Radiology Case Reports 17 (2022) 3005–3008

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

# HIV-associated dementia presenting predominantly with clinical motor deficits: A case report☆,☆☆

*Laura McLean, BA*[a,*], *Stephen Aradi, MD*[b], *Roy Waknin, MD*[c], *Brittany Rea, MD*[c], *Marc A. Camacho, MD, MS, FACR*[c]

[a] *University of South Florida, Morsani College of Medicine, Tampa, FL 33612, USA*
[b] *Department of Neurology, University of South Florida, Morsani College of Medicine, Tampa, FL, 33612, USA*
[c] *Department of Radiology, University of South Florida, Morsani College of Medicine, Tampa, FL 33612, USA*

ARTICLE INFO

*Article history:*
Received 24 May 2022
Accepted 26 May 2022

*Keywords:*
HIV
Neuroradiology
HIV-associated dementia
Emergency Radiology

ABSTRACT

HIV-associated dementia is commonly seen in older individuals and presents as a subcortical dementia associated with concentration, attention, and memory impairments. Motor signs, such as difficulty with gait, and mood changes are less prominent findings but are considered during diagnosis. We present a case of HIV-associated dementia in a young 29-year-old man who presented with progressive lower extremity weakness and difficulty ambulating.



## Introduction

Human immunodeficiency virus (HIV)-associated dementia is defined as a marked interference with day-to-day functioning and impaired cognitive testing. The neurocognitive dysfunction is directly caused by HIV, rather than an opportunistic infection, and the risk increases over time [1].

## Case Report

We present a case of a 29-year-old man with a history of bipolar disorder and SARS-CoV2 positive in August of 2021 whose father urged him to come to the emergency department for progressive lower extremity weakness and difficulty ambulating for two months. During the two weeks prior to presen-

*Abbreviations:* HAD, HIV-associated dementia; HANDs, HIV-associated neurocognitive disorders.

☆ Competing Interests: There is no conflict of interest to declare.

☆☆ Funding: None.

* Corresponding author.
E-mail address: Lauramclean@usf.edu (L. McLean).

https://doi.org/10.1016/j.radcr.2022.05.076

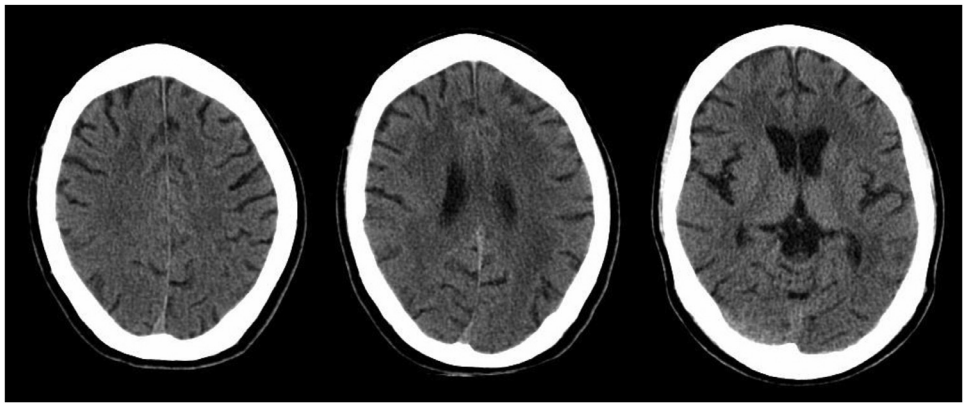

**Fig. 1 – Noncontrast computed tomography (CT) of the head reveals confluent areas of hypoattenuation in the periventricular white matter and centrum semiovale. Mild generalized cerebral atrophy advanced for age is present.**

tation, his ability to ambulate declined precipitously and he was unable to walk at presentation. He also reported mild urinary urge and hesitancy. The patient denied changes in attention, concentration, or sleep. Risk factors include unprotected sex starting at age 19. Mental status examination was notable for a flat affect with preserved language, attention and concentration, and delayed recall. There was bilateral lower extremity weakness predominantly of hip flexion, knee flexion, and ankle dorsiflexion. Deep tendon reflexes were normal with the exception of 3-4 beats of clonus at the ankles. Tone was spastic in the legs, and plantar responses were extensor. Vibration, proprioception, and temperature sensation were normal.

