Case Report

Human Immunodeficiency Virus-Associated Dementia: Two Case Reports

Abstract

Human immunodeficiency virus (HIV) continues to be a serious public health problem in our country in the world and has serious effects on the central and peripheral nervous system. HIV-associated dementia (HAD), which may develop due to HIV infection, causes subcortical dementia that can progress with marked slowdown in reaction time and psychomotor speed, impaired cognitive flexibility, emotional lability, and apathy. Neurocognitive tests are the most appropriate tools for the neurocognitive assessment and staging of the disease. In this context, the Addenbrooke's Cognitive Examinations Revised (ACE-R) test may be preferred in the neurocognitive evaluation of patients considered to have HAD, in terms of its repeatability and easy applicability, as it allows us to evaluate many neurocognitive functions in detail.

Keywords: *Addenbrooke cognitive examination test, human immunodeficiency virus, human immunodeficiency virus-associated dementia*

Nefise Eda Arslanoğlu[1], Nazli Gamze Bülbül[1], Mehmet Güney Senol[1], Mehmet Fatih Özdag[1]

[1]Department of Neurology, Sultan Abdülhamid Han Research and Training Hospital, Istanbul, Turkey

Introduction

Human immunodeficiency virus (HIV) causes primary failure of the immune system and makes the body vulnerable to infections and some types of cancer as a result.[1] Transmission routes are as follows: sexually transmitted from mother to baby, transmitted to medical personnel, transmitted by injector, and other tools. In our country, 45.6% of cases are observed sexually, and 0.97% are observed with the use of intravenous substances. HIV was first seen in the world in the United States in 1981 and in our country in 1985. According to the data of the Department of Infectious Diseases and Early Warning of the General Directorate of Public Health of the Ministry of Health of the Republic of Turkey, from 1985 to December 31, 2021, there were 30,293 HIV-seropositive individuals and 2083 acquired immunodeficiency syndrome cases. 81.2% of the cases were male, 18.8% were female, and 16% were made up of foreign nationals. The most common age ranges of the disease are 25–29 and 30–34, and the transmission route of 53.08% of the cases is unknown.[2] In addition to the direct effects of HIV infection on the immune system with the decrease of CD4 T-lymphocytes, it also has serious effects on the brain, spinal cord, and peripheral nerves in the nervous system. HIV-related neurological complications are seen in 40%–50% of patients and may be the first symptom in 10%.[2,3]

Although the incidence of neurological complications has decreased considerably in the postantiretroviral treatment (ART) period, neurocognitive deficits in HIV cannot be prevented.[4] Although ART treatment reduces cognitive decline and has positive effects on patients' daily life activities, there is still no complete cognitive improvement.[5] In previous studies, even in young people with HIV infection acquired in early childhood, moderate neurocognitive impairments may be observed. In another study, it was reported that 71% of patients with HIV infection are at risk for cognitive impairment.[6] Vascular and metabolic comorbidities such as diabetes mellitus, metabolic syndrome, and obesity, which are observed with increasing frequency in elderly people, also increase the prevalence of HIV-related neurocognitive impairment.[7,8] Slow response times, marked slowing of psychomotor speed, poor cognitive flexibility, and emotional lability or apathy can often be seen in HIV-associated neurocognitive disorder (HAND). HIV-associated

How to cite this article: Arslanoğlu NE, Bülbül NG, Senol MG, Özdag MF. Human immunodeficiency virus-associated dementia: Two case reports. J Neurobehav Sci 2022;9:72-6.

