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Progressive Multifocal Leukoencephalopathy in a Patient with Advanced HIV: A Case Report

Case Report

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Abstract

Background: Progressive Multifocal Leukoencephalopathy (PML) is a demyelinating central nervous system disorder caused by JC virus reactivation in immunocompromised individuals, particularly those with advanced HIV. Although rare, its occurrence alongside pulmonary tuberculosis (TB) poses significant diagnostic and therapeutic challenges.

Case Presentation: We report the case of a 34-year-old male who presented with prolonged fever, Productive cough, significant weight loss, and progressive neurological decline. He was diagnosed with advanced HIV infection (CD4 count: 95 cells/μL) and pulmonary TB, confirmed by sputum CBNAAT. Neuroimaging revealed lesions suggestive of PML, later confirmed by cerebrospinal fluid analysis detecting JC virus DNA. The patient was initiated on anti-tubercular therapy, followed by antiretroviral therapy after stabilization. Systemic improvements included increased appetite and weight gain of 8kg; however, neurological recovery remained limited.

Conclusion: This case underscores the complexity of managing advanced HIV with concurrent opportunistic infections like PML and TB. Early diagnosis using advanced imaging and molecular diagnostics, along with multidisciplinary management strategies, is critical for optimizing outcomes. However, neurological prognosis in PML remains poor, highlighting the need for innovative therapeutic approaches targeting JC virus and enhancing myelin repair.

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Keywords: Progressive Multifocal Leukoencephalopathy; JC virus; HIV/AIDS; Opportunistic infections; Antiretroviral therapy; Immune reconstitution

Introduction

Progressive Multifocal Leukoencephalopathy (PML) is a severe, demyelinating disease of the central nervous system (CNS) caused by the reactivation of the JC virus (JCV), a polyomavirus that resides latently in the kidneys and lymphoid tissues of most individuals. In most individuals, it remains a latent infection with a prevalence of 0.22 and incidence of 0.11 per 100,000 people.[1]

it is particularly virulent in patients with immunosuppressive conditions such as AIDS, post solid organ and bone marrow transplant recipients, malignancies, and chronic inflammatory conditions.[2]JCV reactivates and causes progressive destruction of oligodendrocytes, the myelin-producing cells in the brain. The resulting demyelination manifests as subacute neurological deficits.

Its clinical presentation includes progressive focal neurological dysfunction. Aphasia/dysarthria, monoparesis, hemiparesis, ataxia, cortical blindness, and visual field defects are commonly reported. Mental status changes such as confusion, dementia, and even coma are seen [3].

PML is an opportunistic infection that occurs in approximately 3–5% of individuals with untreated HIV, especially those with a CD4

count below 200 cells/μL. Although antiretroviral therapy (ART) has significantly reduced the incidence of PML, its presence remains an ominous marker of advanced immunosuppression.[4]

This case report describes a 34-year-old male presenting with advanced HIV infection, pulmonary tuberculosis (TB), and PML. The interplay of multiple opportunistic infections and profound immunosuppression complicated the diagnostic and therapeutic approach. This case emphasizes the importance of a multidisciplinary strategy in managing HIV patients with complex clinical presentations.

Case Presentation

A 34-year-old male labourer from Faridabad, Haryana, presented to the emergency department with complaints of intermittent fever and Productive cough in the last two months duration, accompanied by progressive neurological decline over one month. The neurological symptoms included reduced verbal output, and complete dependence for ambulation. His wife provided the history, which was deemed reliable.

The patient had a significant history of chronic smoking (smoking index of 320) and daily alcohol consumption for over eight years. He reported substantial weight loss, from 56 kg to 31 kg over the past eight months, and decreased appetite. There was no prior history of tuberculosis, diabetes mellitus, hypertension, or other chronic illnesses.

On examination, the patient appeared cachexic with a BMI of 10.7 kg/m^2. He was conscious but disoriented to time, place, and person. Neurological examination revealed gaze-evoked nystagmus and reduced verbal response. Respiratory examination revealed normal vescicular breath sounds but no other significant findings. Meningeal signs were absent, and reflexes were intact.

Laboratory investigations revealed hemoglobin levels of 13.3 g/dL, a total leukocyte count of 11,000/mm^3 with a differential count showing neutrophils at 88%, lymphocytes at 7%, monocytes at 4%, and eosinophils at 1%. Platelet count was elevated at 4.6 lakhs/mm^3, with a MCV(mean corpuscular volume) of 84 fL and a HCT(Hematocrit)

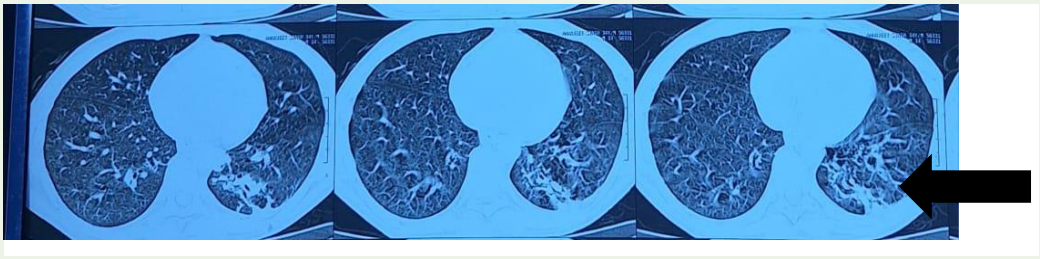

Figure 1: CECT Chest showing multiple branching trees in bud lesions in various segment of bilateral lower lobe.

