AIDS Research and Therapy

CASE REPORT

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Myelopathy as the first manifestation of AIDS

Yuanyuan Li[1], Qianru Yang[1], Hong Lin[1], Qiong Zhou[1], Fangfang Ge[1] and Jiankuan Shi[1*]

Abstract

Background Human immunodeficiency virus (HIV) is a retrovirus mainly infecting immune cells. Central nervous system diseases in HIV-infected patients can be caused by HIV or opportunistic infections. Neurological diseases associated with HIV have diverse manifestations and may occur in early or late stages. This article reports an HIV patient with myelopathy as initial symptom and negative spinal cord magnetic resonance imaging (MRI) and reviews common classifications of HIV-related spinal cord diseases.

Case presentation A 50-year-old male presented with weakness in both lower limbs and gait disorders for more than three months. Physical examination and various tests ruled out many possible causes. Given positive HIV and syphilis antibody in serological examination, normal spinal cord MRI and electromyogram, and after excluding other potential diagnoses through comprehensive analysis, the diagnosis of HIV-related myelopathy was established.

Conclusions Spinal cord lesions caused by HIV infection involve multiple aspects in terms of etiology and mechanism. HIV infection-related vacuolar myelopathy (HIV-VM) is the most common and typical spinal cord lesion. It usually appears at a relatively late stage of HIV infection, but it may also occur in the early stage and even serve as the initial manifestation of newly diagnosed HIV. The diagnosis of HIV myelopathy is usually exclusionary. In imaging, it often shows high T2 signal and spinal cord atrophy on spinal cord MRI, or it may also appear normal.

Clinical Trial Not applicable.

Keywords HIV-associated myelopathy, Spinal cord magnetic resonance imaging, HIV, Acute infection, HIV-associated neurological syndrome

Background

Globally, HIV-1 infection accounts for the vast majority of HIV cases. Among 33 million HIV-infected people, only 1 to 2 millions are caused by the relatively uncommon HIV-2 virus [1]. Globally, HIV-1 infection accounts for the vast majority of HIV cases. Among 33 million HIV-infected people, only 1 to 2 millions are caused by the relatively uncommon HIV-2 virus [2]. The degree of immunosuppression plays a critical role in determining both the risk and type of central nervous system (CNS) complications that may arise in HIV-infected individuals [3]. Others include malignant tumors (such as lymphoma), cerebrovascular diseases [4]. At the initial stage of infection, HIV invades the central nervous system and crosses the blood-brain barrier through infected monocytes. This mechanism is called the "Trojan horse" mechanism [5]. As early as 1 to 2 weeks after infection, the virus can be detected in the cerebrospinal fluid. Within 3 months after initial infection, changes will occur in brain structure, most of which show mild neurological symptoms [6]. During the seroconversion period, more severe neurological manifestations such as acute meningoencephalitis and acute inflammatory demyelinating polyneuropathy may occur, but usually there is no specific

*Correspondence:
Jiankuan Shi
shijiankuan@163.com
[1]Department of Neurology, Xi'an International Medical Center Hospital, xitai road, gaoxin District, Xi'an city, Shaanxi Province, China

imaging manifestation or no imaging manifestation at all [6, 7].

HIV-related neurological diseases have various manifestations.First, primary HIV infection: like acute meningoencephalitis, acute & chronic inflammatory demyelinating polyneuropathies, distal symmetric polyneuropathy,

cerebrovascular disease, myelitis, and HIV-associated neurocognitive disorder.Second, treatment side effects: neuropathy, stroke, and neuropsychiatric disorders.Third, opportunistic infections: toxoplasmosis, lymphoma, John Cunningham(JC) virus infection, cryptococcal meningitis, cytomegalovirus encephalitis, tuberculous meningitis, and varicella-zoster virus.

encephalitis.Fourth, immune response-related diseases: immune reconstitution inflammatory syndrome and CD8 encephalitis [1, 8]. Such diseases are usually diagnosed in the late stage of the disease [9]. However, neurological involvement may also occur in the early stage of HIV infection [10–12], making its diagnosis challenging. This article reports a case of an HIV patient with myelopathy as the initial symptom and negative spinal cord MRI, and reviews the common classifications of HIV-related spinal cord diseases.

