BMC Proceedings

BioMed Central

Oral presentation

Deconstructing progressive multifocal leukoencephalopathy

Igor J Koralnik[1,2]

Address: [1]Neurology Department, Beth Israel Deaconess Medical Center, Boston, MA 02215, USA and [2]Division of Viral Pathogenesis, Beth Israel Deaconess Medical Center, Boston, MA 02215, USA

Email: Igor J Koralnik - ikoralni@bidmc.harvard.edu

from Infectious diseases of the nervous system: pathogenesis and worldwide impact
Paris, France. 10–13 September 2008

Published: 23 September 2008

BMC Proceedings 2008, **2**(Suppl 1):S23

This abstract is available from: http://www.biomedcentral.com/1753-6561/2/S1/S23

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the brain caused by the reactivation of the human polyomavirus JC (JCV), which occurs in the setting of immunosuppression. Individuals at risk of developing PML include patients with AIDS or lymphoproliferative disorders, organ transplant recipients, and patients treated with immunosuppressive or immunomodulatory therapies for inflammatory or autoimmune diseases.

JCV remains latent in kidneys and lymphoid organs, and reaches the brain via hematogenous route. There, JCV causes a productive and lytic infection of oligodendrocytes leading to areas of demyelination and associated neurologic deficits. PML was recognized and named fifty years ago, before the discovery of its etiologic agent, and before the availability of modern neuroimaging techiques. However, we now recognize that PML may not always be progressive, that it can present as a single lesion, that it may not be restricted to the white matter, and that it may harbor inflammatory features. Therefore, JCV encephalopathy may be a more appropriate term to describe all the facets of this disease.

Indeed, while the classic presentation of PML is devoid of inflammation, novel inflammatory forms of PML have been observed in the context of an immune reconstitution inflammatory syndrome (IRIS), in HIV^+ patients receiving highly active antiretroviral therapy (HAART). This inflammatory reaction, characterized by contrast enhancement of PML lesions on MRI and inflammatory infiltrates in the brain parenchyma, may be associated with life-threatening edema and may require treatment with corticosteroids.

Moreover, in addition to glial cells, JCV can also infect cerebellar granule cell neurons (GCN), leading to cerebellar atrophy and associated cerebellar dysfunction in immunosuppressed individuals. This novel clinical entity, dystinct from PML, was named JCV granule cell neuronopathy (JCV GCN). A deletion in the carboxy-terminus of the VP1 gene, encoding the major viral capsid protein, appears to be associated with the GCN tropism of JCV.

There is no treatment for PML, and survival at one year does not exceed 50%. However, individuals who are able to mount a cellular immune response against JCV, mediated by $CD8^+$ cytotoxic T lymphocytes (CTL), have a prolonged survival and a better clinical outcome. These CTL could be detected in the blood and CSF of PML survivors. Furthermore, $CD8^+$ T cells are present in PML lesions, and aggregate around JCV-infected glial cells. Therefore, immunotherapies aiming at boosting JCV-specific cellular immune response, such as dendritic-cell based immunotherapy, may be a valid treatment option for PML.

Supported by NIH NINDS grants R01 041198 and 047029, R21 051124 and K24 060950 to IJK.