Received : 26-07-2022
Revised : 05-08-2022
Accepted : 12-08-2022
Published : 31-08-2022

Orcid
Nefise Eda Arslanoğlu: {ORCID: 0000-0001-9533-6874}
Nazli Gamze Bülbül: {ORCID: 0000-0001-8560-0774}
Mehmet Güney Senol: {ORCID: 0000-0001-6397-9293}
Mehmet Fatih Özdag: {ORCID: 0000-0003-1853-0467}

Address for correspondence:
Mrs. Nefise Eda Arslanoğlu, Department of Neurology, Sultan Abdülhamid Han Research and Training Hospital, Istanbul, Turkey.
E-mail: edasidali@hotmail.com

Access this article online

Website: www.jnbsjournal.com

DOI: 10.4103/jnbs.jnbs_22_22

Quick Response Code:

Ethics committee approval: There is no need for ethics committee approval.

dementia (HAD) is included in the subclassification of HAND.[9,10] Here, it is aimed to discuss two cases followed up with HAD, together with detailed examination, neurocognitive test results, and neuroimaging results in the light of literature. We consider that this case study, which examines neuroimaging and neurocognitive test results related to HIV-related dementia, will contribute to the literature.

Two Case Reports

Case 1

A 58-year-old female patient was admitted to the neurology outpatient clinic with the complaint of forgetfulness. When her anamnesis was questioned in more detail, it was learned that she was a homemaker, that she was being followed up and treated with a diagnosis of acquired immunodeficiency in our infectious diseases clinic, and that the complaint of forgetfulness had increased for 6 months. She stated that he forgot the place where she put the things, the words she would say in everyday life, and her routine chores. She had hypertension on her resume but was not taking medication. There was no feature in her family history. In her neurological examination, she was conscious, cooperative, and oriented. Cranial nerve examination was normal. She had moderate dysarthria. Neither motor lateralizing findings nor cerebellar pathological findings were detected. Deep tendon reflexes were normoactive. The Babinski's sign was found to be bilaterally positive. Romberg test was positive. When hemogram and biochemistry values are examined, erythrocyte sedimentation rate: 55 mm/h. HIV RNA (macro) value resulted in 598 IU/mL, CD4: 12.52/mm^3, and CD8: 18.13 mm^3. Cranial magnetic resonance (MR) examination revealed that lesions adjacent to the left lateral ventricular corpus, which may be compatible with the lacunae at the level of both the corona radiata, thalamus, basal ganglia and the lentiform nucleus. Diffuse nodular and patchy T2 fluid-attenuated inversion recovery (FLAIR) signal increases were observed in the frontoparietal, occipital, and subcortical deep white matter. T2 FLAIR signal enhancement areas in basal ganglia, external capsules and left thalamic localization; diffuse millimetric focal gradient ECHO hypointensities were reported in bilateral cerebellar hemispheres, brain stem and basal ganglia, and in both cerebral hemispheres [Figure 1]. Brain glucose metabolism was reported as normal in brain positron emission tomography (PET) examination. ACE-R test was used for the neurocognitive evaluation of the patient. In the ACE-R test, attention and orientation functions were partially preserved (13/18). While recording memory was preserved in memory processes, short-term memory, retrograde memory, recall, and recognition skills were impaired (9/26). While there was mild impairment in verbal fluency functions (6/14), language functions were preserved (20/26). While the perceptual skills, one of the visual-spatial functions, were preserved, the planning ability was impaired (9/16). In the clock-drawing test, planning and conceptualization were affected. As a result, it was interpreted that there is a deterioration in the temporolimbic type of memory processes and a deterioration in the ability to maintain attention and planning ability, which is one of the complex attention functions. The patient was considered to have HAD the current findings. Oral and written consent was obtained from the patient.

