Higher EBV response is associated with more severe gray matter and lesion pathology in relapsing multiple sclerosis patients: a case-controlled magnetization transfer ratio study

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Objective: To evaluate associations between Epstein-Barr virus (EBV)-specific humoral response and magnetization transfer ratio (MTR)-derived measure in multiple sclerosis (MS) patients and healthy controls (HCs).

Background: EBV infection has been associated with higher clinical activity and risk of multiple sclerosis MS. However, studies regarding the anti-EBV humoral response and its effect on non-conventional MRI imaging are currently lacking.

Design/Methods: The study included 101 MS patients (69 relapsing-remitting MS (RRMS) and 32 secondary-progressive MS (SPMS)) and 41 HCs who underwent clinical, serological, and MRI investigations. MTR values of T1-, T2-lesion volume (LV), normal-appearing (NA) brain tissue (NABT), gray matter (NAGM) and white matter (NAWM) were obtained. Enzyme-linked immunosorbent assay was used to quantify anti-Epstein Barr nuclear antigen (EBNA) antibody levels. Partial correlations corrected for MRI strength were used and Benjamini-Hochberg-adjusted p-values <0.05 were considered significant.

Results: MS patients had significantly higher anti-EBNA titer when compared to HCs (median 107.9 U/ml vs. 27.8 U/ml, p<0.001). Although numerically higher in the RRMS group, there were no significant anti-EBNA titer differences between the RRMS and SPMS subgroups (median 132.6 U/ml vs. 80.4 U/ml). Within the MS group, higher serum anti-EBNA titer was significantly correlated with lower T1-LV MTR (r=-0.287, p=0.035). Within the RRMS group, higher serum anti-EBNA titer was associated with T1-LV MTR (r=-0.524, p<0.001) and NAGM MTR (r=-0.308, p=0.043). These associations were not present in HCs nor in SPMS patients.

Conclusions: Greater EBV humoral response measured as anti-EBNA antibodies is associated with lower GM MTR changes and focal destructive lesion pathology in RRMS patients.