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Brain Lesions, A Common Cause for Misdiagnose of HIV Encephalitis (Case-Report)

Ina Rezhdo*, Najada Como, Migena Qato, Arjan Harxhi

Infectious Disease Service
Department of Infectious Disease, Faculty of Medicine
University Hospital Center "Mother Theresa" Tirana, Albania

Abstract

Background: HIV encephalitis is a complication of HIV infection that affects nearly half of HIV-infected patients, manifesting as neurocognitive dysfunction with varying severity. The clinical presentation can range from being asymptomatic or causing mild neurocognitive impairment to severe dementia, accompanied by peripheral nerve symptoms such as seizures and hemiparesis. Typically, initial manifestations in these patients prompt an imaging evaluation, alongside laboratory tests. Brain imaging often reveals lesions that are not pathognomonic for any specific condition. Given that these neurological symptoms overlap with a wide range of other diseases, patients are often first admitted imaging, and histopathological evaluations are essential in establishing the correct diagnosis and identifying the underlying cause of these syndromes as the case progresses.

Aim and Method: We present the case of a 47-year-old woman who was admitted to the neurosurgery clinic at University Hospital Center Mother Theresa with a diagnosis of secondary brain lesions of unknown origin, which ultimately revealed encephalitis in an end-stage HIV patient.

Conclusion: In conclusion, an accurate diagnosis relies on a combination of symptomatology, clinical neurologic evaluation, laboratory testing including infective pathogens (especially HIV),

Address for correspondence: Ina Rezhdo*, Infectious Disease Service, Department of Infectious Disease, Faculty of Medicine, University Hospital Center "Mother Theresa" Tirana, Albania. Rr. "Dibres", No. 371, Tirana, Albania. E-mail: ina.rezhdo@gmail.com

radiological studies and invasive procedures when necessary.

Keywords: Brain, Encephalitis, HIV, Lesion, Misdiagnose.

INTRODUCTION

HIV encephalopathy is a potential complication of HIV infection, caused by inflammation of the brain. It can affect both brain volume and structure, leading to a variety of mental health symptoms and intellectual challenges. HIV is a virus that targets and weakens the immune system, increasing the risk and severity of complications (1,2,3,4). One such complication is HIV encephalitis, which refers to brain inflammation typically resulting from the virus's effects or opportunistic infections like toxoplasmosis (5,6).

HIV encephalopathy generally appears in advanced stages of HIV, often many years after the initial infection. It is most common in individuals who do not take effective HIV medications and those with a very low CD4+ cell count, a type of white blood cell responsible for fighting infections (7,8).

HIV encephalitis, also known as HIV-associated neurocognitive disorder (HAND), includes a spectrum of neurocognitive impairments of varying severity following HIV infection (9,10,11,12). The clinical presentation of this condition varies from asymptomatic or minor neurocognitive impairment to severe dementia. In addition, it is the most severe of the three forms of HAND:

- **Asymptomatic neurocognitive impairment**: This form has no symptoms of cognitive decline.
- **HIV-associated mild neurocognitive disorder**: A person with this disorder may have mild symptoms of cognitive decline.
- **HIV encephalitis**: HIV encephalitis causes severe symptoms of cognitive decline.

Prompt and effective administration of antiretroviral therapy (ART) is currently considered the most effective treatment for managing HIV encephalitis.

CASE PRESENTATION

A 47-year-old woman, A. I., was admitted to the Emergency Unit of University Hospital Mother Theresa with a diagnosis of cerebral tumor and a right frontal cerebral lesion, pending biopsy. The patient first presented to the emergency care unit on 13.12.2022 with complaints of vomiting, headache, and left-sided hemiparesis, which had started earlier that day. She was promptly brought to the emergency service as soon as the symptoms began. Clinical and biochemical tests, neurological assessments, and a head CT scan were performed, revealing a hypodense right frontal formation with cerebral tissue edema. After further physical examinations and consultations, she was hospitalized in the Neurosurgery Service.

The patient had a history with the Neurosurgery Service, having been hospitalized 10 days earlier and subsequently undergoing a biopsy of the cerebral lesion. During her first hospitalization, her complaints included paresis and tremor in her

left hand, along with one episode of generalized contractions without loss of consciousness. Imaging revealed a parenchymal cerebral lesion (2 cm x 2 cm) surrounded by cerebral edema. A biopsy of the right frontal lesion was taken during the intervention. She was discharged from the Neurosurgery Service in good condition, pending biopsy results, and was prescribed Keppra 500 mg, 2x1.

