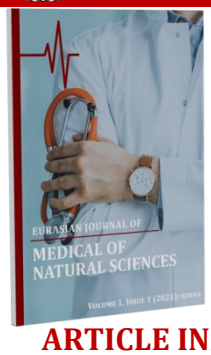
EURASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
Innovative Academy Research Support Center
IF = 7.921 www.in-academy.uz



CENTRAL NERVOUS SYSTEM INVOLVEMENT IN HIV INFECTION

Tadjiev Botir Mirkhashimovich
Kuldoshov Akhmedzhon Shamsuddinovich
Department of Infectious Diseases, Children's Infectious Diseases, Phthisiology and Pulmonology
Tashkent State Medical University
https://doi.org/10.5281/zenodo.15674101

ARTICLE INFO

Received: 08th June 2025
Accepted: 15th June 2025
Online: 16th June 2025

KEYWORDS

HIV infection, central nervous system, neurological complications, HIV-associated neurocognitive dysfunction (hand), cerebral toxoplasmosis, cryptococcal meningitis, progressive multifocal leukoencephalopathy, antiretroviral therapy, opportunistic infections, neuroinflammation.

ABSTRACT

Central nervous system (CNS) involvement in HIV infection is one of the most serious and commonly encountered neurological complications in HIV-positive individuals. The human immunodeficiency virus can penetrate nervous system cells at the early stages of infection, leading to a wide range of clinical manifestations—from mild cognitive impairment to severe dementia, as well as opportunistic infections and malignancies. The most common CNS-related conditions associated with HIV include HIV-associated neurocognitive disorders (HAND), cerebral toxoplasmosis, cryptococcal meningitis, and progressive multifocal leukoencephalopathy. Early diagnosis and timely initiation of antiretroviral therapy (ART) play a crucial role in the prevention and management of these conditions. This paper discusses the main clinical forms, mechanisms of CNS involvement, diagnostic methods, and current treatment strategies for neurological complications of HIV infection.

ПОРАЖЕНИЕ ЦЕНТРАЛЬНОЙ НЕРВНОЙ СИСТЕМЫ ПРИ ВИЧ-ИНФЕКЦИИ

Таджиев Ботир Мирхашимович
Кулдошов Ахмеджон Шамсуддинович
Кафедра инфекционных болезней, детских инфекционных болезней, фтизиатрии и пульмонологии
Ташкентский государственный медицинский университет
https://doi.org/10.5281/zenodo.15674101

ARTICLE INFO

Received: 08th June 2025
Accepted: 15th June 2025
Online: 16th June 2025

KEYWORDS

ВИЧ-инфекция, центральная нервная система, неврологические осложнения, ВИЧ-ассоциированная

ABSTRACT

Поражение центральной нервной системы (ЦНС) при ВИЧ-инфекции является одним из наиболее серьезных и часто встречающихся неврологических осложнений у ВИЧ-инфицированных лиц. Вирус иммунодефицита человека может проникать в клетки нервной системы на ранних стадиях инфекции, что приводит к широкому спектру клинических проявлений — от легких когнитивных нарушений до тяжелой деменции, а также оппортунистических инфекций и злокачественных новообразований. Наиболее распространенные состояния

EURASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
Innovative Academy Research Support Center
IF = 7.921 www.in-academy.uz

нейрокогнитивная дисфункция (рука), церебральный токсоплазмоз, криптококковый менингит, прогрессирующая мультифокальная лейкоэнцефалопатия, антиретровирусная терапия, оппортунистические инфекции, нейровоспаление.

ЦНС, связанные с ВИЧ, включают ВИЧ-ассоциированные нейрокогнитивные расстройства (HAND), церебральный токсоплазмоз, криптококковый менингит и прогрессирующую мультифокальную лейкоэнцефалопатию. Ранняя диагностика и своевременное начало антиретровирусной терапии (АРТ) играют решающую роль в профилактике и лечении этих состояний. В данной статье обсуждаются основные клинические формы, механизмы поражения ЦНС, методы диагностики и современные стратегии лечения неврологических осложнений ВИЧ-инфекции.

