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■ CASE REPORT ■

Rapidly Progressive Dementia Caused by Neurosyphilis Coinfection with HIV

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Neurosyphilis occurring among human immunodeficiency virus (HIV)-positive patients has rarely been reported in Korea, although the coexistence of primary or secondary syphilis and HIV has been previously reported. We report a case of a 36-yr-old man who presented with rapidly progressive dementia due to neurosyphilis and HIV coinfection. Syphilis and HIV coinfection should be considered as a differential diagnosis of dementia in young patients since prompt therapeutic intervention could result in good clinical outcome.

Key Words: *Neurosyphilis, HIV, Dementia*

INTRODUCTION

Recognition of dementia associated with infectious agents is important because its treatment could reverse the cognitive decline/abnormality in the patients thereof. It is particularly important to consider the possibility of syphilis, the human immunodeficiency virus (HIV), Lyme disease, and chronic meningitis as the cause in such circumstances. Syphilis and HIV coinfection has become increasingly common, in which case HIV makes it more likely for syphilis to present with non-typical features [1]. Central nervous system (CNS) involvement in syphilis patients includes syphilitic meningitis, meningovascular syphilis, tabes dorsalis, and general paresis. In contrast to the pre-antibiotic era, late neurosyphilis (tabes dorsalis or general paresis) is rare and early forms (asymptomatic, meningitis, and meningovascular syphilis) are more frequent in HIV-infected patients due to earlier initiation of highly active antiretroviral therapy (HAART) [2]. In Korea, the coexistence of primary and secondary syphilis and HIV has been reported since 1994, but, until now, there have been no reports on dementia associated with coinfection of neurosyphilis and HIV. We report a patient who presented with rapidly progressive dementia caused by neurosyphilis and HIV coinfection.

CASE REPORT

A 36-yr-old man was brought to the Department of Neurology at Asan Medical Center because of violent behavior and cognitive impairment. He was unmarried and made a living as a call taxi driver. He had no family history of dementia or stroke, and no previous history of drug abuse. Because he lived alone, his family could not provide information regarding his personal life such as sexual preference. During the fall of 2005, he showed signs of herpes zoster infection in the right leg, at which time he demonstrated an irritable personality along with mild dysarthria. The following year, he visited another hospital where he underwent brain MRI. Afterwards, he showed progressive emotional instability and worsening dysarthria. However, he was physically strong enough to continue driving a taxi. In December 2006, he was involved in a motor vehicle accident, after which his family persuaded him to stop driving. In February 2007, he developed urinary incontinence and frequently showed unusual repetitive behaviors such as walking continuously back and forth within his home. A month later, his memory worsened. He ate less and wandered around continuously. In August, he was unable to participate in daily conversations and showed episodes of violent behavior and emotional incontinence.

Complete neurological examination could not be performed owing to poor cooperation of the patient. He could answer a few questions such as his phone number and home address, but refused to respond to any other questions. Frontal lobe releasing signs were elicited. There was gegenhalten paratonia in his arms. Ill-defined reddish lesions were scattered on his face. His hands and feet showed signs of cutaneous fungal infection. The Korean version of Mini-Mental State Examination (K-MMSE) score [3] was 2.

His initial vital signs were stable. Chest CT revealed chronic tuberculous empyema. Brain MRI demonstrated diffuse cortical atrophy, especially prominent in bilateral temporal lobes on axial T1-weighted images and a mild degree of high signal intensities in the periventricular white matter on fluid attenuated inversion recovery (FLAIR) images (Fig. 1). [^{18}F] fluorodeoxyglucose positron emission tomography (FDG PET) revealed hypometabolism in bilateral temporal lobes (Fig. 2). The cerebrospinal fluid (CSF) disclosed pleocytosis with elevated protein and a normal pressure of 15 cm H_2O (Table 2). Venereal disease research laboratory (VDRL) test on the serum and CSF were all positive (Table 1, 2). Serum Treponema Pallidum hemagglutination (TPHA) and fluorescent treponemal antibody absorption test (FTA-ABS) were also reactive. The serum was positive for HIV antibody and the Western blot test for HIV was positive. The CD4 cell count was 214 cells/mL. The patient was treated with aqueous penicillin G (24 million units per day) for 14 days. To control his behavior, olanzapine was given intramuscularly which was later changed to oral quetiapine fumarate 25 mg/day. His condition improved dramatically after the

