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Case Report

Progressive Multifocal Leukoencephalopathy in a Patient on Antiretroviral Therapy- A Case Report

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Introduction

Progressive multifocal leukoencephalopathy (PML) is a disease of the central nervous system which affects the white matter and causes demyelination. JC polyomavirus (JCV) causes a lytic infection of oligodendrocytes in this condition. In 2009 a study of 400 healthy blood donors was conducted, in which 58% of the study population were found to be exposed [1]. JCV infection is highly prevalent in the human population, which leads to a chronic, asymptomatic infection, but incidence of PML in the general population is very low. Wild-type JCV infection is benign, whereas PML is associated with the presence of mutated virus that acquires genetic alterations. The emergence of PML also depends on impaired host immune function, thus the susceptibility to this disease is driven by the convergence of viral and host factors [2]. One of the major conditions which leads to disease in JC virus infection is HIV-AIDS. Other factors include haematological malignancies, Systemic lupus erythematosus and chronic immunosuppressive therapies.

Case Presentation

A 30-year-old PLHA patient on ART since 2007 presented to us with complaints of disoriented behaviour and irrelevant speech. His clinical stage at the start of ART was level III and his baseline CD4 was 257 cells/cu.mm. He was on irregular treatment with fluctuations in CD4 counts along the course of treatment.

On examination, patient was afebrile, semiconscious, disoriented, with sluggish response to stimuli. Cardiorespiratory system examination was normal. On neurological examination patient was stuporous, with a Glasgow coma scale of 10/15. Loss of memory and bladder incontinence was evident. Pupils were reacting to light. On motor system examination, paraparesis was observed. No signs suggestive of extrapyramidal or lower motor neuron derangements were present.

Lab investigations revealed normal blood counts, liver and renal function tests. His serial CD4 counts were analysed and a decline from 510 in Feb 2016 to 123 in July 2016 was noted. CSF analysis was within normal limits. MRI showed T2/ FLAIR bilateral diffuse asymmetric white matter hyper intensities in the cerebral hemispheres causing mass effect compressing on the left lateral ventricle suggestive of progressive multifocal leukoencephalopathy **(Fig 1).** Anti JC virus antibody in CSF proved positive. Patient was counselled regarding strict adherence to ART.

On discharge, patient's higher functions improved with resolution of bladder incontinence and significant improvement in the behavioural symptoms. CD4 counts at one month follow up were 313 cells/ cu.mm.

He is on regular follow up and is able to do his routine activities of daily living without assistance with occasional mood disturbances on and off.

Discussion

Kidney is considered to be the primary site of infection of JC virus and approximately 19-27% of adults shed JCV in their urine chronically. The prevalence of shedding is dependent on gender and age [7]. JCV is rarely found in blood, and though there have been reports of JCV in brain, bone marrow, tonsil and peripheral blood lymphocytes, viral tropism and lifecycle beyond kidney is still not

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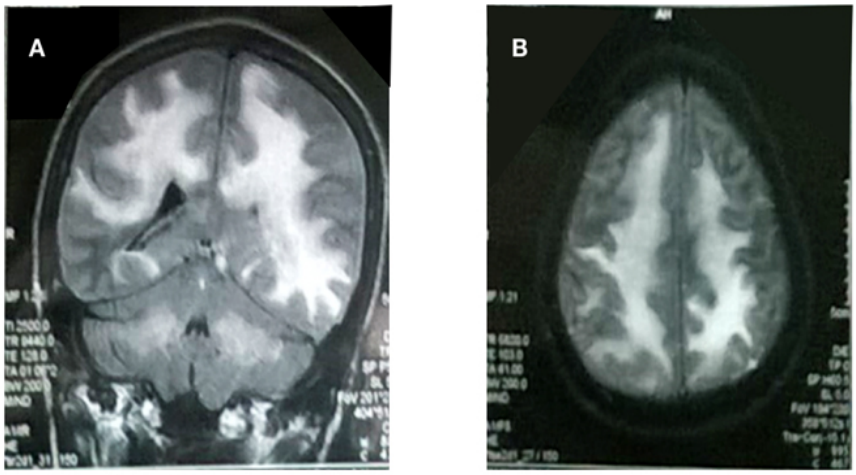

Fig 1. T2 weighted FLAIR coronal (A) axial (B) showing bilateral asymmetric FLAIR hyper intensity in periventricular and subcortical white matter in a patient with progressive multifocal leukoencephalopathy

fully understood. It is less known how JCV accesses the central nervous system (CNS) and ultimately infects oligodendrocytes in the brain. Recent data suggest that viral mutations in the VP1 capsid protein and/or the noncoding control regions (NCCRs) might result in a change in tropism or replication capacity that is permissive for pathogenic demyelinating brain infection [3,4].

The transformation of JCV from a benign peripheral infection to a rare pathogenic brain infection depends on the both host and viral factors. Apart from viral mutations, significant changes in the host immune functions are also required. HIV-AIDS is the most common context where PML is observed [5,6].

Patients diagnosed with PML present with rapidly developing focal deficit such as motor deficit, sensory deficit, visual deficit, cognitive decline. Neuroimaging is characterised by white matter lesions. However, it has to be differentiated from HIV encephalopathy. In PML, the white matter involvement in bilateral, asymmetric, well delineated. Periventricular and subcortical white matter are the most common sites involved. Basal ganglia involvement is variable. The lesions do not show contrast enhancement and lack mass effect. It is not confined to vascular territories. However, PML occurring in the setting of Immune Reconstitution Inflammatory Syndrome (IRIS) is associated with contrast enhancement. In HIV encephalopathy, the white matter involvement in symmetric, bilateral and poorly delineated. Periventricular white matter is the most common site involved. The lesions lack contrast enhancement and mass effect. However, the occurrence of focal neurological deficit favours a diagnosis of PML, Table 1. Table 2 shows the various causes of white matter lesions with or without mass effect in HIV Positive individuals [7,8].

Specifics of white matter involvement	Progressive Multifocal Leukoencephalopathy	HIV Encephalopathy
Symmetricity	Bilateral asymmetric	Bilateral symmetric
Delineation	Well delineated	Poorly delineated
White matter involvement	Periventricular and subcortical white matter with or without basal ganglia involvement	Periventricular white matter.
Contrast enhancement	No contrast enhancement	No contrast enhancement
Mass effect	No mass effect	No mass effect

Table 1. Neuroimaging differences in the white matter involvement in Progressive Multifocal Leucoencephalopathy and HIV Encephalopathy.

White matter lesion without Mass Effect	White matter lesion with mass effect
Progressive multifocal leukoencephalopathy	CNS Lymphoma
HIV Leukoencephalopathy	Toxoplasma encephalitis
Cytomegalovirus encephalitis	Tuberculoma
	Neurocysticercosis
	Cerebral Abscess
	PML with immune reconstitution*

Table 2. White matter lesions with or without mass effect in HIV positive patients.*As seen in our patient.

Conclusion

Prognosis of PML varies depending on comorbidities. Unmanaged PML leads to a mortality rate of 30-50% within the first three months of diagnosis. [9] Intervention can improve the chance of survival in some patients, though it is likely that some significant neurological deficits will be permanent. Immune reconstitution in the early stages of HAART therapy can produce white matter involvement with mass effect. Recent studies indicate that restoration of immune function can cause viral clearance and may lead to resolution of PML. We were able to conclude from our case that proper immune constitution may mask asymptomatic JC virus infection and also prevent rapid deterioration in the condition of the patient, which we observed in our patient as a rare entity.

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