

## A Cerebellar Tremor in a Patient with Human Immunodeficiency Virus-1 Associated with Progressive Multifocal Leukoencephalopathy

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Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system (CNS) caused by JC virus infection in oligodendrocytes, especially in patients with acquired immunodeficiency syndrome (AIDS). Movement disorders associated with PML are very rare. Here, we report a case of PML in an AIDS patient who presented with a cerebellar tremor, caused by lesions in the cerebellar outflow tract. A cerebellar tremor can be a rare clinical manifestation in patients with PML.

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**Key Words:** Progressive multifocal leukoencephalopathy, Acquired immunodeficiency syndrome, Cerebellar tremor.

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system (CNS), caused by a lytic infection of oligodendrocytes with JC virus (JCV), a human polyomavirus. PML usually occurs in immunocompromised individuals, especially in patients with acquired immunodeficiency syndrome (AIDS).<sup>1,2</sup> Pathologically, any part of the white matter in the CNS can be involved; consequently, diverse neurological symptoms can be seen, depending on the site of involvement. However, movement disorders associated with PML are very rare.<sup>3,4</sup> Here, we report a patient with PML infected with human immunodeficiency virus (HIV) who presented with a cerebellar tremor caused by white matter lesions in the cerebellar outflow tract.

### Case Report

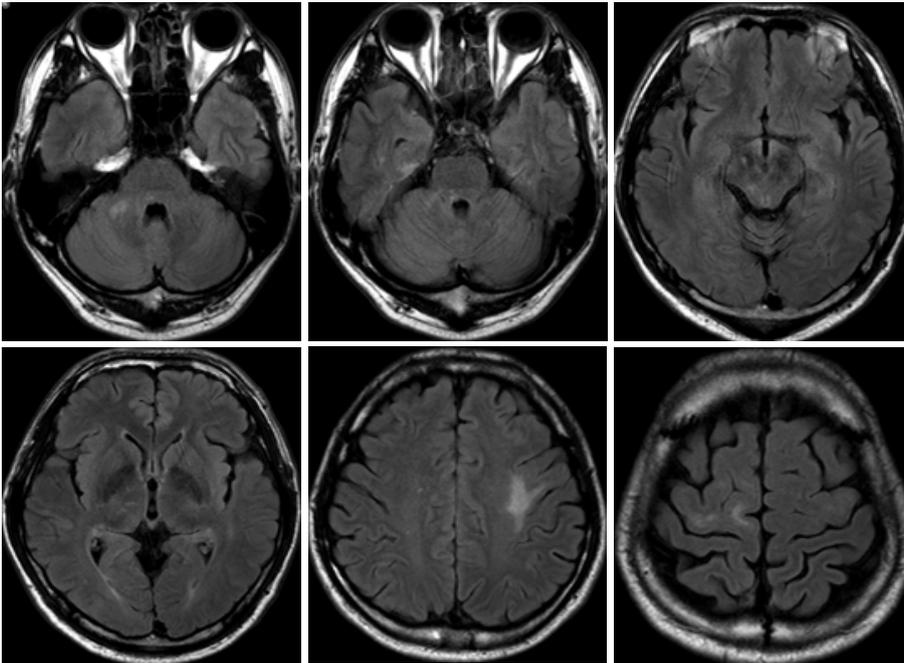
A previously healthy 34-year-old man visited another university hospital complaining of progressive weakness of the right extremities. The initial imaging findings showed hyperintensities in the left frontoparietal white matter, right superior cerebellar peduncle, and right posterior pons on fluid-attenuated inversion-recovery (FLAIR) images and hypointensities on T1 images, with no enhancement (Figure 1). A serology work-up to evaluate possible causes of immunocompromise followed. Based on positive laboratory findings in the HIV serology test and typical magnetic resonance imaging (MRI) findings, the patient was diagnosed with presumptive PML, combined with AIDS.<sup>2</sup> Efforts to identify JCV DNA in cerebrospinal fluid (CSF) and plasma failed and JCV was detected only in urine by PCR analysis. After beginning highly active antiretroviral therapy (HAART), the number of CD4<sup>+</sup> T-cells increased, from 70 to 180 cells/mm<sup>3</sup>, and negative conversion of HIV RNA copies was noted. However, the weakness of the right extremities slowly worsened. Five months after the initial symptom onset, he felt that his head was shaking and soon after, he developed tremulous movements of the left hand that gradually worsened.

