CEREBRAL TOXOPLASMOSIS WITH DECUBITUS ULCERS AS HUMAN IMMUNODEFICIENCY VIRUS COINFECTION: A NEGLECTED CASE FROM A SEROCONCORDANT COUPLE

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ABSTRACT

Cerebral toxoplasmosis is a severe opportunistic infection of the advanced stage of human immunodeficiency virus (HIV). Complications of decubitus ulcers are a threat that increases morbidity and mortality. A 56-year-old woman came with an open wound on her lower back, accompanied by weakness of the right limbs and left leg for a month. There was a history of brain swelling with craniotomy intervention a month before admission. The patient and her husband were confirmed HIV positive. On physical examination, there was a decubitus ulcer in the sacral region with right hemiparesis and left leg monoparesis. CD4+ levels were 42 cells/µL (4.9%), and anti-toxoplasma IgG was more than 300 IU/mL. There was a cerebral abscess in the left hemisphere with midline deviation to the right on a head CT scan with contrast. Head MRI with contrast showed tuberculomatosis with multiple nodular lesions in the right and left hemispheres. Surgical debridement was performed. Pharmacological therapy includes antiretroviral, antibiotics for cerebral toxoplasmosis, and prophylaxis. Improving awareness of HIV in seroconcordant couples is important for the early management and prevention of severe opportunistic infections and their complications.

Keywords: Cerebral Toxoplasmosis; Coinfection; Decubitus Ulcers; HIV; Seroconcordant

Received: Month Year, *Accepted: Month Year,* *Published: Month Year*

INTRODUCTION

Human immunodeficiency virus (HIV) infection remains a global health problem. Around 39.9 million people worldwide are living with HIV in 2023, with the majority of them being adults aged 15-49 years. Around 86% of them know their HIV status, while there are still 5.4 million people who do not know they are living with HIV. The mortality remains high, but the trend is decreasing every year because of increased use of antiretroviral therapy (ART) (UNAIDS, 2024). In Indonesia, the number of HIV infection was 543 thousand people with prevalence varying according to population, such as men who have sex with men (MSM) at 25.8%, injecting drug users at 28.8%, transgender people at 24.8%, and female sex workers at 5.3% (Kemenkes RI, 2022).

The high stigma and discrimination against people living with HIV/AIDS (PLWHA) in society have an impact on individuals, families, communities, and health service providers. The UNAIDS report (2023) states that 4.6% of PLWHA experience stigma and discrimination, and the level of violence against women PLWHA reaches 32%. Social threats to PLWHA make some people afraid to reach health facilities, thus encouraging people to be neglected. Fear of

carrying out voluntary counseling and testing (VCT) in risk groups causes delays in HIV diagnosis, expansion of access to pre-exposure prophylaxis (PrEP) for vulnerable groups, and ART for PLWHA who develop into advanced stages of HIV, which has a high risk of complications and mortality (Adiansyah *et al*., 2023).

Cerebral toxoplasmosis is a severe opportunistic infection of HIV/AIDS caused by the obligate intracellular parasite, *Toxoplasma sp.* The prevalence rate in 2019 from several hospitals in Bandung, Indonesia, is 12.9%. Cerebral toxoplasmosis can occur in 30-40% of PLWHA who do not receive toxoplasmosis prophylaxis, especially with an HIV viral load of more than 50 copies/mL and a CD4+ lymphocyte count of less than 100/mm³ (Dian *et al*., 2023). Common clinical manifestations are impaired mental status (75%), neurological deficits (70%), headache (50%), fever (45%), weakness, and cranial nerve disorders. Cerebral toxoplasmosis is a neurological emergency that requires acute-phase treatment and maintenance to prevent recurrence (Yostila & Armen, 2018).

Decubitus ulcers are local tissue damage caused by compression of soft tissue over bony prominences and external pressure over a long time. The prevalence rate varied. Generally, it occurs in 5-11% of acute care settings and 15-25% of long-term care settings. Some high-risk factors associated are immobilization, decreased pain sensation, and malnutrition (Mahmuda, 2019). Decubitus ulcers in cerebral toxoplasmosis patients develop as a complication of neurological deficits that lead to prolonged periods of bed rest, which reduce quality of life (Elsheikha *et al*., 2021). Immunodeficiency and poor nutritional status can delay wound healing due to altered immune response. Thus, it potentially causes other complications, including infection and sepsis (Cidral *et al*., 2016).

