

Case Report

People living with HIV presenting with hemiparesis: what are the possible causes?

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ABSTRACT

People living with HIV (PLWH) are commonly associated with opportunistic infections, particularly with low CD4 count, less than 200 cells/ μ L. Neurological manifestation can be occurred 70% in PLWH and the most symptoms is hemiparesis, seizure, headache, behavioural changes, decrease of consciousness, and cognitive impairment but depends on the localization of the brain lesions. We present a case of 53-year-old man with initial presentation of right hemiparesis and was on highly active antiretroviral therapy (HAART). With laboratory and CT-scan result, the patient diagnosed with stroke ischemic and occurred at the same time with toxoplasma encephalitis (TE) as an opportunistic infection. In PLWH, many possible causes involve central nervous system-caused hemiparesis. The initial differential diagnosis should be considered to prevent delayed treatment and potential of severe complications.

Keywords: Hemiparesis, HIV, PLWH, Stroke, TE

INTRODUCTION

Neurological manifestation can be occurred 70% in PLWH leading to morbidity and mortality.^{1,2} Most common occurred in late stages with the progression of the immunodeficiency but also can be affected in every stage of the HIV infection. Neurological problems associated with HIV can arise either directly from the HIV infection itself or indirectly due to opportunistic infections. These problems are caused by inflammatory, demyelinating, or degenerative processes.³

The neurological symptoms vary based on infection stage, opportunistic infections, the level of immunosuppression, and whether the patient is receiving HAART.^{1,2}

In this case report, we present of possible diagnosis in PLWH with neurological manifestation can be occurred with multiple diagnosis such as stroke ischemic and TE at the same time.

CASE REPORT

A 53-year-old man was admitted to a hospital with a clinical manifestation of right-sided hemiparesis started 1 week ago. He had no slurring of speech or facial drooping. He also has no complaints neither of headache nor fever. He also has no history of nausea, vomiting or diarrhoea. He was on HAART with regimen TLD (Tenofovir, lamivudine, and dolutegravir) for 6 months and has a history of tuberculous lung with 6 months complete with anti-tuberculous drug (ATD) 1 year ago. He also denied history of hypertension, diabetes, hyperlipidaemia, and smoking.

On physical examination, the level of consciousness was *compos mentis*, blood pressure 170/110 mmHg, regular heart rate 72 times per minute, respiratory rate 20 times per minute, temperature 36.8°C, and oxygen saturation 99% on room air. The pupils are equal, reactive, and round to light and accommodation. The neurological examination showed no meningeal signs, hyperreflexia, increased

muscle tone, right hemiparesis with motoric strength of 3/5 in both upper and lower extremities, sensory deficits and cortical findings were absent. No generalized lymphadenopathy was found on the examination.

Laboratory results found WBC 6.670/ μ L, hemoglobin 11.7 g/dL, and platelet 191.000/ μ L. Electrolyte examination found sodium 141 mmol/L, potassium 2.8 mmol/L, and chloride 103 mmol/L. Random blood sugar examination was 113 mg/dL. Liver function and renal function test was within normal range. Cholesterol total 154 mg/dL, direct HDL 57 mg/dL, direct LDL 84 mg/dL, and triglyceride 94 mg/dL. The chest radiologic examination showed within normal with no pulmonary infiltrates. Computed tomography (CT) scan findings subacute ischemic cerebral infarction at left internal capsula, chronic ischemic cerebral infarction at right thalamus, right and left corona radiata, and left pedunculus cerebellum, ischemic of the small vessel at anterior peri cornu et right and left ventricle lateralis posterior (Figure 1). The patient was assessed with ischemic stroke, hypertension stage II, and hypokalemia at the initial hospitalization, so he was treated with potassium chloride 25 meq per 24 hours, aspirin 80 mg OD, amlodipine 10 mg OD, methylprednisolone injection 62.5 mg BID, and citicoline injection 500 mg BID.