Case presentation

A 50-year-old male was hospitalized due to weakness in both lower limbs and gait disturbance lasting over three months. The symptoms emerged spontaneously more than three months before admission.The patient has distal muscle weakness in both lower limbs, leading to an abnormal, scissor-like gait as described by relatives. No obvious fecal or urinary incontinence, swallowing or speech dysfunction, limb numbness, breathing difficulty, thoracolumbar girdle sensation, cognitive decline, vision loss, mental or behavioral changes, headache, dizziness, or fever was observed. The patient has no significant past medical history. Physical examination shows that the patient is conscious, with normal cognitive function, negative cranial nerve examination, grade 5- muscle strength in the distal end of both lower limbs, active tendon reflexes in all four limbs, positive pathological signs in both lower limbs, no cerebellar signs, negative meningeal irritation signs, no spinal cord lesion level, no sensory disturbance of deep and superficial sensations, and no urinary and fecal disorders. His spinal cord MRI, brain MRI and electromyogram are normal (Fig. 1).

His serological examination shows positive HIV and positive syphilis antibody. Lumbar puncture was performed. The cerebrospinal fluid test results suggest central nervous system infection (Table 1).

The metagenomic detection report of the complete set of pathogenic microorganisms in cerebrospinal fluid only detects HIV (Table 2; Fig. 2). Figure 2: Human immunodeficiency virus 1 Genome coverage map(coverage rate 82.11%).

Considering that the patient is mainly manifested as weakness in the lower limbs and gait disturbance, with a history of three months, no other underlying diseases or special drug exposure history in the past. The neurological examination suggests upper motor neuron paralysis (spastic paralysis). The localization diagnosis considers spinal cord involvement. He has an acute onset and a short course. There is no family history and no trauma history before getting sick. Therefore, we first excluded spinal cord diseases caused by neurodegenerative diseases, hereditary diseases, trauma, etc. Considering that his spinal cord MRI (cervical and thoracic spinal cords) is normal (no abnormal signals or obvious morphological changes of the spinal cord), we excluded spinal cord space-occupying lesions, tumors, vascular diseases, drug poisoning or side effects and other etiologies. His electromyogram is also normal. There is no evidence to support that he has immune-related peripheral neuropathy or motor neuron disease. His serological syphilis antibody is positive, but we did not find syphilis antibody in the tested cerebrospinal fluid, so neurosyphilis is not considered. After completing the metagenomic detection of the complete set of pathogenic microorganisms in cerebrospinal fluid, no Mycobacterium tuberculosis and other bacteria were found, so spinal tuberculosis is not considered. And the metagenomic detection report of the complete set of pathogenic microorganisms in cerebrospinal fluid only detects HIV. In conclusion, after excluding potential differential diagnoses it is considered that the diagnosis of HIV-related myelopathy is established. The patient was transferred to a specialized hospital for diagnosis and treatment one day after a definite diagnosis.

The patient underwent a CD4 cell count test in an infectious disease specialist hospital. The result indicated that the CD4 cell count was significantly low(Table 3). Antiretroviral drugs were administered. (Since the specialist hospital is not affiliated with the author's institution, the specific treatment plan cannot be provided.) At present, the patient's limb weakness and gait disorder have been remarkably improved. The patient can ascend and descend stairs easily without assistance.

Discussion and conclusions

The problem of spinal cord lesions resulting from HIV infection is growing increasingly prominent. Its etiology and mechanism are intricate, and diagnosis and treatment are extremely challenging. HIV-related spinal cord lesions not only inflict great pain on patients but also pose a formidable challenge to medical workers. The etiology and mechanism of it involve multiple aspects [13]. On one hand, the HIV virus itself has neurotropism and can directly damage the nervous system, including the

