

## Difficulties in establishing a definitive diagnosis of intracerebral hemorrhage in patients with HIV/AIDS



Yuriz Bakhtiar<sup>1</sup>, Muhamad Thohar Arifin<sup>1\*</sup>, Adrian Pratama<sup>2</sup>

### ABSTRACT

**Introduction:** Neurological disorders are observed in about 70% of HIV/AIDS cases, of which intracranial mass lesions characterize 10-20%. In addition, the incidence of intracerebral hemorrhage is frequently associated with several etiologies, including toxoplasmosis and cerebral tuberculosis. This manifestation has been attributed the most common opportunistic infections in developing countries. Therefore, a CT scan of the head is commonly used to provide similar images, and consequently mimic SOL or general brain tumors. Meanwhile, laboratory examinations merely use rapid tests without any serologic assessment for opportunistic infections, which prompts difficulties in the confirmatory diagnostics process.

**Case Presentation:** This paper reports two HIV/AIDS cases with neurological disorders. The first involved two patients with multiple SOLs, while the second was a patient with both SOL and intracerebral hemorrhages. Furthermore, the difficulties in establishing an SOL diagnosis by merely relying on head CT scans are observed in these reports, as only toxoplasmosis and tuberculoma were detected. The dilemma of performing a brain biopsy has also been considered an impeding factor.

**Conclusion:** intracerebral hemorrhage is prevalent and is also considered another cause of neurological disorders and is still a challenging diagnosis in person with HIV/AIDS.

**Keywords:** Intracranial Mass Lesion, SOL, HIV/AIDS.

**Cite This Article:** Bakhtiar, Y., Arifin, M.T., Pratama, A. 2021. Difficulties in establishing a definitive diagnosis of intracerebral hemorrhage in patients with HIV/AIDS. *Bali Medical Journal* 10(1): 437-441. DOI: 10.15562/bmj.v10i1.2249

<sup>1</sup>Department of Neurosurgery, Faculty of Medicine, Universitas Diponegoro-Dr. Kariadi Hospital, Semarang, Indonesia.

<sup>2</sup>Department of Neurosurgery, Salatiga City Hospital, Indonesia.

\*Corresponding author:  
Muhamad Thohar Arifin;  
Department of Neurosurgery, Faculty of Medicine, Universitas Diponegoro-Dr. Kariadi Hospital, Semarang, Indonesia;  
[thohar@fk.undip.ac.id](mailto:thohar@fk.undip.ac.id)

Received: 2021-02-05

Accepted: 2021-04-20

Published: 2021-04-30

### INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is a set of clinical symptoms or diseases instigated by the human immunodeficiency virus (HIV) infection. In addition, a CD4<sup>+</sup> count less than 200/ $\mu$ L, the presences specific opportunistic infections or malignancies classified as AIDS-defining illness serve as confirmatory assessment techniques.<sup>1</sup> Moreover, 70% of the total HIV patients are known to present with neurological disorders, of which about 10-20% demonstrate intracranial focal mass/lesions during radiologic examination.<sup>2</sup> This phenomenon is possibly triggered by opportunistic infections, HIV-related tumors, and cerebrovascular disorders.<sup>3</sup> However, toxoplasmosis, primary central nervous system lymphoma (PCNSL), progressive multifocal leukoencephalopathy (PML), cryptococcal abscess, and tuberculoma have been identified as the major causes of infections.<sup>3,4</sup> The most predominant perpetrators are tuberculosis and toxoplasma infection.<sup>3</sup>

The neurological manifestations arising from these focal intracranial lesions are highly non-specific.<sup>1,5</sup> These include headaches, changing mental status, seizures, and focal neurological deficits, and are known to be extremely common in every case.<sup>1,5</sup> Moreover, fever is frequently observed in cases associated with infection, including tuberculosis, toxoplasmosis, and cryptococcal abscess,<sup>5</sup> while cranial nerve paralysis is associated with lesions in the basal area of the brain, following tuberculosis and cryptococcal abscess.<sup>5</sup> In addition, radiological examinations with Computed Tomography (CT) scans are used to generate results identical to one another.<sup>6</sup> However, masses in the form of tumors, with a capacity to either enhance contrast or not, portray specifically difficult diagnostics properties.<sup>1,4,5</sup>

