SPHINGOLIPID CLUB

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MEETING BOOK

Investigating the Impact of Epstein-Barr Virus on Sphingolipid Composition in Extracellular Vesicles of Multiple Sclerosis Patients

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Background. Multiple sclerosis (MS) is a chronic autoimmune disease characterized by the immune system's attack on the central nervous system, leading to demyelination and neurodegeneration. Epstein-Barr virus (EBV) has been recognized as a crucial risk factor in the development of MS, as almost all MS patients show evidence of past EBV infection. Extracellular vesicles (EVs) have been proposed as key players in the development of MS, due to their immunomodulatory potential and ability to cross the blood-brain barrier. Moreover, an increase in EBV-related proteins has been found in the circulating EVs of MS patients. Recent studies suggested that sphingolipid metabolism may be disrupted in MS, contributing to disease process. In light of this evidence, our aim was to study a possible link between MS and EBV, by assessing selective changes in EV sphingolipids.

Methods. Plasma-derived EVs from an exploratory cohort (n=24) of MS patients, on anti-CD20 or on other immunomodulating therapies, and healthy controls, were isolated by ultracentrifugation. Size and number of EVs was determined by nanoparticle tracking analyzer (NTA). Sphingolipids from patients' plasma and EVs were analyzed by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). The same approach was carried out on EVs from EBV- and EBV+ B lymphocyte-derived cell lines.

Results. EVs produced by EBV+ cell lines showed a significant increase in the concentration of dihydroceramides, ceramides, hexosylceramides, gangliosides GM3 and globosides GB3 (the last two precursors of the ganglio and globo series respectively) (all, $p<0.05$). No significant changes were observed in the plasma of MS patients, while a significant increase in sphingomyelins and hexosylceramides was seen in EVs from patients in anti-CD20 therapy compared to those from patients on other immunomodulating therapies (both, $p<0.05$).

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