Table 1. Laboratory data of the patient

Test	Result	Normal range	Test	Result	Normal range
WBC (103 /µL)	1.7	4-10.5	**ALT (U/L)**	62	<55
Neutrophils (%)	68.3	40-72	**AST (U/L)**	30	5-34
Lymphocyte (%)	22.4	25-45	**Glucose (mg/dL)**	90	74-100
Hb (g/dL)	13.6	12-16	**Urea (mg/dL)**	32	14-40
RBC (106/ µL)	4.67	4-5.6	**Creatinine (mmol/L)**	0.65	0.57-1.11
PLT (103 /µL)	150	150-400	**K (mmol/L)**	3.8	3.5-5.1
CRP (mg/dL)	0.1	<0.5	**Na (mmol/L)**	136	136-145

On admission, her physical examination showed stable vital signs, altered consciousness, no signs of wasting syndrome, a temperature of 36.8°C, dehydrated skin and mucosa, oxygen saturation of 97%, and blood pressure of 110/80 mmHg.

Objective examination upon admission: oriented, negative Kerning and Brudzinski signs, isochoric pupils, photoreactive pupils, preserved oculomotor, sinister hemiparesis.

A head MRI was performed, showing right frontal lesions with pronounced perifocal edema, along with additional cerebral and cerebellar lesions. The biopsy results revealed a cerebral tissue fragment with hyperemia, neutrophilic and perivascular infiltrations, and small parenchymal granulations. Histopathological changes were compatible with encephalitis of unclear origin.

Laboratory analysis showed leukopenia and absolute lymphopenia (WBC = 1.7K/uL; lymphocytes = 0.4K/uL). Other results, including RBC, CRP, renal and liver function, glucose, and urinalysis, were normal (Table 1). Tumor markers were negative (CEA, AFP, CA 19-9, CA 15-3), except for elevated CA 125.

After consulting an infectious disease specialist and undergoing specific tests, including HIV, HBsAg, Anti-HCV, Toxo IgM and IgG, and CMV IgM and IgG, the patient tested positive for HIV. She was transferred to the Infectious Disease Service on 19.12.2022. Upon arrival, the patient's condition was severe. She was in a forced bed position, with altered consciousness, somnolent but slow and correct responses to verbal stimuli. She appeared pale, with skin and mucous membranes showing candidiasis. Neck stiffness was absent, and Kerning and Brudzinski signs were negative. Hemodynamically stable,

with a heart rate of 76 bpm and blood pressure of 110/75 mmHg, vesicular breath sounds, and rales on auscultation (O2 saturation 94%). Abdominal examination showed no peritoneal signs, and diuresis was present. Left-sided hemiparesis was also observed. The absolute CD4+ T-cell count was 18 cells/mm³ (5%). Blood and urine cultures were negative, as were the Wright, Widal, Weil-Felix, and Mantoux tests. Following admission, the patient was treated with antibiotics (Ceftriaxone, Levofloxacin, Metronidazole), steroids, and anti-edematous therapy. Due to the contractions. A head CT showed increased edema in the right frontal region and compression of the right lateral ventricle (Figure 1). Clinically, the patient exhibited frequent seizures and entered status epilepticus despite antiepileptic therapy. She was in a forced bed position, stuporous, responding minimally to painful stimuli.

On the 17th day of admission, her condition deteriorated, with bradycardia, hypotension, and oxygen saturation falling to 88%. Despite resuscitative efforts with inotropic drugs and CPR, the patient was pronounced deceased.