MARKAZIY NERV TIZIMINING ZARARI IN OIV INFEKTSIONLARI

Tojiyev Botir Mirhashimovich
Qo'ldoshov Axmedjon Shamsuddinovich
Yuqumli kasalliklar, bolalar yuqumli kasalliklari, ftiziatriya va pulmonologiya kafedrasi
Toshkent davlat tibbiyot universiteti
https://doi.org/10.5281/zenodo.15674101

ARTICLE INFO

Received: 08th June 2025
Accepted: 15th June 2025
Online: 16th June 2025

KEYWORDS

OIV infektsiyasi, markaziy asab tizimi, nevrologik asoratlar, OIV bilan bog'liq neyrokognitiv disfunktsiya, miya toksoplazmozi, kriptokokk meningit, progressiv multifokal leykoensefalopatiya, antiretrovirus terapiya, opportunistik infektsiyalar, neyroinflamasyon.

ABSTRACT

qayta boshlash. OIV infektsiyasida markaziy asab tizimining (MNS) shikastlanishi OIV bilan kasallangan odamlarda eng jiddiy va keng tarqalgan nevrologik asoratlardan biridir. Odamning immunitet tanqisligi virusi infektsiyaning dastlabki bosqichida asab tizimining hujayralariga kirib, engil kognitiv buzilishdan og'ir demansgacha, shuningdek, opportunistik infektsiyalar va malign o'smalarga qadar keng klinik ko'rinishlarga olib keladi. OIV bilan bog'liq bo'lgan markaziy asab tizimining eng keng tarqalgan kasalliklariga OIV bilan bog'liq neyrokognitiv buzilish, miya toksoplazmozi, kriptokokk meningit va progressiv multifokal leykoensefalopatiya kiradi. Erta tashxis qo'yish va antiretrovirus terapiyani (ART) o'z vaqtida boshlash ushbu holatlarning oldini olish va davolashda muhim rol o'ynaydi. Ushbu maqolada markaziy asab tizimining shikastlanishining asosiy klinik shakllari, mexanizmlari, diagnostika usullari va OIV infektsiyasining nevrologik asoratlarini davolashning zamonaviy strategiyalari muhokama qilinadi.

Introduction. Human Immunodeficiency Virus (HIV) infection continues to pose a major global health challenge, affecting millions of individuals worldwide. Beyond its well-documented effects on the immune system, HIV has profound implications for the central nervous system (CNS), which often remain underdiagnosed and undertreated. The virus can

invade the CNS early in the course of infection, sometimes within days to weeks after exposure, leading to a range of neurological manifestations that can severely impair the quality of life and functional capacity of affected individuals [1]. The CNS is a critical site of HIV persistence, even in the presence of effective antiretroviral therapy (ART). HIV enters the brain primarily via infected monocytes and lymphocytes, crossing the blood–brain barrier through a "Trojan horse" mechanism. Once in the CNS, the virus can infect microglial cells, astrocytes, and perivascular macrophages, leading to neuroinflammation and neuronal injury [2]. This neuropathogenesis may result in a spectrum of neurological complications, including opportunistic infections, HIV-associated neurocognitive disorders (HAND), HIV encephalopathy, and cerebrovascular diseases [3]. The incidence of HIV-related CNS complications has changed significantly in the era of combination antiretroviral therapy (cART). While the introduction of cART has led to a notable decline in severe opportunistic infections such as cryptococcal meningitis and toxoplasmosis, milder but chronic forms of neurocognitive dysfunction, such as HAND, have become more prevalent [4]. HAND affects nearly 30–50% of individuals living with HIV, even those with suppressed viral loads, suggesting that neuroinflammation and viral reservoirs in the brain continue to drive pathology despite systemic viral control [5]. Clinical presentations of CNS involvement in HIV are highly variable and can range from subtle cognitive and behavioral changes to severe motor deficits, seizures, and altered consciousness. Diagnostic evaluation typically includes neuroimaging, cerebrospinal fluid (CSF) analysis, and neuropsychological testing, although challenges remain in differentiating between primary HIV-related pathology and secondary complications caused by co-infections or malignancies [6]. Timely identification and management of CNS complications in HIV-infected individuals are vital. Delayed diagnosis may result in irreversible neurological damage and increased morbidity and mortality. Moreover, the choice of antiretroviral drugs with high CNS penetration effectiveness (CPE) scores has been shown to influence treatment outcomes and may help reduce the risk of neurocognitive decline [7]. Recent research has also focused on the potential role of adjunctive therapies, including anti-inflammatory agents, neuroprotective strategies, and cognitive rehabilitation techniques, in managing CNS complications in HIV. However, further studies are needed to establish standardized protocols for screening, prevention, and treatment [8]. This article aims to provide a comprehensive overview of central nervous system involvement in HIV infection, discussing its pathophysiological mechanisms, clinical features, diagnostic approaches, and management strategies. Understanding the neurological aspects of HIV is essential for clinicians, researchers, and public health professionals involved in the care of people living with HIV.

