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CHAPTER 29

NEUROLOGICAL MANIFESTATIONS OF HIV: UPDATE

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ABSTRACT

HIV-associated neurological manifestations compromise the central nervous system (CNS) and peripheral nervous system (PNS), resulting in complications such as encephalitis, progressive multifocal leukoencephalopathy (PML), HIV-associated dementia, and peripheral neuropathies. These conditions stem from inflammation and neurotoxicity induced by the virus, affecting immune and supportive cells such as microglia and astrocytes. This study conducted a systematic review using the Research Portal of the Virtual Health Library, with a search limited to Brazilian articles that addressed neurological alterations in HIV. Ten articles were selected based on strict inclusion criteria. The results pointed to representative data on the prevalence, pathophysiology, and available therapies for neurological complications of HIV, highlighting the persistence of neurocognitive disorders even in patients on antiretroviral therapy (ART). While PML was evidenced as a significant complication, with a low survival rate among those affected. The discussion reinforces that, despite the advances in ART, factors such as advanced age, prolonged immunosuppression, and barriers to drug penetration in the CNS contribute to the persistence of neurocognitive changes. Personalized therapeutic strategies, combined with multidisciplinary integration, are essential for the management of these patients. It is concluded that the neurological complications of HIV remain a relevant clinical challenge. Continuous research and the development of more effective therapies are indispensable to improve the quality of life of patients and reduce the impacts of these manifestations.

Keywords: HIV. Neurological complications. Diagnosis. Therapy. Revision.

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INTRODUCTION

The main characteristic of HIV (Human Immunodeficiency Virus) is its ability to compromise the immune system, but its manifestations in the central nervous system (CNS) and in the peripheral nervous system (PNS) are also of great clinical relevance (Aráujo et al. 1996).

HIV-associated infections can lead to a number of neurological complications, which can occur at different stages of infection. CNS HIV can cause encephalitis, progressive multifocal leukoencephalopathy, and HIV-associated dementia, resulting in cognitive, motor, and behavioral changes. These conditions are often related to inflammation and neurotoxicity induced by the virus and activated immune cells, which although it does not directly affect neurons, according to Gáscón (2022) HIV is associated with infections in CNS support cells, such as microglia and astrocytes. This group of cells constitutes a fundamental cell group to preserve the conditions of the interstitial environment in the nervous tissue. In addition, they play an essential role in coordinating immune responses, in addition to synthesizing and releasing amino acids that are used by neurons. In addition, these cells also regulate the balance of ions that are crucial for the action potential in neuronal membranes. However, the infection of these cells is considered a factor that can trigger inflammation in the nervous tissue resulting in pathogens mentioned above.

In the PNS, HIV can cause peripheral neuropathies, which is a secondary involvement due to infection by the virus and also the result of occasional pathogenesis such as those mentioned in the paragraph above. In this way, the symptoms manifest as pain, weakness and loss of sensation in the extremities. As already mentioned, these neuropathies may be a consequence of the virus itself or the use of antiretroviral drugs (Santana et al. 2023; Gáscón, 2022).

Also from this perspective, progressive multifocal leukoencephalopathy (PML) is a disease that causes the loss of myelin in the brain and is caused by the John Cunningham virus (JCV). PML was a rare and fatal complication associated with hematologic cancers or inflammatory disorders prior to the HIV epidemic. According to studies (Santana et al. 2023) between 1958 and 1982, only 230 cases were recorded. With the advent of combination antiretroviral therapy (CART), HIV has become the leading cause of PML-related immunosuppression. Also in this study, the indices show that 3 to 5% of people living with HIV/AIDS develop PML, with a survival rate of only 10% after one year.

METHODS

The systematic review was carried out in January 2025 using the Research Portal of the Virtual Health Library in order to identify relevant studies in Brazil on the complications and neurological manifestations caused by HIV in this group. To this end, the search process used the following keywords: (neurological complications) and (HIV), limited to the title, abstract and subject fields. This database was accessed through the Virtual Health Library (http://pesquisa.bvsalud.org). The research was carried out in stages and in the state of the art the sources were presented in LILACS (28), MEDLINE (10), CUMED (5), BINACIS (2), BDENF (1) and Index Psicologia (1).

Articles were selected that met the following criteria: articles developed in Brazil and containing information on neurological changes in HIV. A total of 10 articles were selected meeting these criteria. In this sense, this study aims to identify studies published in the literature that evaluate the neurological alterations caused by HIV.

