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Diagnostic Assessment & Prognosis

An individual with human immunodeficiency virus, dementia, and central nervous system amyloid deposition

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Abstract Human immunodeficiency virus (HIV)–associated neurocognitive disorder (HAND) is found in 30%–50% of individuals with HIV infection. To date, no HIV+ individual has been reported to have a positive amyloid PET scan. We report a 71-year-old HIV+ individual with HAND. Clinical and neuropsychologic evaluations confirmed a progressive mild dementia. A routine brain MRI was normal for age. [18F]Fluorodeoxyglucose–PET revealed mild hypermetabolism in bilateral basal ganglia and hypometabolism of bilateral parietal cortex including the posterior cingulate/precuneus. Resting state functional MRI revealed altered connectivity as found with individuals with mild AD. CSF examination revealed a low Aβ42/tau index but a low phospho-tau. An amyloid PET/CT with [18F]florbetaben revealed pronounced cortical radiotracer deposition. This case report suggests that progressive dementia in older HIV+ individuals may be due to HAND, AD, or both. HIV infection does not preclude CNS Aβ/amyloid deposition. Amyloid PET imaging may be of value in distinguishing HAND from AD pathologies.

Keywords: Human immunodeficiency virus; HIV; HIV-associated neurocognitive disorder; HAND; Dementia; Alzheimer's disease; Amyloid PET; Functional MRI; Biomarker

1. Introduction

More than 36.9 million individuals worldwide are infected with human immunodeficiency virus (HIV) in 2014 [1]. HIV infection has largely changed from a fatal illness to a chronic manageable condition since the introduction of combination antiretroviral treatment (cART) in 1996. HIV-infected adults older than 55 years comprise the fastest growing age group in the HIV+ population [2]. HIV-associated neurocognitive disorder (HAND) occurs in 30%–50% of HIV+ individuals treated with cART [3]. The etiology of HAND remains unclear but may be due to viral infection and inflammation accelerating CNS aging [4] and decreasing cognitive reserve. It is currently unknown whether chronic HIV infection and/or treatment are risk factors for Alzheimer's disease (AD). As an increasing fraction of the HIV+ populace advances into the geriatric age range, clinicians will be challenged to differentiate HAND from other dementias of aging, including AD.

Putative biomarkers of AD pathology, including cerebrospinal fluid (CSF) proteomics—Aβ/amyloid, tau, phospho-tau, and others, and amyloid PET neuroimaging are supportive of a clinical diagnosis of AD pathology [5] in HIV-uninfected individuals. Only one case of HAND and biomarker-supported AD has been reported—with abnormal [18F]fluorodeoxyglucose-PET and CSF

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proteomics [6]. However, a review of CSF AD biomarkers in subjects with HAND reveals low amyloid levels in both diagnoses, increased phospho-tau in AD, and inconsistent tau levels in HAND [7]. To date, no HIV+ individual has been reported to have a positive amyloid PET scan. In fact, Ances et al. [8] suggest that HAND is *not* associated with increased CNS fibrillar amyloid as detected by amyloid PET imaging because all five subjects examined were negative, but the oldest was 67 years old. Given the aging HIV+ populace, we report the sentinel case of a possible new emerging epidemic of HAND/AD.

2. Methods and results

2.1. Case study

The subject is a 71 year-old man with a 14-year history of HIV infection diagnosed after presenting with flu-like symptoms and a viral pneumonia. He was subsequently treated with cART. He and his wife noted mild short-term memory problems for 5 years with insidious onset and a more noticeable decline in the last 3 years. His symptoms manifested by comprehension difficulty, forgetting recent conversations, and difficulty with multitasking. Functionally, he stated that he took longer to complete projects and sometimes made mistakes. He could no longer work as an attorney. His spouse stated that he had trouble learning new skills such as using his cellular telephone. As calculations became more challenging, his spouse assumed household financial management. He currently shops independently but requires a list. He performs personal care and basic activities of daily living with minimal or no assistance. He describes his mood as fearful of his cognitive disorder. He remains socially active, exercises daily, and enjoys weekly religious services. He denies aggression, anxiety, agitation, hallucinations, delusions, paranoia, and suicidal ideation. He has a long-standing history of sleep problems. His spouse also reports frequent (2–3 times a week) episodes of violent movements and screaming while dreaming. The patient reports these events as acting out his dreams. His spouse also reports occasional jerks of his extremities during sleep. Review of clinical records indicates a stable HIV infection with consistent compliance with cART (most recently abacavir, lamivudine, darunavir, and ritonavir). He also takes atorvastatin for hypercholesterolemia. There is no history of CNS infection or injury, stroke, transient ischemic attack, or alcohol or drug abuse. He had one episode of loss of consciousness with a minor head injury secondary to syncope in 2002. His mother died at age 89 years with probable AD; his father died at age 71 years with parkinsonism and dementia.

His physical and neurologic examination was remarkable only for cognitive impairment. His Mini-Mental State Examination [9] score was 22/30, and Montreal Cognitive Assessment [10] score was 20/30. He recalled zero of five words on delayed recall. He had difficulty with repetition and gave concrete answers to similarities. He named only

Table 1
Neuropsychologic evaluations demonstrate progressive cognitive decline

Task	Evaluation 1	Evaluation 2 (27 mo later)
Working memory and information processing speed		
Working Memory Index	Average (50th percentile)	Low average (23rd percentile)
Arithmetic	High average (75th percentile)	Average (50th percentile)
Digit span	Average (5F/4B; 25th percentile)	Borderline (5F/2B; 9th percentile)
Processing speed index	Borderline (8th percentile)	Impaired (5th percentile)
Digit symbol coding	Impaired (5th percentile)	Impaired (5th percentile)
Symbol search	Low average (16th percentile)	Borderline (9th percentile)
Executive functioning		
Rey complex figure copy	Impaired: poor planning and organization; inaccurate	Impaired: poor planning and organization; inaccurate
WAIS-IV picture completion	Borderline (9th percentile)	Average (50th percentile)
WAIS-III picture arrangement	Borderline (9th percentile)	Low average (16th percentile)
Language		
Phonemic verbal fluency (FAS)	Superior (Σ = 60, 91st percentile)	Low average (Σ = 29, 13th percentile)
Semantic verbal fluency (animals)	Low average (Σ = 18, 23rd percentile)	Impaired (Σ = 11, 1st percentile)
Boston naming test	Impaired (47/60 correct)	Impaired (40/60 correct)
Repeatable battery for the assessment of neurocognitive status		
Total score	Not tested	Impaired (1st percentile)
Attention	Not tested	Impaired (1st percentile)
Immediate memory	Not tested	Impaired (<1st percentile)
Visuospatial/constructional	Not tested	Low average (14th percentile)
Language	Not tested	Impaired (<1st percentile)
Delayed memory	Not tested	Low average (14th percentile)
Fine motor speed and coordination		
Grooved pegboard dominant (R)	Impaired (Σ = 121 s, 2nd percentile)	Impaired (Σ = 121 s, 2nd percentile)
Grooved pegboard nondominant	Impaired (Σ = 133 s, 3rd percentile)	Impaired (Σ = 121 s, 2nd percentile)

WAIS, Wechsler Adult Intelligence Scale.