On admission to our hospital, HIV RNA copies were seen again (41.2/mL) and the CD4<sup>+</sup> T-cell count had decreased to 10.2 cells/mm<sup>3</sup>. The neurological examination revealed asymmetric bilateral motor weakness, which was more severe on the right side (IV) than on

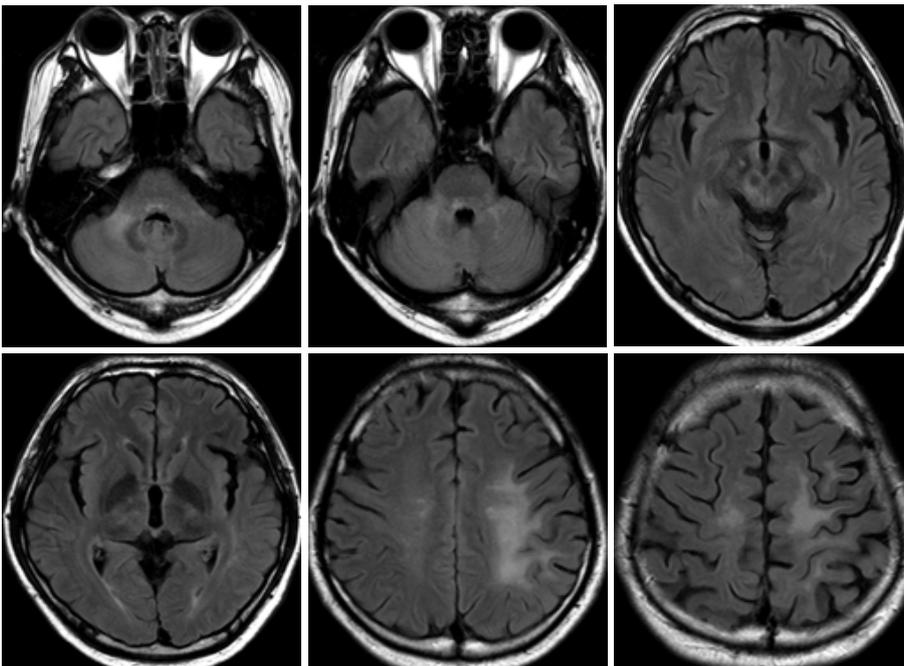
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**Figure 1.** The initial MRI shows multifocal lesions involving in left frontoparietal white matter, right superior cerebellar peduncle, and right posterior pons on fluid-attenuated inversion recovery images.



**Figure 2.** A follow-up MRI taken 2 months after onset of the tremor revealed new lesions involving the right thalamus, right retrorubral area, and right posterior pons with extension of the frontoparietal white matter lesions.

the left ( $IV^+$ ). Superficial and deep sensations were preserved. Deep tendon reflexes were hyperactive bilaterally and plantar reflexes were extensor bilaterally. When the arms were outstretched, there were large-amplitude, oscillatory, rhythmic movements, with a frequency of 3-4 Hz primarily in the head and left arm. This tremor was augmented on goal-directed movements, while no tremor was seen while resting or sleeping. His higher cognitive functions were unremarkable and his Mini-mental State Examination (MMSE) score was 30. He refused a CSF study to detect JCV DNA. Followup

MRI taken 2 months after the onset of the tremor revealed new lesions involving the right thalamus, right retrorubral area, and right posterior pons with extension of the frontoparietal white matter lesions (Figure 2). The introduction of steroid, topiramate (150 mg), and clonazepam (1.5 mg) tended to moderate the amplitude of the tremor.

## Discussion

In patients with HIV-1-associated PML not treated with

antiretroviral therapy, the diagnostic sensitivity and specificity of virological analysis of the CSF are 72-92% and 92-100%, respectively.<sup>4</sup> Although we failed to detect JCV DNA in the CSF, our patient was compatible with presumptive (clinical) PML, based on the typical clinical and neuroimaging characteristics.<sup>2</sup>

The most common presenting signs of PML are hemiparesis or monoparesis, visual defects, language dysfunction, personality changes, and ataxia. The clinical characteristics of PML can be variable, with multiple neurological deficits. Of the rarer combined neurological deficits, several types of movement disorder associated with PML have been reported. Singer, et al.<sup>5</sup> reported a patient with PML presenting with a rapidly progressive akinetic-rigid syndrome, while Bhatia, et al.<sup>6</sup> reported parkinsonism, combined with cognitive impairments. Others have reported patients with PML presenting with hyperkinetic movement disorders, such as tremor or dystonia.<sup>7</sup> Except for one report of very unusual PML by Bhatia, et al., the structural lesions responsible for the movement disorders have been localized to the basal ganglia or areas related to basal ganglia circuits; parkinsonism or dystonia was associated with PML lesions involving in the basal ganglia, whereas tremor was associated with lesions in the cerebellar output pathways.

Regarding the pathomechanisms of the cerebellar tremor in our patient, the PML lesions involving the midbrain and thalamus could disrupt the contralateral cerebellar outflow pathway, leading to an intention tremor. Similarly, Stockhammer, et al.<sup>3</sup> reported a patient with PML presenting with Hol-

mes' tremor-like phenomenon: a jerky tremor during rest and intentional components during goal-directed movements. Although detailed comparison of the midbrain lesions between our case and the case of Stockhammer, et al. is impossible because of the lack of imaging data, a difference in the involvement of the substantia nigra may lead to different types of tremor.

In summary, our case illustrates that cerebellar tremor can be a rare clinical manifestation in patients with PML.

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