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Case Report

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Juvenile amyotrophic lateral sclerosis in 16 years old girl with HIV

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Abstract

There has been demonstrated that HIV could induce the induction of Amyotrophic lateral sclerosis (ALS) syndrome. The exact mechanism of pathogenesis is not fully understood and classic ALS and HIV-associated ALS are different in some key aspects. Our patient was a 16 years old girl who presented with progressive speech difficulties, gait disturbance, and upper and lowers limb weakness associated with atrophy, fasciculation, and hyperreflexia. After three months she experienced dysphagia. She had thenar atrophy in both hands and anterior forearms. Babinski's signs were present bilaterally. There was a pattern of diffuse chronic denervation with fasciculations in the four limbs according to electromyogram (EMG) results. Further tests showed the following findings: Positive HIV serology, a CD4+ count of 290 cells/mm3, and plasma HIV–RNA level was 31000 copies/ml; cerebral spinal fluid (CSF) analysis showing 22 cells/mm3 and protein analysis showing 77 mg/dL. It seems to be sufficient evidence that HIV infection is a potential cause of ALS-like syndrome; however, until knowing the exact pathological mechanism, possible coincidental HIV infection in patients with ALS syndrome should be considered.

Keywords: Amyotrophic lateral sclerosis, HIV infection, Case report, Juvenile, ALS

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Introduction

Amyotrophic lateral sclerosis (ALS) is one of the most common motor neuron diseases which is characterized by progressive neurodegeneration of upper and lower motor neurons (1). Although several genetic forms of ALS have been reported, the etiologies of a major number of ALS cases have been to be elucidated (1). The viral etiology of ALS has been proposed in the 1960s and 1970s when persistent poliovirus infection was hypothesized as a possible cause of motor neuron degeneration (2). In recent years, other viral causes of ALS syndrome have been proposed. As an example, it has been revealed ALS syndrome could be caused by the human T-cell lymphotropic virus type 1 (HTLV-1) causes ALS syndrome (3). Over the past years, several cases of ALS or ALS-like syndrome have been identified in association with human immunodeficiency virus type 1 (HIV) infection. Moreover, HIV infection is associated with other forms of motor neuron disease such as brachial amyotrophic diplegia (4). HIV-associated ALS is distinguishable from classic HIV in some key points, including early onset of disease and proper response to antiretroviral (ARV) therapy in some cases. Clinical course of ALS-associated HIV could be very fast, sometimes disease progresses in weeks or months. While the classic form of ALS usually occurs in older patients, HIV-associated ALS is observed in patients under 40 years and particularly in male patients (5). Here, we report a case with HIV infection and ALS syndrome and discuss the relationship between ALS syndrome and HIV infection and the related clinical comments.

Case presentation

A 16 years old girl presented with progressive speech difficulties, gait disturbance, and upper and lower limb weakness associated with atrophy, fasciculation, and hyperreflexia. After three months she experienced dysphagia. She had thenar atrophy in both hands and anterior forearms. Babinski's signs were present bilaterally. Deep tendon reflex

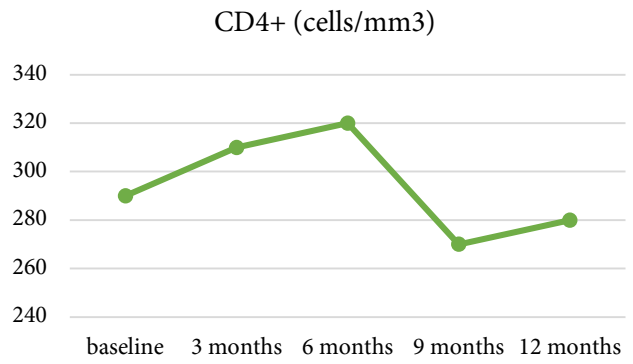

Figure1. Representation of longitudinal CD4+ level

was presented in the ankles. The physical, cognitive, autonomic, and sensory functions were normal. Brain and spinal cord MRI revealed no abnormality (Figure1). There was a pattern of diffuse chronic denervation with fasciculations in the four limbs according to electromyogram (EMG) results. My family history was negative for neurological disorders. The initial diagnosis was amyotrophic lateral sclerosis (ALS), but the other tests showed the following findings: Positive HIV serology, a CD4+ count of 290 cells/mm3 (Figure 1), and plasma HIV– RNA level was 31000 copies/ml; cerebral spinal fluid (CSF) analysis showing 22 cells/mm3 and protein analysis showing 77 mg/dL.