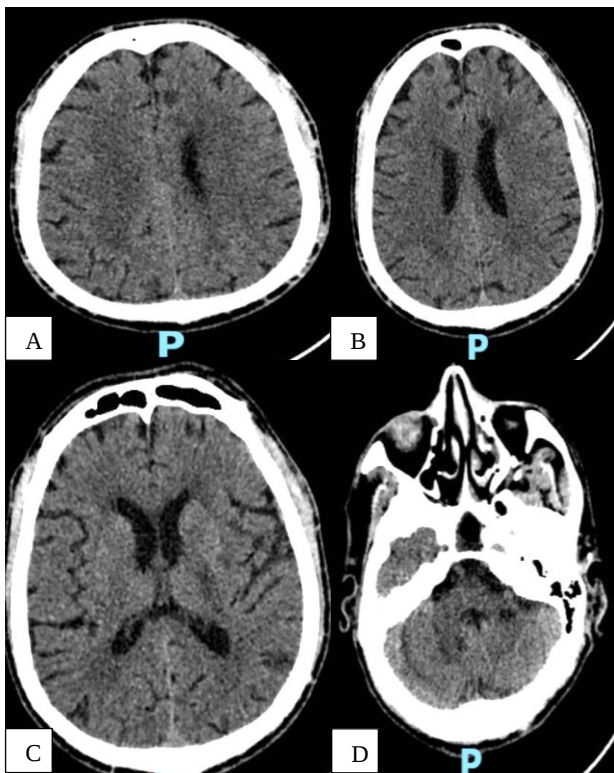


Figure 1 (A-D): Patient's head CT-scan examination findings.

After the potassium was corrected with a result of 3.7 mmol/L, the right hemiparesis still persisted with improvement in motoric strength at the upper extremities at 4/5 and at the lower extremities still at 3/5 points. Then the patient was checked for toxoplasma IgG antibodies and

the result is >20.000 considered to be positive, indicating toxoplasma infection.

The patient was given clindamycin 600 mg QID, cotrimoxazole 960 mg BID, and methylprednisolone injection 62.5 mg BID was continued from the first day of admission until the patient was discharged. After 8 days on the ward, the patient was discharged with residual right hemiparesis on maintenance of clindamycin 600 mg QID, cotrimoxazole 960 mg BID, methylprednisolone 4 mg BID, aspirin 80 mg OD, and amlodipine 10 mg OD and continuing ARV with regimen TLD OD.

DISCUSSION

The patient's clinical presentation with pure motor hemiparesis, we initially expected an ischemic stroke caused by small-vessel disease with CT scan findings of hypodense lesion with a result of subacute and chronic ischemic cerebral infection represent stroke ischemic. HIV vasculopathy is also linked with a higher incidence of cerebrovascular accidents due to procoagulant tendencies.³ Stroke incidence also shown consistently increased 1.4-1.5 fold higher in HIV infection.⁴ HAART also increases the risk of stroke (2-6%) in PLWH, although still controversial with the data on the frequency of stroke, particularly ischemic stroke. Ischemic stroke was also reported soon after starting HAART, but the mechanism is still unclear and should exclude the unmasking of opportunistic infections as part of immune reconstitution (IRIS).^{1,4} Therefore, the patient was also given aspirin and antihypertensive at initial treatment.

Other than vasculopathy in HIV patients, infection in HIV can also cause ischemic strokes through several mechanisms such as cardioembolism, opportunistic infections, neoplasia, coagulopathy, and hyperviscosity.⁴ HAART also known to cause metabolic syndrome such as nucleoside reverse transcriptase inhibitors and some protease inhibitors increased prevalence of type II diabetes and glucose intolerance by inhibiting cellular glucose uptake and insulin resistance, and also increased cholesterol, triglycerides, and dyslipidemia. Protease inhibitors also added risk to thrombotic events because increased of fibrinogen, d-dimer, and protein S deficiency.⁴

After evaluated from the acute onset of time, no risk factors and history of diabetes, hypertension, smoking, and the laboratory result of lipid profile was normal, we also suspected with opportunistic infection in this patient. The most possible of opportunistic infection in PLWH is TE, so we examined the laboratory testing of toxoplasma IgG antibodies and the result is >20.000 and CT scan patient's finding ischemic of the small vessel also showed vasculitis represent the patient also infected with TE. TE affects 3-40% of individuals with HIV infection and the most common opportunistic infection causes focal to diffuse encephalitis or other focal cerebral lesions.⁵ The clinical manifestations of cerebral toxoplasmosis are varied, particularly in PLWH such as fever, headache, altered

sensory and/or motor function with focal neurological deficit to disorientation, hemiparesis, confusion, decreased level of consciousness, ambulatory gait, speech abnormalities, and seizures associated to a focal lesion or disseminated encephalitis.^{5,6}

In immunosuppression advanced disease and CD4 count ≤ 200 cell/mm³ more than 90% of cases of focal lesion in CNS is because of toxoplasmosis.³ In Kalavathi et al study showed 9 cases from 15 cases (60%) with symptoms of focal neurological deficits hemiparesis with UMN facial nerve palsy.³