Literature Reviw. The relationship between HIV infection and central nervous system (CNS) pathology has been a subject of extensive research since the early years of the HIV/AIDS epidemic. Early studies in the pre-antiretroviral therapy (pre-ART) era described severe and rapidly progressive neurological syndromes, including HIV-associated dementia (HAD), opportunistic infections such as toxoplasmosis and cryptococcal meningitis, and primary CNS lymphomas [9]. These conditions were often markers of late-stage disease and were strongly associated with high mortality. With the advent of combination antiretroviral therapy (cART) in the mid-1990s, the incidence of severe opportunistic neurological

complications significantly decreased. However, this therapeutic advancement unveiled new challenges, particularly the rise in milder, chronic neurocognitive impairments among HIV-positive individuals [10]. These impairments were categorized under the term HIV-associated neurocognitive disorders (HAND), encompassing a spectrum from asymptomatic neurocognitive impairment (ANI) and mild neurocognitive disorder (MND) to HAD [3]. Several cohort studies, including the CHARTER (CNS HIV Antiretroviral Therapy Effects Research) and MACS (Multicenter AIDS Cohort Study), have been instrumental in establishing the prevalence and clinical features of HAND. Heaton et al. (2010) reported that despite viral suppression, approximately 50% of HIV-positive individuals showed signs of neurocognitive impairment, especially in domains such as attention, processing speed, memory, and executive function [5]. This finding highlighted the need to look beyond viral load as the sole marker of CNS health in HIV patients. Neuropathological studies revealed that chronic immune activation and neuroinflammation are key drivers of neuronal damage in HIV infection. Microglial activation, astrocytosis, and the release of neurotoxic cytokines, such as TNF-α and IL-6, have been identified in post-mortem brains of HIV-positive individuals, even those receiving effective ART [11]. Moreover, HIV Tat and gp120 proteins have been shown to exert direct neurotoxic effects, exacerbating synaptic dysfunction and neuronal apoptosis [12]. The concept of the central nervous system viral reservoir has further complicated the management of HAND. While plasma HIV RNA levels may be undetectable, the virus can persist in a latent or replicative form within CNS cells, protected by the blood–brain barrier. This phenomenon, known as CSF viral escape, has been observed in a subset of patients, where detectable viral RNA is found in cerebrospinal fluid (CSF) despite effective systemic suppression [7], [13]. Pharmacokinetic studies have emphasized the importance of drug penetration into the CNS. The CNS Penetration-Effectiveness (CPE) score, developed by Letendre et al., has become a useful tool for selecting ART regimens with higher neuroprotective potential [14]. Drugs like zidovudine, abacavir, and nevirapine have shown better CNS penetration, while others such as tenofovir and atazanavir have relatively poor CNS distribution [15]. Nevertheless, high CPE scores do not always correlate with better neurocognitive outcomes, suggesting that factors beyond drug distribution, such as host immunity, comorbidities, and aging, also play critical roles [16]. In recent years, the intersection of aging and HIV has emerged as a significant research focus. As people with HIV live longer due to improved treatment, they are increasingly facing age-related neurodegenerative conditions, including Alzheimer's disease and Parkinsonism. Studies have reported overlapping neuropathological features such as beta-amyloid deposition and tau pathology in older HIV-infected individuals, raising concerns about compounded neurodegeneration [17]. In terms of diagnostic tools, advances in neuroimaging and biomarker research have enhanced the detection of CNS involvement in HIV. MRI with diffusion tensor imaging (DTI), magnetic resonance spectroscopy (MRS), and positron emission tomography (PET) have provided insights into white matter integrity and neuroinflammation in vivo [18]. CSF biomarkers, including neurofilament light chain (NFL), β2-microglobulin, and neopterin, have shown promise in distinguishing between HAND and other neurological disorders [19]. Efforts to develop adjunctive treatments for HAND have yielded mixed results. Trials using memantine, selegiline, and minocycline have not