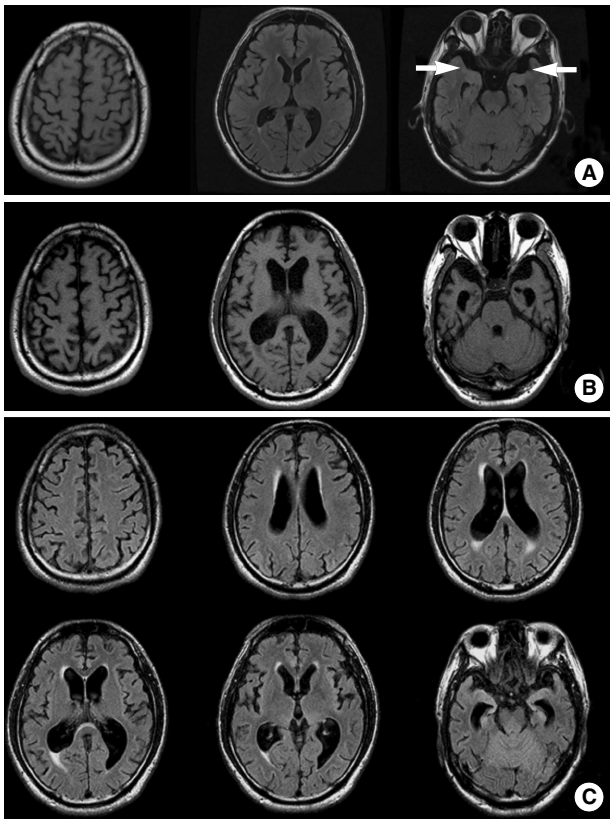

Fig. 1. Progressive cortical atrophy seen on brain magnetic resonance imaging (MRI). (A) Axial T1-weighted image performed in 2006 shows diffuse cortical atrophy, particularly in bilateral medial temporal lobes (arrow), accompanied by secondary ventricular dilatation. (B) Follow-up MRI acquired in 2007 revealed progression of diffuse cortical atrophy. (C) Fluid attenuated inversion recovery (FLAIR) images of 2007 disclosed mild degree of high signal intensities in the periventricular white matter.