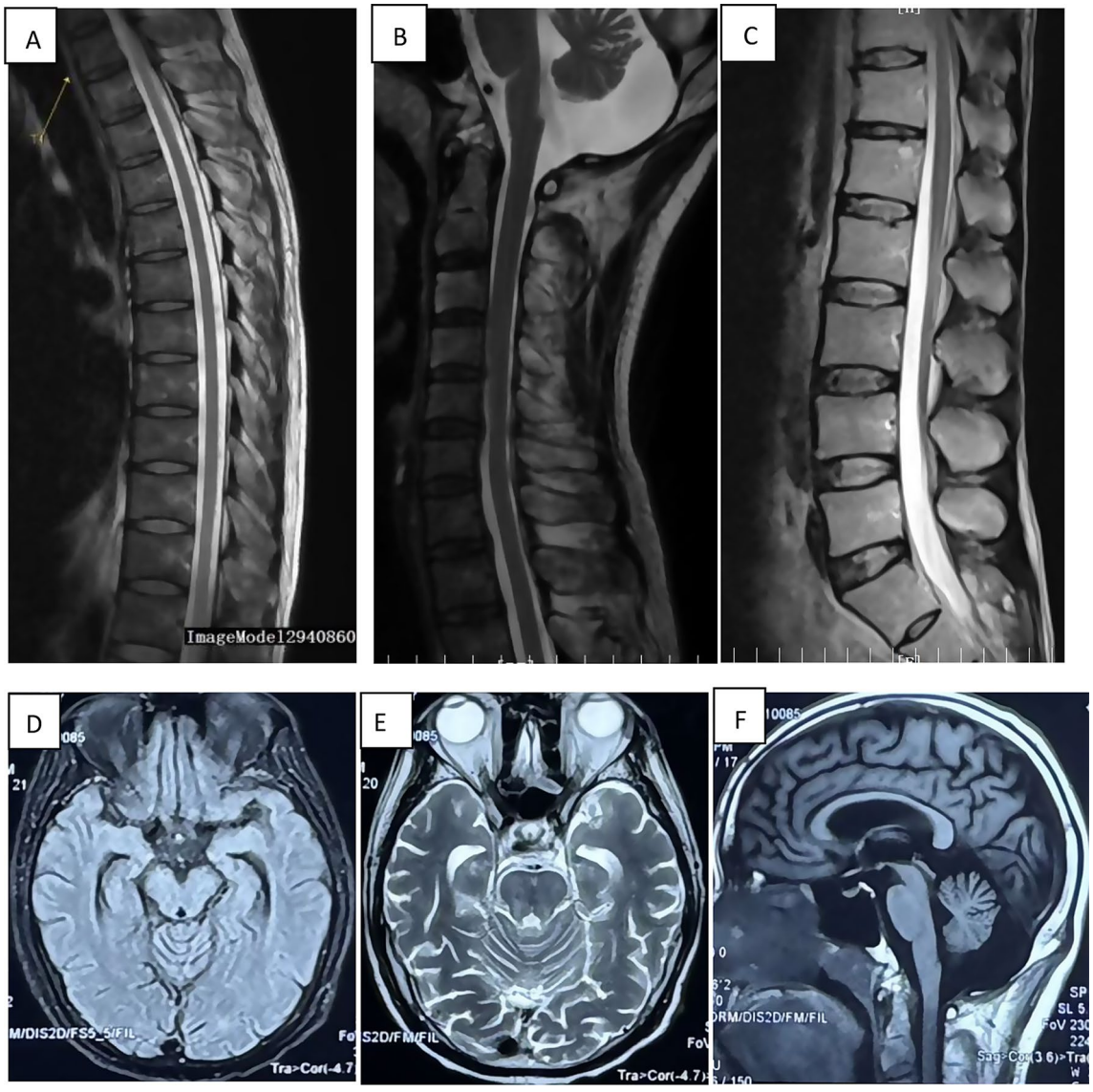

Fig. 1 **A**: Thoracic spinal cord segmental MRI T2-weighted; **B**:cervical spinal cord segmental MRI T2-weighted; **C**: lumbar spinal cord segmental MRI T2-weighted; **D**: Axial T2 FLAIR; **E**: Axial T2-weighted; **F**: Sagittal T1-weighted

Table 1 Cerebrospinal fluid laboratory results

Project	Result	Reference Interval
Cerebrospinal fluid cell count	13(10^6/L)	0–8(10^6/L)
Cerebrospinal fluid total protein TP-C	658 mg/L	150–450 mg/L
Glucose GLU	2.73mmol/L	2.22–3.89mmol/L
Chlorine CL	129.20mmol/L	120–132mmol/L
Lactate dehydrogenase LDH	26U/L	0–40U/L
Lactic acid LAC	1.97	0.5–2.2mmol/L
Intracranial pressure	110mmH2O	90–190mmH2O
Cerebrospinal fluid cell classification	Lymphocyte ratio (84.6%)	-
Cerebrospinal fluid appearance	Colorless, clear and transparent	Colorless, clear and transparent

spinal cord [14–17]. On the other hand, the immune deficiency caused by HIV infection makes patients susceptible to various opportunistic infections and tumors [2, 3, 8], and these factors may also indirectly lead to spinal cord lesions (Table 4 [13]).

HIV indirectly mediates spinal cord injury through immune regulation, degeneration, or related infections and tumors. The pathological manifestations are diverse, ranging from cytotoxic necrosis to demyelination and vasculitis. Clinically, HIV vacuolar myelopathy and opportunistic infections dominate in uncontrolled diseases [13].