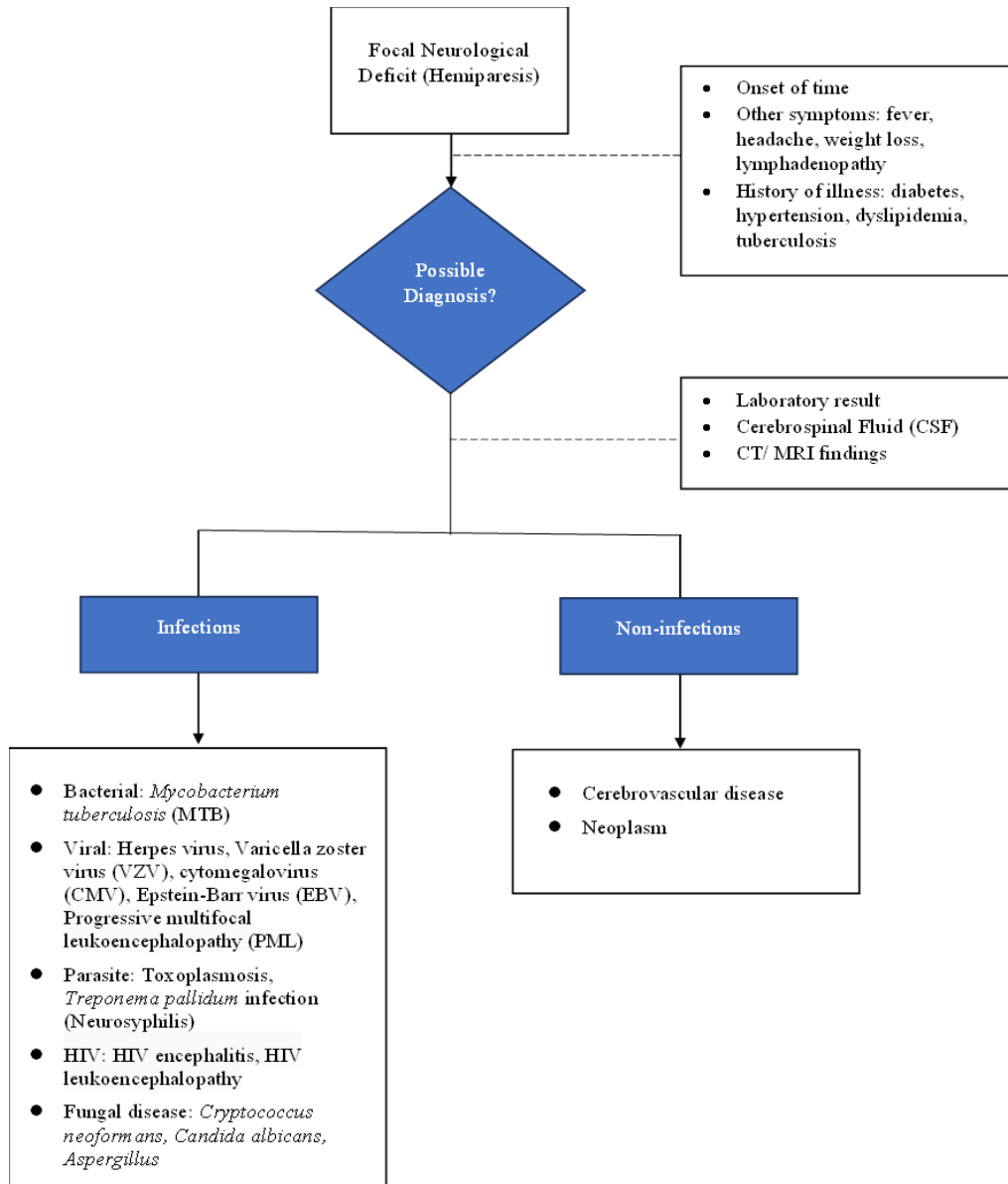


Figure 2: Algorithm to considering possible causes of hemiparesis in PLWH.

