



## Case Report

# AKINETIC MUTISM AS A NEUROPSYCHIATRIC SYMPTOM OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY : A COMPLICATIONS OF HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

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## ABSTRACT

*Progressive Multifocal Leukoencephalopathy (PML) is a rare complication of Human Immunodeficiency Virus (HIV) infection. The disease carries a poor prognosis, with rapid progression and death usually occurring within 6 months. Mental disorders are a fairly common symptom in patients with PML (1/3 of cases). A 39-year-old male came with akinetic mutism. He has difficulty communicating, is unwilling to speak, has lost voluntary movements, and lacks motivation and initiative to perform daily activities. Managing this case is quite challenging, requiring careful history taking, physical examination, and selecting appropriate supporting tests. The management of this case involves a neurologist, internist, psychiatrist, and nutritionist. Correct diagnosis and treatment lead to clinical improvement. On the 15th day of treatment, the patient began to speak briefly with his family. Furthermore, his sleep has improved. Recognising this rare case earlier can be a clinical experience if at some point a similar case is found.*

**Keywords:** Akinetic mutism, HIV, PML, Rare case

## INTRODUCTION

Akinetic mutism (AM) is the loss of voluntary movement (akinesia) and the absence of speech (mutism), although the eyes are open and eye movements in response to stimuli are still present. The patient appears fully conscious but exhibits no affective reactions, no desire to eat or drink, and little or no speech.<sup>1</sup> AM in this case is part of HIV (Human Immunodeficiency Virus)-associated neurocognitive disorder (HAND), also known as HIV encephalopathy.<sup>2</sup> HAND occurs due to diffuse brain damage. HAND, a complication of HIV, can be associated with Progressive Multifocal Leukoencephalopathy (PML). The prevalence of PML is very low, but the disease still carries a poor prognosis, with rapid progression and death usually occurring within 6 months.<sup>3</sup> There is no data in Indonesia regarding akinetic mutism associated with PML.

The 39-year-old male patient was diagnosed with PML, a complication of HIV infection. Patients tend to be quiet and have no motivation to communicate or carry out simple activities. Examination and treatment of HIV patients with various neuropsychiatric complications is challenging, requiring a multidisciplinary approach. In this case, it was difficult to obtain the patient's medical history due to communication difficulties, and the patient had not lived with his family for a long time. The selection of tests and treatments must be carefully tailored to the patient's condition.<sup>4</sup>

The purpose of this case report is to identify this rare case and provide clinical experience for similar cases. In addition to intensive medical treatment, family support significantly contributed to the patient's recovery.

## **PATIENT AND OBSERVATION**

### **Patient Information**

Mr. F, 39, was consulted in Neurology on February 2, 2022, complaining of a tendency to be quiet. This tendency to be quiet had been present for approximately two months, worsening three days before admission. Initially, the patient spoke only one or two words, sometimes incoherently. He also often did not recognize family members. He was sometimes seen daydreaming and smiling to himself. He was constantly fiddling with the buttons on his shirt and pants. He refused to talk and did not answer or respond to questions. His sleep was disturbed. He ate well when fed. He was willing to eat and opened his mouth when fed. He could finish one portion of food at each meal. There was no history of head trauma. There was a fever, not too high, that came and went. The headache had been present for two months, accompanied by nausea and vomiting. There were no seizures.

History of being admitted to PON Hospital in mid-December 2021 with a diagnosis of Acute Cognitive Impairment due to suspected Meningoencephalitis, suspected pulmonary TB, and HIV on ARVs. The patient was then taken home by his family to Makassar and admitted to Wahidin Sudirohusodo Hospital. After discharge, the patient's condition improved slightly but worsened approximately 5 days later (weakness, vomiting, headache, and frequent forgetfulness), leading to his being readmitted to Wahidin Sudirohusodo Hospital.

His family history of HIV was known to him two months ago, and he is taking ARVs. His history of pulmonary TB began four months ago, and he has not continued OAT treatment to date. His history of Hepatitis B dates back to 2017. There is no history of diabetes mellitus or hypertension. His family is unaware of any drug use. His family is unaware of any history of promiscuity.

### **Clinical Findings**

Physical examination revealed a 39-year-old man in a recumbent position, wearing a black collared shirt with white stripes, his lower body covered by a brown blanket. His face appeared appropriate for his age, his build was medium, he appeared still, tilted to the right, and his eyes were closed, and he was taking adequate self-care (with assistance). He appeared to be fiddling with his shirt buttons.

