Med Microbiol Immunol
DOI 10.1007/s00430-015-0437-7

ORIGINAL INVESTIGATION

EBV and vitamin D status in relapsing-remitting multiple sclerosis patients with a unique cytokine signature

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Received: 12 July 2015 / Accepted: 8 September 2015

Abstract Multiple sclerosis, a debilitating autoimmune and inflammatory disease of the central nervous system, is associated with both infectious and non-infectious factors. We investigated the role of EBV infection, vitamin D level, and cytokine signature in MS patients. Molecular and serological assays were used to investigate immune biomarkers, vitamin D level, and EBV status in 83 patients with relapsing-remitting multiple sclerosis and 62 healthy controls. In total, 98.8 % of MS patients showed a history of EBV exposure compared to 88.6 % in the healthy group ($p = 0.005$). EBV DNA load was significantly higher in MS patients than healthy subjects ($p < 0.0001$). Using a panel of biomarkers, we found a distinct transcriptional signature in MS patients compared to the healthy group with mRNA levels of CD73, IL-6, IL-23, IFN-γ, TNF-α, IL-15, IL-28, and IL-17 significantly elevated in MS patients ($p < 0.0001$). In contrast, the mRNA levels for TGF-β, IDO, S1PR1, IL-10, and CCL-3 were significantly lower in MS patients compared to healthy controls ($p < 0.0001$). No significant differences were found with the mRNA levels of IL-13, CCL-5, and FOXP3. Interestingly, in MS patients we found an inverse correlation between vitamin D concentration and EBV load, but not EBNA-1 IgG antibody levels. Our data highlight biomarker correlates in MS patients together with a complex interplay between EBV replication and vitamin D levels.

Keywords Epstein–Barr virus · Relapsing-remitting multiple sclerosis · Vitamin D · Immune biomarker signature

Abbreviations

EBV	Epstein–Barr virus
RRMS	Relapsing-remitting multiple sclerosis
PRMS	Primary remitting multiple sclerosis
EDSS	Expanded Disability Status Scale
EBNA-1	EBV nuclear antigen 1
EBNA-2	EBV nuclear antigen 2
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
IDO	Indoleamine 2,3-dioxygenase
S1PR1	Sphingosine-1-phosphate receptor 1
CNS	Central nervous system

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Published online: 13 September 2015