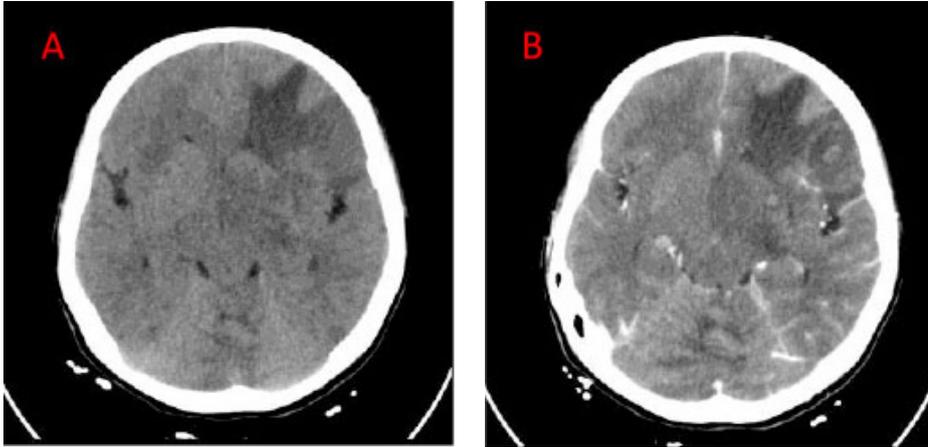
The epidemiological data of HIV and AIDS in Indonesia, from January to June 2019 showed 22,600 and 2,912 cases, respectively, with 2,565 and 747 in Central Java.<sup>7</sup> Based on the data obtained at the VCT Polyclinic in Regional General Hospital (RSUD), Salatiga, a total of 45

positive cases were recorded in 2019. Furthermore, 6 patients (13%) presented with neurological disorders, and focal lesions on head CT scan, of which 5 possessed a CT space-occupying lesion (SOL), and 1 demonstrating multiple SOL with intracerebral hemorrhage. Therefore, both case types were reported in this study, comprising 2 patients for the first and 1 for the second case. The availability of assessment tools at the study location was limited, as the healthcare providers merely relied on head CT and the laboratory tool for rapid HIV test. Hence, the inability for a patient's condition to allow for brain biopsy connotes difficulties in the definitive diagnosis of SOL.

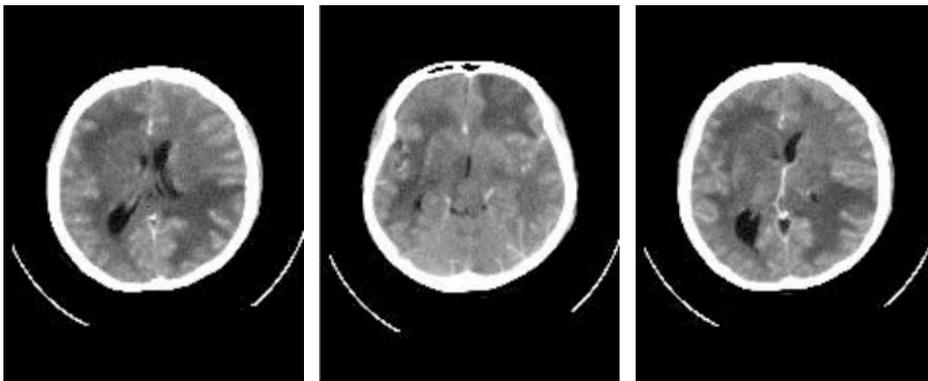
### CASE REPORTS

#### Case 1 – Multiple space-occupying lesions (SOL) in HIV/AIDS

A total of 2 patients presented with similar head CT images, characterized by multiple SOLs. Particularly, the first was a 23-year-old woman admitted to the polyclinic of neurological diseases at RSUD Salatiga,



**Figure 1.** (A) CT with plain images and (B) contrast images, indicating multiple lesions with a thin ring enhancement along with perifocal edema in the left frontal lobe. This was slightly enhanced with the target sign in the middle.



**Figure 2.** Multiple space-occupying lesions with prominent perifocal edema of approximately 3 lesions in (A) right frontal lobe and (B) left frontal lobe and mass with minimal ring enhancement with a target sign on (C) left parietal lobe.

with complaints of severe sleep-disturbing headaches for over 10 days prior to the admission. This manifestation was accompanied by nausea and vomiting, alongside a fever over 3 days. The previous diagnosis showed HIV and pulmonary tuberculosis (TB), while the current vital sign examination revealed fever at 38°C. In addition, physical and neurological assessments show the patient to be within normal limits.