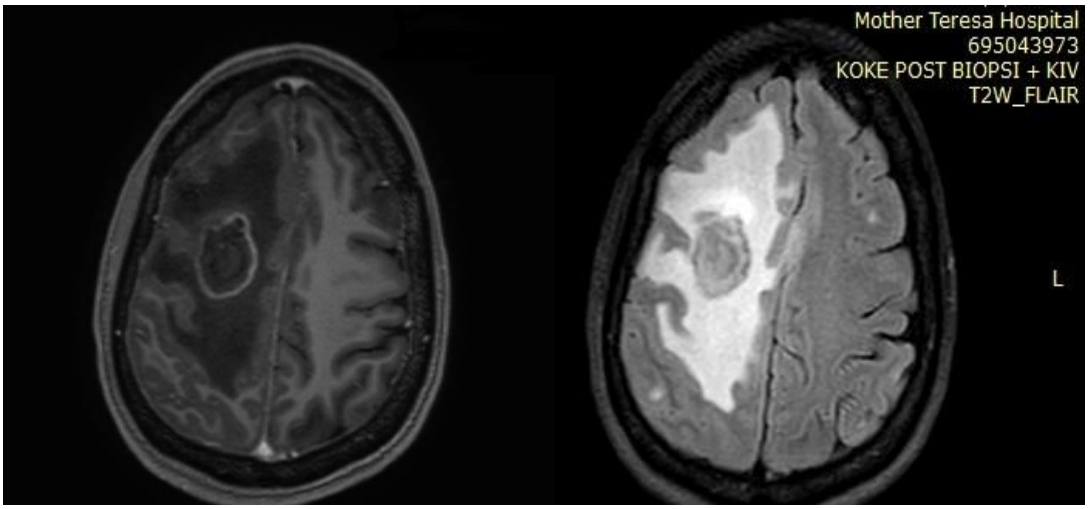

Figure 1. Cerebral frontal dexter lesion with surrounding perifocal edema

low CD4+ count and risk of opportunistic infections, treatment was supplemented with Sulfamethoxazole/Trimethoprim, Fluconazole, and ART (Dolutegravir, Lamivudine, Tenofovir). Empirical antitubercular treatment was also initiated.

Ten days after starting treatment, the patient's condition worsened, presenting with epileptic seizures, loss of consciousness, and muscle

DISCUSSION

In the clinical presentation of neurological disorders, healthcare professionals must first perform cerebral imaging examinations to evaluate the presence of space-occupying brain lesions. Once such lesions are identified, the next step is making the correct differential diagnosis. The case must initially be evaluated by both a neurologist and a neurosurgeon to determine the nature of the lesion. If the diagnosis remains

inconclusive, further exploration using detailed imaging techniques like MRI or invasive methods such as brain biopsy is necessary. In neuropathologic practice, brain biopsies revealing encephalitis without identifying the specific origin are often classified as Encephalitis Not Otherwise Specified (pathologic ENOS). Some patients with ENOS diagnosed through biopsy may also present with clinical ENOS. Additionally, patients initially suspected of having neoplastic, demyelinating, or degenerative diseases may end up diagnosed with ENOS following a brain biopsy (13,14).

In HIV infection, cerebral lesions can often be misdiagnosed as tumor-related neurological conditions or other neurosurgical causes. The clinical spectrum of neurological disorders associated with HIV infection often overlaps with other neurological conditions, and includes:

Dementia. Advanced HIV can lead to HIV-associated dementia or AIDS dementia complex, both of which impair cognitive function and can be life-threatening. However, they can often be prevented with the proper administration of antiretroviral therapy (ART) (15).

Viral infections. HIV can increase your risk for several viral infections that strike the nervous system. Cytomegalovirus infections can negatively affect cognitive function, physical control (like the use of legs and arms and bladder control), vision and hearing, and your respiratory system, causing problems like pneumonia. People with AIDS are also likely to develop a herpes virus infection, like shingles, inflammation in the brain, and inflammation, in the spinal cord. Another condition, progressive multifocal leukoencephalopathy (PML) is also caused by a virus. PML is aggressive and dangerous. In some circumstances, it can be controlled with antiretroviral medicines (16,17,18,19).

Fungal and parasitic infections. Cryptococcal meningitis is caused by a fungus and leads to serious inflammation of the spinal cord and brain. A parasite can cause an infection called toxoplasma encephalitis (20), which often leads to confusion, seizures, and extremely painful headaches. Both of these infections can be life-threatening.

Neuropathy. HIV can cause damage to nerves throughout the body, resulting in significant pain or weakness, known as neuropathy. Neuropathy is most common in people with advanced HIV.

Vacuolar myelopathy. This condition occurs when tiny holes develop in the fibers of the nerves of the spinal cord. It causes difficulty walking, particularly as the condition gets worse. It's common in people with AIDS who aren't receiving treatment and also in children with HIV (21).

Psychological conditions. People with HIV or AIDS often develop anxiety disorders and suffer from depression. They may also experience hallucinations and significant changes in behavior.

Lymphomas. Tumors called lymphomas (22) often strike the brain of people with HIV. They're often related to another virus, similar to the

herpes virus. Lymphomas can be life-threatening, but good management of HIV can make treating lymphomas more successful.

Neurosyphilis. If an HIV-infected person also has syphilis that goes untreated, it can quickly progress and damage the nervous system. It can cause the nerve cells to break down and lead to loss of vision and hearing, dementia, and difficulty walking (23).

Some of the reasons above give an early orientation through HIV diagnosis to a patient with cerebral lesions from the neurologist and neurosurgeon. In this case report, the initial hospitalization of the patient was a diagnostic failure, as testing for infectious agents like HIV, which could cause cerebral damage, was not considered.

CONCLUSION

In conclusion, an accurate diagnosis relies on a combination of symptomatology, clinical neurologic evaluation, laboratory testing including infective pathogens (especially HIV), radiological studies and invasive procedures when necessary.

