# Psychosis in Progressive Multifocal Leukoencephalopathy: Management and Social Underpinnings

Laila Hussain, DO[1], Sree Jadapalle, MD[2], Joe Shortall, DO[3]
[1,3]Campbell University Cape Fear Valley Medical Center Psychiatry Residency Program, Fayetteville, NC
[2]Dept of Psychiatry, Cape Fear Valley Medical Center, Fayetteville, NC
[1]LHussain2@capefearvalley.com, [2]SJadapalle@capefearvalley.com, [3]JShortall2@capefearvalley.com

## Abstract

We present a case of a bisexual black male with HIV and multiple hospitalizations at various facilities over the span of a year who presented with a constellation of neurologic and psychotic symptoms. Previous medical workups had focused on HIV-related illness, and psychiatry consultants had diagnosed him with schizophrenia and vascular dementia. During admission at our hospital, the patient was eventually diagnosed with progressive multifocal leukoencephalopathy (PML) and PML-induced psychosis successfully treated with Haloperidol and Paliperidone.

A literature review was conducted through multiple databases including Pubmed, JAMA, and Cochrane, with further exploration of articles that emphasized pathophysiology and social factors impacting the management and outcomes of HIV/PML, and current literature on the role of white matter dysfunction in schizophrenia.

Through this case report, we discuss the role of stigma on treatment adherence and outcomes in minority and underserved populations. We also aim to offer insights into the current understanding of white matter pathology in the role of psychosis and implications for continued research that can guide the development of novel therapies.

## Introduction

Progressive Multifocal Leukoencephalopathy (PML) is a rare disease of the central nervous system involving the infiltration of oligodendrocytes by John Cunningham (JC) virus, and an AIDS-defining illness. Symptoms develop over weeks, and while the classic neurologic symptoms such as motor deficits, altered mentation, ataxia, and visual disturbances are well documented, there are few reports on psychiatric symptoms in PML[6]. We discuss a case of PML-associated psychosis successfully treated with antipsychotics.

While there has been a decrease in the incidence of PML in patient's with HIV and improvement of 1-year survival rates from 10% to >50%, studies indicate that individuals of minority racial and sexual backgrounds are at greater risk for contracting HIV and are less likely to access both medical and mental health care due to stigma[2,4]. Current literature also supports the role of white matter pathology, demyelination, and oligodendrocyte dysfunction in both PML and psychosis.

## Case Description

A 38-year-old black male with a history of poorly-controlled HIV presented to the ED on involuntary commitment petitioned by local police after being found wandering through traffic. The patient was disoriented and tangential and reported noncompliance with home medications for the past week. He was medically admitted with psychiatry consultation due to bizarre behaviors and psychosis.

The patient's parents denied any known psychiatric history apart from behavioral issues as a child or family psychiatric history. They recalled that he was diagnosed with HIV around 2014 but was poorly compliant with medications, and were unaware of how he contracted the virus. They noticed an acute change in his behaviors and personality about a year prior, deteriorating memory, and gait instability, requiring multiple hospital visits over the past months.

Chart review revealed no psychiatric history until a diagnosis of paranoid schizophrenia two months prior at another local hospital after presenting with similar symptoms. He was initially admitted to the inpatient psychiatric unit but was transferred to the medical floor for further medical workup due to neurological symptoms. MRI brain at that time showed evidence of HIV encephalopathy, and he was started on appropriate prophylactic and HAART treatments. He continued to be diagnosed with schizophrenia treated with Haloperidol and Paliperidone (Invega). Although the patient had reportedly been diagnosed with HIV in 2014, previous ED visit records did not include a diagnosis of HIV until 2020.

**Labs**

| | | | | |
|---|---|---|---|---|
| 5.3 | 12.1 / 36.3 | 301 | | |
| 140 | 108 | 13 | 104 | CD4: 251 |
| 3.9 | 27 | 1.40 | | HIV-1 PCR: 1240 |
| | | | | TSH: 45.6 |
| | | | | UDS: Negative |

*Table 1: Patient's HIV studies and initial labs, including CBC remarkable for normocytic anemia, CMP remarkable for AKI, and elevated TSH (which remained elevated upon discharge despite treatment).*

During our evaluation, he endorsed visual hallucinations of deceased relatives, intermittent auditory hallucinations, and paranoid delusions of being harmed by others. He was initially continued on Invega monotherapy for psychosis but returned to dual therapy with Haldol due to persistent psychosis and agitation. He eventually transitioned from oral Invega to Invega Sustenna. Further medical workup of a repeat MRI head showed evidence indicative of PML. By discharge, he continued to exhibit cognitive deficits but his psychosis had resolved.