The patient was treated with a diagnosis of severe cephalgia. Therefore, the CD4<sup>+</sup> test performed on day 3 of therapy showed 35/μL. Figure 1 showed a head CT scan with contrast performed on day 6 and multiple SOLs were identified. Subsequently, the individual was admitted to the neurosurgery unit with conservative

care and was then discharged on day 8.

The second patient was a 50 years-old woman admitted to the emergency unit of RSUD Salatiga with decreased consciousness for over three hours before admission, after an episode of vomiting. In addition, previous medical history shows headaches, while the vital signs indicate fever at 39 °C, using a Glasgow Coma Scale (GCS) E<sub>2</sub>M<sub>4</sub>V<sub>2</sub>. The other physical examination results were within the normal limits, while neurological examination was difficult to perform due to the decreased consciousness.

The treatment commenced in the neurology unit, following a diagnosis of suspected space-occupying lesion (SOL). In addition, a CT examination of the head with contrast was performed

on day 3 of treatment and multiple SOLs were observed. Figure 2 showed the presentation with prominent vasogenic edema and a differential diagnosis of tuberculosis abscess, alongside brain metastases, and diffuse astrocytoma. The patient was then referred to the neurosurgery department and advised to perform voluntary counseling and testing (VCT). The results showed a positive reaction on the rapid HIV test, and the patient was treated conservatively prior to death on day 5.

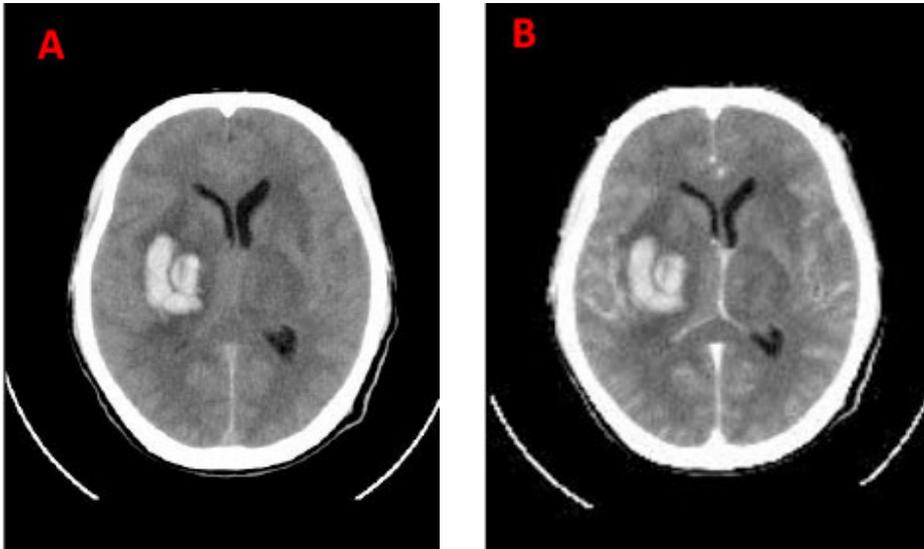
### Case 2 – Space-occupying lesions with intracerebral hemorrhage in HIV/AIDS

A 42 years-old man was admitted to the Polyclinic of Internal Diseases at RSUD Salatiga, with complaints of fever spanning through a 7 days period. The fever subsided following the provision of antipyretics and up again subsequently. In addition, the patient also presented with headache and diarrhea for over 10 days, while a hyperpyrexia temperature of 39.9°C, and GCS 15 were recorded following the assessment of vital signs. The lungs possessed rough wet crackles on the right hemithorax upon physical examination, while the laboratory tests indicated paratyphi titer BO: 1/160, and X-rays showed lobar pneumonia.

The patient was then treated in the internal medicine unit with a febrile working diagnosis for 7 days with typhoid fever and pneumonia. Subsequently, there were reports on the experienced of communication difficulties, and was further referred to the neurological department, where the anti-HIV test was positive. The results of GCS E2M3V2 and head the CT showed decreased consciousness due to the presence of SOL in the left thalamus (Figure 3). This was accompanied by intracerebral hemorrhage in the right parietal lobe. Subsequently, the patient was admitted to neurosurgery and was provided with conservative therapy before death on day 9 of the treatment.