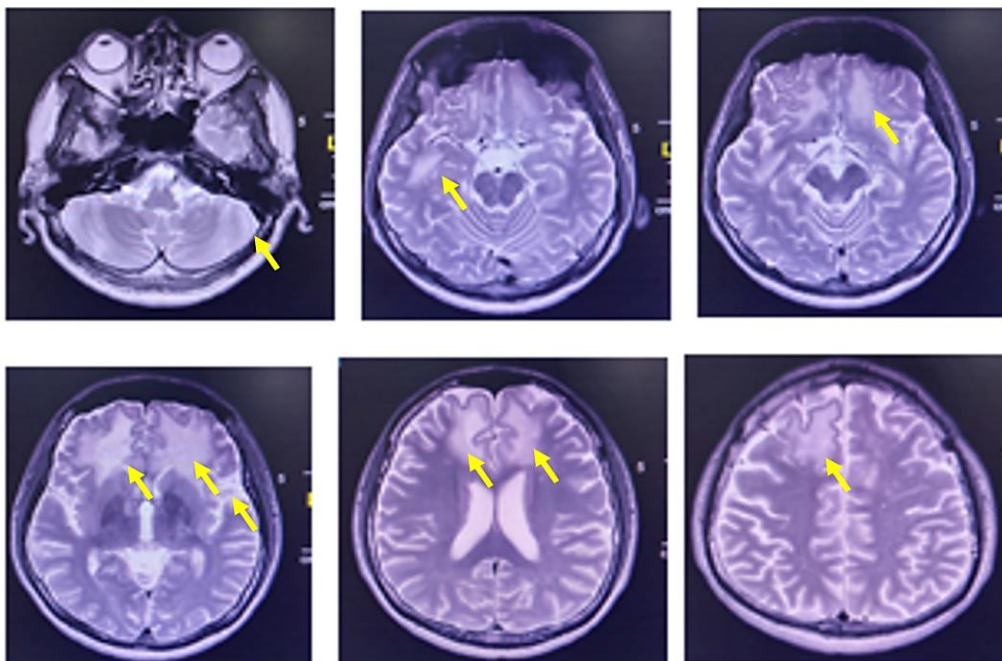
Blood pressure was 130/90 mmHg, pulse rate 88 beats per minute, regular, with adequate lifting power, respiratory rate 18 breaths per minute, and a temperature of 36.5°C. GCS 4/5/6 with impaired higher cortical function. Internal and neurological examinations were within normal limits. Psychiatric examination revealed impaired/foggy consciousness, hypoactive psychomotor skills, and absent eye and verbal contact. Mood was difficult to evaluate, affect was limited, harmony was inappropriate, and empathy was intangible. Orientation, memory, attention span, and abstract

thinking were difficult to evaluate. Hallucinations, illusions, depersonalization, and derealization were difficult to evaluate. Thought flow and thought content are difficult to evaluate. Laboratory examinations revealed the following:

**Tabel 1. Laboratory Finding**

Parameters	Result	Reference Range
WBC	5,2	4,00-10,00 [ $10^3/\text{mm}^3$ ]
RBC	4,05	4,20-5,40 [ $10^6/\text{mm}^3$ ]
HGB	12,6	11,0-16,5 g/dL
HCT	39	37,0-47,0%
PLT	174	224 [ $10^3/\text{mm}^3$ ]
Random blood glucose	117	<200 mg/dL
SGOT	20	<40 U/L
SGPT	24	<41 U/L
ureum	0.86	0,67-1,50 mg/dl
Creatinin	25	16,6-48,5 mg/dl
Potassium	4.5	3,5-5.,0 mmol/l
Sodium	137	135-145 mmol/l
CD4 count	14	500-1.200 sel/ $\text{mm}^3$
HbSAg	Reactive	Nonreactive
Anti-HCV	Nonreactive	Nonreactive
Anti-TOXO IgG	Nonreactive	Nonreactive
Anti-TOXO IgM	Nonreactive	Nonreactive
Anti-CMV IgG	Reactive	Nonreactive
Anti-CMV IgM	Nonreactive	Nonreactive
Anti-Rubella IgG	Nonreactive	Nonreactive
Anti-Rubella IgM	Nonreactive	Nonreactive

A contrast-enhanced MRI of the head revealed multifocal hypointense lesions on T1W1, hyperintense on T2W1 and FLAIR, and partially restricted lesions on DWI/ADC in the white matter of the bilateral frontotemporal lobes, the right parietooccipital and periventricular lobes, and the left cerebellum consistent with progressive multifocal leukoencephalopathy (PML).