CASE

A 56-year-old married woman came to the PKU Muhammadiyah of Surakarta Hospital with a main complaint of a single open wound on her lower back for a month. The wound was covered with a black layer and pus at the edges, the depth could not be estimated. Initially, she felt itching in her lower back and a small wound that progressively enlarged over time. Other complaints were fatigue, mouth ulcers, weakness in the right limbs and left leg, unable to speak but still understand speech, difficulty opening her mouth, and difficulty swallowing. On medical history, she was hospitalized with fatigue, walking and memory disorder, and weakness in her extremities a month before admission. She also had intermittent fever, soft yellow diarrhea five times a day without mucus or blood, and weight loss. Supporting examinations from her previous hospitalization showed that she was HIV positive with a brain swelling that required intervention. She underwent craniotomy and received antibiotics for cerebral toxoplasmosis at that time. On a deep alloanamnesis, she had never experienced vaginal discharge, multiple sexual partners, shared needles, tattoos, donated blood, or received blood transfusions. Furthermore, she had never smoked, consumed alcohol, or abused drugs. Her husband had previously been confirmed HIV positive two months before, with complaints of weight loss, painful urination without discharge, diarrhea, fever, bloody coughing, and stomach infection. He never admitted anything about his probable HIV transmission. Thus, several risk factors could not be ascertained.

On physical examination, she was *compos mentis* (E4M5Vafasia), BP 107/72 mmHg, HR 94 beats/minute, RR 20 breaths/minute, T 36.7 ℃, SpO2 97% with nasal cannula 3 liters/minute. Head inspection showed a post-craniotomy lesion on the left temporal side (Figure 1). A single decubitus ulcer was found in the sacral region, approximately 11 x 9 cm, with a black covering along the wound and pus on the edge (Figure 2). Neurological examination revealed right hemiparesis and monoparesis of the left leg. Physiological reflexes were

biceps +1/+2, triceps +1/+2, patella +1/+1, and achilles +1/+1. Pathological reflexes were negative. Motor strength was 2/4/2/2 with normal sensitization. There was no peripheral edema with a normal capillary refill test (CRT).

Figure 1. Post-craniotomy with an asymmetrical head on the left temporal side

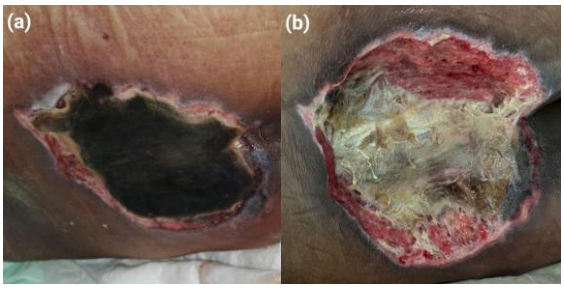

Figure 2. (a) A single decubitus ulcer lesion at admission and (b) post-debridement with a bone depth

Initial electrocardiogram (ECG) showed sinus tachycardia, HR 150 beats/minute. Laboratory examination showed erythrocytes 3.96 million/uL, Hb 13.1 g/dL, leukocytes 15.42 x 10^3/uL, platelets 369 x 10^3/uL, random blood glucose 127 mg/dL, SGOT 79 U/L, SGPT 59 U/L, PT 12.6 seconds, APTT 28.3 seconds, creatinine 0.5 mg/dL, albumin 2.9 g/dL, eGFR 125 ml/min, sodium 117.6 mmol/L, and potassium 4.58 mmol/L. Three methods of anti-HIV testing were confirmed reactive with an absolute CD4+ decrease of 42 cells/µL (4.9%) and a CD4:CD8 ratio of 0.07. Anti-toxoplasma IgG was more than 300 IU/mL. Pus culture from the sacral ulcer lesion showed *Escherichia coli* with multiple antibiotic resistance to ampicillin, ampicillin-sulbactam, ceftriaxone, and trimethoprim-sulfamethoxazole. Chest X-ray (CXR) showed bronchopneumonia suspected of pulmonary tuberculosis (TB) (Figure 3). Head CT scan (HCTS) with contrast showed cerebral abscess with extensive tentacle edema in the left hemisphere and midline deviation to the right of 1.2 cm. Head MRI with contrast showed multiple nodular lesions in the right and left hemispheres, approximately 3.5 x 2.8 x 3.5 cm, with extensive perifocal edema in the left temporal and midline deviation to the right of 0.5 cm (Figure 4).

