Remission of HIV-associated myelopathy after highly active antiretroviral therapy

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ABSTRACT

HIV-associated myelopathy is the leading cause of spinal cord disease in HIV-infected patients. Typically, it affects individuals with low CD4 T cell counts, presenting with slowly progressive spastic paraparesis associated with dorsal column sensory loss as well as urinary disturbances. Other aetiologies must be first ruled out before establishing the diagnosis. We report here the case of a 37-year-old woman with advanced HIV disease, who developed HIV-associated myelopathy. The patient showed a gradual improvement after beginning with highly active antiretroviral therapy and, finally, she achieved a complete functional recovery. In addition, neuroimaging and neurophysiological tests normalized.

KEY WORDS: HIV-associated myelopathy, AIDS, HAART

Case History

In September 1996, a 37-year-old HIV-infected female patient presented with a 3-month history of progressive difficulty in walking. During that time she had noticed mild numbness and loss of joint position sense in her lower limbs, together with hesitancy of micturition. She also complained of pins and needles, as well as soreness in her lower limbs, mostly affecting the distal part of the legs. Six years previously, the patient had found out she was HIV positive (by heterosexual contact) and a recent control staged her disease as B3 (30 CD4 T cells/µL). She had been taking zidovudine, didanosine and trimethoprim/sulfamethoxazole, as primary prophylaxis, for the previous 3 years. Her past medical history was otherwise unremarkable. There was no drug abuse. Physical examination revealed a cachectic woman with lower limb weakness of pyramidal type, Grade 4 power (Medical Research Council scale), increased tone, brisk reflexes and ankle clonus. Both plantar responses were extensor. Sensory abnormalities included impairment of joint position sense in the feet, with no sensory level. In the upper limbs there was an increased tone and mild hyperreflexia, but power remained normal. The rest of the examination was unremarkable.

Routine haematology and biochemistry were normal, apart from mild anaemia (haemoglobin level of 10.5 g/dL) and a CD4 T cell count of 180/mm³. Both vitamin B12 and folate levels were within normal limits (B12: 419 pg/mL, normal range 165-920 pg/mL; folate: 6.3 ng/mL, normal range 2.2-17 ng/mL). Cerebrospinal fluid (CSF) analysis revealed a protein level of 53 mg/dL, with 1 white cell per high power field and a normal glucose level (47 mg/dL). CSF cultures yielded negative results for bacteria, including mycobacteria and fungi. It was negative for cryptococcal antigen as well. ELISA-based serological tests for cytomegalovirus (CMV), herpes simplex virus (HSV) and human T-lymphotropic virus type I and II (HTLV-I and II), both in serum and CSF, together with tests for syphilis, were all negative. Cervical and dorsal magnetic resonance imaging (MRI) showed T2-weighted hyperintensity within the spinal cord, between the level of C2 and C7, especially in the dorsal areas, with neither signs of spinal cord compression nor contrast enhancement (Figure 1A). Brainstem auditory evoked potentials, as well as visual evoked potentials, were normal. Somatosensory evoked potentials (SSEP) revealed a significant increase in the latency of the N20 waves of the upper limbs (median nerve) as well as the P37 waves of the lower limbs (posterior
Treatment with zidovudine, lamivudine and ritonavir was then initiated, leading to a progressive immunological recovery and a slow improvement of symptoms. Walking, power and sensation were normal after three years of follow-up. In May 1997, the MRI normalized (Figure 1B), together with a parallel and gradual improvement of SSEP, which became normal in March 2001 (Table 1).

In order to simplify the antiretroviral regimen, ritonavir was replaced by efavirenz in 2002. Currently, the patient is asymptomatic and her HIV viral load stays below 50 copies/mL, with a CD4 cell count between 800 and 1200 cells/µL.

**Discussion**

In the pre-HAART era, HM usually developed in the advanced stages of the HIV infection, with a progressive course until the patient’s death. Even though pathologic abnormalities of HM were found at autopsy in 22-55% of patients with advanced HIV infection, signs and symptoms of myelopathy had only been recorded in 26-60% of these patients during life.2,7 The pathogenesis of HM remains elusive, with no evidence for a direct effect of HIV on the spinal cord. Diagnosis is largely clinical and it is also based upon the presence of MRI changes, most commonly spinal cord atrophy or intrinsic cord signal abnormalities.10 Slowing or absence of waves in the SSEP also supports the diagnosis. Other possible causes of spinal cord disease mimicking this condition must be first ruled out before a diagnosis can be made. These include infections caused by CMV, HSV-2, HTLV-I and II, toxoplasma, tuberculosis and syphilis, as well as vitamin B12 deficiency, lymphoma, multiple myeloma, ischaemia and spinal cord compression.12 In the present case, all these conditions were excluded.

So far, four other cases have been published in the literature, reporting a remission of symptoms after initiating HAART, although neurophysiological tests were not carried out in two of them.3,4 Furthermore, in one case report, HM was the first symptom of HIV infection in a patient who preserved his CD4 count but showed high values of viral load.1 Eyer-Silva et al described a patient with symptomatic recovery after starting on lopinavir. This patient was previously under HAART, with unsuccessful viral control. SSEP here were only carried out after starting the treatment and recovery was incomplete.3 Finally, there is another patient in whom symptomatic recovery could be confirmed after initiating HAART, but in this case slight impairment of central conduction time could be demonstrated.6 Our patient is the first case showing full recovery after beginning with antiretroviral therapy. This recovery was documented by clinical, neuroimaging and neurophysiological tests. Clinical response correlated well with viral control, while neurophysiological parameters followed a slower recovery. Although the pathogenesis of HM is unknown, the clinical improvement that seems to parallel the immunological recovery in this patient suggests that HIV is likely to be the cause of this disease, either directly or due to an abnormal secretion of cytokines.

**References**


**Table 1: Somatosensory evoked potentials (in msec)**

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<th>1996</th>
<th>1998</th>
<th>2001</th>
<th>Normal values</th>
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<tr>
<td>N20 left</td>
<td>24.1</td>
<td>18.7</td>
<td>19.4</td>
<td>18.81±0.93</td>
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<tr>
<td>N20 right</td>
<td>25.4</td>
<td>18.8</td>
<td>19.8</td>
<td>18.94±1.07</td>
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<tr>
<td>P37 left</td>
<td>50.4</td>
<td>47</td>
<td>37.3</td>
<td>37.16±2.64</td>
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<tr>
<td>P37 right</td>
<td>53.8</td>
<td>48.6</td>
<td>39.5</td>
<td>36.80±3.02</td>
</tr>
</tbody>
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N20: median nerve. P37: tibial posterior nerve.