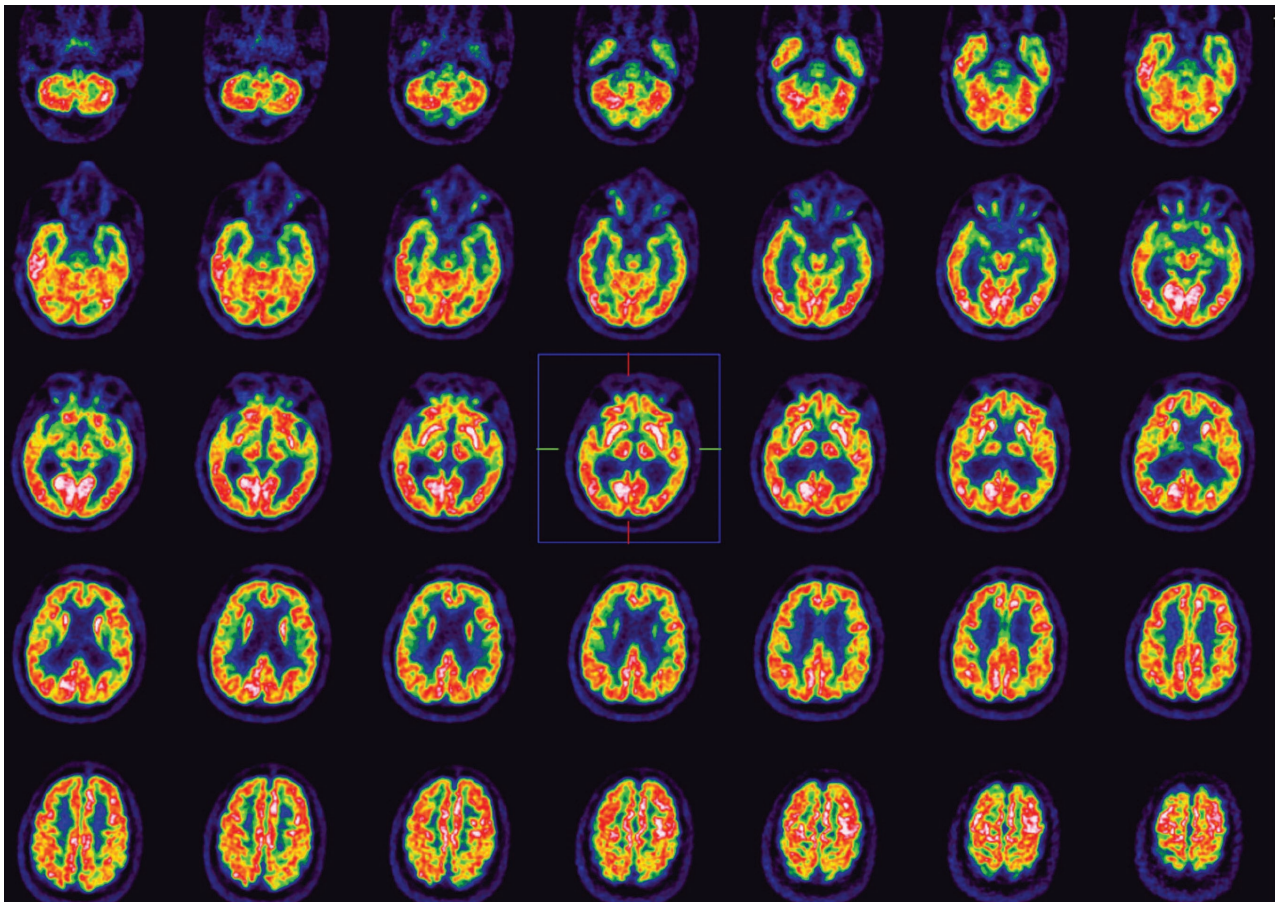

Fig. 2. Positron emission tomography (PET) in 2007. Fluorodeoxyglucose (FDG) PET showed hypometabolism in bilateral temporal lobes.

Table 1. The laboratory findings of serum

	VDRL (titer)	TPHA	FTA-ABS	CD4 cells (/μL)
2007/09/28	1:512	Reactive	Reactive	234
2007/10/08	1:256			
2008/03/21	1:128			427
2008/08/06	1:128			460
2008/12/09	1:128			592
2009/03/19	1:32			611
2009/09/01				524

VDRL, venereal disease research laboratory; TPHA, Treponema Pallidum hemagglutination; FTA-ABS, fluorescent treponemal antibody absorption test.

Table 2. The laboratory findings of CSF

CSF	2007/ 09/28	2007/ 10/08	2008/ 03/21	2008/ 09/05	2009/ 03/19
HIV RNA copies/mL	36,000		<25	Not detected	Not detected
WBC count (/mm^3) (lymphocyte %)	30 (71)	9 (72)	0		2 (19)
Protein (mg/dL)	130	144	48		41
Glucose/serum BST (mg/dL)	65/107	59/110	61/		85/108
VDRL	1:32	1:32	1:16		1:4
ADA	8	6.2	Not done		

HIV RNA, human immunodeficiency virus ribonucleic acid; VDRL, venereal disease research laboratory; ADA, adenosine deaminase; BST, blood sugar test.

administration of penicillin G. He exhibited childish behaviors, intermittent violent personality, and a silly smile, but he was able to carry conversations with others. Ten days later, the K-MMSE score was six. Following the penicillin G therapy, antiretroviral treatment was initiated. Lopinavir/ritonavir 400 mg/100 mg, zidovudine 300 mg, and lamivudine 150 mg (HAART, highly active antiretroviral therapy) were administered twice a day. Forty days later, the K-MMSE score was improved to twenty-four and the Montreal cognitive assessment-Korean version (MOCA-K) [4] score was eighteen. His condition improved to a degree where he could

carry out activities of daily living with little assistance. The VDRL titer decreased from 1:512 to 1:128 in the serum (Table 1) and from 1:32 to 1:16 in the CSF. The CSF pleocytosis improved and became normal on follow-up test. The CSF protein also declined significantly from 130.2 mg/dL to 48.1 mg/dL (Table 2). A year later, aggravation of cognitive decline and violent behavior were again noted and were considered to be related to HIV-associated dementia. Since then, he has been treated with antipsychotics and HAART.

DISCUSSION

To the best of our knowledge, this patient was the first case in Korea to present with rapidly progressive dementia caused by coinfection of neurosyphilis and HIV. The clinical features of neurosyphilis and HIV coinfection are extremely variable and interpretation of the laboratory data is difficult. One of the major concerns regarding the coexistence of HIV and syphilis is that syphilis might facilitate HIV acquisition and transmission [5]. The interaction between syphilis and HIV infection is complex and remains incompletely understood. Furthermore, the management of neurosyphilis in an HIV-infected patient is controversial [6]. In Korea, primary and secondary syphilis with HIV coinfection has already been reported in 1994 [7], and with time clinicians are likely to encounter more and more cases of neurosyphilis and HIV coinfection attributed to the increasing incidence of HIV infection. It is necessary to note that syphilis and HIV coinfection is potentially an important cause of various neurological problems.

