



The cellular immune response against JC virus is instrumental in the containment of progressive multifocal leukoencephalopathy

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CD8⁺ cytotoxic T lymphocytes (CTL) are the effectors of the cellular immune response against viruses. We have previously shown that the presence of JCV-specific CTL is associated with a favorable outcome in patients with progressive multifocal leukoencephalopathy (PML), and we have characterized two 9 amino acid epitopes of the major capsid protein VP1 which are recognized by CTL of HLA A*0201⁺ PML survivors. To determine the role of this cellular immune response in the acute phase of PML, the presence of these JCV-specific CTL was determined in the blood of 26 patients who developed PML less than ten months before immune evaluation (3.7 ± 2.5). The early detection of JCV-specific CTL had an 87% predictive value for subsequent control of PML, while the absence of such cells had an 82% predictive value for a subsequent active form of the disease ($p = 0.0009$). In individual patients, an increase in JCV-specific CTL preceded a significant clinical improvement while a drop of CTL was associated with an exacerbation of PML. Since JCV infects 85% of healthy individuals, we hypothesized that the cellular immune response may be instrumental in containing JCV replication, and the development of PML. Of 11 healthy individuals tested, 8 (73%) had detectable JCV-specific CTL. The frequency of these cells in the blood was low, and varied from 1/2,500 to less than 1/100,000 PBMC. These results indicate that CD8⁺ T cell response against JCV is commonly found in immunocompetent people, and suggest that these cells might protect against the development of PML. Acknowledgments: this work was supported by Public Health Service grant R01 NS/AI 41198 and NS 047029, R21 NS 046243 and the Harvard Center For AIDS Research grant P30-AI28691.