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REFERENCES

1. Moulignier A. HIV and the central nervous system. Rev Neurol 2006;162(1):22–42.

2. Bowen LN, Smith B, Reich D, Quezado M, Nath A. HIV associated opportunistic CNSinfections: pathophysiology, diagnosis and treatment. Nat Rev Neurol 2016;12(11):662–674.

3. Sonneville R, Magalhaes E, Meyfroidt G. Central nervous systeminfections inimmunocompromised patients. Curr Opin Crit Care 2017;23(2):128–133.

4. Mamidi A, DeSimone JA, Pomerantz RJ: Central nervous systeminfections in individuals with HIV-1 infection. J Neurovirol 2002;8:158–167.

5. Luft BJ, Hafner R, Korzun AH, et al. Toxoplasmic encephalitis inpatients with theacquired immunodeficiency syndrome. Members of the ACTG 077p/ANRS 009 StudyTeam. N Engl J Med 1993;329(14):995–1000.

6. Luft BJ, Remington JS. Toxoplasmic encephalitis in AIDS. ClinInfect Dis 1992;15(2):211–222.

7. AIDS-related focal brain lesions in the era of highly active antiretroviraltherapy A. Ammassari, A. Cingolani, P. Pezzotti, A. De Luca, R. Murri, M.L.Giancola, L.M. Larocca, A. AntinoriNeurology 2000;55(8):1194-200

8. Antinori A, Giancola ML, Grisetti S, et al. Factors influencing virological response to

antiretroviral drugs in cerebrospinal fluid of advanced HIV-1infected patients. AIDS 2002;16(14):1867-76.

9. Le LT, Spudich SS. HIV-Associated neurologic disorders andcentral nervous systemopportunistic infections in HIV. Semin Neurol 2016;36(4):373–381.

10. Snider WD, Simpson DM, Nielsen S, et al. Neurological complications of acquiredimmune deficiency syndrome: analysis of 50patients. Ann Neurol 1983;14(4):403–418.

11. Rosenblum ML, Levy RM, Bredesen DE. Neurosurgical implications of the acquiredimmunodeficiency syndrome (AIDS). Clin Neurosurg 1988;34:419–445.

12. Price RW. Neurological complications of HIV infection. Lancet 1996;348(9025):445–452.

13. Solomon T, Michael BD, Smith PE, et al; National Encephalitis Guidelines Development and Stakeholder Groups. Management of suspected viral encephalitis in adults: Association of British Neurologists and British Infection Association National Guidelines. J Infect 2012;64(4):347-373.

14. Hornef MW, Iten A, Maeder P, Villemure JG, Regli L. Brain biopsy in patients with acquired immunodeficiency syndrome: diagnostic value, clinical performance, and survival time. Arch Intern Med 1999;159(21):2590-2596.

15. Ances BM, Ellis RJ. Dementia and neurocognitive disorders due to HIV-1infection. Semin Neurol. 2007;27(1):86-92.

16. Dousset V, Armand JP, Lacoste D, et al. Magnetization transferstudy of HIV encephalitis and progressive multifocal leukoencephalopathy. AJNR Am J Neuroradiol 1997;18:895901

17. Levy RM, Bredesen DE, Rosenblum ML. Opportunistic centralnervous system pathology in patients with AIDS. Ann Neurol 1988;23(suppl):S7–S12.

18. Tan IL, Smith BR, von Geldern G, Mateen FJ, McArthur JC. HIV associated opportunistic infections of the CNS. Lancet Neurol 2012;11(7):605–617.

19. Collazos J. Opportunistic infections of the CNS in patients withAIDS. CNS Drugs 2003;17(12):869–887.

20. C.E. Offiah, I.W. Turnbull. The imaging appearances of intracranial CNS infectionsin adult HIV and AIDS patients. Clinical Radiology 2006;61:5, 393-401.

21. Di Rocco A, Werner P. Hypothesis on the pathogenesis of vacuolar myelopathy, dementia, and peripheral neuropathy in AIDS. J Neurol Neurosurg Psychiatry 1999;66(4):554.

22. Bower M, Fife K, Sullivan A, et al. Treatment outcome in presumed and confirmed AIDS-related primary cerebral lymphoma. Eur J Cancer 1999;35(4):601–604.

23. Berger JR, Cohen BA. Opportunistic infections of the nervoussystem in AIDS. In: Gendelman HE, Grant I, Everall IP, LiptonSA, Swindells S, eds. The Neurology ofAIDS. Oxford, UnitedKingdom: Oxford University Press 2005:485–529.