Patient was found to be HIV positive with high viral load and CD4 count of 86 cells/mm$^3$. Additionally, he was found to be positive for EBV, HSV1, treponemal antibody, and RPR. Since the patient denied having ever been diagnosed or treated for syphilis in the past, the result suggested a new, untreated infection.

Noncontrast computed tomography (CT) of the head was obtained in the emergency department which revealed confluent areas of hypoattenuation in the periventricular white matter and centrum semiovale (Fig. 1).

Magnetic resonance imaging (MRI) of the brain was performed which demonstrated confluent bilateral T2/FLAIR hyperintense signal (Fig. 2A and B) and mildly T1 hypointense signal (Fig. 2C) in the periventricular white matter and centrum semiovale with relative sparing of the subcortical white matter and subcortical U-fibers suggestive of HIV encephalitis. No associated enhancement was appreciated on contrast-enhanced images (Fig. 2D). Additionally, generalized atrophy that was advanced for his age was noted. Contrast enhanced MRI of the spine was unremarkable.

Based on the clinical and radiographic findings, a diagnosis of HIV-associated dementia was made. The patient was treated for syphilis with Penicillin G and started on Trimethoprim/sulfamethoxazole (Bactrim) for *Pneumocystis jiroveci* pneumonia prophylaxis. He was also started on HIV-antiretroviral therapy (ART), bictegravir-emtricitabine-tenofovir (Biktarvy) and followed up outpatient for formal neuropsychological and cognitive evaluation.

## Discussion

Initially, our patient's clinical presentation with subacute progressive spastic paraparesis was concerning for spinal cord involvement (ie, myelopathy), specifically the corticospinal tracts given the bilateral nature of his progressive weakness. MRI of the spine was unremarkable, ruling out spinal injury secondary to trauma or mass effect. Extensive laboratory data was collected to evaluate for etiologies of myelopathy; myelopathy in the setting of immunosuppression can occur secondary to opportunistic infections such as VZV, EBV, HTLV1, syphilis, and rarely PML [2–5]. Additionally, myelopathy has rarely been documented in those following infection with SARS-CoV2, which our patient had in August of 2021, although viral product is not detected in the CSF in the majority of these cases [6]. HIV vacuolar myelopathy was considered, but this usually involves the sensory tracts, which were intact in our patient [7]. HIV can also cause motor neuron disease that can be predominantly upper motor neuron, but this is not very common [8]. Other causes of progressive spastic paraparesis include nutritional deficiencies (B12, copper, vitamin E, folate), toxicities (nitrous oxide, others), or hereditary causes (eg, adult onset adrenomyeloneuropathy, hereditary spastic paraplegia, etc.), though our patient's symptom time course is faster than typical for most genetic causes [9–12].

### *HIV-associated dementia*

HIV-associated dementia (HAD) is a category of the HIV-associated neurocognitive disorders (HANDs) first described by the neurologist Bradford Navia and colleagues in 1986 with nearly 50% of patients presenting with either motor or behavioral changes [13]. Fortunately, with the increased use of ART, the incidence of HIV-associated CNS disease has significantly decreased from 5.9 per 100 person-years in 1994 to 0.5 in 2002 [14]. However, people over the age of fifty continue to be the most affected by HAND with a relatively constant or increased prevalence for this age group [15]. Risk factors for developing HAD include a low CD4 count (<200 cells/mm$^3$), longer