Case 2

A 47-year-old male patient was admitted to our neurology outpatient clinic with complaints of progressive forgetfulness for 4 months. When his anamnesis was questioned in more detail, he stated that he forgot and burned food on the stove twice, once lost his phone, and had disruptions in his daily life activities. While he was working in a medical waste unit in a hospital, he had an HIV-infected syringe stuck in his hand and his HIV serology was positive in his examinations. Thereupon, he was followed up in the infectious diseases clinic and his treatment was arranged. When the patient's history is questioned, it was learned that he had hypertension but did not use medication and had a history of head trauma due to a traffic accident 2 years ago. There were no features in his family history. In neurological examination, he was conscious, cooperative, and oriented. Cranial nerve examination was normal. Neither motor lateralizing findings nor cerebellar pathological findings were detected. Deep tendon reflexes were normoactive. The Babinski's sign was found to be bilaterally negative. The tandem walk was impaired. When the laboratory values were examined, no significant pathology was detected in the hemogram and biochemistry. HIV RNA (macro) resulted in 4353 IU/mL, CD4: 7.35/mm^3, and CD8: 3.17/mm^3. Cranial magnetic resonance imaging (MRI) examination revealed that the posterior fossa was consistent with a 70 mm × 86 mm × 35 mm retrocerebellar arachnoid cyst surrounding the left cerebellar hemisphere [Figure 2]. When the patient's past medical records were examined, it was seen that the existing arachnoid cyst was present in the cranial computed tomography (CT) taken after a head trauma 2 years ago and its sizes did not change [Figure 3]. In the brain PET examination, it was interpreted that there were 18-fluorodeoxyglucose PET/CT findings consistent with hypometabolism in a global patch pattern, except for both occipital and frontal cortices and basal ganglia, and these findings suggested inflammatory/vascular processes involving the cortical area. In the ACE-R test used for neurocognitive evaluation, attention and orientation functions were partially preserved (13/18); there was deterioration in memory processes such as anterograde memory, short-term memory, retrograde memory, recall, and recognition skills (8/26). There was severe deterioration in verbal fluency functions (5/14). He counted 11 words in semantic fluency test and only 3 words in lexical fluency test. There was a deterioration in the naming of the

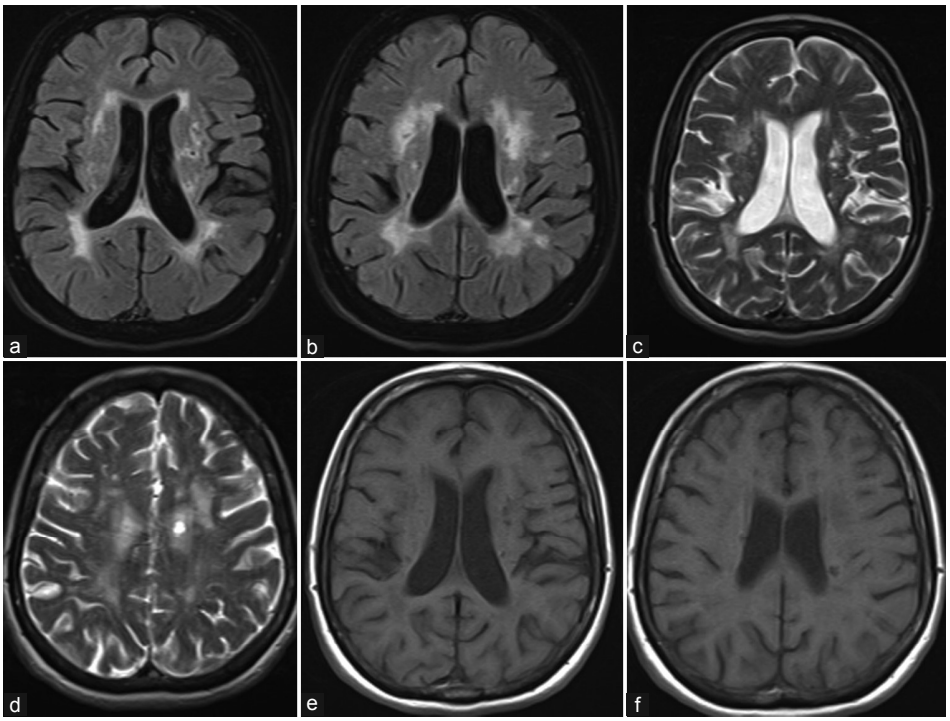

Figure 1: Cranial MRI FLAIR (a,b), T2 (c,d), and T1 (e,f) axial sequences of Case 1. MRI: Magnetic resonance imaging, FLAIR: Fluid-attenuated inversion recovery

