HIV-related Neurocognitive Disorder with Hallucinations and Delusions: A Case Report

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Case Report

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Abstract

Background: In patients with human immunodeficiency virus (HIV) infection, HIV-associated neurocognitive disorder (HAND) occurs in 18-50% of cases. Symptoms, including memory impairment, impaired attention, concentration, executive dysfunction, slowed motor speed, apathy, personality changes, and abnormal behavior vary. However, psychotic symptoms, such as hallucinations and delusions, are rare. We report a case of HAND with hallucinations, delusions, abnormal behavior, irritability, and decreased motor and attention-processing speeds that were successfully treated with risperidone and aripiprazole.

Case presentation: A 39-year-old Japanese man with a 6-year history of HIV presented to our hospital with delusions, hallucinations, and cognitive dysfunction. Five years ago, he was admitted to our department with abnormal behaviors, such as trespassing in his residence and immobility. He was diagnosed with HAND after HIV secondary brain disease was ruled out. He was admitted with auditory and visual hallucinations. However, his symptoms improved with risperidone (4 mg). Two years previously, he stopped taking risperidone and became irritable. He was admitted to our department in October of the same year with hallucinations, delusions, slow movement, and decreased spontaneity. Misperception, delusions, abnormal behavior, and prolonged response latency were observed at the time of admission. On the third day of admission, aripiprazole was administered, and the dose was titrated to 30 mg. His hallucinations, delusions, abnormal behavior, and irritability disappeared. One year later, in March, a cognitive function test showed that his motor speed, attention-information processing speed, and activity had improved.

Conclusions: This patient presented with HAND hallucinations, delusions, abnormal behavior, hyperirritability, and cognitive dysfunction. Risperidone and aripiprazole effectively alleviated these symptoms, and the cognitive dysfunction showed reversible improvement. Clinicians should be aware of the possibility of hallucinations and delusions, which are rare symptoms in treating HAND. Additionally, they should consider the possibility of improved cognitive function and provide appropriate treatments.

Background

Human immunodeficiency virus (HIV) is no longer a fatal infection but a manageable chronic disease that can lead to a nearly normal life span. Understanding its pathogenesis, advances in antiretroviral drugs, and promotion of social awareness have dramatically improved the treatment and prognosis of HIV-positive individuals [1].

It has been recognized that neurocognitive impairments have no explanation other than the HIV infection with the increasing longevity of HIV-infected patients. The HIV-associated neurocognitive disorder (HAND) concept has been defined for research and clinical purposes in patients with mild cognitive impairment not captured by conventional diagnostic criteria [2]. HAND, which ranges from asymptomatic neurocognitive impairment to severe cognitive dysfunction, occurs in 18–50% of patients with HIV-
infected. HAND symptoms include memory impairment, impaired attention and concentration, executive dysfunction, slowed motor speed, apathy, personality changes, and abnormal behavior. However, affective disorders and psychotic symptoms are rare, with few prior reports of psychotic symptoms in particular [3].

In this report, we describe a case of HAND with hallucinations, delusions, irritability, abnormal behavior, decreased motor speed, and decreased attention-information processing speed successfully treated with risperidone and aripiprazole.

