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Original Research Paper

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EXTENSIVE PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN YOUNG HIV PATIENT WITH SUBNORMAL CD4+ COUNT: A CASE REPORT

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ABSTRACT Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system due to the reactivation of the JC virus, which usually occurs in immunocompromised patients and is a major opportunistic infection associated with HIV infection. We report a case of a extensive progressive leukoencephalopathy in HIV patient with subnormal CD4+ count.

KEYWORDS : Humanimmunodeficieny virus infection, Acquired immunodeficiency syndrome, PML(Progressive Multifocal Leukoencephalopathy), JC virus, Opportunistic infection, CD4+ count

INTRODUCTION:

Progressive multifocal leukoencephalopathy (PML) is a rare, serious, and usually fatal demyelinating disease caused by human polyomavirus (JCV). The incidence of this opportunistic infection has risen dramatically during the AIDS epidemic. PML is the result of reactivation of latent JC virus infection in the setting of cellular immunodeficiencies. Cases associated with HIV account for 85% of all cases. PML is the only known clinical manifestation of JC virus infection. This disease has been diagnosed in 1%–4% of HIV-infected patients in developed countries in the pre–highly active antiretroviral therapy (HAART) era. The incidence of PML has decreased less dramatically when compared to other central nervous system (CNS) diseases in the HAART era. PML has rarely been reported in HIV-infected patients from developing countries in general, and India in particular. The clinical entity of PML is to be suspected in HIV-infected patients who present with focal neurologic deficits. The lesions of PML begin as small foci of demyelination in subcortical white matter that eventually coalesce. The cerebral hemispheres, cerebellum, and brainstem may all be involved. Patients typically have a protracted course with multifocal neurologic deficits, with or without changes in mental status. Approximately 20% of patients experience seizures. Ataxia, hemiparesis, visual field defects, aphasia, and sensory defects may occur. Headache, fever, nausea, and vomiting are rarely seen. Their presence should suggest another diagnosis. MRI typically reveals multiple, non-enhancing white matter lesions that may coalesce and have a predilection for the occipital and parietal lobes. The lesions show signal hyper intensity on T2-weighted images and diminished signal on T1-weighted images.

The measurement of JC virus DNA levels in CSF has a diagnostic sensitivity of 76% and a specificity of close to 100%. Prior to the availability of ART, most patients with PML died within 3–6 months of the onset of symptoms. Paradoxical worsening of PML has been seen with initiation of ART as an immune reconstitution syndrome. There is no specific treatment for PML; however, a median survival of 2 years and survival of >15 years have been reported in patients with PML treated with ART for their HIV disease. Despite having a significant impact on survival, only ~50% of patients with HIV infection and PML show neurologic improvement with ART. Studies with other antiviral agents such as cidofovir have failed to show clear benefit. Factors influencing a favourable prognosis for PML in the setting of HIV infection include a CD4+ T-cell count >100/μL at baseline and the ability to maintain an HIV viral load of <500 copies/mL. Baseline HIV-1 viral load does not have independent predictive value of survival. PML is one of the few opportunistic infections that continues to occur with some frequency despite the widespread use of ART. To the best of our knowledge, PML as a presenting manifestation of AIDS is very rarely reported from Indian literature.

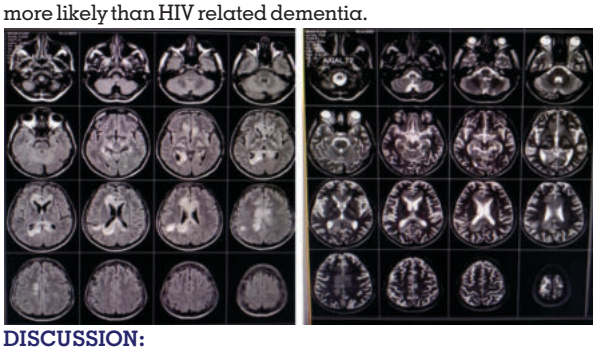
Case Report:

A 36 year old male Hindu patient came to GMERS hospital morbi on 8th July, 2023 with complaining of low grade fever, decrease appetite, increased sleep for last 1 month. Then he developed complain of unable to walk himself, bizarre behaviour, decreased cognitive function, loss of control over bladder and bowel for last 7days. No history of vomiting, headache, neck pain, involuntary movement, loss of consciousness.

Patient is a known case of HIV-AIDS since 8 year. Patient was treatment defaulter for last 2 year. No history of Tuberculosis, Diabetes mellitus, Hypertension, IHD, CV stroke,

On Admission vital, temperature- normal, pulse- 92/min, Bp-124/76mmhg, RS-nad, CVS-nad, CNS- concious & not fully oriented to time place person, RR-18/min, Spo2-98%on RA.