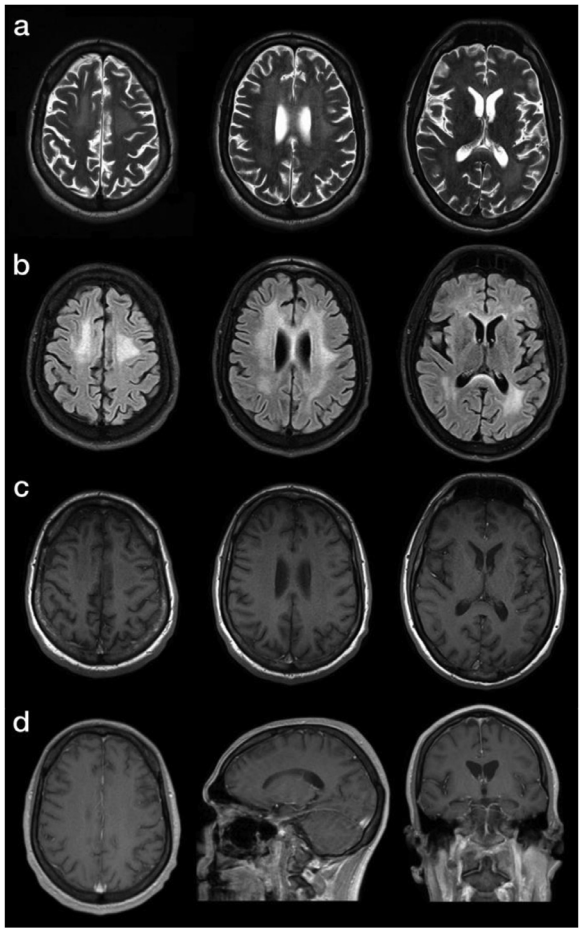


**Fig. 2 – Axial T2 (A), FLAIR (B), and T1 (C) magnetic resonance imaging (MRI) of the brain demonstrate confluent bilateral T2/FLAIR hyperintense signal and mildly T1 hypointense signal in the periventricular white matter and centrum semiovale with relative sparing of the subcortical white matter and subcortical U-fibers. Post-contrast T1 images (D) did not show any associated enhancement. Additionally, generalized atrophy that is advanced for his age was noted.**

HIV infection duration, and older age [16]. Formal neuropsychological testing is required for diagnosis; however, comprehensive neuropsychological testing is costly and may not be readily accessible. Therefore, HAD may be diagnosed based on severe cognitive and motor dysfunction that significantly impairs functioning [17].

In addition to the motor (eg, ataxia, leg weakness, and loss of fine-motor coordination) and cognitive changes that may occur, a minority of patients may present with mood-changes such as mania and psychosis [18]. Notably, the prevalence of bipolar disorder type 1 in HIV patients is almost 6 times higher than the prevalence for the general population in the United States [19]. In severe dementia, patients may present with mutism, paraplegia, and myoclonus [13].

Imaging of the brain may support the diagnosis of HIV-associated dementia (HAD). The most sensitive imaging modality for detecting HAD is MRI of the brain, which should include axial DWI, T2, TIRM/FLAIR, and T1 series [17]. The third ventricle may be enlarged early in the disease course [20]. Gray matter atrophy of the cerebral cortex, which may also be visualized on CT, may be responsible for cognitive dysfunction, while motor impairment, including pyramidal and extrapyramidal signs, are due to involvement of upper motor neurons and the corticospinal tracts and basal ganglia, respectively. In the later stages of the disease, bilateral symmetrical lesions affecting the periventricular regions and centrum semiovale can be seen [21]. To differentiate between HAND and progressive multifocal leukoencephalopathy (PML), PML does not usually present in a bilateral confluent diffuse pattern. PML can enhance when associated with immune reconstitution inflammatory syndrome (IRIS) in HIV, while HAND should not exhibit enhancement. Additionally, the subcortical U-fibers are typically spared in HAND [22,23]. If mass effect or enhancement is present, a diagnosis other than HAD must be considered [24].