The patient was seen by outpatient psychiatry 2 weeks after discharge. He continued to display cognitive and gait impairments, but his mother reported no psychotic symptoms. He was continued on Haldol 7.5 mg PO BID and Invega Sustenna 134 mg IM monthly but was lost to follow-up. He continued to visit outpatient neurology and completed a repeat MRI ~9 months post-hospitalization, with findings consistent with HIV leukoencephalopathy and subsequent HIV dementia.

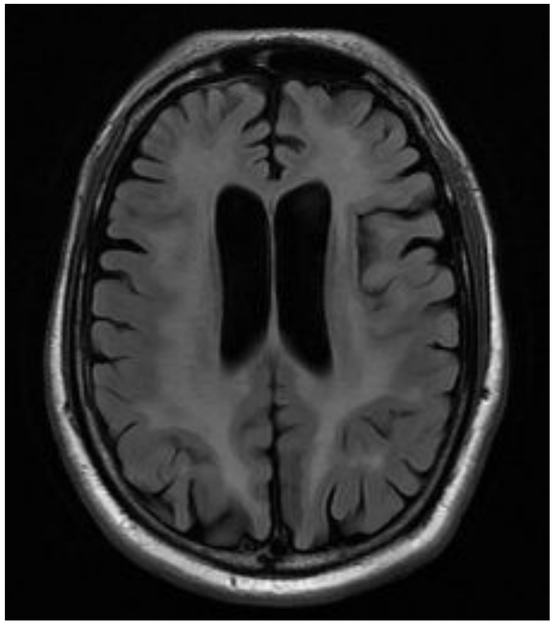

*Image 1: Patient's MRI brain with and without contrast showing periventricular hyperintensities consistent with PML. [1]*

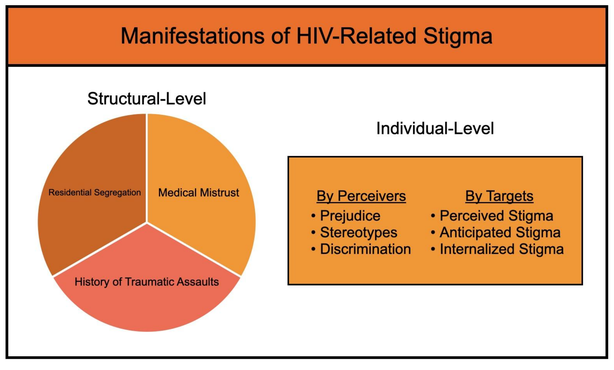


*Figure 1: The Stigma and HIV Disparities Model which identifies societal stigmas that contribute to racial/ethnic health disparities. [2]*
**Targets are those who possess the devalued characteristics. Perceived stigma involves the assessment of experiencing stigma by perceivers in the past, and anticipated stigma involves the expectation of experiencing such stigma in the future. Internalized stigma is the act of devaluing one's self or group based on one's stigma.*

## Discussion

Our patient presented with classic neurologic symptoms associated with PML and profound psychotic symptoms. This case is the only reported case to our knowledge, of PML-induced psychosis treated successfully with Haloperidol and Paliperidone. Post-mortem and neuroimaging studies of patients with schizophrenia have shown evidence of decreased volume and structural abnormalities in prefrontal cortex (PFC) white matter and a decrease in the number of oligodendrocytes in cortical areas suggestive of a role of white matter dysfunction in the pathogenesis of psychosis[5]. Studies have also shown antipsychotics to affect myelin proliferation and differentiation, but results among various studies have been mixed. Further research and understanding of these findings may help guide the development of novel treatments and therapeutic targets for psychosis[3].

Research has shown that stigma has been cited as the most prominent barrier to engagement in HIV care[2]. Stigma towards those experiencing psychosis may have also contributed to our patient receiving misdiagnoses. These combined factors contributed to the delay in diagnosis of PML and may explain our patient's lack of engagement with outpatient care and medication compliance.

## Conclusions

- PML has the potential to be misdiagnosed as a primary psychotic disorder as it can present with psychosis due to the demyelinating process affecting oligodendrocytes
- Studies have implicated white matter and myelin alteration on the development of schizophrenia, and continued research may drive the development of novel treatments and therapeutic targets for psychosis
- Stigma is the primary barrier to accessing treatment for HIV, PML, and psychosis.

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