HIV infection-related vacuolar myelopathy (HIV-VM) is the most common and typical spinal cord lesion. In fact, this belongs to a pathological diagnosis. It mainly

Table 2 Cerebrospinal fluid full set of pathogen microorganism metagenomic detection report, only HIV was detected

Genus				Species/Type/Subtype		
Type	Name	Sequence Number	Relative Abundance	Name	Sequence Number	Coverage
Single-stranded RNA (SSRNA)	Lentivirus	4062	98.42%	Human immunodeficiency virus type 1	4055	82.11%

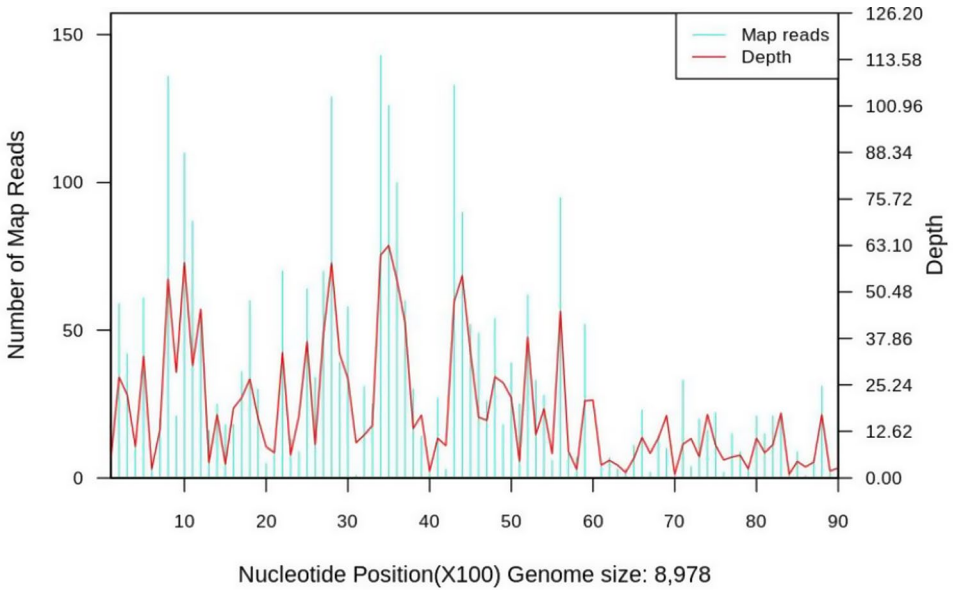

Fig. 2 Human immunodeficiency virus 1 Genome coverage map(coverage rate 82.11%)

Table 3 The patient's CD4 count

Project	Result	Reference Interval
CD4 cell count	34cells/μl	414-1123cells/μl
CD4 Lymphocyte Ratio	9%	34-70%

presents as slowly progressive spastic paraplegia, bladder and rectal dysfunction, and sensory disturbances [18, 19]. The pathophysiological mechanism of HIV myelopathy is currently unclear. The neurotoxic factors secreted by HIV-infected monocytes and the impaired utilization of B12 as a source of methionine in transmethylation metabolism are currently popular pathological hypotheses [20]. These factors can lead to multifocal vacuolization of the spinal cord tracts and histologically related pallor of the myelin sheath, so it is called vacuolar myelopathy [21, 22]. Before the introduction of antiretroviral therapy (ART), HIV-related myelopathy (HIV-VM) was extremely common and was mostly diagnosed only after the patient's death. Postmortem autopsy studies on AIDS patients reported that the proportion of pathological evidence of HIV-VM ranged from 22–55% [21, 23]. However, due to the difficulty and often delay in diagnosis, the actual prevalence is likely to be underestimated.

In the time course of HIV infection, HIV-VM usually appears at a relatively late stage, but in a few cases, it may also occur in the early stage of the disease [11, 24, 25]. There are reports that HIV vacuolar myelopathy may serve as the initial manifestation of newly diagnosed HIV [23, 26, 27]. In the literature on HIV infection-related myelitis, there are also two reports of transverse myelitis as the first manifestation of acute HIV infection [10, 17].