Case presentation

A 39-year-old Japanese man with HIV presented to our hospital with delusions, hallucinations, and cognitive dysfunction. He was diagnosed with HIV infection 6 years ago and continued to work while being treated with antiretroviral drugs (dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg). Five years ago, his activity and speech decreased, and on August 3 of the same year, he stopped moving when he was out. The patient underwent further examination and treatment. The patient experienced visual and auditory hallucinations with critical patient content. Blood tests did not detect HIV-ribonucleic acids. Ribonucleic acid (RNA) and his cluster of differentiation (CD) 4 T-lymphocyte count was 996 cells/μL, indicating that treatment for HIV infection was controlled. Electroencephalography revealed sporadic slow waves at approximately 6 Hz. Head magnetic resonance imaging (MRI) showed age-inappropriate mild cerebral atrophy but no other abnormal intracranial signals, including white matter signals. Head single-photon emission computed tomography (SPECT) showed decreased blood flow in the bilateral parietal lobes, precuneus, and cerebellum. However, these findings were nonspecific, and secondary brain diseases, such as opportunistic infections secondary to HIV infection and neurodegenerative diseases, were ruled out. Finally, the patient was diagnosed with HIV-associated neurocognitive disorder. The patient was prescribed risperidone (4 mg); his symptoms resolved, and he was discharged. After discharge, he was able to work and lead a normal life. However, around March two years ago, he became reluctant to take risperidone because of somnolence and began taking it irregularly. Risperidone was discontinued upon request in May of the same year. The patient continued to receive antiretroviral medications. Subsequently, his facial expressions became increasingly difficult, and his irritability increased. In June of the same year, he stopped working. In November of the previous year, he began to have attention and short-term memory deficits, such as losing his wallet and forgetting where he had left his medications. He discontinued the antiretroviral medications around the same time. In September of the same year, he started experiencing hallucinations and delusions, like seeing his sister’s hair floating towards his face and delusions that his brother was responsible for his father’s death and the closure of the family's restaurant. He also developed autistic tendencies and anhedonia. Since October of the same year, his ability to respond to his family's attempts at communication has become limited. On October 5, year, when the patient went shopping with his brother, he became completely immobile and was admitted to our hospital.
When we examined him, he was lying on his bed with closed eyes and did not respond to our calls. After some time, he could open his eyes and assume a sitting posture. However, he loudly sighed when asked questions and took a long time to respond. He ignored our calls and stared at the faces and names of medical personnel. Antiretroviral medication was restarted on the first day of hospitalization. Aripiprazole 12 mg was initiated on the third day of hospitalization. He misidentified the medical personnel as relatives. He also admitted to delusions that the world had broken and a big fight was happening outside the hospital. He took a long time to respond, often only sighing and not responding. He was also seen making challenging comments to medical personnel. On the fifth day of admission, he showed abnormal behavior, such as unlocking the lock in another patient's protection room. A total of 24/30 points on the Mini-Mental State Examination (MMSE) showed decreased disorientation of place and time. The score on the Japanese version of the MoCA was 27/30, with deficits in trial-making, sentence recitation, and word recall. Laboratory tests showed no abnormalities in electrolytes, liver, kidney, or thyroid function, and HIV-RNA quantification was 20 copies/mL with a CD4+ count of 771 cells/μL, indicating that treatment for HIV infection was serologically successful. Electroencephalography revealed slow waves scattered at approximately 6 Hz. Head MRI showed slight cerebral atrophy. However, no abnormalities were observed, such as HIV-associated leukoencephalopathy or vascular lesions (Figure 1). Head SPECT showed nonspecific mild hypoperfusion in the left cerebral hemisphere and mildly increased blood flow in the right frontotemporal and left temporal lobes (Figure 2). After the aripiprazole dose was increased to 30 mg, his delusional complaints ceased, his challenging attitude disappeared, and he could spend time in the ward peacefully. However, he continued to have an attention disorder, slowness of movement, and sluggish reactions, such as being distracted by the attending physician's nameplate, window, or television during the examination and unable to carry on a conversation. On the 17th day after admission, abnormal behaviors were observed, such as attempting to climb the patio fence and removing the wall clock from the wards. Detailed cognitive testing was deemed necessary, and the Brief Assessment of Cognitive Scale for Schizophrenia was version (BACS-J). The results showed that motor function, attention, and information-processing ability were impaired by a -2 standard deviation or more (Table 1). On day 22 of hospitalization, he was treated with 400 mg aripiprazole long-acting injections, with no apparent psychiatric exacerbations or adverse events. The patient was discharged on day 36 of hospitalization.

After being discharged, the patient maintained regular visits to our hospital and received a 400 mg aripiprazole long-acting injection. One year later, in January, his response slowness noticeably improved. His activity level also increased, and by March of that same year, he had even started working part-time. We administered the BACS-J test to assess his cognitive function during an outpatient visit on March 16 of the same year. The results showed improved motor function and attention processing speed (Table 1). He continued to work part-time and received treatment at our hospital without hallucinations, delusions, abnormal behavior, or irritability. The MMSE score on August 31 of the same year was 30. Head SPECT showed no change in the nonspecific mild hypoperfusion in the left cerebral hemisphere and improvement in increased blood flow in the right frontotemporal and left temporal lobes. (Figure 3).
Discussion and Conclusions

This case report presents two important clinical and pathophysiological findings in HAND. The first was the presence of hallucinations and delusions associated with HAND, and the second was the efficacy of risperidone and aripiprazole in treating psychotic symptoms and reversible improvement in cognitive function.