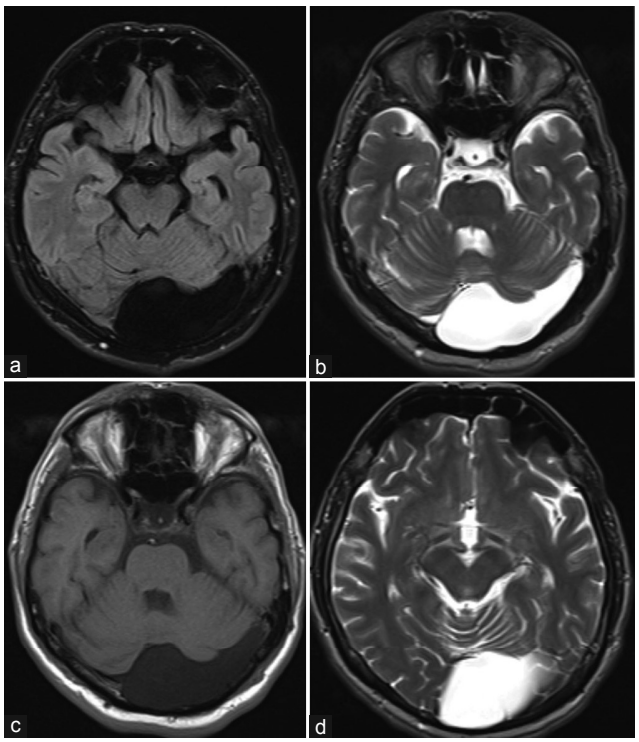

Figure 2: Cranial MRI FLAIR (a), T2 (b,d), and T1 (c) axial sequences of Case 2. MRI: Magnetic resonance imaging, FLAIR: Fluid-attenuated inversion recovery

confrontal associated with the left posterior areas (13/26). While the perceptual skills, one of the visual-spatial functions, were preserved, the planning ability was impaired (9/16). In the clock-drawing test, planning and conceptualization were affected. There were difficulties in learning verbal information. He could not retrieve any of the seven words in long-term memory, and he recognized three words in recognition, recognized one word by forced choice, and misrecognized one word. As a result, it was interpreted that there is a deterioration in the temporolimbic type of memory processes and a deterioration in the ability to maintain attention and planning ability, which is one of the complex attention functions. The patient was considered to have HAD the current findings. Oral and written consent was obtained from the patient.

Discussion

Cross-sectional studies show that about half of HIV-infected patients have cognitive impairment. Although a decrease in neurocognitive deterioration has been observed with ART treatments, providing the etiology, prognosis, and optimal treatment regimen in these patients still remains a great responsibility.[11] HIV-dementia complex is a subcortical dementia that progresses with progressive deterioration in attention and concentration, slowdown in psychomotor speed, and behavioral changes and results in death in less than a year.[9] In a consensus conducted in Italy in 2006, the subclinical classifications for HAND were determined as asymptomatic neurological impairment, mild neurocognitive impairment, and HIV-related dementia (HAD).[10] When its pathogenesis was examined, it was found that there were generalized atrophy in the brain, white matter changes causing leukoencephalopathy, microglial nodules typical of viral encephalitis, and multinuclear giant cells seen in staining