There are differing algorithms for when to initiate ART in patients with HIV-associated dementia given their clinical history. Treatment options for ART-naïve patients with a CD4 count less than 200 cells/μL should include further assessment for opportunistic infections, such as the JC virus responsible for PML. However, JC virus PCR CSF negativity is of poor sensitivity, so clinical monitoring [25] and follow-up imaging is important to help differentiate HIV versus PML encephalopathy. The initiation of ART in the setting of profoundly elevated viral load and depleted CD4 counts, as well as in the setting of certain opportunistic infections, can precipitate IRIS, so close clinical monitoring is necessary in these cases [26].

Proper diagnosis of HIV-associated dementia is important as to not mistake this for progressive multifocal leukoencephalopathy, adult-onset leukodystrophy, B12 or other vitamin deficiencies, endocrine disorders (eg, thyroid or adrenal dysfunction), substance use, or psychiatric disorders in the setting of HIV, as additional testing, treatment, and prognosis are different.

## Patient Consent Statement

Appropriate patient consent has been obtained for this case study.

## Authorship Contribution statement

All authors had access and equal role in writing the manuscript.

## REFERENCES

[1] Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, Leblanc S, et al. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. J Neurovirol 2011;17(1):3–16. doi:10.1007/s13365-010-0006-1.

[2] Nagel MA, Niemeyer CS, Bubak AN. Central nervous system infections produced by varicella zoster virus. Curr Opin Infect Dis 2020;33(3):273–8. doi:10.1097/qco.0000000000000647.
[3] Enríquez-Ruano P, Navarro CE, Ariza-Varón M, Calderón-Castro ADP. Myelopathy secondary to human T-lymphotropic virus and Treponema pallidum infection: case report. Spinal Cord Ser Cases 2019;5:93. doi:10.1038/s41394-019-0238-0.
[4] Singh JR, Ibraheem K, Jain D, Yogendra K. Myelitis: A Rare Presentation of Epstein Barr Virus. J Assoc Physicians India 2019;67(3):93–5.
[5] Murayi R, Schmitt J, Woo JH, Berger JR. Spinal cord progressive multifocal leukoencephalopathy detected premortem by MRI. J NeuroVirol 2015;21(6):688–90. doi:10.1007/s13365-015-0342-2.
[6] Garg RK, Paliwal VK, Gupta A. Spinal cord involvement in COVID-19: a review. J Spinal Cord Med 2021:1–15. doi:10.1080/10790268.2021.1888022.
[7] Di Rocco A, Simpson DM. AIDS-associated vacuolar myelopathy. AIDS Patient Care STDS 1998;12(6):457–61. doi:10.1089/apc.1998.12.457.
[8] Lorenzoni PJ, Ducci RD, Dalledone GO, Kay CSK, de Almeida SM, Werneck LC, et al. Motor neuron disease in patients with HIV infection: Report of two cases and brief review of the literature. Clin Neurol Neurosurg 2018;171:139–42. doi:10.1016/j.clineuro.2018.06.006.
[9] McDermott C, White K, Bushby K, Shaw P. Hereditary spastic paraparesis: a review of new developments. J Neurol Neurosurg Psychiatry 2000;69(2):150–60. doi:10.1136/jnnp.69.2.150.
[10] Shamim D, Alleyne K. X-linked adult-onset adrenoleukodystrophy: psychiatric and neurological manifestations. SAGE Open Med Case Rep 2017;5. doi:10.1177/2050313x17741009.
[11] Hadzic A, Glab K, Sanborn KV, Thys DM. Severe Neurologic Deficit after Nitrous Oxide Anesthesia. Anesthesiology 1995;83(4):863–6. doi: 10.1097/00000542-199510000-00028.
