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Pathogenesis of leukoencephalopathies in HIV+ patients

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The use of HAART in the treatment of HIV infection has led to a marked reduction in AIDS-associated morbidity and mortality, but PML is still observed with a relevant prevalence in AIDS patients. Interestingly, several PML cases show a prolonged survival and a new PML-like leukoencephalopathy, called non- determined leukoencephalopathy (NDLE) or encephalopathy of unknown origin, without evidence of JCV active infection, has been reported. It is likely that the immune system plays a role in both slowing the progression of PML, due to its affect on JCV replication, and in contributing to the genesis of NDLE in HIV+ HAART-treated patients. In fact it can be hypothesized that the result of an improved immune status upon HAART could also lead to an imbalanced expression of cytokines and immunomodulators by peripheral lymphocytes that may induce white matter lesions consistent of those seen in PML patients. In order to study the pathogenesis of these HIV-associated leukoencephalopathies, we are performing extensive evaluation of the immune system function, of the genetic background, and neurotropic viruses, JCV included, search on biological samples collected at different times of the diseases in patients with suspected NDLE, with PML, and in patients without any neurological disorders. So far, the data obtained on the patients enrolled suggest that no viruses seem to be involved in NDLE, but on the basis of the immunological results we confirm our hypothesis that an imbalance of the immune system plays a significant role in NDLE pathogenesis.