According to conventional diagnostic criteria, HIV-associated dementia is defined as 1) acquired abnormalities in at least two cognitive domains (excluding motor domains) that impair work or daily activities and 2) acquired impairment of motor or executive functions or abnormalities in specific psychoneurotic or psychosocial functions (such as motivation, emotional control, and social behavior) that meet one of these criteria [2]. However, these criteria cannot identify patients with mild neurocognitive disorders and vary in estimating clinical severity because the degree of neurocognitive impairment is not well specified. A new disease concept called HAND was proposed to address these issues, and criteria were proposed to classify neurocognitive disorders into three categories: asymptomatic neurocognitive disorders, symptomatic neurocognitive disorders, and HIV-related dementia [2].

HAND presents various clinical symptoms, including memory impairment, executive dysfunction, slowness of thought and speech, attention disorders, multitasking disorders, impaired impulse control, and impaired judgment [1]. However, the comorbidity of affective disorders and psychosis in HAND is low [3] and reports on psychotic symptoms in particular are scarce. Expanding to HIV infection, a previous study indicated 26 patients with hallucinations or delusions after HIV infection and reported 14 patients with delusions and 23 with hallucinations [4]. This study also found that patients with opportunistic brain infections or metabolic encephalopathy were likelier to exhibit impaired consciousness, disorientation, attention, and memory than patients without HIV-related brain disease. Thus, we conclude that psychotic symptoms in HIV-infected patients are related to the systemic and cerebral complications of HIV infection rather than the psychotic process itself. However, our patient showed no HIV-RNA activation during the exacerbation of cognitive and psychiatric symptoms, and various tests revealed no secondary brain diseases. HAND occurs in patients with good blood viral control. This is because when HIV infects the central nervous system (CNS), the blood-brain barrier partially restricts the entry of anti-HIV drugs, the microglia that serve as HIV reservoirs are long-lived [5], and HIV entering the CNS forms a biological environment that is isolated from the peripheral blood and is thus more susceptible to antiretroviral drugs. HIV within the CNS has an independent genetic profile, which may alter its susceptibility profile to antiretroviral drugs [6]. When HIV enters the CNS, it infects microglia, astrocytes, and other cells, causing neurological damage through various mechanisms, including the release of inflammatory cytokines, the production of neurotoxins that induce neuronal apoptosis, increased levels of reactive oxygen species and nitric oxide, and increased permeability of the blood-brain barrier [7]. In this case, treatment improved the areas of elevated blood flow observed in the right frontotemporal and left temporal lobes on the head SPECT (Figure 2 and Figure 3). These findings may suggest an improvement in CNS inflammation. A previous study found no correlation between head
SPECT blood flow patterns and cognitive impairment severity or brain atrophy in HAND [8]. These differences suggest that hallucinations and delusions in HAND may be because of inflammation in the brain. This patient presented with various psychotic symptoms, including misidentification of medical personnel as related to him, delusions of victim relationships, delusions of a world-defeating experience, sub-catatonia and visual hallucinations, and affective disorders such as increased irritability. This report is the first of young patients with HAND and good HIV control showing various psychiatric symptoms.

Based on the severity of the criteria, this case was classified as HIV-related dementia because of the two domains (motor function and attention-processing speed) and major obstacles to daily life before treatment. After treatment, the patient's condition improved to asymptomatic neurocognitive impairment, which did not interfere with daily life. Previous reports have described cases of HIV-associated dementia with cognitive and motor impairments and improved levels of daily living following initiation of antiretroviral therapy [9] [10]. These reports suggest that cognitive decline because of HAND may be reversible with pharmacotherapy, even in severe conditions like HIV-related dementia. However, most case reports of improved cognitive function were because of antiretroviral drugs, and a few articles have suggested that other drugs have a significant effect. Irritability, lethargy, memory impairment, hallucinations, delusions, and slowed motor speed appeared and worsened after treatment with antiretrovirals alone, suggesting that risperidone and aripiprazole effectively improved the symptoms. In particular, aripiprazole allowed detailed cognitive changes in the BACS assessment. Possible reasons for the reversible improvement in cognitive function with antipsychotic drugs include the possibility that the improvement in psychotic symptoms also contributed to the improvement in cognitive function and that antipsychotic drugs suppressed the pro-inflammatory effects of microglia and increased their anti-inflammatory effects [7].

