A Case of Cerebellar Dysarthria as the Presenting Symptom of HIV Infection

Zeba Siddiqi***, Ritu Karoli**, Jalees Fatima*, Rahul Dey#, Khursheed Kazmi#

Abstract

A 37 year old man presented with progressive dysarthria for 2 weeks. A week later he developed ataxia and bilateral cerebellar signs including intention tremors, dysmetria and dysdiadokokinesia. During evaluation for aetiology of cerebellar dysarthria, MRI brain revealed asymmetric altered signal intensities in bilateral cerebellar hemispheres and right side of pons suggesting demyelinating lesions. ELISA for Human Immune Deficiency virus-1 was positive. We kept a presumptive diagnosis of Progressive Multifocal Leukoencephalopathy (PML) on the basis of clinico-radiological picture. PML is an under investigated and under diagnosed CNS infection seen in HIV patients with advanced disease. We present an unusual case report where isolated cerebellar involvement occurred as the first AIDS defining event in the absence of appreciable immunodeficiency in a patient with previously undiagnosed HIV infection.

Introduction

HIV is a global menace with over 5 million people living with HIV/AIDS in India. AIDS virus is known to be a neurotropic virus and CNS involvement is seen as presenting complaint in 10% of cases, with a spectrum of neurological manifestations. Isolated cerebellar symptoms in HIV have been reported rarely and usually result from opportunistic infections. Mechanisms of CNS involvement can be via demyelination due to autoimmunity elicited by viral proteins, secondary to lymphomas, secondary to cell mediated immunodeficiency or other general and systemic complications of HIV. The prominent demyelinating CNS lesions reported in HIV are acute disseminated encephalomyelitis, multiple sclerosis like demyelination and progressive multifocal leukoencephalopathy. We present a 37 year old male with subacute cerebellar involvement in the form of bilateral, asymmetrical demyelination as the first AIDS defining event in the absence of appreciable immunodeficiency with previously undiagnosed HIV infection.

Case Report

A 37 year old male presented to the medical out patients department with complaints of low grade fever and body ache of 8 months duration and slurring of speech for 20 days. He did not have difficulty in walking, any motor deficits, bowel bladder involvement, loss of consciousness, facial deviation, nasal regurgitation of fluids, emotional lability or any abnormal movements. There was no history suggestive of raised intracranial tension, seizures, head injury, anorexia or weight loss. The patient denied having vaccinations or upper respiratory infections in the recent past. There was no history of alcohol, drug abuse or previous illness and his family history was unremarkable. His appetite and sleep were normal. General physical examination was normal, higher mental functions and cranial nerves were intact, motor examination was normal, plantars were flexors bilaterally and there was no sensory loss. Speech was characteristically slow, slurred and scanning. Gait was normal but patient could not perform tandem walking. Fundoscopy was done which was unremarkable. His complete blood counts, liver and kidney function tests and serum electrolytes; were within normal limits. Cerebro spinal fluid (CSF) analysis showed 10 cells, all lymphocytes with 56 mg/dl sugar, 140 mg/dl proteins and no oligoclonal bands. PCR for tubercular antigen was negative. It was VDRL nonreactive and negative for...
cryptococcal infection. On brain imaging, CT scan was normal but MRI revealed asymmetrical altered signal intensities in bilateral cerebellar hemispheres and pons on the right side. The lesions were hypointense on T1 weighted images and hyperintense on T2 (Figure 1) and FLAIR suggestive of demyelination/ischaemia. A subsequent MR angiography of cerebral circulation was done which was normal. Taking into account his acute demyelinative illness, the patient was prescribed pulse Methylprednisolone therapy but no improvement was observed. Rather, a week post admission, the patient deteriorated and developed ataxia. On examination, he had broad based gait, bilateral intention tremors, bilateral horizontal nystagmus, bilateral dysdiadochokinesia bilateral dysmetria and left plantar became extensor. He was tested by ELISA for HIV that came out to be positive for type 1 virus and was subsequently confirmed by western blot assay. His CD4 counts were 582 cells/µL and HIV viral load was 24,000 RNA copies/ml at the time of diagnosis. On the basis of patient’s clinical and radiological picture and after ruling out other possibilities, we formulated a probable diagnosis of PML. The patient was transferred to regional ART centre for further workup and initiation of HAART but despite treatment, he showed progressive worsening, and died three months later.