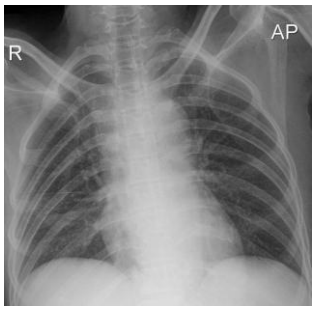

Figure 3. Bronchopneumonia with suspected pulmonary TB

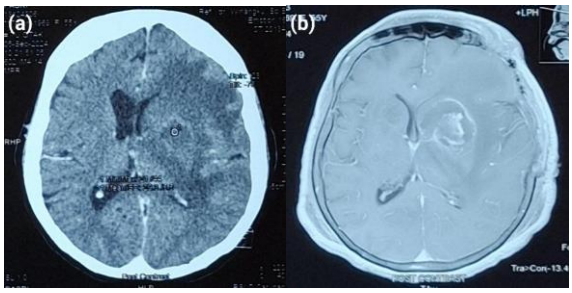

Figure 4. (a) Cerebral abscess with extensive tentacle edema in the left hemisphere on HCTS with contrast and (b) multiple nodular lesions in both hemispheres on head MRI with contrast

She was diagnosed with stage 4 HIV and cerebral toxoplasmosis coinfection with sacral decubitus ulcers. She was managed with surgical debridement for the ulcers, oral clindamycin 4 x 600 mg and cotrimoxazole 960 mg once daily after her cerebral toxoplasmosis medication for six weeks, ART TLD (tenofovir 300 mg, lamivudine 300 mg, dolutegravir 50 mg) once daily, ceftazidime injection 3 x 2 grams daily, oral moxifloxacin 300 mg once daily, and oral isoniazid 300 mg once daily for TB prophylaxis. Ikamicetin

ointment, 15 grams, was given to prevent infection in the post-debridement ulcer.

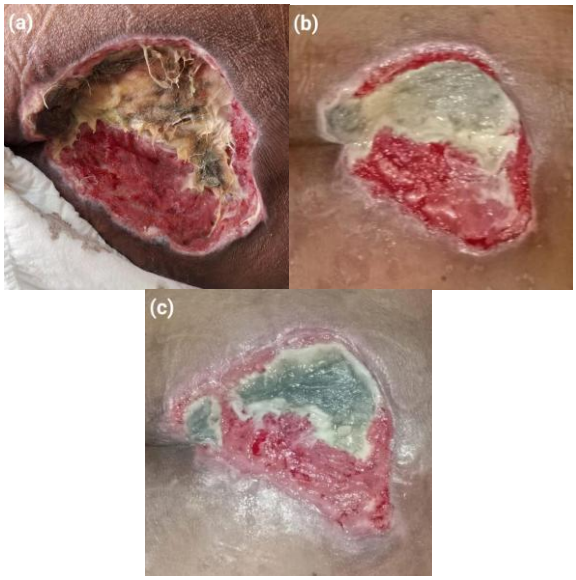

Figure 5. Wound healing progression of post-debridement ulcer on (a) day 3, (b) day 6, and (c) day 21 after discharge

After five days of hospitalization, she was allowed to be discharged with regular daily care of her post-debridement ulcer and following medication. Furthermore, she was advised to use a decubitus bed and antiseptic soap to prevent the occurrence of decubitus ulcers and other infections. She was followed up three, six, and twenty-one days after discharge with improved wound healing and general condition (Figure 5).

DISCUSSION

The diagnosis of HIV infection, in this case, was based on the presence of immunodeficiency symptoms, a history of positive HIV status in the partner, and confirmed with a laboratory test. Neurological deficits were found as a result of cerebral toxoplasmosis based on radiological study and the increase of anti-toxoplasma IgG, which led to immobilization and decubitus ulcers. Based on WHO criteria, the patient was diagnosed with stage 4 HIV coinfection with cerebral toxoplasmosis (WHO, 2021).

Cerebral toxoplasmosis is the most common intracranial opportunistic infection in HIV patients, which causes high morbidity and mortality. It occurs because of the reactivation of a latent infection and causes neurological symptoms, such as headache, disorientation, drowsiness, hemiparesis, and loss of consciousness (Laksono *et al*., 2024). It has predilection in the cortex and basal ganglia of the brain, which results in movement disorders, such as Parkinsonism, ataxia, chorea, ballismus, and rigidity. Other clinical manifestations are cranial nerve palsies, speech disorders, meningeal or cerebellar signs, psychiatric symptoms, and lethargy. Several diagnostic tools are used to confirm the clinical presentation through serological tests, cerebrospinal fluid (CSF) analysis, histopathology, and neuroimaging (Chandra, 2022).

