CASE REPORT

Movement disorder in a patient with Human Immunodeficiency Virus on an anti-retroviral therapy: A Case Report

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Abstract

Human Immunodeficiency Virus associated neurocognitive dysfunction can present as a case of movement disorder in a patient with prolonged anti-retroviral therapy. Diagnosis was made after ruling out space occupying lesions, nutritional deficiencies and infectious causes through brain imaging and cerebrospinal fluid analysis. With multidisciplinary care and change of antiretroviral therapy to drugs with higher cerebrospinal fluid penetration, symptoms of the patient improved over a span of six months. Delayed neurological damage due to Human Immunodeficiency Virus can present with isolated cerebellar symptoms.

Keywords: Human immunodeficiency Virus, White matter disease, Neurocognitive impairment.

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Introduction

Human Immunodeficiency Virus (HIV) is a neurotropic virus which infects the central nervous system (CNS) early in the disease course and can result in neurological and psychological symptoms.[1] Movement disorders in HIV can be due to direct or a variety of opportunistic infections.[2] We report a case of HIV patient seen in July, 2017 at the Sindh Institute of Urology and Transplantation (SIUT). Patient was on anti-retroviral therapy (ART) for many years and developed walking difficulty with a tendency to fall.

Case Report

A 49-year-old female, widowed, lady health visitor by profession was found to be HIV positive 6 years back when she underwent a cholecystectomy. She contracted HIV from her husband who died due to the illness, 25 years back. Her disease remained stable on Tenofovir (TDF), Lamivudine (3TC) and Efavirenz (EFV) with undetectable viral load and optimal cluster of differentiation count 4 (CD4 count).

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During the last year, she started complaining of walking difficulty, tendency to fall, dizziness, frequent crying and episodes of panic attacks. These symptoms were not associated with fever, drowsiness, limb weakness, seizures or memory loss. Her symptoms were slowly progressive in nature and she had to leave her job as she was unable to carry out normal physical activities at home.

On examination, patient was alert, well oriented but very anxious. Motor and sensory systems were intact. She had a wide-based gait with abnormal heel to shin test and dysdiadochokinesia. Patient was unable to maintain her balance while walking. Her cranial nerve examination was unremarkable except that she had nystagmus. Rest of the physical examination was normal.

Complete blood picture, liver and renal function tests were normal. The CD4 cell count was 288 which dropped from 599 six months back (Normal Value- 500 to 1,400 cells per cubic millimeter) and the viral load was undetectable. Thyroid stimulating hormone (TSH) was 0.8mIU/L (Normal Value- 0.4 to 4.0 milli-international units per liter), HbA1c was 5.3% (normal range - 4%-5.6%.) and vitamin B12 levels

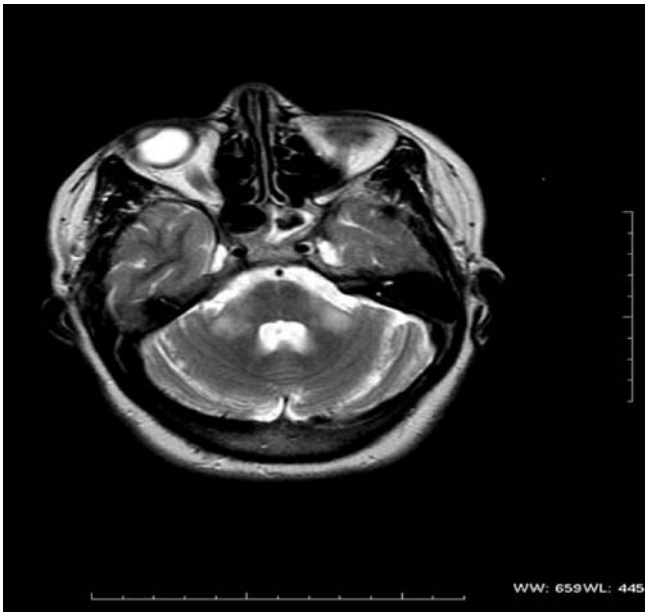

Figure-1: High intensity signals bilaterally in the middle cerebellar peduncles suggestive of neurodegenerative disease.

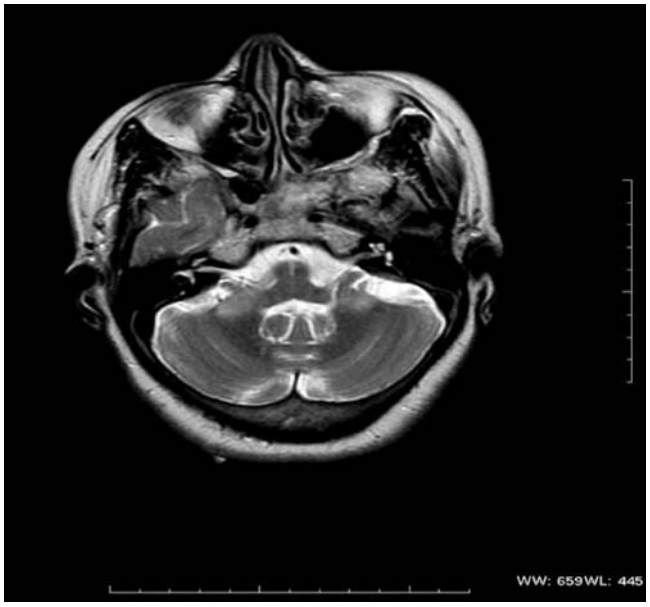

Figure-2: Symmetrical bilateral distribution of high intensity signals in the middle cerebellar peduncles which is unchanged from the previous MRI done 6 months earlier.

was 106 pg/ml (normal level > 450pg/ml).

