

21. Title: When PCR Fails, The 'Open-Ring' Sign as a Diagnostic Anchor in Probable HIV-Associated PML: A Case Report

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Background: Progressive multifocal leukoencephalopathy (PML) is a potentially fatal demyelinating central nervous system (CNS) disorder caused by the reactivation of the John Cunningham Virus (JCV) in immunodeficient individuals, particularly those with advanced AIDS. A definitive diagnosis requires either histopathological evidence from a brain biopsy or compatible clinico-radiological features combined with positive CSF JCV PCR. The clinical reality, however, is quite often more complicated. Baseline lymphocyte counts may remain normal in those with advanced AIDS, misleading the diagnostic process. Additionally, CSF JCV PCR has a sensitivity of only 74% without ultrafiltration, meaning false negatives can occur. In such cases, the presence of compatible clinico-radiological features alone without a positive PCR defines "possible PML". This case report explores how clinicians must resort to advanced neuroimaging to serve as diagnostic "anchors" in order to initiate life-saving therapy on time, especially when molecular testing fails.

The Case: A 29-year-old female was referred to Civil Hospital Ahmedabad (CHA) with a 15-day history of low-grade fever, generalized pulsatile headache, and static weakness in left-sided upper and lower extremities. There were no other associated complaints or significant past or family history. Neurological examination revealed right-sided ptosis and diplopia without ophthalmoplegia and right-sided facial deviation. Initial investigations by a private physician had suggested Tuberculous Meningitis (TBM) due to early MRI findings and blood reports that only showed severe Iron Deficiency Anemia (IDA) without lymphopenia, which initially misled the diagnosis. Thus, at CHA, CSF studies were performed, but they were negative for ZN stain and CBNAAT and TBM was ruled out. Meanwhile, routine HIV screening revealed a reactive HIV-1 status, and repeat hemograms discovered newfound lymphopenia (12%) with a CD4+ T cell count of 159/cumm (6%), confirming WHO Clinical Stage IV. Consequently, CSF JCV PCR and other opportunistic infection screens were done, but they all came back negative. Despite this, a follow-up MRI with spectroscopy was performed. It turned out to be pivotal as extensive white matter hyperintensities in the periventricular, subcortical, and juxtacortical regions were found in the T2-FLAIR images. Post-contrast T1W images also demonstrated a characteristic "peripheral open-ring enhancement" without leptomeningeal involvement, while DWI showed restricted diffusion at the active leading edge. MRS provided biochemical confirmation of active demyelination through a marked Choline/NAA inversion. Based on this strong clinico-radiological correlation, a diagnosis of probable PML was made. Following multidisciplinary counselling, a Tenofovir, Lamivudine, Dolutegravir regimen (TLD) and prophylactic Trimethoprim-Sulfamethoxazole (TMP-SMX) therapy were initiated.

Conclusion: This case highlights two major diagnostic pitfalls. First, initial lymphocyte counts may be misleading, as patients can present with advanced disease despite normal baseline counts. Second, it also demonstrates that molecular testing may yield false negatives and leave a diagnostic vacuum. In such cases, clinicians must rely on pathognomonic radiological signs—specifically, open-ring enhancement and DWI leading edge—alongside MRS markers to initiate immediate antiretroviral therapy. Radiological recognition in the context of HIV remains a highly critical clue for diagnosis, emphasizing the importance of routine HIV screening in high-risk patients with neurological symptoms.

Key Words: Leukoencephalopathy, Progressive Multifocal; HIV Infections; Polymerase Chain Reaction; False Negative; Neuroimaging.

Figure:

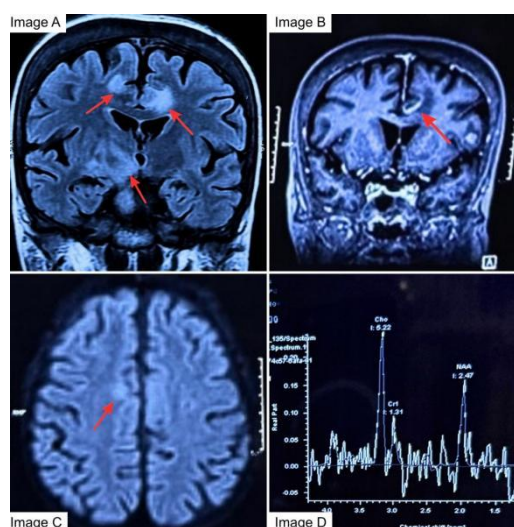


Figure 1: Multimodal Neuroimaging of Probable PML. (A) Coronal FLAIR showing extensive distribution in the subcortical white matter and pons. (B) Axial T1-weighted post-contrast image reveals characteristic peripheral open-ring enhancement. (C) DWI demonstrating the active leading edge of the demyelinating plaque. (D) MR Spectroscopy showing metabolic shifts (Cho/NAA inversion) consistent with active demyelination and neuronal loss

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