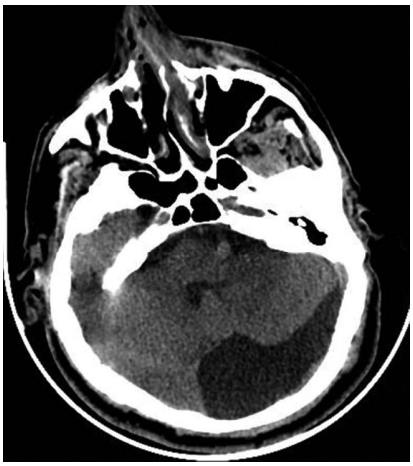

Figure 3: BT examination of Case 2

specific to HIV-infected cells.[10] Recent studies have shown that HAND is not associated with CD4 T-lymphocyte count and cerebrospinal fluid HIV RNA concentration. Although no HAND-specific neuroimaging findings are known, hyperintense white matter lesions with unclear boundaries can be seen symmetrically on cranial MRI examinations.[10] Currently, no treatment methods are known for HAND-treated HIV cases other than current ART methods.[12]

Neurocognitive tests were used for the neurocognitive evaluation and staging of the disease. In these tests, speech areas, attention skills, executive functions, abstraction skills, learning-remembering and memory processes, information processing speed, and motor functions are evaluated in detail.[12,13] In previous studies, the Mini-Mental Test (MMT), the Montreal Cognitive Assessment Scale, and the International HIV Dementia Scale were generally used.[3] We used the ACE-R test for neurocognitive evaluation in both cases. ACE was prepared at the University of Cambridge and Addenbrooke Hospital Neurology Clinic in 2000 and revised in 2005 and started to be used as ACE-R.[14] ACE-R is a test that can be applied in an average of 15–20 min and includes MMT, and is used for early diagnosis and differential diagnosis of dementia, to follow-up patients. There are a total of five subtests in the ACE-R test. The test is evaluated out of 100 points. These subtests are attention and orientation (18 points), memory (26 points), fluency (14 points), language functions (26 points), and visuospatial functions (16 points). In the ACE-R Turkish validity study, 73 limit values were determined to distinguish Alzheimer's disease from normal healthy people at the educational level of over 11 years, and 88 limit values were determined to distinguish patients with mild cognitive impairment from normal healthy people.[14] When the ACE-R test results of both the cases were evaluated, the ACE-R total score of the first case was 56/100, and the second case was 48/100.

A subcortical dementia is seen in HAD, especially as specific gray matter nuclei in the white matter tracts and subcortical areas are affected. As a result, slowed reaction time, significant slowdown in psychomotor speed, weakening of cognitive flexibility, emotional lability, and apathy can be observed clinically. It has been determined that HIV-seropositive individuals have lower neurocognitive performance than the control group, and neurocognitive test scores are found to be lower, especially in the areas of language functions, attention, orientation, concentration, memory, and praxis.[12,13,15] When the ACE-R tests were examined, temporolimbic type involvement, impaired attention maintenance, and planning skills were observed, and with the current findings, HIV-related dementia (HAD) was considered in both cases. The factors affecting the low detection of neurocognitive test scores have been investigated in previous studies. No direct relationship was found with age, gender, education level, body mass index, clinical stage, alcohol/substance use, concomitant cardiovascular/metabolic/psychiatric diseases, anemia, presence of opportunistic infections, and CD4 T-cell count.[15]

In conclusion, HAD should be kept in mind in clinical practice in patients followed up with HIV infection and in patients with rapidly progressive memory impairment and behavioral changes. In the neurocognitive evaluations of patients with suspected HAD, ACE-R test can be preferred in terms of being a test that evaluates memory, attention, orientation, fluency, language functions and visuospatial functions in detail, as well as reproducibility, including MMT, short duration, and easy applicability.

Patient informed consent

Patient informed consent was obtained.

Ethics committee approval

There is no need for ethics committee approval.

Financial support and sponsorship

No funding was received

Conflicts of interest

There are no conflicts of interest to declare.

Author contribution subject and rate

- Nefise Eda Arslanoğlu (40%): Contributed with literature research, writing of manuscript and treatment of patient.
- Nazlı Gamze Bülbül (30%): Contributed with comments on manuscript and treatment of patient.
- Mehmet Güney Şenol (15%): Organized the report and supervised the report write-up.
- Mehmet Fatih Özdağ (15%): Contributed with comments on manuscript organization and write-up.

