. In our case the patient presented with progressively unsteady gait, slurred speech, and limb clumsiness. Examination revealed gait ataxia, impaired limb coordination, dysarthria, and abnormal eye movements. CD4 lymphocyte counts was very low 26 cells/mm^3. Neuroimaging studies showed prominent cerebellar atrophy. We report a syndrome of unexplained, isolated degeneration of the cerebellum occurring in association with HIV infection.

INTRODUCTION

HIV/AIDS is one of the leading causes of death worldwide, and one in every 100 adults aged 15 to 49 in HIV-infected patients. HIV is classified among the lentiviruses, a family of viruses characterized in part by their tendency to cause chronic neurologic disease in their animal hosts. All levels of the neuraxis can be involved, including the brain, meninges, spinal cord, nerve, and muscle. In developing countries, opportunistic infections of the central nervous system (CNS) account for most of the reported neurologic morbidity and mortality but as newer antiretroviral therapy have greatly increased life expectancy, there is growing concern about the chronic viral neurotoxicity that can lead to progressive brain atrophy and associated neuropsychological/neurocognitive impairment as well as movement disorders. Cognitive impairments might range from minor cognitive motor disorders to HIV-associated dementia, often with progressive deterioration ultimately leading to death. Although there is no proven treatment, some evidences suggest that, despite the poor CNS penetration of most antiretrovirals, effective antiretroviral therapy may attenuate neurotoxicity and halt progression of symptoms(1).

HIV infection is associated with progressive striatal, hippocampal, and white matter volume loss, starting in the medically asymptomatic stage, and accelerating later (2). Newer MRI-based studies have revealed that atrophy may be seen in as many as 10–15% of infected patients, with common involvement of areas concerned with motor control such as the basal ganglia (3), and primary, supplementary motor, and prefrontal cortices (4). The caudate and adjacent ventricles are enriched in the virus, so atrophy may progress as the virus spreads out radially into cortical projection areas (5).

Classically defined as a motor control center, the cerebellum is increasingly recognized as contributing to general cognitive processing and emotional control (6). Studies in rats have associated HIV infection with increased cerebellar neuronal death (7), but the extent of cerebellar atrophy in HIV patients and how it relates to symptoms is unknown.

We report an interesting case of an 18 year old patient presenting as symmetric, progressive cerebellar ataxia later found to be HIV positive.

CASE REPORT

A 18 year old male presented to us with 3 months history of gradual onset, symmetric, progressive difficulty in walking, impairment of vision and inability to perform fine activities due to increased tremors for which he was admitted to our ward. The patient was being treated at a peripheral centre and was treated with steroids following which his symptoms did not improve. After few days patient developed genralised dermatitic rashes. There is past history of ATT intake for suspected pulmonary tuberculosis for a full course of 6 months after which the patient became asymptomatic. There was no history of seizures, sensory symptoms or bowel bladder dysfunction. Patient was non-alcoholic; chronic tobacco abuser. No prior history of blood tansfusions or surgical interventions.

On general examination he was malnourished, having pallor and generalized dermatitis rash. His vitals were stable. Cognition was intact except for minor attention deficits. Cranial nerve examination was within normal limits. Pupils and fundus were normal. On motor system examination, tone was reduced in all four limbs, power 4+ in all limbs. The results of physical examination were notable for severe dysarthria, nystagmus, finger-nose-finger and heel-knee-shin dysmetria, intention tremor, and impaired rapid alternating movements. Superficial and deep reflexes were intact with pendular knee jerk. Cerebellar signs were present in both upper and lower limb. His gait was broad based, with inability to perform tandem walking. Sensory and autonomic signs and signs of meningeal irritation were absent.