In conclusion, this patient showed HAND with hallucinations, delusions, abnormal behavior, hyperirritability, and cognitive dysfunction. Risperidone and aripiprazole were effective for these symptoms, and the cognitive dysfunction improved reversibly. Clinicians should be aware of the possibility of hallucinations and delusions, which are rare symptoms in treating HAND. They should also consider the possibility of improvement of cognitive function and provide appropriate treatment interventions.

**Abbreviations**


CD4; cluster of differentiation 4

CNS; Central nervous system

HAND; Human immunodeficiency virus associated neurocognitive disorder.

HIV; Human immunodeficiency virus.
MMSE; Mini-mental state examination
MRI; Magnetic resonance imaging
RNA; Ribonucleic acid
SPECT; Single photon emission computed tomography

**Declarations**

**Ethical Approval and Consent to participate**

All actions described in this case report were conducted according to the ethical guidelines. This was a case report, and the Ethics Committee of the University of Occupational and Environmental Health approved the review. Informed consent was obtained from all the patients for participation in this study.

**Consent for publication**

Informed consent was obtained from the patient to publish anonymous information in this manuscript.

**Availability of data and materials**

The data supporting the findings of this report are available from the corresponding author upon reasonable request.

**Competing interests**

All authors do not have any conflict of interest.

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**Author’s Contributions**

JI and NO investigated and made the most significant effort to draft the manuscript. JI and NO wrote the original draft and manuscript. JI, HT, and MA contributed to the patient’s treatment. The SI provided expert advice on head imaging findings. NO, HT, AI and RY supervised and revised the manuscript. All the authors have read and approved the final manuscript. All authors agree with the journal to which this article has been submitted.

**Acknowledgements**

None.
References


Table

Table 1 Change of The Brief Assessment of Cognition in Schizophrenia Japanese Version•BACS-J•
<table>
<thead>
<tr>
<th></th>
<th>Before treatment, points Z-Score</th>
<th>After treatment, points Z-Score</th>
</tr>
</thead>
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<tr>
<td>Verbal memory</td>
<td>61 (+1.44)</td>
<td>56 (+0.84)</td>
</tr>
<tr>
<td>Working memory (Digit sequencing)</td>
<td>19 (-0.81)</td>
<td>21 (-0.25)</td>
</tr>
<tr>
<td>Motor function (Token motor task)</td>
<td><strong>62 (-3.01)</strong></td>
<td>96 (+0.49)</td>
</tr>
<tr>
<td>Fluency task</td>
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<td></td>
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<tr>
<td>Semantic fluency</td>
<td>16 (-0.74)</td>
<td>16 (-0.74)</td>
</tr>
<tr>
<td>Word fluency</td>
<td>28 (+0.18)</td>
<td>28 (+0.18)</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>44 (-0.47)</td>
<td>47 (-0.20)</td>
</tr>
<tr>
<td>Symbol coding task</td>
<td><strong>33 (-3.29)</strong></td>
<td>53 (-1.50)</td>
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<tr>
<td>Executive function (Tower of London)</td>
<td>16 (-0.95)</td>
<td>17 (-0.50)</td>
</tr>
</tbody>
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**Figures**


Head MRI—fluid-attenuated inversion recovery

Head MRI showed slight cerebral atrophy. However, no abnormalities, such as HIV-associated leukoencephalopathy or vascular lesions.
Head SPECT statistical analysis image by 99m Tc-ECD

Head SPECT shows nonspecific mild hypoperfusion in the left cerebral hemisphere and mildly increased blood flow in the right frontotemporal and left temporal lobes.
Figure 3

Head SPECT statistical analysis image by 99m Tc-ECD

Head SPECT showed no change in the nonspecific mild hypoperfusion in the left cerebral hemisphere and improvement in increased blood flow in the right frontotemporal and left temporal lobes.