### DISCUSSION

HIV infection and AIDS predisposes an individual to serious neurological complications,<sup>1</sup> particularly associated with: (1) HIV infections, (2) opportunistic infections, (3) AIDS-related malignancies,



**Figure 3.** (A) CT with plain images and (B) Contrast images that showing SOL in the left thalamus with intracerebral hemorrhage in the right parietal lobe.

and (4) complications from HIV medications.<sup>1</sup> The prevalence rate is high, at 40-70%, and is accompanied by focal lesions' appearance. This manifestation is common in developing countries, and is usually caused by tuberculosis and toxoplasmosis infection, while sources from PCNSL, PML, and cryptococcal abscesses are less common.<sup>2,4</sup>

### Case 1 – Multiple space-occupying lesions (SOLs) in HIV/AIDS

Both HIV/AIDS patients in case 1 share common clinical symptoms, including fever and headaches, with multiple SOLs present on head CT scan. These clinical manifestations have the potential to instigate opportunistic infections, especially cerebral toxoplasmosis. Based on the Indonesian socio-economic perspective as a low-income and developing country, this predisposed disease is first suspected due to the incidence of 55%, and being the most common in HIV/AIDS cases.<sup>1,8</sup> Furthermore, the infection is accompanied by the clinical and neurological manifestations of headaches, fevers, altered mental status, focal neurological deficits, seizures, behavioral changes, cranial nerve palsy, ataxia, and visual disturbances.<sup>1,4,8,9</sup> The head CT examination of both patients showed the presence of multiple SOLs, with target sign in the frontal and parietal regions, alongside minimal ring enhancement and

surrounding edema. This assessment is consistent with the radiological findings of cerebral toxoplasmosis.<sup>1,4,5,8,9,10</sup>

PCNSL with these disease characteristics have a very rare incidence rate of less than 5% even in developed countries. Also, the neurological manifestations vary depending on the location of the lesion in the brain, with a predominance of seizures, while the imaging diagnosis process using MRI prompts the less prioritization of this outcome.<sup>1,4,5,11,12</sup> The PML is also not highlighted as a differential diagnosis in both cases for similar reasons.<sup>13,14</sup> Moreover, cerebral cryptococcal is known to be the second most common opportunistic infection, with initial clinical features including respiratory disorders and fever, followed by neurological manifestations, encompassing headaches, signs of meningeal irritation, and paralysis of the cranial nerves after the infection reaches the brain through hematogenous means. The head CT scan is a less predictable differential diagnosis in contrast with the clearer identification through MRI. However, cerebral cryptococcus tends to produce identical images in some cases, which is comparable to SOL or brain tumors.<sup>5,15,16,17</sup>

Cerebral tuberculosis or tuberculoma is the second most frequent case of opportunistic infection after toxoplasmosis in developing countries, characterized

by fever, headache, and cranial nerve paralysis as the most common clinical manifestations.<sup>1,5</sup> In addition, head CT examination showed the tendency for tuberculoma to display an image of multiple mass lesions. This is a relatively rare form of the target lesions, with ring enhancement and mass effects.<sup>18,19,20</sup> Also, tuberculomas are known to produce images of a calcified area, featuring no contrast enhancement to the surroundings.<sup>21</sup> This manifestation was suspected with the first patient in case 1, due to a previous pulmonary tuberculosis history.

It is difficult to reach a definitive diagnosis in both patients with cases 1, due to limited radiological examination, which relied only on head CT scan. The unavailability of other laboratory tests also fueled this challenge to diagnose opportunistic infections in HIV/AIDS, as well as the dilemma in determining the criteria for brain biopsy, as a definitive standard for the diagnosis of intracranial disorders. Moreover, a brain biopsy is possibly performed in the case of toxoplasmosis particularly when (1) the lesion is large with a mass effect, together with a threat of brain herniation, (2) the solitary lesion enhanced the contrast with negative anti-toxoplasma IgG results, (3) the patients fail to respond to treatment for 10 -14 days, the incidence of clinical worsening, or enlarged lesion.<sup>8</sup> The conduction of brain biopsy in patients with toxoplasmosis often leads to worse conditions, and indicates the need for medication.<sup>8</sup> This approach also provides better outcomes for cases with tuberculoma compared to surgery.<sup>20,21</sup>