RESULTS

The analysis carried out allowed us to obtain reliable and representative data of the clinical reality, thanks to the rigorous criteria adopted for this study. This article addresses the neurological manifestations associated with the Human Immunodeficiency Virus (HIV), exploring from the most prevalent alterations to those less frequent, but clinically relevant. The study gathers up-to-date data on the pathophysiology of these manifestations, as well as available and emerging therapies that aim to mitigate the neurological impacts of HIV, contributing to better clinical management of patients.

DISCUSSION

Human immunodeficiency virus (HIV) infection transcends immune impairment, also affecting the central nervous system (CNS) and resulting in several neurological complications. Since the beginning of the epidemic, it has been observed that HIV can cause cognitive deficits, behavioral changes, and motor dysfunctions, significantly impacting the quality of life of patients (Christo, 2010).

With the advent of antiretroviral therapy (ART), there has been a reduction in HIV-associated mortality. However, even with treatment, many patients continue to have HIV-associated neurocognitive disorders (HAND). These disorders range from asymptomatic impairments to more severe forms, such as HIV-associated dementia. Studies indicate that the prevalence of HAND remains significant in the era of ART, affecting higher cognitive functions such as memory, attention, and executive functions (Pansera, 2017).

The impact of HIV on the CNS occurs due to the invasion of the virus into resident immune cells, such as macrophages and microglia, which release neurotoxic inflammatory cytokines. This inflammatory process can lead to neuronal degeneration and synaptic dysfunction, impairing higher cognitive functions (Cordeiro, 2019).

Recent studies indicate that the prevalence of neurocognitive alterations in patients with HIV remains significant, even in patients under regular treatment. Research has identified high rates of cognitive impairment in cohorts of newly diagnosed patients (Silvany, 2018).

In the context of vertical transmission, the damage can be even more pronounced. Children infected with HIV during the perinatal period are at increased risk of cognitive impairment, as the infection occurs during a critical period of CNS development. These patients often have deficits in motor skills and school performance (Souza, 2014).

The diagnosis of HIV-associated neurocognitive alterations requires a multidimensional approach. It is essential to perform a detailed clinical evaluation, complemented by neuropsychological examinations, neuroimaging, and analysis of the cerebrospinal fluid. The use of biomarkers to detect CNS inflammation, such as the presence of specific proteins in the cerebrospinal fluid, has shown promise in the early identification of these alterations (Midya; Chakraborty, 2015).

Risk factors such as older age, detectable viral load, and low CD4+ T lymphocyte count for prolonged periods are associated with the development of these complications. Patients with a lower CD4+ T nadir have a higher susceptibility to HIV-associated dementia, indicating that severe immunosuppression is directly linked to the severity of neurological damage (Christo, 2010).

While ART has brought significant advances, challenges remain. Not all antiretroviral drugs have good CNS penetration, allowing HIV to persist in viral reservoirs. These reservoirs may be responsible for ongoing neurological damage, even in patients with an undetectable viral load in peripheral blood (Cordeiro, 2019).

Therapeutic combination strategies with drugs with high CNS penetration can minimize the impacts of neurological changes. However, the side effects and long-term toxicity of these drugs still pose a challenge in clinical practice (Pansera, 2017).

The therapeutic approach should be personalized and multidisciplinary. Proper management of neurocognitive alterations requires the integration of neurologists, infectious disease specialists, and mental health specialists, in addition to including psychosocial support (Silvany, 2018).

CONCLUSION

HIV-associated neurological changes continue to be a relevant concern, especially due to the longevity achieved by patients with the advent of ART. Continuous research and development of new therapies are key to better understanding the underlying mechanisms of these changes and promoting effective interventions that improve patients' quality of life. Thus, it is possible to see that since the introduction of TARC, there has been a significant reduction in the incidence of PML among patients with HIV, although this decrease has been smaller than in other opportunistic infections.

Therefore, understanding the neurological manifestations of HIV is crucial for effective management of the disease and for improving patients' quality of life. HIV-associated neurological changes represent a significant concern, especially with regard to the increase in patients' life expectancy due to advances in antiretroviral therapies (ART). Despite improvements in treatment, many patients continue to face neurocognitive disorders that affect their quality of life. Thus, the scientific review highlights the need for a multidisciplinary approach to the management of these complications, involving neurologists, infectious disease specialists, and mental health professionals.

The identification of risk factors, such as low CD4+ T lymphocyte count and advanced age, is essential to understand the severity of neurological manifestations. Continued research and the development of new therapies are essential to improve the understanding of the neurological changes caused by HIV and to implement interventions that can improve the quality of life of affected patients.

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