demonstrated consistent neurocognitive improvement [20]. However, recent research into anti-inflammatory agents, gut–brain axis modulation, and cognitive rehabilitation strategies is ongoing and may offer novel therapeutic avenues [21]. Despite these advances, gaps remain in understanding the long-term evolution of CNS complications in HIV-infected populations. More research is needed to identify early biomarkers, personalize ART regimens for neuroprotection, and develop targeted interventions to mitigate neurological decline in both young and aging HIV populations.

Conclusion. Central nervous system (CNS) involvement in HIV infection remains a significant clinical and public health concern, even in the era of effective combination antiretroviral therapy (cART). While the incidence of severe opportunistic neurological infections has declined markedly, chronic and often subtle neurocognitive impairments—collectively known as HIV-associated neurocognitive disorders (HAND)—continue to affect a substantial proportion of people living with HIV. These complications not only diminish quality of life but also interfere with adherence to therapy, daily functioning, and long-term health outcomes. The pathogenesis of CNS involvement in HIV is complex and multifactorial, involving viral persistence in the brain, chronic immune activation, neuroinflammation, and direct neuronal injury. Despite plasma viral suppression, HIV can establish latent reservoirs in the CNS, creating challenges for both treatment and eradication efforts. Furthermore, aging, comorbidities, and co-infections may exacerbate cognitive decline in this population, necessitating a multidisciplinary and personalized approach to care. Timely diagnosis and appropriate management of CNS complications require the integration of clinical assessment, neuroimaging, cerebrospinal fluid (CSF) analysis, and neuropsychological testing. The use of antiretroviral regimens with higher CNS penetration scores, alongside ongoing monitoring and potential adjunctive therapies, is crucial in mitigating neurological damage. Emerging diagnostic tools and biomarkers also offer promise for earlier detection and targeted interventions. Continued research into the mechanisms of HIV neuropathogenesis, improved neuroprotective strategies, and the development of effective adjunctive treatments will be essential to address the unmet neurological needs of individuals living with HIV. Understanding and addressing CNS involvement is a critical step toward comprehensive HIV care and improving long-term outcomes for patients worldwide.

References:

1. Бокша В.А., Петров А.В. Неврологические осложнения ВИЧ-инфекции: современные подходы к диагностике и лечению // Журнал неврологии и психиатрии им. С.С. Корсакова. — 2021. — Т. 121, № 5. — С. 23–30.
2. Гусев Е.И., Насонова В.А., Бурцев А.Г. СПИД и поражение нервной системы. — М.: ГЭОТАР-Медиа, 2019. — 288 с.
3. Антонов А.А., Козлова Н.М. Влияние ВИЧ на когнитивную функцию и ЦНС // Вестник инфекционной патологии. — 2020. — № 4. — С. 15–20.
4. UNAIDS. Global HIV & AIDS statistics — Fact sheet. — 2023. URL: https://www.unaids.org (дата обращения: 20.05.2025).
5. Clifford D.B., Ances B.M. HIV-associated neurocognitive disorder. Lancet Infect Dis. — 2013; 13(11): 976–986. doi:10.1016/S1473-3099(13)70269-X