In terms of imaging, HIV myelopathy often shows high T2 signal on spinal cord MRI, commonly seen in the thoracic spinal cord. The lateral and posterior cords of the common spinal cord are involved, and the cervical spinal cord may also appear [23, 28]. Spinal cord atrophy is another common feature of long-term myelopathy [22, 28]. There are also reports that magnetic resonance imaging of patients with HIV myelopathy may show a normal-appearing spinal cord and has no obvious correlation with the severity of the patient's clinical symptoms [28]. Ernst F et al. [29]reported a case of a patient who had been previously diagnosed with HIV and presented with progressive weakness and difficulty walking. However, there was no abnormal signal on thoracic spinal cord magnetic resonance. After excluding other opportunistic infections, due to the significantly increased HIV load in the cerebrospinal fluid (CSF), HIV-related vacuolar myelopathy was diagnosed. HIV-VM is an exclusionary diagnosis. Negative or non-specific MRI results cannot rule out HIV-VM. In this case, the possible structural and functional damage of spinal cord cells must not be ignored.

Table 4 Human immunodeficiency virus (HIV)-associated spinal cord diseases

Disease	Prevalence	Pathophysiology	Key Diagnostic Tests	Treatment Methods
CD4 count > 500 cells/L				
Primary HIV-associated acute transverse myelitis	Case report	HIV-mediated immunotoxicity	CSF HIV RNA, exclusion of other diseases	Combined antiretroviral therapy (cART)
Immune-mediated transverse myelitis	Case report	Unknown	MRI, CSF oligoclonal bands	Corticosteroids
HIV-associated motor neuron disease	Case report	Unknown	MRI, EMG/NCS	Intravenous immunoglobulin (IVIG)
CD4 count < 500 cells/L	No data	No data	No data	No data
HIV myelitis	8-10% (pathological examination)	HIV-mediated immunotoxicity	CSF HIV RNA, exclusion of other diseases	Combined antiretroviral therapy (cART)
Vacuolar myelopathy	7-55% (pathological examination)	Unknown	Exclusion of other diseases	Supportive treatment
Primary central nervous system lymphoma	Case report	Intramedullary or leptomeningeal spread	CSF cytology examination, biopsy of mass lesion	Steroids, radiotherapy, systemic chemotherapy
Cytomegalovirus (CMV) radiculomyelitis	Case report	Necrosis, small and medium vessel vasculitis	CSF CMV PCR	Intravenous ganciclovir ± foscarnet sodium
Herpes simplex virus (HSV) sacral radiculomyelitis	Case report	Necrosis, small and medium vessel vasculitis	CSF HSV PCR	Intravenous acyclovir
Varicella-zoster virus (VZV) myelitis	Case report	Necrosis, medium vessel vasculitis	CSF VZV PCR or VZV IgM/IgG	Intravenous acyclovir
Spinal syphilis	Case report	Large vessel vasculitis, meningomyelitis, gumma, tabes dorsalis	CSF Venereal Disease Research Laboratory test (VDRL)	Intravenous penicillin
Spinal tuberculosis	Case report	Vertebral compression, paravertebral abscess, radiculomyelitis, tuberculoma	CSF acid-fast staining, culture or PCR, biopsy of mass lesion	First-line anti-tuberculosis drugs and corticosteroids

The main treatment methods for HIV-related myelopathy are still initiating highly active antiretroviral therapy (HAART) and symptomatic and supportive treatment. Other authors also claim that after receiving highly active antiretroviral therapy, the symptoms and signs of HIV-VM have completely recovered [30–33]. It has been reported that the symptoms of HIV-related acute transverse myelitis completely resolved and the imaging results turned negative after initiating HAART treatment [10]. However, the impact of HAART on specific neurological complications of HIVM is still controversial and may not be able to stop the progression of the disease [20, 26, 31, 34, 35]. Some studies have shown that patients with HIV-VM may benefit from immunoglobulin treatment, but this still requires further research [36]. In a phase II, double-blind, placebo-controlled study, L-methionine was used to treat AIDS-related myelopathy. The results showed that L-methionine is safe and well tolerated, but there is no significant benefit in any clinical indicators [20].

Given the common latency between initial HIV infection and symptom appearance or diagnosis, along with the fact that HIV can impact patients' spinal cord function, when coming across patients showing distinct spinal cord symptoms yet having a normal spinal cord MRI, one should stay alert and conduct HIV screening.

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Author contributions
YL, QZ, and QY collected and analyzed the data of the patients. YL analyzed the data and wrote the manuscript. JS, FG, and HL conceptualized the report and provided overall supervision. All authors read and approved the final manuscript.

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Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
The patient was verbally informed of the nature and purpose of the report, and signed the informed consent forms.

Consent for publication
The patient provided signed consent for publication of the case.

Clinical trial number
Not applicable.

Competing interests
The authors declare no competing interests.

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