**Figure 1. MRI Brain with Contrast**

### **Diagnostic assessment**

The diagnosis in this patient was HIV stage IV with complications of PML, CMV infection, and Hepatitis B infection. The patient's symptoms of akinetic mutism gave rise to a diagnosis of HIV-associated neurocognitive disorder (HAND). The patient's axis I psychiatric diagnosis was other specified mental disorders due to known physiological condition (F.06.8) with axis II and IV not yet evaluable, axis V GAF Scale 50 – 41.

### **Therapeutic interventions**

The neurologist gave the patient citicholine, mecobalamine, and ranitidine. The internist gave the patient an IV of 0.9% sodium chloride 1500cc/24 hours, one FDC ARV tablet every 8 hours, cotrimoxazole 960 mg/24 hours, clindamycin 300 mg/8 hours, and ganciclovirum 500 mg/12 hours. The psychiatrist gave the patient risperidone 2 mg/12 hours and lorazepam 0.5 mg/12 hours.

### **Follow-up and outcome of interventions**

On the second day of treatment, the patient frequently rocked the bed and bit his lip until it bled. He had difficulty sleeping. Therefore, the lorazepam dose was increased by 1 mg/12 hours and fluoxetine was added at 10 mg/12 hours. On the fourth day of treatment, the patient was calmer but slept more, so the doses of risperidone and lorazepam were reduced to 1 mg/12 hours and 0.5 mg/12 hours, respectively. On the seventh day of treatment, the patient was calmer and slept longer, so the risperidone dose was reduced again to 1 mg/12 hours. However, his sodium level dropped to 126 mmol/L, so he was given 500 cc of 3% sodium chloride every 24 hours. On the tenth day of treatment, the patient was able to speak, although not clearly. On the thirteenth day, the patient began to speak a little to his family, so on the fifteenth day, the patient was discharged.

### **Informed Consent**

The family was told that the case would be brought to light and made public. The family agreed.

### **DISCUSSION**

Patients with HIV infection can develop various complications. One complication that can occur in the brain and spinal cord is PML. PML is a demyelinating disease of the brain caused by oligodendrocyte lysis by the JC virus that occurs in immunosuppressed patients due to either HIV infection or other causes.<sup>4</sup> The cause of PML is the John Cunningham virus (JCV), which is commonly spread in the community, but the basic pattern of JCV is not pathogenic. Seroepidemiological data show that the majority of the human population (75-80%) is infected with JCV and approximately half are infected during childhood. This virus can reside in renal epithelial cells and is often found in urine but does not cause symptoms of the disease.<sup>5</sup> Approximately 5% of patients with HIV develop PML.<sup>6</sup> Complications that arise are usually associated with low CD4 lymphocyte counts ( $<200$  per  $\text{mm}^3$ ).<sup>7</sup>

The exact mechanism by which HIV affects PML remains unknown. However, HIV infection appears to directly or indirectly impact JCV activation. Experimental evidence suggests a direct link between HIV infection and increased PML incidence in AIDS patients through cross-regulation of the JCV promoter by the HIV-encoded transregulatory protein, Tat. Tat is a potent transcriptional transactivator of the HIV long terminal repeat and also plays a critical role in HIV replication. Tat has the ability to regulate JCV transcription from the viral promoter through the

Tat-responsive cis-element present in the JCV regulon. Tat can also be secreted from HIV-infected cells and taken up by adjacent uninfected and/or infected cells, modulating the expression of Tat-responsive promoters, including JCV. Furthermore, Tat may also indirectly modulate JCV regulation, possibly through Tat-induced upregulation of cytokines and several other regulatory proteins.<sup>6</sup>

The clinical symptoms of PML that appear in patients depend on which area of the brain is infected. Visual disturbances are the most common symptom (35-45%). One-third of cases present with mental deficits, including emotional lability and memory problems, similar to dementia. Motor impairments occur in 25-33% of cases. The disease progresses slowly, leading to death within 4-6 months, although clinical signs and symptoms are usually stable for a considerable period.<sup>4</sup>