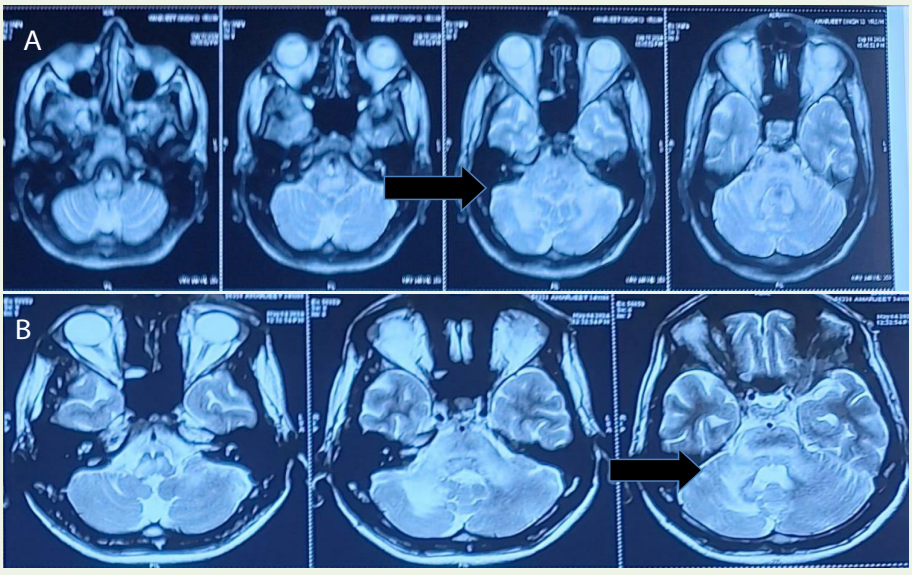

Figure 2: (A): CEMRI T1 weighted image showing Hypointense altered signal intensity lesion involving the pons. (B): T2 weighted image showing hyperintense altered signal intensity lesion involving the bilateral cerebellar peduncles and deep white matter of right cerebellar parenchyma

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of 42%. Liver function tests were within normal limits, with serum bilirubin levels (total/direct) of 0.6/0.2 mg/dL and transaminases (OT/PT) and ALP(Alkaline phosphatase) measured at 26/61 and 103 U/L, respectively. Serum electrolytes were stable with sodium and respectively, potassium levels at 136 mEq/L and 3.47 mEq/L, respectively. Calcium and phosphate levels were noted at 9.34 mg/dL and 4.32 mg/dL, and total protein/albumin levels were 6.1/3.8 g/dL. Inflammatory markers showed an ESR (Erythrocytic sedimentation rate) of 40 mm/hour and CRP(C-Reactive Protein) of 87 mg/L.

Cardiac evaluation with electrocardiography (ECG) indicated normal sinus rhythm, while chest X-ray (PA view) displayed prominent bronchovascular markings with patchy opacities in the right upper lung zone. Abdominal ultrasonography demonstrated normal findings for the liver, portal vein, spleen, and bilateral kidneys in terms of size, shape, and echotexture. A 2D echocardiogram revealed no abnormalities.

Urine analysis showed 2 pus cells per high-power field, with no proteinuria or hematuria, and cultures were sterile. Common infectious diseases were ruled out, with negative results for Typhidot, WIDAL, malaria card test, Rapid malarial antigen test(RMAT), and peripheral smear for malaria. Blood cultures also yielded no growth. Non-contrast CT (NCCT) of the head was normal, and cerebrospinal fluid (CSF) analysis revealed 10 lymphocytic cells, glucose at 62 mg/dL, protein at 97 mg/dL, and adenosine deaminase (ADA) levels of 6 U/L. Cryptococcal antigen, Gram stain, and bacterial/fungal cultures were negative. Additionally, tests for EBV, CMV, and HSV were negative.

Sputum CBNAAT confirmed the presence of *Mycobacterium tuberculosis*. Fungal (KOH) and acid-fast bacillus (AFB) stains, along with bacterial cultures, were negative. HIV-1 and 2 were reactive by ELISA, with a CD4 count of 95 cells/µL. Serologies for HBsAg, anti-HCV, VDRL, Brucella, and TORCH profile were negative. Thyroid function tests were normal, as were serum ACE levels at 12 U/L and ANA results.