CT or magnetic resonance imaging (MRI) also can be shown multiple ring-enhancing lesions in typical locations with surrounding edema strongly suggestive of cerebral toxoplasmosis.^{1,7} Cerebral toxoplasmosis is typically diagnosed through MRI in patients with clinical suspicion, followed by detection of *Toxoplasma gondii* in blood serum, body fluids including cerebrospinal fluid (CSF), and/or biopsied or autopsied CNS tissue.⁵ The diagnosis should be confirmed with antibody and PCR testing.¹ Serological testing for IgG or IgM, but not always show positive results. Lumbar puncture should be performed to

monitored regularly and the response to treatment should be evaluated by improvements in signs and symptoms, overall well-being, and weight gain.³

First-line treatment using a combination of pyrimethamine and sulfadiazine but co-trimoxazole (trimethoprim-sulfamethoxazole) has also been proven to be effective.¹ Clindamycin can be the alternative therapy to sulfadiazine but has higher cutaneous side effects.⁸ Folinic acid also must be given along with pyrimethamine to prevent marrow suppression and hematologic toxicity.^{8,9} The

recommended initial therapy is at least given for 6 weeks and maintenance therapy is commonly continued lifelong to prevent recurrence or discontinued if patients asymptomatic and maintained CD4+ counts >200 cells/ μ L for at least 6 months.⁸

Even though the patient is on HAART, the prevalence of opportunistic infections remains high in patients adhering to their medications. Progression of HIV infection and level of patient immunity influence the possible opportunistic infection. Milder infections affected skin infections such as herpes zoster in an early stage, whereas in serious infections affected CNS such as toxoplasmosis or cryptococcal meningitis in late stages with severe immune suppression.⁶

The central nervous system involvement is hard to differentiate because have a similar clinical manifestation depending on the localization of the brain lesions especially in PLWH with a high risk of opportunistic infection. Considering possible causes of hemiparesis in PLWH should be divided into infection and non-infection diseases to make a possible differential diagnosis.¹⁰ (Figure 2) We also present from several case report and literature review of PLWH with clinical manifestation and added information about etiology, symptoms, additional laboratory test, neuroimaging findings, and the definitive treatment from most common opportunistic infections. (Table 1).

Table 1: The possible causes of common opportunistic infections in PLWH.

Possible causes	TE ^{11,12}	ME TB ¹¹	Neuro-syphilis ^{13,14}	PML ¹⁵⁻¹⁷	CMV ¹⁸⁻²⁰	VZV ²¹
Etiology	<i>Toxoplasma gondii</i>	<i>Mycobacterium tuberculosis</i>	<i>Treponema pallidum</i>	JC virus	Cytomegalovirus	Varicella zoster virus
Symptoms	Fever, headaches, psychomotor or behavioural changes, memory loss	Fever, persistent cough, weight loss, night sweats	Headache, loss of hearing and vision, dementia, sensory ataxia	Gait disturbances, cognitive impairment, progressive weakness, speech disturbances, visual field defects	Retinitis, uveitis, polyradiculopathy, pneumonia, enteritis	Bilateral weakness
Laboratory test	IgG antibodies, PCR, NAAT	GeneXpert, culture, AFB staining	VDRL, <i>T. pallidum</i> agglutination assay	PCR, JCV DNA	CMV IgG, CMV IgM, CMV Antigen PP65, CMV DNA PCR	VZV PCR, VZV IgG
Neuro-imaging CT/MRI	Multiple ring-enhancing lesions surrounding edema Location: Basal ganglia and cortico-sub-cortical union	Tuberkuloma	Left hemipons infarction, vasculitis	Single or multiple and round- or sector-shaped abnormal in periventricular or subcortical white matter	-	Lesions in deep white matter Large-vessel occlusions, small-vessel infarcts, intraparenchymal and subarachnoid hemorrhage
Therapy	Sulfadiazine and pyrimethamine, clindamycin	ATD (2 RHZE + 10RH) and corticosteroids	Penicillin G 21 days	Corticosteroids, but no specific treatment proven	Valganciclovir IV (5 mg/kg) BID within 3 weeks then 1 dose/day	Acyclovir IV 14 days and corticosteroid

ME TB=Meningoencephalitis tuberculosis; TE=Toxoplasma encephalitis; PML=Progressive multifocal leukoencephalopathy; CMV=Cytomegalovirus; VZV=Varicella zoster virus; JC virus= John Cunningham polyomavirus; VDRL=Venereal disease research laboratory (VDRL); NAAT=Nucleic acid amplification assays; ATD=Anti-tuberculous drug.

CONCLUSION

The patient presented hemiparesis in PLWH must be thought of the possible caused of diagnosis. The neurological manifestation in PLWH so challenging, as the symptoms are not specific and depends on the affected brain lesion, they can be misdiagnosed so the initial differential diagnosis should be made to prevent the delayed treatment and potential of severe complications of diseases with worsening long-term outcomes in patients.

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