### Case 2 – Multiple space-occupying lesions (SOLs) with intracerebral hemorrhage in HIV / AIDS

The Patient with HIV/AIDS in case 2 present with clinical manifestations in the form of fever, pneumonia, and rapidly progressive impairment in consciousness. Moreover, non-enhancing SOL was observed to the contrast on the left thalamus alongside intracerebral hemorrhage through a head CT scan. The incidence of intracerebral abnormalities as in the previous case was assumed to result from cerebral toxoplasmosis, being the most common opportunistic infection

in developing countries. Meanwhile, differential diagnoses with tuberculoma and cryptococcal abscess were not ruled out, due to the presence of pneumonia. The MRI and other laboratory examinations are important to attain a proper diagnosis, and the deficiency prompted diagnostic difficulties.

The incidence of Intracerebral hemorrhage in HIV infection was 1.85 and 1.87 times higher compared to non-HIV, and in people over 40 years of age.<sup>22</sup> This manifestation potentially increases to 4.46 times in patients with CD4<sup>+</sup> count <200 cells/ $\mu$ L,<sup>22</sup> and is likely associated with HIV-induced vasculitis.<sup>23</sup> Furthermore, lower counts are implicated in arterial remodeling, which is caused by (1) endothelial dysfunction, immunosuppression and inflammation. These result in lipohyalinosis, and is estimated to damage small blood vessels in the brain, as well as (2) the non-atherosclerotic dolichoectatic arterial phenotype, resulting from chronic immunity disorders in HIV.<sup>23</sup> The presence of SOL or intracerebral hemorrhage associated with condition deterioration and possibly death of patients is difficult to determine. Therefore, SOL biopsy or hematoma evacuation is considered high importance, although a declining condition is a common reason not to perform this assessment.

## CONCLUSION

HIV/AIDS is an infectious disease with a high incidence rate worldwide, especially in Indonesia. The sufferers often present with clinical symptoms of neurological disorders, resulting from focal brain lesions. These are predominantly caused by cerebral toxoplasmosis, tuberculoma, especially in developing countries, while other triggers include primary central nervous system lymphoma, progressive multifocal leukoencephalopathy, and cryptococcal abscess.

The clinical manifestations of intracerebral disorders in HIV/AIDS are indistinguishable, as fever, headaches, and decreased consciousness are predominant in patients at Salatiga Hospital. Moreover, radiological examinations, especially using CT scan, provide inconclusive results and often produce similar SOL or

brain tumors. This assessment technique is insufficient to attain a definitive diagnosis of intracranial disorders in HIV/AIDS, without MRI and laboratory examination using the rapid HIV test in the absence of serology to detect other opportunistic infections. In addition, intracerebral hemorrhage is prevalent and is also considered another cause of neurological disorders.

## ETHICAL CONSIDERATION

All patients had received signed written informed consent regarding publication of their medical data in medical journal.

## FUNDING

This report doesn't received any specific grant from government or any private sectors.

## ACKNOWLEDGMENTS

No funding to declare. The authors are grateful to all staff of the Department of Radiology, Department of Neurology, and Department of Neurosurgery, RSUD Salatiga, Indonesia for the support.

## AUTHOR CONTRIBUTION

Muhamad Thohar Arifin and Yuriz Bakhtiar responsible for conception and design, or acquisition of data, or analysis and interpretation of data. Yuriz Bakhtiar, Muhamad Thohar Arifin, and Adrian Pratama responsible for drafting the article or revising it critically for important intellectual content; and. All author agree for the final approval of the version to be published.

## DISCLOSURE OF CONFLICTS OF INTEREST

The authors report no relevant conflict of interest, related to this study. They confirm reading the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## REFERENCES