According to the diagnosis of AIDS and ALS, antiviral therapy (zidovudine, lamivudine, and Abacavir) along with riluzole 50mg twice a day started. However, her weakness progressed after one year.

Discussion

According to a review study conducted in 2014, isolated lower motor neuron (LMN) syndrome was present in 32% of HIV-associated ALS patients, and mixed LMN and upper motor neuron (UMN) was present in 57% of patients (5). However, some studies indicated that isolated LMN syndrome is more frequent than mixed UMN and LMN involvement (3).

Our patient showed mixed UMN and LMN syndrome and coincident identification of HIV infection. While many studies have reported the beneficial clinical effect of ARV therapy on a patient's outcome, her weakness progressed after one year of ARV therapy. However, a case report study by Satin et al., demonstrated three patients with HIV-associated ALS with mixed UMN and LMN involvement and slow disease progression with proper clinical response to ARV therapy (6). Unlike clinical response in our patient, MacGowan et al., reported a 32-year-old woman with HIV-associated ALS who recovered from motor neuron deficit after initiation of ARV therapy (7). Consistently, another case reported by Sinha et al., reported a 37-year-old male with HIV-associated ALS with concomitant tuberculosis who recovered after treatment with ARV therapy and antitubercular treatment (8). However, Von Giesen et al. reported two male partners infected with the same HIV strain but only one of them presented with HIV-associated ALS and showed no response to ARV therapy (9).

ALS occurring in HIV-infected patients could be either secondary to HIV infection or a rare coincidence. However, the pathogenesis of ALS-associated HIV is not understood and remains controversial (5). HIV does not infect motor neurons, but it could damage microglia and macrophages in CNS, and autopsy studies failed to HIV infection from motor neuron damage (10, 11). Therefore, it has been proposed that damage to motor neurons following HIV infection could be due to the production of neurotoxic cytokines and chemokines as a consequence of viral infection (12). Clinically, HIV-associated ALS differs from classic ALS at some points, including younger age of disease onset, rapid progression of the disease, high protein in CSF, and partial clinical response to ARV therapy. Moreover, in contrast to classic ALS which has invariable disease progression, clinical outcomes in HIV-associated ALS range from complete recovery to rapid progression and death (5). In fact, classic ALS is a monophasic disease with irreversible progression; however, HIV-associated ALS has a polyphasic progressive course and could be reversible with ART therapy (3, 13). Administration of corticosteroids and IVIg showed no clinical benefit in HIV-associated ALS patients, but ART therapy is the most effective method for progression control in these patients (5). It has been proposed that HIV could selectively mutate to infect motor neurons, suggesting the explanation of the efficacy of ARV therapy for the treatment of HIV-associated ALS (5). A comparative study conducted by Moodley et al. in 2018, revealed that HIV-associated ALS patients were younger, showed more severe disease at onset, and have longer survival if treated with ARV therapy, compared to patients with classic ALS syndrome (14).

In summary, ALS could infrequently occur following HIV infection. There is no certain pathophysiological mechanism following HIV infection is not understood and further studies are required to better elucidate the causal relationship. It should be considered that classic ALS and HIV-associated ALS are different in some key aspects, including the age of onset, male-to-female ratio, rapid progression, variable progression, and response to ARV therapy.

Declarations

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Conflict of interest

The authors have no conflicts of interest to disclose.

Consent for publication

This manuscript has been approved for publication by all authors.

Informed consent was taken from the patient

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