

Neurologic Disorders in the People Infected with HIV Receiving Antiretroviral Therapy

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Editorial

The Neuroinfectious Diseases primarily involve alterations in the functions of central nervous system (CNS) which radiates from spinal cord to muscles and nerves [1]. The clinical conditions in encephalitis, acquired immunodeficiency syndrome (AIDS) and meningitis may be appropriately cited here. In these diseases, the brain membrane invaded by any bacteria or virus causes inflammation which may lead to disability in an infected person or even death. The complications generated under these clinical conditions include dementia [2,3]. The people living with human immunodeficiency virus (HIV)/AIDS (PLWHA) may develop neuropathy and lymphoma. In order to manage the neuroinfectious diseases, significant advancements have been made, still their early diagnosis and suitable treatment stay as a major challenge. With extensive travel of the people these days worldwide, there is rampant spread of new infections of many viruses such as chikungunya, corona virus, dengue, Ebola virus, enterovirus, Hanta, influenza viruses, Marburg, severe acute respiratory syndrome, West Nile and HIV-1 in small span of time which cause re-emergence of many new diseases such as measles, meningococcal meningitis, poliomyelitis and AIDS. Though, the application of antiretroviral therapy (ART) drugs has caused significant decrease in the incidence of infections leading to many neurological disorders, still specific and early diagnosis is a challenge for proper treatment and management of such neurological syndromes which might reverse the immune-suppression [4]. The burden of undiagnosed central nervous system (CNS) infections so often goes largely under recognized [1,5]. According to the recent World Health Organization (WHO) reports, about 36 million people are infected with HIV-1 today; out of it, about 19 million people are receiving ART [6]. Though the ARTs have helped increase the longevity of PLWHAs, the neurologic complications develops in about 40 percent of them. The HIV-1 infection has been found to affect both the peripheral nervous system and the CNS causing neurologic dysfunctions. It also affects the muscles [7]. The symptoms of neurologic disorder in the HIV infected individuals may include the development of acute demyelinating polyneuropathy (AIDP) and aseptic meningitis [8]. However, the accurate and specific symptoms for diagnosis in such clinical conditions are still being explored. It has been found that HIV-1 infection leads to develop inflammation without invading the neurons which may cause harm to the spinal cord, brain and functioning of nerve cells [9]. Because of neurologic dysfunctions, the symptoms of behavioral changes, confusion, cognitive motor impairment, forgetfulness, damage to the peripheral nerves, headaches, loss of sensation, and progressive weakness develop [10-12]. In addition, the PLWHA using ARTs may complain for anxiety, depression, fever, lack of coordination, pain, swelling in organs, seizures, spinal cord problems, and even coma [7,8,13]. The clinical conditions of neurological complications

developed due to HIV-1 infections and ART intake could be of many types such as:

(1) Dementia: It relates trouble in thinking, remembering and understanding. In the advanced stage of HIV infections, a complex clinical condition of dementia or AIDS associated dementia develops which may impair the cognitive function. It can be life-threatening too [3].

(2) Fungal and parasitic infections: The opportunistic infections by a fungus may cause Cryptococcal meningitis which induces serious inflammation in the brain and spinal cord. Also a parasite infection can induce toxoplasma encephalitis. Under this clinical condition, symptoms of confusion, painful headaches and seizures may occur [14,15].

(3) Lymphomas: Tumors in HIV -1infected individuals may influence the brain [16].

(4) Neuropathy: It relates to the damage to neurons in the HIV-1 infected patients, causing pain or weakness. The HIV-1 infection in the advanced stage causes neuropathy [17].

(5) Neurosyphilis: An HIV-infected individual having syphilis is difficult to be treated. Such a clinical condition augments deterioration of CNS causing dementia, loss of hearing and vision, and difficulty in walking [18].

(6) Vacuolar myelopathy: It associates with the damage of myelin sheath of neurons and hence it develops holes in the nerve fibers and spinal cord. It results into development of problems in walking. It has been found prevalent in children and acute PLWHA [19].

(7) Psychological status: The PLWHA people often develop anxiety and depression with altered behavior [20].

(8) Opportunistic infections with other viruses: The PLWHA people invite several infections by other viruses such as cytomegalovirus infections can negatively affect cognitive function, hearing and vision and respiratory system. PLWHA may also develop inflammation in the brain and the spinal cord due infection by herpes virus [21].

It is evident from the existing reports that the exact modes of alterations in neuroimmune communications leading to development of neurological disorders in the PLWHA receiving ART have not been properly studied. HIV/AIDS, now recognized as a chronic disease, has been shown to cause neuroinflammation and dementia associated with high rates of death [9]. Further, the use of ART by HIV infected individuals has made their neuropathology highly complicated. Some workers have indicated that the PLWHAs receiving ARTs which are able to penetrate CNS and help clear HIV from brain via complete suppression of viral replication have frequently displayed depression,

neurocognitive dysfunction and neuropsychiatric problems [11,22-24]. These findings indicate that the etiology pertaining to these clinical conditions is fully due to replication of HIV in brain. Rather, it suggests that neuro HIV induced dysfunction could be due to perturbations in the neuroimmune cross-talk. The recent reports have pointed out that the application of ARTs alone or in the presence of other drugs may induce alterations in both the neurochemical cross talk and neurological disorders. Since the PLWHA continue taking ARTs for long term with other drugs, this clinical condition becomes acute in aged population infected with HIV [25]. The smooth neuron communication and CNS functions are driven by a proper network of interactions among different key factors produced by accessory/ supporting cells such as astrocytes, cytokines, CNS-microphages, microglia, neurons and neurotropic factors. These factors are responsible to maintain the health of neurons and sound bidirectional neurochemical communication [10-12]. A complex array of interactions among these factors helps maintain smooth nerve impulse transmission and protect the neurons. Any aberration in these interactions caused by HIV-1 infection or application of ART may cause changes in the functions of immune cells; some of them being associated to perturbations in the uptake of neurotransmitters, chemotaxis, CNS maintenance, damaged neurons, phagocytosis and production of cytokines. These changes lead to the occurrence of neuroinflammation and abnormal functions of neurons, which adversely affects neuronal circuits resulting into behavioural and cognitive defects [11].

In view of the growing incidences of neurological disorders in PLWHA using ARTs, extensive research is required to properly understand pathophysiological conditions of the person suffering from such clinical conditions so as to develop specific diagnostic tools and to start early treatment to save lives. Simultaneously, the implementation of proper guidelines for the management of this disease and generation of sufficient awareness among the masses by spreading information on these issues especially about the emerging and re-emerging infections are required.

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