1. Winn RH. Youmans & Winn Neurological Surgery. 7th edition. Philadelphia: Elsevier; 2017.

2. Bhigjee AI, Naidoo K, Patel VB, Govender D. Intracranial Mass Lesions in HIV-positive Patients – The KwaZulu/Natal Experience. *S Afr Med J*. 1999;89:1284-8.
3. Mochan A, Modi M, Modi G. Management of HIV-associated focal brain lesions in developing country. *Q J Med*. 2004;97:413-21.
4. Greenberg MS. Handbook of Neurosurgery. 8th edition. New York: Thieme; 2016.
5. Tan IL, Geldern GV, Smith BR, Mateen FJ, McArthur JC. HIV-associated opportunistic infections of the CNS. *Lancet Neurol*. 2012;11:605-17.
6. Cunliffe CH, Fischer I, Monoky D, Law M, Revercomb C, Elrich S, et al. Intracranial Lesions Mimicking Neoplasms. *Arch Pathol Lab Med*. 2009;133:101-23.
7. Directorate General of Disease Prevention and Control, Ministry of Health, Republic of Indonesia. Report on the Development of HIV AIDS & Sexually Transmitted Infectious Diseases (PIMS), Quarter II of 2019; 2019.
8. Vidal JE. HIV-related Cerebral Toxoplasmosis Revisited: Current Concepts and Controversies of an Old Disease. *Journal of International Association of Providers of AIDS Care*. 2019;18:1-20.
9. Naqi R, Azeemuddin M, Ahsan H. Cerebral toxoplasmosis in a patient with acquired immunodeficiency syndrome. *J Pak Med Assoc*. 2014;316-8.
10. Ramachandran R, Radhan P, Anand R, Subramanian I, Santosham R, Sai V. CNS toxoplasmosis in immunocompetent individuals. *Radiology Case Reports* 2014;1:908.
11. Laing RB, Flegg PJ, Brettle RP, Leen CL, Burns SM. Clinical features, outcome and survival from cerebral toxoplasmosis in Edinburgh AIDS patients. *Int J STD AIDS*. 1996;7(4):258-64. doi: [10.1258/0956462961917933](https://doi.org/10.1258/0956462961917933).
12. Grommes C, DeAngelis LM. Primary CNS Lymphoma. *J Clin Oncol*. 2017;35:2410-8.
13. Tan CS, Koralknik IJ. Beyond progressive multifocal leukoencephalopathy: expanded pathogenesis of JC virus infection in the central nervous system. *Lancet Neurol*. 2010;9(4):425-37.
14. Nery FG, Franca M, Vasconcelos C. Progressive Multifocal Leukoencephalopathy in an HIV Patient With High CD4 T Cell Count: A Case Report. *J Med Cases*. 2010;1(3):103-7.
15. Maziarz EK, Perfect JR. Cryptococcosis. *Infect Dis Clin North Am*. 2016;30(1):179-206.

16. Paiva ALC, Aguiar GB, Lovato RM, Zanetti AVD, Panagopoulos AT, Veiga JCE. Cryptococcoma mimicking a brain tumor in an immunocompetent patient: case report of a extremely rare presentation. *Sao Paulo Med J*. 2018;136(5):492-6.
17. Ulett KB, Cockburn JW, Jeffree R, Woods ML. Cerebral cryptococcoma mimicking glioblastoma. *BMJ Case Rep*. 2017;2017:bcr2016218824. doi: [10.1136/bcr-2016-218824](https://doi.org/10.1136/bcr-2016-218824).
18. Shih RY, Koeller KK. Bacterial, Fungal, and Parasitic Infections of the Central Nervous System: Radiologic-Pathologic Correlation and Historical Perspectives. *Radio Graphics*. 2015;35:1141-69.
19. Mensah KA, Akoto H. Imaging Appearances, Diagnosis and Treatment of Atypical Brain Abscess: Review of the Literature. *AJMAH*. 2017;3(1):1-17.
20. Vidal JE, Hernandez AV, Oliveira ACP, Souza AL, Madalosso G, Silva PRM, et al. Cerebral Tuberculoma in AIDS Patients A forgotten diagnosis?. *Arq Neuropsiquiatr*. 2004;62(3-B):793-6.
21. Monteiro R, Carneiro JC, Costa C, Duarte R. Cerebral tuberculomas - A clinical challenge. *Respiratory Medicine Case Reports*. 2013;9:34-7.
22. Chow FC, He W, Bacchetti P, Regan S, Feske SK, Meigs JB, et al. Elevated rates of intracerebral hemorrhage in individuals from a US clinical care HIV Cohort. *Neurology*. 2014;83:1705-11.
23. Hatleberg CI, Ryom L, Kamara D, Wit SD, Law M, Philips A, et al. Predictors of Ischemic and Hemorrhagic Strokes Among People Living With HIV: The D:A:D International Prospective Multicohort Study. *E Clinical Medicine*. 2019;13:91-100.



This work is licensed under a Creative Commons Attribution