

## JC VIRUS GRANULE CELL NEURONOPATHY AND HYPER-IgE IN HIV DISEASE

The polyomavirus JC (JCV) is the causative agent of progressive multifocal leukoencephalopathy (PML) in immunosuppressed patients. JCV is a neurotropic virus that causes productive infection of oligodendrocytes and restrictive infection of astrocytes. The concept of narrow host cell selection of JCV has been challenged by recent case studies. It was reported that JCV can also cause productive infection of cerebellar granular neurons (CGN) independently of PML infection in the cerebral hemisphere. This novel syndrome was called JCV granule cell neuronopathy (JCV-GCN).<sup>1,2</sup> Isolated cerebellar degeneration due to JCV infection restricted to the cerebellum in the absence of typical features of PML in HIV disease was only reported in one case.<sup>1</sup>

Hyperimmunoglobulinemia E (hyper-IgE) and eosinophilia have been described in some HIV-infected patients.<sup>3</sup> The immunoglobulin E (IgE) level was correlated with immune status. Very high IgE level (20- to 100-fold above normal) usually occurred with significant decrease in CD4 cells. These patients usually presented with atopic dermatitis and recurrent soft tissue infection.

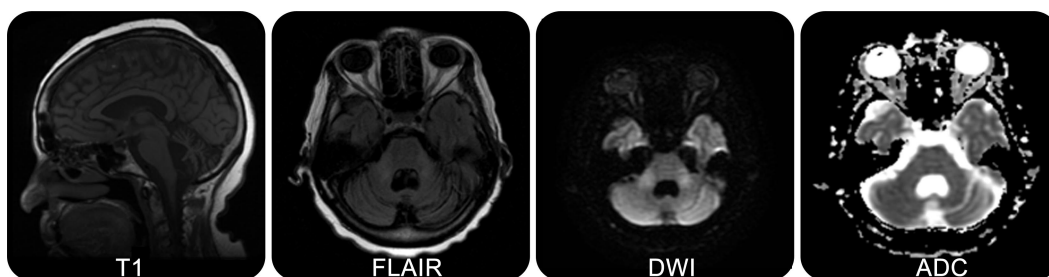
**Case report.** A 58-year-old right-handed black woman had unremarkable past medical history and family history. In early January 2010, she initially developed slurred speech, followed by ataxia on her left side. In March 2010, she developed ataxia on her right side and lost the ability to walk. She developed episodic vertigo and diplopia. Physical examination in early July 2010 was remarkable for severe scanning dysarthria, ataxic pursuit eye movements, saccadic overshoot, and conjugate nystagmus on upgaze. She could not perform finger-nose or heel-knee-shin movements or sit up because of severe extremity and truncal ataxia. Deep tendon reflexes were normal and the plantar responses were flexor. Sensation and cognitive examinations were normal. Serologic studies for infection, hepatitis, toxoplasmosis, autoimmune, and paraneoplastic disease were negative. Stool study

was negative for parasites. Blood cell count revealed eosinophilia with percentage of 39.5% (normal < 5%) and absolute count of  $0.9 \times 10^3/\text{mL}$  (normal <  $0.5 \times 10^3/\text{mL}$ ). Serum proteinogram showed immunoglobulin A 575 mg/dL (normal < 400 mg/dL), immunoglobulin G 1,820 mg/dL (normal < 1,600 mg/dL), immunoglobulin M 137 mg/dL (normal < 230 mg/dL), and IgE 91,200 IU/mL (normal < 100 IU/mL), without monoclonal spike. Anti-HIV1 antibodies were positive. CD4 cell count was  $6/\text{mm}^3$ . HIV1 RNA level was 154,180 copies/mL. CSF analysis showed erythrocytes  $0/\text{mm}^3$ , leukocytes  $0/\text{mm}^3$ , glucose 56 mg/dL, and protein 36.3 mg/dL. PCR for cytomegalovirus, herpes simplex virus 1 and 2, varicella zoster virus, Epstein-Barr virus, and HIV were negative in CSF. JCV PCR was positive in CSF. Brain MRI (figure) revealed severe cerebellar atrophy. Fluid-attenuated inversion recovery (FLAIR) images and T2 sequences showed areas of slight hyperintensity in bilateral middle cerebellar peduncles (MCP), which were restrictive on diffusion-weighted imaging but not on apparent diffusion coefficient. There was no hypointensity on T1 and no enhancement with gadolinium.

The patient was treated with highly active antiretroviral therapy (HAART) (ritonavir/lopinavir, zidovudine, and lamivudine) and re-examined 10 weeks later. There was improvement of ataxia on her left side, but the rest of the examination was unchanged. Laboratory results showed serum IgE level of 49,900 IU/mL, eosinophils of 5.1% in percentage and  $0.1 \times 10^3/\text{mL}$  in absolute count, CD4 cell count of  $39/\text{mm}^3$ , and HIV RNA level of 237 copies/mL.

**Discussion.** Biopsy was not performed in this case so pathology was not available. But the clinical, laboratory, and radiologic features are consistent with JCV CGN. Typical clinical and radiologic features of PML were not present. The slight hyperintensity in bilateral MCP on MRI FLAIR and T2-weighted images is of uncertain meaning, although it is tempting

**Figure** Diffuse cerebellar atrophy was demonstrated by MRI



ADC = apparent diffusion coefficient; DWI = diffusion-weighted imaging; FLAIR = fluid-attenuated inversion recovery.

to postulate that this is an extremely limited form of leukoencephalopathy associated with this particular type of JCV infection. It could be related to a cerebellar form of PML as it has been reported that cerebellar involvement was frequent in HIV-infected patients with PML.<sup>4</sup> However, the MCP involvement was rare without typical PML and usually showed hypointensity on T1-weighted images.<sup>5</sup> Furthermore, this MCP hyperintensity may simply be a nonspecific metabolic signal change due in some way to the effects of the infection, since the MCPs can be prominently involved in diverse and unrelated conditions such as the cerebellar form of multiple system atrophy, adult Alexander disease, and adult vanishing white matter disease.<sup>6</sup>

The significance of hyper-IgE is uncertain but may reflect impaired immune response. Her symptoms and laboratory results improved after HAART therapy, which has good CNS penetration.<sup>7</sup> The eosinophilia resolved and IgE level was decreased by half after 10 weeks' treatment. It is unlikely that her symptoms were due to parasite infection or other immunologic disorders. JCV CGN should be suspected in cerebellar degeneration in HIV-infected patients. This patient expands the spectrum of JCV-related CNS disease.

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*Disclosure: The authors report no disclosures.*

*Received October 30, 2010. Accepted in final form January 11, 2011.*

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*Neurology* 2011;76;1941-1942

DOI 10.1212/WNL.0b013e31821d751e

**This information is current as of May 30, 2011**

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