Neurological complication in HIV patients

K Ritarwan*

Department of Neurology, Faculty of Medicine Universitas Sumatera Utara, JalanBunga Lau No 17, KemenanganTani, Medan Tuntungan, Kota Medan, Sumatera Utara-20136, Indonesia
*Corresponding author: kiking@usu.ac.id, kikingritarwan@gmail.com.

Abstract. Human Immunodeficiency Virus (HIV) is neurotropic and immunotropic, making them massive destruction of both systems. Although their amount has been reduced, there is still neurological presentations and complications of HIV remain common in the era of combination antiretroviral therapy (cART). Neurological opportunistic infections (OI) occur in advanced HIV diseases such as primary cerebral lymphoma, cryptococcal meningitis, cerebral toxoplasmosis, and progressive multifocal encephalopathy. Neurological problem directly related to HIV appear at any stage in the progress of HIV disease, from AIDS-associated dementia to the aseptic meningitis of primary HIV infection observed in subjects with an immune deficiency. The replication of peripheral HIV viral is able to be controlled in the era of effective antiretroviral therapy. Non-HIV-related neurological disease such as stroke increased important as the HIV population ages.

1. Introduction

Human immunodeficiency virus (HIV) is both neurotropic and immunotropic virus causing progressive destruction to the immune system through infection of CD-4 T-Lymphocyte. Infection by HIV can involve the nervous system early in the course of the disease and at multiple levels from the brain to the peripheral nerve and muscle. Infection may be regarded as primary when the pathological changes are the direct result of HIV alone or secondary in the case of opportunistic infections.[1] The spectrum of HIV infection has gradually widened in the last decade. The global molecular epidemiological of HIV approximately 39.5 million of HIV infected adult and children.[1] In the South East Asian, there have been 5.6 million infections. The Asia Pacific NeuroAids Consortium (APNAC) study reported the people of Jakarta involve neurocognitive impairment was 11%, and neuropathy was 17%. In South Africa, the incidence of HIV was 2.1% (approximately 2400 new infection each day), and 40% of all death was due to AIDS.[2,3] Neurologic consequences of HIV are as primary and secondary disorders. The primary neurologic disorder complications are such as HIV dementia in adults, encephalopathy in children, HIV-associated myelopathy, and distal peripheral neuropathy. Secondary disorders complications are such as an opportunistic infection resulting from HIV immunosuppression.[3,4]

2. Neurologic complications associated with Human Immunodeficiency Virus

2.1. Primary CNS Lymphoma

There has been a marked increase in Central Nervous System (CNS) Lymphoma since the beginning of the AIDS Epidemic.[3] The increase cannot, however, be entirely attributed to AIDS because the
incidence of CNS Lymphoma has increased in the non-AIDS Population. The majority of primary CNS Lymphoma (PCNSL) occur sporadically in person with no apparent immune deficiency. The incidence of PCNSL among immunocompetent persons has been increasing over the past 25 years, with a peak incidence between age 50 and 65 years. PCNSL account for about 3% of all primary brain tumors in adults. PCNSL is disproportionately among patients with HIV infection or iatrogenic immunodeficiency states, particular recipients of organ transplants.[3,4]

Patients present with a combination of altered mental status and local neurogenic symptoms. Neurologic deficit often progresses rapidly, and the diagnosis appears around 2 to 3 months. A seizure is less common than among patients with gliomas. Lymphomatous infiltration of the posterior vitreous and/or retina (often asymptomatic) occur in 10% to 20% of patients and is usually asymptomatic when present at the time of initial diagnosis.[4] PCNSL is unique among primary brain tumors in that corticosteroids not only reduce peritumoral cerebral edema but also have a direct oncolytic effect and can produce significant (but temporary) clinical and radiographic improvement. PCNSL is highly responsive to whole brain RT (3,500 to 5,000 cGy), but following RT alone the tumor recurs quickly and the median survival is only 12 to 18 months. The most active single agents for PCNSL are methotrexate or cytarabine, which have good penetration into the brain parenchyma and CSF when given in high intravenous doses.[4,5]