The patient in this case is a 39-year-old man who complained of a tendency to be quiet for the past two months, which worsened in the past three days. The patient experienced akinetic mutism (AM), which is the loss of voluntary movement (akinesia) and inability to speak (mutism), although the eyes are open and eye movements in response to stimuli are still present. The patient appears fully conscious, but has no affective reactions, no desire to eat or drink, and little or no speech. AM in this case is part of HIV-associated neurocognitive disorder (HAND), also known as HIV encephalopathy. The triad of symptoms in HAND includes subcortical dementia symptoms, namely impaired memory and psychomotor speed, depressive symptoms, and movement disorders.<sup>2</sup> HIV-associated dementia (HAD) is HAD with neurocognitive impairment 2 SD below the mean in  $\geq 2$  cognitive domains with marked impairments in activities of daily living/functioning. In this case, the symptom of akinetic mutism can be classified as HAD because it meets the criteria mentioned above. The prognosis for HAD is usually poor. Fifty to seventy-five percent die within 6 months.<sup>8</sup>

Axis I diagnosis for this patient was F06.8 (Other specified mental disorder due to known physiological condition) is made due to the presence of brain disease, damage, or dysfunction, or systemic physical illness in the form of PML and HIV that is known to be associated with one of the mental syndromes in the form of akinetic mutism that may be related in time. The second criterion is the recovery from the mental disorder after improvement or removal of the underlying cause. However, in this patient, the underlying disease is PML which cannot be cured. The final criterion is that there is currently no evidence that points to an alternative cause of another mental syndrome.<sup>9</sup>

The test to detect PML is the histopathological triad with detection of JCV protein and/or JCV DNA. This test is quite difficult to perform. Therefore, JCV DNA testing from cerebrospinal fluid and imaging studies can be performed. This patient underwent a head MRI to confirm the diagnosis of PML. An MRI examination revealed extensive lesions in the brain parenchyma, particularly in the bilateral frontal lobes. This is consistent with the symptoms of akinetic mutism, which is typically associated with lesions in the cortical-subcortical pathway, particularly the frontal lobes.<sup>1</sup>

Currently, there is no specific therapy for the cause of PML. Treatment focuses on the presenting symptoms. HIV often coexists with other illnesses, so doctors usually focus on treating HIV itself and other infections.<sup>10</sup> Management of this patient is quite challenging. HIV itself is difficult to treat. Their relatively silent behavior presents challenges in assessment and treatment. Hyponatremia, hepatitis B infection, and cytomegalovirus infection also pose challenges. The patient received multidisciplinary care, resulting in significant clinical improvement during her 15-day hospital stay. Family support significantly aids the patient's recovery. Fifteen days into hospitalization, the patient began to show a willingness to communicate with her family.

Several case reports have examined the symptoms of PML in HIV-positive patients. The case described by Tandi et al. (2025)<sup>11</sup> involved a patient with seizures, blurred vision, occasional diplopia in the right eye, fatigue, and right upper limb weakness with a tingling sensation and confusion. The seizures improved with antiepileptic medication. Brrang RK et al. (2024)<sup>12</sup> presented a case report of PML in HIV-positive patients with similar symptoms. The patient experienced a relapse 2 months after discharge. Li L et al. (2023)<sup>13</sup> described PML with progressively worsening symptoms. The patient then died 2 weeks following his discharge. Li et al. (2025)<sup>14</sup> described a case of PML with dizziness and headache. Intravenous immunoglobulin (IVIG) treatment is an effective treatment option for individuals presenting with early PML-IRIS. However, its efficacy, optimal duration, and dosing regimen in advanced cases require validation through larger-scale controlled studies. Clinicians are advised to make individualized treatment decisions by carefully weighing the benefits against the potential risks associated with IVIG therapy while closely monitoring for any adverse reactions.

Post-outpatient follow-up requires even more challenging management. Families must be provided with clear and effective education to support their recovery. Patients are encouraged to attend regular check-ups to monitor CD4 counts, HIV viral load, and ARV continuation. When contacted by phone several days later, the family reported that the patient was beginning to communicate well with their family.

The prevention of PML is crucial due to poor prognosis. It is found that even if these patients continue antiretroviral therapy after a period of non-compliance, the damage caused by the JC virus is often extensive and irreversible. In the hope of the near future, many useful and definite therapies will surface to help those HIV living with PML patient especially with these antiviral agent, immunomodulator and passive immunization.<sup>15</sup>

## **CONCLUSION AND SUGGESTION**

A 39-year-old man was diagnosed with akinetic mutism, a condition associated with HAND. The patient was treated in hospital with the collaboration of several physicians. Knowledge of infections that can occur in HIV patients will help establish a diagnosis and provide appropriate treatment tailored to the patient's needs. Managing HIV-associated PML requires a comprehensive approach involving early recognition, timely diagnosis, and prompt initiation of ART and supportive therapies.

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## **CONFLICT OF INTEREST**

There is no conflict of interest.

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