Discussion

HIV has assumed epidemic proportions since its discovery. The disease can be latent for several years before manifesting itself. HIV is a neurotropic virus and CNS involvement is seen in approximately 10 percent of cases of HIV. Neurological involvement in HIV can be due to opportunistic infections, drug toxicity, malignancy, cerebrovascular disease or as a consequence of direct HIV infection. Neurological diseases associated with HIV-1 are becoming more common as antiretroviral therapy improves patient survival. Demyelinating CNS disorders in HIV are rare and are due to acute multiple sclerosis like leukoencephalopathy, acute disseminated encephalomyelitis (ADEM) or PML.

Multiple sclerosis has a female preponderance, presents with sensory symptoms, optic neuritis and pyramidal signs. Presence of oligoclonal bands in CSF are diagnostic. MRI reveals typical sharply demarcated lesions mostly in periventricular region. ADEM is an immune mediated disorder of CNS that presents as multifocal neurological dysfunction, chiefly monophasic and selflimiting. It is also known as ‘Parainfectious’ or ‘Postvaccinial’ as it is known to occur following exposure to an antigen that subsequently triggers autoimmune destruction of the nervous system. ADEM typically affects white matter but may involve cortical grey matter and basal ganglia.

The other important yet underdiagnosed neurological complication of HIV is progressive multifocal leukoencephalopathy (PML). PML is a demyelinating disease of CNS that is caused by JC virus which is a member of Papovaviridae group. The virus is found in 80% of healthy population but is manifested only in immunosuppressed individuals such as patients with AIDS, leukaemia, tumours or those undergoing transplants and in patients receiving immune therapy with monoclonal antibodies. PML is an illness with insidious onset and steady progression of focal symptoms that include behavioural, speech, cognitive, motor or visual impairment. CSF analysis is usually normal with slight elevation of proteins. On MRI, PML lesions are hypointense on T-1 weighted and hyperintense on T-2 and FLAIR sequences with no mass effect. A combination of characteristic clinical picture and typical imaging findings support a “presumptive diagnosis” of PML. For a “definitive diagnosis”, along with clinical and imaging findings, there should be evidence of JC virus in CSF or typical histopathological changes with demonstration of JC virus DNA in infected cells (Table 1).

Histopathologically, the second most common site of involvement after the supratentorial white matter is the cerebellum and adjacent pons. Brain biopsy carries a sensitivity of 74-92% and a specificity of 92-100% in PML. Where other opportunistic infections occur when CD4 counts are < 200 cells/µL, PML is typically seen in patients with higher CD4 counts. Since the
onset of AIDS epidemic in 1981, the incidence of PML has increased significantly and now HIV associated cases account for up to 85% of all cases of PML. It is estimated that PML affects 4% of HIV patients but there are only a few case reports in literature.8

There are few studies associating HIV with demyelinating illnesses and among them, those with cerebellar involvement as an initial presentation are rarer. Berger et al first described 7 HIV patients with neurological diseases resembling multiple sclerosis.9 In 1992, Berger jr et al again described a case of relapsing and remitting leukoencephalopathy who had recently seroconverted for HIV and presented with limb weakness, bilateral optic neuritis, leg pain and spasm early in the course of disease. Deshpande and Patnaik from Mumbai, India reported four HIV cases associated with CNS demyelination. Three of them presented with hemiplegia while one of them presented with cerebellar involvement.10

Our patient was not a known case of HIV and presented to us with dysarthria of 20 days duration. Other signs of bilateral cerebellar involvement subsequently evolved. He was diagnosed to be HIV positive with relative sparing of immune competency. After pondering upon all possible causes of cerebellar demyelination in patients of HIV and taking into account our patient’s progressive worsening and the clinico-radiological picture, a presumptive diagnosis of PML was instituted. Due to technical difficulties we could not isolate JC virus or perform histopathological examination therefore we cannot say with authority that he was a patient of PML. Although the patient was sent to an ART centre for further management, his condition deteriorated and he died three months later.

To conclude, it is imperative for the general physicians to be aware that HIV can present as subacute cerebellar involvement as the first AIDS defining illness in a relatively immunocompetent patient.

References


<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Typical Clinical Feature</th>
<th>Typical Imaging Feature</th>
<th>CSF JCV DNA</th>
<th>Typical Histopathology with Demonstration of JCV DNA / Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite PML</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Definite PML</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Presumptive PML</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 1: Diagnostic Criteria of PML