2.2. Progressive Multifocal Leuкоencephalopathy (PML)
HAART has had a profound influence on survival in PCNSL patients and should be aggressively pursued.[4,5] PML is a multifocal demyelinating disease. There has been areport as a non-metastatic complication of neoplasia. PML agent of JC Virus (human papillomavirus) which infects and destroy oligodendrocytes.[6,7] Clinical features include progressive dementia, visual loss, spastic quadriaparesis, and ataxia. HIV associated PML has a median survival time of 2 to 4 months. The diagnostic procedure was EEG, MRI Scan, and CSF. The EEG showed a progressive slowing of activity over both hemispheres. The MRI scan reveals extensive white matter lesions bilaterally on T2-weighted imaging. The diagnosis is established by detection of JC virus DNA in the CSF by polymerase chain reaction or brain biopsy. The treatment included intravenous cytarabine improved survival.[8]

2.3. Cerebral Toxoplasmosis
There are three common opportunistic infections in patients with HIV infection, such as Toxoplasmosis, Cytomegalovirus, and Cryptococcus.[1,4] Toxoplasma gondii produces as asymptomatic infection in adults but can cause a severe and potentially fatal encephalitis in immunosuppressed persons, particularly following organ transplantation or complicating AIDS. Clinical features include seizure, focal neurological deficits, dystonia, hemiballismus, cranial nerve palsy, and ataxia. In 4-CD found less 200/mm³. The lumbar puncture, CSF analysis reveals lymphocytic pleocytosis, xanthochromia, and elevated protein contents.[4,6,8,9] The CT-scan shows singles or multiple contrasts enhancing lesion with nodular or ring-enhancement structures. The MRI scans are often more sensitive than CT scanning and reveal additional parenchymal lesions. Serum antitoxoplasma antibodies usually detected in active disease, but lower or absent do not exclude the diagnosis.[4]

The combination therapy with pyrimethamine is given in a loading dose 50 to 200mg/day for 2 to 6 weeks. A Combination of clindamycin and pyrimethamine is an effective alternative therapy for patients who cannot tolerate sulfadiazine.[4,8,10]

2.4. Cytomegalovirus infection
The CMV is a DNA virus of herpesvirus group, which produces swelling of infected cells that contain large intranuclear inclusion. The clinical features include altered mental status, seizures, thefocal neurological deficit. Cytomegalovirus DNA can be demonstrated in the CSF using the PCR reaction.
The use of the antiviral agent's ganciclovir or foscarnet, alone or in combination, increase survival time for several weeks.[5,6,9]

2.5. HIV associated neurocognitive disorder (HAND)

The HAND is the new definition of what used to be called AIDS Dementia Complex - the phenotype form of HIV encephalitis.[1] The hands is the most common cause of dementia in young people, and one of the treatable dementias. It usually has an insidious onset and chronic, progressive course, bringing disability to many HIV patients. Also, this syndrome may cause poor adherence to HIV care, job loss, decline of driving ability, and lesser adherence with HIV medication, with increased morbidity and mortality.[7,11]

In 2007, new criteria were published defining how to diagnosis HAND, including a wide spectrum of HIV related cognitive impairments, as follow:
- Asymptomatic neurocognitive impairment (ANI)
- Mild cognitive-motor disorders (MCMD)
- HIV associated dementia (HAD).

The definition asymptomatic neurocognitive impairments (ANI) was patients no complaint (asymptomatic) impairment in two or more neuropsychological and one or more standard deviation below the mean for matched controls. MCMD same as ANI but patients have mild complaints. HAD was significant impairment (loss of activities of daily living) and impairment in two or more neurophysiological symptoms and two or more standards deviation below the mean for matched controls.[8,11]

The creation of very active antiretroviral therapy (HAART) as the essential HIV treatment has led to significant reduction in the prevalence of severe HIV-associated dementia (HAD) and central nervous system (CNS) opportunistic infection.[8,11]

3. Conclusions

Neurological opportunistic infections and diseases occurred in advanced HIV disease are such as cryptococcal meningitis, primary cerebral lymphoma, progressive multifocal encephalopathy, and cerebral toxoplasmosis. Neurological disease directly related to HIV can be found in any stage of the progress of HIV disease, from AIDS-associated dementia to the aseptic meningitis of primary HIV infection observed in subjects with immune deficiency. In the era of effective antiretroviral therapy, where peripheral HIV viral replication is largely controlled, non-HIV-related neurological disease. Cranial CT and MRI present cortical atrophy, but the degree of atrophy has not correlated with the grade of dementia.

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