Immobilization in cerebral toxoplasmosis can occur due to several factors related to the effects on the central nervous system (CNS), the development of infection, and immunodeficiency. Significant neurological deficits, including spastic motor disorders and altered consciousness, can result in prolonged immobility. Patients may be unable to move and change body position, increasing the risk of developing ulcers due to continuous pressure (Muchamad & Sofro, 2023). Prolonged pressure on certain areas, especially on bony prominences, causes ischemia and tissue necrosis, resulting in pressure ulcers (Mulianto & Rosmarwati, 2023). An altered immune system in HIV infection is associated with a slower healing process for decubitus ulcers. A systematic review showed that lower CD4+ counts correlated with longer healing times and increased susceptibility to wound infections in HIV-positive individuals (Ottu, 2022).

Patients with stage 3 or 4 HIV who are planned for ART and/or have a CD4 count <200 cells/µL (including pregnancy) are recommended to be given cotrimoxazole two weeks before the administration of ART. In this case, cotrimoxazole 960 mg was given from the beginning of diagnosis for six weeks because of the late diagnosis (Laksono *et al*., 2024). The standard therapy for cerebral toxoplasmosis is an initial dose of pyrimethamine 100 mg, followed by maintenance therapy of 50 mg in combination

with sulfadiazine 1000 mg every 6 hours or clindamycin 600 mg every 6 hours for 6 weeks. Since the patient was confirmed with cerebral toxoplasmosis, the patient was given clindamycin 600 mg after six weeks of prophylaxis (Dunay *et al*., 2018). Delaying ART administration reduces overlap side effects with cotrimoxazole, such as nausea, vomiting, hepatotoxicity, and others (Laksono *et al*., 2024).

Decubitus ulcers compromise the integrity of the skin and create an open wound that serves as a portal of entry for microorganisms. It increases the risk of infection, especially in grades 3 and 4 ulcers, where underlying tissue may be exposed (Mahmuda, 2019). Surgical wound debridement was successfully performed in this case. An antibiotic was applied to the post-debridement wound to prevent severe infection with a ceftazidime 2 gram and ikamicetin ointment. In cases where the ulcer is complicated, ceftazidime may be useful in combination with other antibiotics to increase efficacy against multidrug-resistant organisms. A retrospective study showed that a combination of topical and systemic antibiotics is particularly noteworthy when the ulcer is infected or there is a presence of cellulitis (Mulianto and Rosmarwati, 2023).

Other medications are also given to our patient because of the suspicion of pulmonary TB. Moxifloxacin is effective against several pathogens associated with community-acquired pneumonia (CAP) and bronchopneumonia involving multiple bacterial agents (Kuzman *et al*., 2014). HIV causes a decrease in CD4+ T cells, which are critical for mounting an effective immune response to TB (Yang *et al*., 2022). Therefore, prophylaxis should be administered in conjunction with ART. Isoniazid has been shown to significantly reduce the incidence of active TB among individuals with latent TB infection. The standard dose in adults is 5-15 mg/kg for 6 or 9 months with a maximum dose of 300-900 mg (CDC, 2020).

In this case, the patient was diagnosed late due to fear of stigma and discrimination. Furthermore, low knowledge about HIV in patients and families made it difficult to provide appropriate advice. Several factors cause delays in HIV diagnosis, including sociodemographic factors and health system barriers. Lack of awareness about HIV routine testing in high-risk individuals is a barrier to the current public health. Moreover, seroconcordant couples are advised to check their HIV status because sexual health outcomes are interrelated between partners (Bendera *et al*., 2024). Absence of checking HIV status leads to delays in management that contribute to severe disease. A study has reported that delayed HIV diagnosis is associated with poor treatment response. Moreover, HIV infection with lower CD4+ counts tends to have a higher mortality rate (Candevir *et al*., 2023). Improving awareness about HIV testing among couples is needed to prevent it. An open discussion between partners significantly increases the couple's willingness to take the test together. Studies show that couples who discuss HIV testing are almost five times more likely to participate in VCT. Therefore, management can be performed earlier to reduce severe complications (Muhindo *et al*., 2015; Hampanda *et al*., 2023).

CONCLUSION

A neglected stage 4 HIV with cerebral toxoplasmosis coinfection that progressed to a sacral decubitus ulcer has been reported. The diagnosis was confirmed based on clinical presentation, laboratory, and radiological study. Several medications, including prophylaxis, were administered. Surgical debridement was performed for the ulcer, with a good improvement in post-debridement wound healing along follow-up. A delayed management of HIV infection and its complications could have been prevented by improving awareness among high-risk couples, sexual partners, and the community. Therefore, comprehensive management can be performed to reduce morbidity and mortality.

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