References

1. Arseniou S, Arvaniti A, Samakouri M. HIV infection and depression. Psychiatry Clin Neurosci 2014;68:96-109. doi: 10.1111/pcn.12097.
2. Tümer A, Ünal S. HIV/AIDS epidemiyolojisi ve korunma. Aile Toplum 2001;4:4.
3. Ünlütürk Z, Değirmenci E, Kutlu SS. Acquired ımmune deficiency syndrome showing ıts first symptom with nervous system ınvolvement. Turk J Neurol 2020;26:165-72. doi: 10.4274/tnd.2020.95676.
4. Maschke M, Kastrup O, Esser S, Ross B, Hengge U, Hufnagel A. Incidence and prevalence of neurological disorders associated with HIV since the introduction of highly active antiretroviral therapy (HAART). J Neurol Neurosurg Psychiatry 2000;69:376-80. doi: 10.1136/jnnp.69.3.376.
5. Spudich S. HIV and neurocognitive dysfunction. Curr HIV/AIDS Rep 2013;10:235-43. doi: 10.1007/s11904-013-0171-y.
6. Shivaswamy RP, Ashok A, Jayaram SC, Thandure V, Dowerah J. A study of neurocognitive dysfunction in HIV-positive patients in a tertiary care center in South India. J Datta Meghe Inst Med Sci Univ 2021;16:108-14. doi: 10.4103/1319-4534.322599.
7. Temereanca A, Ene L, Rosca A, Diaconu CC, Luca A, Burlacu R, *et al*. Neurocognitive ımpairment in the combined antiretroviral therapy era in a romanian cohort of young adults with chronic HIV ınfection. AIDS Res Hum Retroviruses 2020;36:367-72. doi: 10.1089/AID.2019.0132.
8. Nix LM, Tien PC. Metabolic syndrome, diabetes, and cardiovascular risk in HIV. Curr HIV/AIDS Rep 2014;11:271-8. doi: 10.1007/s11904-014-0219-7.
9. Eggers C, Arendt G, Hahn K, Husstedt IW, Maschke M, Neuen-Jacob E, *et al*. HIV-1-associated neurocognitive disorder: Epidemiology, pathogenesis, diagnosis, and treatment. J Neurol 2017;264:1715-27. doi: 10.1007/s00415-017-8503-2.
10. Clifford DB, Ances BM. HIV-associated neurocognitive disorder. Lancet Infect Dis 2013;13:976-86. doi: 10.1016/S1473-3099(13)70269-X.
11. Simioni S, Cavassini M, Annoni JM, Abraham AR, Bourquin I, Schiffer V, *et al*. Cognitive dysfunction in HIV patients despite longstanding suppression of viremia. AIDS 2010;24:1243-50. doi: 10.1097/QAD.0b013e3283354a7b.
12. Valcour V, Paul R. HIV infection and dementia in older adults. Clin Infect Dis 2006;42:1449-54. doi: 10.1086/503565.
13. Vásquez E, Lee EE, Zhang W, Tu X, Moore DJ, Marquine MJ, *et al*. HIV and three dimensions of Wisdom: Association with cognitive function and physical and mental well-being: For: Psychiatry Research. Psychiatry Res 2020;294:113510. doi: 10.1016/j.psychres.2020.113510.
14. Yıldız S. ACE R Adaptation for Turkish Population. Master degree thesis; 2011.
15. Sumonu TA, Imarhiagbe F, Owolabi LF, Ogunrin OA, Komolafe MA, Ilesanmi OS. Cognitive functions in newly diagnosed patients with HIV infection in a tertiary health facility: Assessment using community screening interview for dementia. eNeurologicalSci 2017;9:8-13. doi: 10.1016/j.ensci.2017.10.001.