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

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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 to 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 tuberculosis 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.

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⁺ count less than 200/μL, the presences specific opportunistic infections or malignancies classified as AIDS-defining illnesses serve as confirmatory assessment techniques. Moreover, 70% of the total HIV patients are known to present neurological disorders, of which about 10-20% demonstrate intracranial focal mass lesions during radiologic examination. This phenomenon is possibly triggered by opportunistic infections, HIV-related tumors, and cerebrovascular disorders. However, toxoplasmosis, primary central nervous system lymphoma (PCNSL), progressive multifocal leukoencephalopathy (PML), cryptococcal abscess, and tuberculosis have been identified as the major causes of infections. The most predominant perpetrators are tuberculosis and toxoplasma infection.

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

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.\(^5\) 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,
CASE REPORT

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) E₂M₄V₂. 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, particularly associated with: (1) HIV infections, (2) opportunistic infections, (3) AIDS-related malignancies,

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+ 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. 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.
and (4) complications from HIV medications. 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.

**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. 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. 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.

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. The PML is also not highlighted as a differential diagnosis in both cases for similar reasons. 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 such as meningeal irritation, and paralysis of the cranial nerves after the infection reaches the brain through hematogenous means. The patient with HIV/AIDS in case 2 was assumed to have a predominance of seizures, while the head CT scan 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.

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

The Patient with HIV/AIDS in case 2 presented 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 tuberculosis and cryptococcal abscesses 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.\textsuperscript{22} This manifestation potentially increases to 4.46 times in patients with CD4\textsuperscript{+} count <200 cells/mL,\textsuperscript{23} and is likely associated with HIV-induced vasculitis.\textsuperscript{24} 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.\textsuperscript{25} 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, tuberculosis, 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**

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**AUTHOR CONTRIBUTION**

Muhammad Thohar Arifin and Yuriz Bakhtiar responsible for conception and design, or acquisition of data, or analysis and interpretation of data. Yuriz Bakhtiar, Muhammad 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**