This patient had clinical features and MRI findings mimicking frontotemporal lobar degeneration. He showed emotional incontinence, irritability, personality change, disinhibition, and cognitive impairment that are quite common in frontotemporal dementia. Brain MRI disclosed prominent atrophy in bilateral frontal and temporal lobes. General paresis is most frequently associated with dementia in neurosyphilis subtypes. The gradual onset and frontotemporal signs are characteristic of this dementia syndrome [8]. Neuroimaging studies of patients with neurosyphilis may reveal frontal and/or temporal lobe atrophy, subcortical changes, and cerebral infarctions [9]. Neurosyphilis should be considered as a possible cause of frontotemporal atrophy in the young age bracket.

HIV-associated dementia (HAD) has been described as a subcortical dementia syndrome and also has been reported to accompany cortical atrophy and hypometabolic changes in the temporal lobes [8]. However, given the fact that this patient had started to improve right after the administration of penicillin and before the use of antiretroviral agents, the main cause of dementia at the time was most likely to be neurosyphilis. Because the exact mechanism of interaction between neurosyphilis and HIV infection is unknown, we cannot completely exclude the possibility of HIV infection as the cause of dementia in this patient. The aggravation of cognitive decline and violent behavior seen after one year of clinical improvement may have been related to HAD.

Before we reached the diagnosis of HIV infection, the patient had a medical history of various opportunistic infections such as chronic pulmonary tuberculosis, herpes zoster, and cutaneous fungal infection. These findings suggested that he was in an immune-compromised state. With the increasing incidence of HIV infection, neurologic manifestations associated with opportunistic infections in HIV have recently been reported in Korea [10, 11]. Considering the dramatic response to penicillin G, his cognitive decline might have been preventable with timely intervention. In that regard, the importance of a comprehensive and systematic approach in the evaluation of dementia cannot be overemphasized.

Syphilis and HIV coinfection should be considered in the differential diagnosis of rapidly progressive dementia in young patients because prompt therapeutic intervention could result in relatively good outcome.

REFERENCES

1. Lynn WA, Lightman S. *Syphilis and HIV: a dangerous combination. Lancet Infect Dis 2004; 4: 456-66.*
2. Poliseli R, Vidal JE, Penalva De Oliveira AC, Hernandez AV. *Neurosyphilis in HIV-infected patients: clinical manifestations, serum venere-*

al disease research laboratory titers, and associated factors to symptomatic neurosyphilis. Sexually transmitted diseases 2008; 35: 425-9.

3. Kang Y. *A normative study of the Korean-mini mental state examination (K-MMSE) in the elderly. The Korean Journal of Psychology 2006; 25: 1-12.*
4. Lee JY, Dong Woo L, Cho SJ, Na DL, Hong Jin J, Kim SK, *et al. Brief Screening for Mild Cognitive Impairment in Elderly Outpatient Clinic: Validation of the Korean Version of the Montreal Cognitive Assessment. J Geriatr Psychiatry Neurol 2008; 21: 104-10.*
5. Zetola NM, Engelman J, Jensen TP, Klausner JD. *Syphilis in the United States: an update for clinicians with an emphasis on HIV coinfection. Mayo Clin Proc 2007; 82: 1091-102.*
6. Zetola NM, Klausner JD. *Syphilis and HIV infection: an update. Clin Infect Dis 2007; 44: 1222-8.*
7. Suh MK EK, Ha GY. *A case of Human Immunodeficiency Virus Infection Associated with Syphilis. Korean J Dermatol 1994; 32: 498-502.*
8. Almeida OP, Lautenschlager NT. *Dementia associated with infectious diseases. Int Psychogeriatr 2005; 17 Suppl 1: S65-77.*
9. Brightbill TC, Ihmeidan IH, Post MJ, Berger JR, Katz DA. *Neurosyphilis in HIV-positive and HIV-negative patients: neuroimaging findings. AJNR Am J Neuroradiol 1995; 16: 703-11.*
10. Yoon JH, Bang OY, Kim HS. *Progressive multifocal leukoencephalopathy in AIDS: Proton MR spectroscopy patterns of asynchronous lesions confirmed by serial diffusion-weighted imaging and apparent diffusion coefficient mapping. Journal of Clinical Neurology 2007; 3: 200-3.*
11. Hong YJ, Jung S, Kim JY, Kwon SB, Song KB, Hwang SH, *et al. Complete binocular blindness as the first manifestation of HIV-related Cryptococcal meningitis. Journal of Clinical Neurology 2007; 3: 212-4.*