[12] Hedera P. Hereditary and metabolic myelopathies. Handb Clin Neurol 2016;136:769–85. doi:10.1016/b978-0-444-53486-6.00038-7.
[13] Navia BA, Jordan BD, Price RW. The AIDS dementia complex: I. Clinical features. Ann Neurol 1986;19(6):517–24. doi:10.1002/ana.410190602.
[14] d'Arminio Monforte A, Cinque P, Mocroft A, Goebel FD, Antunes F, Katlama C, et al. Changing incidence of central nervous system diseases in the EuroSIDA cohort. Ann Neurol 2004;55(3):320–8. doi:10.1002/ana.10827.
[15] Mackiewicz MM, Overk C, Achim CL, Masliah E. Pathogenesis of age-related HIV neurodegeneration. J Neurovirol 2019;25(5):622–33. doi:10.1007/s13365-019-00728-z.
[16] Bhaskaran K, Mussini C, Antinori A, Walker AS, Dorrucci M, Sabin C, et al. Changes in the incidence and predictors of human immunodeficiency virus-associated dementia in the era of highly active antiretroviral therapy. Ann Neurol 2008;63(2):213–21. doi:10.1002/ana.21225.
[17] Eggers C, Arendt G, Hahn K, Husstedt IW, Maschke M, Neuen-Jacob E, et al. HIV-1-associated neurocognitive disorder: epidemiology, pathogenesis, diagnosis, and treatment. J Neurol 2017;264(8):1715–27. doi:10.1007/s00415-017-8503-2.
[18] Owe-Larsson B, Säll L, Salamon E, Allgulander C. HIV infection and psychiatric illness. Afr J Psychiatry (Johannesbg) 2009;12(2):115–28. doi:10.4314/ajpsy.v12i2.43729.
[19] de Sousa Gurgel W, da Silva Carneiro AH, Barreto Rebouças D, Negreiros de Matos KJ, do Menino Jesus Silva Leitão T, de Matos e Souza FG. Prevalence of bipolar disorder in a HIV-infected outpatient population. AIDS Care 2013;25(12):1499–503. doi:10.1080/09540121.2013.779625.
[20] Ragin AB, Du H, Ochs R, Wu Y, Sammet CL, Shoukry A, et al. Structural brain alterations can be detected early in HIV infection. Neurology 2012;79(24):2328–34. doi:10.1212/WNL.0b013e318278b5b4.
[21] Haziot MEJ, Barbosa Junior SP, Vidal JE, de Oliveira FTM, de Oliveira ACP. Neuroimaging of HIV-associated neurocognitive disorders. Dement Neuropsychol 2015;9(4):380–4. doi:10.1590/1980-57642015dn94000380.
[22] Villani LA, Stulberg EL, Abbatemarco JR, Davidson CJ, Kadish R, Renner DR, et al. Biopsy-proven PML in an HIV-negative patient with discoid lupus: failure to detect JC virus in CSF. Clin Neurol Neurosurg 2021;209:106843. doi:10.1016/j.clineuro.2021.106843.
[23] Alleg M, Solis M, Baloglu S, Cotton F, Kerschen P, Bourre B, et al. Progressive multifocal leukoencephalopathy: MRI findings in HIV-infected patients are closer to rituximab- than natalizumab-associated PML. Eur Radiol 2021;31(5):2944–55. doi:10.1007/s00330-020-07362-y.
[24] Smith AB, Smirniotopoulos JG, Rushing EJ. From the archives of the AFIP: central nervous system infections associated with human immunodeficiency virus infection: radiologic-pathologic correlation. Radiographics 2008;28(7):2033–58. doi:10.1148/rg.287085135.
[25] Blankenbach K, Schwab N, Hofner B, Adams O, Keller-Stanislawski B, Warnke C. Natalizumab-associated progressive multifocal leukoencephalopathy in Germany. Neurology 2019;92(19):e2232–e22e9. doi:10.1212/wnl.0000000000007451.
[26] Saag MS, Benson CA, Gandhi RT, Hoy JF, Landovitz RJ, Mugavero MJ, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA Panel,. In: Jama, 320; 2018. p. 379–96. doi:10.1001/jama.2018.8431.