Magnetic resonance imaging (MRI) of the brain showed abnormal signal intensity areas bilaterally in the deep white matter of the cerebellar peduncles, mid brain and the pons which were isointense on T1 weighted Image and hyperintense on T2 weighted Image. These areas did not reveal any enhancement on post contrast T1W1 or any midline shift or a mass effect. Findings were suggestive of neurodegenerative disease (Figure-1). Positron Emission Tomography (PET) scan was not conducted due to unavailability.

Cerebrospinal fluid (CSF) analysis showed glucose of 16mg/dl (Normal Range- 45-80 mg/dL), protein 41mg/dl (Normal range- 20-45 mg/dL) anda total leukocyte count was nil (Normal - 0-5/mm 3). CSF culture, gram stain and acid fast bacilli smear were negative. Mycobacterium tuberculosis, JC (John Cunningham virus) virus and cytomegalovirus polymerase chain reaction (PCR) were all negative. Serum VDRL (Venereal Disease Research Laboratory test) and TPHA (Treponema pallidum haemagglutination) were negative.

Neurology consult was obtained, patient was then placed on vitamin B12 therapy and after 6 months, a repeat level performed was in the normal range. Patient was also started on Buspirone 5mg twice daily and Fluoxetine 20mg daily. However, her symptoms gradually worsened and a repeat MRI of the brain after 6 months of therapy revealed no improvement (Figure-2).

As all of her investigations were negative with no visible change after replacement of vitamin B12, patient was diagnosed as a case of HIV associated neurocognitive disorder (HANDS). Her antiretroviral therapy (ART) was changed from Tenofovir (TDF) to Zidovudine (AZT) due to better blood brain barrier penetration.

Upon a follow up 12 months later, her CD4 count increased to 463 and her symptoms improved with better gait and a decrease in dizziness was noted. She remained stable with no further deterioration at one and a half years of follow up.

Patient consent was obtained before reporting the case.

Discussion

Symptoms of HANDS range from mild cognitive impairment to HIV associated dementia (HAD). HAD is a progressive disabling condition characterized by motor and psychiatric symptoms with death within a year. HAD is also associated with brain atrophy and leukoencephalopathy.[1]

HIV can infect central nervous system (CNS) in two ways, which includes a direct effect or an infection from opportunistic pathogens.[2] The severity of neurocognitive impairment has considerably reduced after the advent of potent combination ARTs. According to Heaton et al,[3] there is a 40-50% reduction in the incidence of HANDS; however, it still remains prevalent in milder forms.

Our patient presented with neurological symptoms after six years on continous ART. With the availability of potent ARTs, HIV has become a chronic disease. Patients are living longer with very low viral loads.

The virus tends to sequester in body compartments as the CNS, where ARTs cannot penetrate in adequate amount. Hence, a milder form of neurocognitive disorder is observed in patients on ARTs with undetectable viral loads in serum. In this era of potent ARTs, chronic HIV patients who are clinically stable and on a prolonged ART do develop neurocognitive disorders, however, a milder form is seen.[4,5]

Clinically, HANDS can present as mood swings, impaired attention, memory deficits, and motor dysfunctions including bradykinesia, gait imbalance and loss of co-ordination.[2] Diagnosis is clinical after the exclusion of opportunistic infections.

Research suggests that HIV virus gains entry in the brain via monocytes. Upon entering the perivascular space of the brain parenchyma, monocytes convert to perivascular macrophages. This is the starting point of activation of

different cells in the brain as well as the release of inflammatory cytokines. Macrophages transfer the virus over to the microglial cells in the brain. Components of the HIV virus namely, glycoprotein (gp120), transcriptional transactivator and viral protein R in the infected microglia mediate increased production of arachidonic acid, nitric oxide, platelet activation factor and tumour necrosis factor, leading to neurotoxic effects with neuronal loss and apoptosis. Astrocytes are also activated and they alter the permeability of the blood brain barrier as a result even more infected monocytes enter the perivascular space.[5]

Isolated cerebellar involvement in HIV patients may be either due to opportunistic infections like JC virus, toxoplasmosis, CNS lymphoma and tuberculoma as a result of primary HIV related degeneration. Isolated cerebellarataxia in HIV is a rare finding. Agrawal et al[6] reported a case of a 40 year old female presenting with ataxia and no infective aetiology was identified, as a result she was labelled as a case of spinocerebellar ataxia secondary to neurodegeneration.

Vitamin B12 deficiency was ruled out as the primary cause of cerebellar ataxia as this deficiency does not present as lesions in the cerebellum but rather with posterior and lateral column involvement in the cervical and thoracic spinal cord.[7] The lack of improvement in our patient's symptoms despite replacement of vitamin B12 and the very atypical MRI findings made the possibility of this brain lesion secondary to the deficiency unlikely. Saylor et al[5] mentioned vitamin deficiencies as one of the co-morbidities which may make the diagnosis challenging.

The best management of HANDS is starting ART as early as possible to combat the entry of the virus into the CNS. Some suggestions have been made regarding the use of ARTs with good CNS penetration. Our patient did show a slight improvement with no further deterioration of the symptoms.

Conclusion

After other causes have been ruled out, physicians should consider HIV associated neurocognitive disorder as a likely aetiology in the era of increased and prolonged use of antiretroviral therapy. Recovery in HANDS depends on the severity of the disease. Management involves multidisciplinary care, especially when dealing with advanced cases.

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