On Investigation, Hb-13.4, TLC-6360(N-69,L-30,E-1,M-0) platelet-2.94lac, RBS-93, S.creat-0.88, S.sodium-138, S.pottasium-4.5, ESR-90, T.billi-1.09, direct-0.84, indirect-0.25, SGPT-21, CRP- 22.65, MP card-negative, dengue-negative, CXR-NAD, Sputum for AFB-negative. HIV VIRAL LOAD-680copies/ml, CD4+T cell- 450. CSF sugar- 67, CSF protein-112, CSF TC- 2cells, CSF ADA- 9.4. MRI BRAIN- Symmetrical involvement of corpus callosum, posterior limb of internal capsule, along cortico-spinal tract in bilateral crus cerebri, bilateral fornix, mammillary bodies, posterior part of medulla, subcortical white matter of bilateral parasaggital anterior frontal lobe, parietal lobe and right peri trigonal white matter which turns slightly hypointense on T1 Wt images with restricted diffusion at splenium of corpus callosum, mamillary bodies. S/o Progressive multifocal leukoencephalopathy more likely than HIV related dementia.



DISCUSSION:

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. PML has been estimated to affect 4% of patients with HIV infection. India has over 5 million people living with HIV/AIDS at present. The expected incidence of PML in Indian HIV-infected population should be significantly large. However, PML is uncommon in India. There is sparse literature on HIV/AIDS with PML from developing countries including India. In the study from All India Institute of Medical Sciences, Delhi, 1.2% of the patients attending the ART clinic had PML. It is less common compared to developed countries, where it has been reported in up to 5% of patients. The non-AIDS population affected by PML is middle-aged and usually harbors either an underlying lymphoproliferative, myeloproliferative, granulomatous disorder or is receiving immunosuppressive therapy. The neurologic signs and symptoms of PML result from the viral destruction of the myelin-producing oligodendrocytes in the CNS. The main pathologic features are atypical astrocytes with enlarged multilobulated nuclei and intranuclear inclusion in oligodendrocytes which are JC virus particles on in situ hybridization. The clinical features are of progressive focal neurological dysfunction. Commonly aphasia/dysarthria, mono paresis, hemiparesis, ataxia, cortical blindness, or visual field defects are reported. Mental status changes such as confusion, dementia, and even coma are seen. Seizures are infrequent (<10%). There are no clinical features of raised intracranial pressure or of systemic infection

The PML cases are referred as

a. Histology-confirmed with the evidence of JCV infection in brain
b. Laboratory-confirmed with the detection of JCV-DNA in CSF
c. Possible with the presence of typical clinical and radiological picture but no demonstration of JCV infection.

One can consider three "stages" to the diagnosis of PML: Clinical suspicion, radiological identification, and etiological confirmation by CSF or tissue analysis. The first of these relies on the character and temporal evolution of focal neurological symptoms and signs as outlined above, along with the setting of disease susceptibility. The second stage in diagnosis entails detection and characterisation of brain lesions by neuroimaging, preferably magnetic resonance imaging (MRI). MRI shows characteristic white matter lesions in brain areas corresponding to the clinical deficits. Because lesions involve demyelination, they are not only hyper intense on T2-weighted and fluid attenuation inversion recovery MRI sequences but also hypointense on T1-weighted sequences, indicating white matter destruction. The later helps distinguish PML from other pathologies, primarily HIV-1 encephalopathy, with more diffuse central white matter changes that are not detected on T1 sequences. While lesions can develop in any part of the brain, including the deep grey matter, they are most common in the subcortical white matter, the white matter of the cerebellar peduncles or hemispheres and in the brain stem. In the classical, noninflammatory form, there is either no or only minimal contrast-enhancement, and no mass effect, unlike cerebral toxoplasmosis and primary CNS lymphoma.

Etiological diagnosis of PML usually relies first on the detection of JCV DNA in CSF by PCR. Among HIV-1-infected, combined ART untreated patients with neurological diseases; the diagnostic sensitivity of this technique was of 72%–92% and specificity of 92%–100%.Thus, a positive result is regarded as diagnostic in the appropriate clinical context. Because the rate of JCV DNA detection increases with progression of PML, lumbar puncture is usually repeated if the initial PCR analysis is negative, but suspicion remains high. When efforts to detect JCV DNA in the CSF fails, brain biopsy is required to achieve an etiological diagnosis of PML.

Various treatment strategies directed against JC virus have been unsuccessful, and HAART remains the only proven effective therapy. Survival has increased substantially after the introduction of HAART with the reported 1-year survival of 39%–56%.

CONCLUSION:

While CD4 counts are an excellent way to estimate the severity of immunodeficiency in AIDS, they are less reliable predictors of PML risk or outcomes than in many Other co-infectious complications. PML is more prevalent in advanced HIV with lower CD4 counts, but the disease does occur occasionally with higher CD4 counts. Clinicians should strongly consider PML in immunocompromised patients with frequent, progressive neurologic symptoms. Implementing CDC guidelines regarding HIV screening can improve early detection in clinical practice.

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