CECT chest showed findings suggestive of Multiple confluent alveolar and branching tree in bud lesions involving apical and anterior segment of right upper lobe,medial segment of right middle,apical and posterior segment of bilateral lower lobe and apical segment of left upper lobe likely Tubercular etiology

CEMRI BRAIN showed findings suggestive of non-enhancing patchy and confluent assymetrical T1 Hypo and T2/Flair iso to hyperintense altered signal intensity lesion involving the pons, bilateral cerebellar peduncles and deep white matter of right cerebellar parenchyma likely demyelination? Progressive multifocal leucoencephalopathy?HIV Encephalopathy

CSF for JC VIRUS QUANTITATIVE - 20650 IU/ML

Sputum CBNAAT was positive for Mycobacterium tuberculosis, confirming pulmonary TB.

Cerebrospinal fluid (CSF) analysis revealed lymphocytic pleocytosis with elevated protein levels, and polymerase chain reaction (PCR) detected JCV DNA, confirming the diagnosis of PML.

In this patient, anti-tubercular therapy (ATT) was initiated for pulmonary TB, along with supportive care to address cachexia and immune suppression. ART was introduced two weeks after ATT commencement to reduce the risk of IRIS. Over five months, the patient experienced systemic improvement, including an 8 kg weight gain and increased appetite. However, neurological recovery was minimal, reflecting the generally poor prognosis associated with PML.

Discussion

This case highlights the challenges of managing coexisting opportunistic infections in patients with advanced HIV. Progressive Multifocal Leukoencephalopathy (PML), resulting from JC virus reactivation in the setting of profound immunosuppression, is a severe condition associated with high mortality rates. Adaptive immunity, particularly cellular responses, plays a crucial role in controlling JC virus.[5]Any impairment, whether primary or secondary, significantly increases the risk of viral reactivation. The use of monoclonal antibodies for treating malignancies and autoimmune conditions has contributed to a rise in secondary PML cases in recent decades.[5]

The coexistence of PML and pulmonary tuberculosis (TB) in this patient underscores the diagnostic difficulties faced in immunocompromised individuals. Both conditions share overlapping symptoms, such as fever, weight loss, and neurological changes, making differentiation challenging. Neuroimaging and advanced molecular techniques proved essential in distinguishing PML from other CNS infections like tubercular meningitis or fungal diseases. New-onset neurological symptoms in immunosuppressed individuals should prompt consideration of PML as a possible diagnosis.[6]Polymerase chain reaction (PCR)-based detection of JC virus DNA in cerebrospinal fluid (CSF) is crucial for confirming the diagnosis.[6]

The American Academy of Neurology (AAN) has established diagnostic criteria for PML. In cases where histopathological analysis is available, the presence of demyelination, bizarre astrocytes, and enlarged oligodendroglial nuclei, along with positive JC virus PCR, immunohistochemistry, or electron microscopy findings, confirms the diagnosis. In the absence of histopathology, a combination of clinical features, radiological findings, and positive CSF PCR for JC virus is used.[6]

The primary management strategy for PML involves immune restoration, as there are no targeted antiviral therapies for JC virus. Antiretroviral therapy (ART) is pivotal in HIV-related PML, as it enhances immune function by increasing CD4 counts and reducing HIV replication. Beyond immune reconstitution, treatment options remain limited. Withdrawal of immunosuppressive therapies, where applicable, and initiation of ART in HIV-positive individuals offer the most substantial survival benefit.[7]

However, in cases with concurrent TB, careful timing of ART initiation is required to mitigate the risk of Immune Reconstitution Inflammatory Syndrome (IRIS), which can exacerbate neurological symptoms.

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This case emphasizes the need for a multidisciplinary approach involving infectious disease specialists, neurologists, radiologists, and critical care teams to address the complexities of managing HIV patients with overlapping opportunistic infections. Despite immune restoration through ART, the prognosis for PML remains poor, with survivors often facing significant neurological impairment. Studies have investigated the effectiveness of 5-hydroxytryptamine antagonists such as mirtazapine and risperidone, nucleoside analogs like cidofovir and cytosine arabinoside, as well as biological treatments including interferon alpha. However, these approaches have not demonstrated conclusive efficacy[8-11]. In recent times, positive results have been observed in patients undergoing treatment with immune checkpoint inhibitors.[12-14]and infusion of virus-specific T cells.[15]

Research efforts are needed to develop novel therapies targeting JC virus and promoting myelin repair.

Conclusion

This case highlights the intricate interplay between advanced HIV, pulmonary TB, and PML in a profoundly immunosuppressed individual. The early recognition of opportunistic infections, timely initiation of ATT and ART, and careful management of IRIS were pivotal in improving the patient's systemic condition with significant improvement in weight gain of 9kg and of increased appetite

While the neurological recovery in this patient was limited, the case underscores the importance of a comprehensive approach to diagnosing and managing complex HIV-associated illnesses. The findings emphasize the role of advanced diagnostics, such as neuroimaging and molecular PCR, in identifying PML and guiding treatment decisions.

This report adds to the growing body of literature on HIV-associated PML and calls for increased awareness, early detection, and resource allocation for managing these challenging cases. Future research into targeted antiviral therapies and adjunctive treatments for PML is essential to improve survival and quality of life for affected patients.

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