In laboratory evaluation, hemogram showed pancytopenia (Hb- 8.68gm, TLC-5100, plt- 1,50,000). Her serum electrolytes, RFT , LFT, chest X - ray, U S G abdomen were normal. HIV by Elisa was positive, CD4 count was 26/µl. Serum B12 and TSH levels were normal. CSF examination showed 10 cells/cumm with all lymphocytes; protein 41 mg/dl; sugar 55 mg/dl and ADA was 5.8. The CSF was also negative for cryptococcal antigen and VDRL. CSF culture did not grow microbes. CSF PCR assay was negative for HSV1, HSV2 and JC Virus. IgM toxoplasma was negative. Regarding dermatitis rash, skin consulation was taken and the patient was diagnosed of having generalized tinea infection. MRI brain revealed age inappropriate cerebellar atrophy with cerebellar atrophy.

The patient was diagnosed with primary cerebellar degeneration associated with HIV disease. The patient was managed symptomatically along with treatment of tinea infection. Patient discharged on continued HAART and supportive therapy with a referral to outpatient physical rehabilitation.

DISCUSSION

HIV crosses the blood-brain barrier and enters the nervous system early, probably concomitant with initial systemic infection (8). The virus has been cultured from brain, nerve, and cerebrospinal fluid (CSF) from persons at all stages of HIV disease, including those without neurologic signs or symptoms (9). Hospital based studies have reported movement disorders in 3% of patients with HIV infection (10). Various movement disorders have been described in HIV patients such as hemichorea-ballismus, myoclonus, dystonia, tremor, and ataxia (11). The pathogenesis of movement disorder in HIV infection remains unclear. The neurologic complications of HIV infection are common and not confined to opportunistic infections. HIV infection-related pathology involving basal ganglia, brainstem and cerebellum may also result in movement disorders(12). Few possible hypothesis explaining these disorders have been proposed; such as development of calcific vasculopathy and ischaemic infarction due to HIV induced hypercoaguable state. Some investigators hold that increased HIV-1 proliferation in the brain is necessary for the development of neurologic dysfunction. Others propose that a macrophage-initiated cascade of events can lead to brain dysfunction and clinical dementia, even in the absence of high viral load in the brain. Activated macrophages, whether infected with HIV or not, are capable of secreting potent neurotoxins, inducing pro-inflammatory cytokines, and generating oxygen free radicals that can damage cells and lead to neuronal dysfunction or death.

In HIV-1 infection, activated brain macrophages and microglia release quinolinic acid, a neurotoxin and N-methyl-D aspartate (NMDA) receptor agonist. Elevated cerebrospinal fluid quinolinic acid levels are associated with region specific cerebral volume loss in HIV infection and has been implicated in the development of cognitive deficits. FDG-PET studies have also shown global cerebral hypometabolism in advanced HIV infection.

Ataxia in HIV infection can also be caused by HIV encephalopathy, vasculitis and opportunistic infections like toxoplasmosis and JC virus which were excluded by appropriate investigations.

In our case the patient presented with bilateral cerebellar symptoms of wide-based gait with dysmetria, abnormal heel-knee-shin test, and dysdiadochokinesia, and was diagnosed

of having HIV disease incidentally. Extensive laboratory work up failed to disclose a cause for subacute ataxia, and thus the patient was labelled a case of primary cerebellar degeneration associated with HIV disease, which is a rare entity. A likely possibility of Isoniazid induced cerebellitis was also considered in this case as this this patient was served ATT for 6 months about one year back. However, this was ruled out owing to absence of MR findings of diffuse cortical hyperintensity in both cerebellar hemispheres and vermis. In the presesnt case, MRI findings of age inappropriate cerebral atrophy with cerebellar atrophy supported our diagnosis.

Treatment of HIV-related movement disorders has uncertain efficacy. Chorea may respond to dopamine receptor blockade, but ataxia, tremors, parkinsonism and other movement disorders in HIV usually fail to respond to available therapies. Our patient however, has shown significant improvement with the symptomatic therapy and HAART.

CONCLUSION

Cerebellar degeneration in HIV is chiefly attributed to infective etiology and lymphoma in available literature. HIV induced cerebellar involvement is not an established entity because of lack of a definite cause and effect relationship and is thus a diagnosis of exclusion.

Conflict of interest: None declared

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