6. Heaton R.K., Franklin D.R., Ellis R.J. et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. Neurology. — 2010; 75(23): 2087–2096.
7. Eggers C., Arendt G., Hahn K. et al. HIV-1-associated neurocognitive disorder: epidemiology, pathogenesis, diagnosis, and treatment. J Neurol. — 2017; 264(8): 1715–1727.
8. ВИЧ-инфекция и СПИД: национальное руководство - 2-е изд., перераб. и доп. / В.В. Покровский [и др.]. - М.: ГЭОТАР-Медиа, 2020. - 696 с.
9. Дроздов, А.А. Современное состояние проблемы дифференциальной диагностики структурных поражений головного мозга у пациентов со СПИДом по данным МРТ (обзор литературы) / А.А. Дроздов [и др.] // Вестник Санкт-Петербургского университета. Медицина. - 2018. - Т. 13, № 4. - С. 403-418.
10. Евзельман М.А., Снимщикова И.А., Королева Л.Я., Камчатнов П.Р. Неврологические осложнения ВИЧ-инфекции. Журнал неврологии и психиатрии им. С.С. Корсакова. 2015;115(3):89–93. DOI: 11.17116/jnevro20151153189
11. Капустин Д.В., Краснова Е.И., Хохлова Н.И., Шишкова О.М., Позднякова Л.Л. Современные аспекты поражения центральной нервной системы у больных ВИЧ-инфекцией (обзор литературы). *Журнал инфектологии*. 2023;15(3):15-28. https://doi.org/10.22625/2072-6732-2023-15-3-15-28
12. Новицкая, О.Н. Особенности диагностики и лечения туберкулёза центральной нервной системы, протекающего на фоне ВИЧ-инфекции: автореф. дис… д-ра мед.наук / О.Н. Новицкая. - М., 2014. - 52 с.
13. Смирнов Н.А., Нагибина М.В., Мартынова Н.Н., Бессараб Т.П., Мазус А.И., Сидорук Л.М., Кулагина М.Г. Некоторые аспекты диагностики и лечения ВИЧ-ассоциированных поражений центральной нервной системы на фоне антиретровирусной терапии. РМЖ. Медицинское обозрение. 2024;8(11):667-673. DOI: 10.32364/2587-6821-2024-8-11-10.
14. Портнова, Р.Г. Оппортунистические инфекции центральной нервной системы у ВИЧ-инфицированных больных/ Р.Г. Портнова // Вестник совета молодых учёных и специалистов Челябинской области. - 2018. - Т. 2, № 4. - С 51-55
15. Тимченко В. Н. Гузеева., В. И, Архипов Ю. А. Поражение нервной системы при ВИЧ-инфекции Десткие инфекции, 2009,№1. С.32-35.
16. Щиголева Е. В. ВИЧ-ассоциированные поражения нервной системы в патогенезе нейроСПИДа // Вестник СМУС74. 2017. №4 (19). URL: https://cyberleninka.ru/article/n/vich-assotsiirovannye-porazheniya-nervnoy-sistemy-v-patogeneze-neyrospida (дата обращения: 18.05.2025).
17. Шнякин, П.Г. Анализ серии случаев токсоплазмоза головного мозга в практике стационара неврологического профиля / П.Г. Шнякин [и др.] // Анналы клинической и экспериментальной неврологии. - 2023. - Т. 17, №1. - С. 75-81.
18. Antinori A, Arendt G, Becker JT, Brew BJ, Byrd DA, Cherner M, Clifford DB, Cinque P, Epsteins LG, Goodkin K, Gisslen M, Grant I, Heaton RK, Joseph J, Marder K, Marra CM, McArthur JC, Nunn M, price RW, Pulliam L, Roberston KR, Sacktor N, Valcour V, Wojna VE: **Updated research nosology for HIV-associated neurocognitive disorders.** *Neurology* 2007, **69:** 1789–1799. 10.1212/01.WNL.0000287431.88658.8b

19. Eggers C., Arendt G., Hahn K. et al. HIV-1-associated neurocognitive disorder: epidemiology, pathogenesis, diagnosis, and treatment. J Neurol. 2017;264(8):1715–1727. DOI: 10.1007/s00415-017-8503-2
20. Meyer AC, Njamnshi AK, Gisslen M, et al. Neuroimmunology of CNS HIV Infection: A Narrative Review. Front Neurol. 2022 Jun 14;13:843801.
21. Paruk HF, Bhigjee AI. Review of the neurological aspects of HIV infection. J Neurol Sci. 2021 Jun 15; 425:117453.
22. Sacktor N., Skolasky R.L., Seaberg E. et al. Prevalence of HIV-associated neurocognitive disorders in the Multicenter AIDS Cohort Study. Neurology. 2016;86(4):334–340. DOI: 10.1212/WNL.0000000000002277
23. Wang Y., Liu M., Lu Q. et al. Global prevalence and burden of HIV-associated neurocognitive disorder: A meta-analysis. Neurology. 2020;95(19):e2610–e2621. DOI: 10.1212/WNL.0000000000010752