Epstein-Barr virus antibodies in serum and cerebrospinal fluid from Multiple sclerosis, Chronic Inflammatory Demyelinating Polyradiculoneuropathy and Amyotrophic Lateral Sclerosis

V. Nocitia,b, G. Frisulloa, A. Martia, M. Luigettia, R. Iorioa, A.K. Patanellaa,b, A. Biancoa, P.A. Tonalia,b, R.L. Grilloc, M. Sabatelli a, A.P. Batocchia,⁎

a Institute of Neurology, Department of Neurosciences, Catholic University, largo Gemelli 8, 00167 Rome, Italy
b Don Carlo Gnocchi Foundation, Italy
c Institute of Microbiology, Catholic University of Rome, Italy

Abstract

Elevated anti-Epstein-Barr virus (EBV) antibody levels are present in serum of Multiple sclerosis (MS) patients but literature lacks of studies comparing anti-EBV antibody levels between MS and other neurological diseases. We evaluate anti-VCA IgG and IgM, anti-EBNA1 IgG, anti-Cytomegalovirus IgG and IgM titres in serum and cerebrospinal fluid (CSF) of 267 MS, 50 Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) and 88 Amyotrophic Lateral Sclerosis (ALS) patients. We found increased titres of anti-EBV-IgG in serum and CSF of MS subjects as compared to CIDP and ALS patients thus providing additional evidence for a possible involvement of EBV in MS.

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1. Introduction

Although the aetiology of Multiple sclerosis (MS) is still unknown, it is believed that MS is caused in a genetically susceptible host by environmental factors that trigger a T-cell autoimmune response against the CNS (Weiner, 2004). Several studies suggest a correlation between viral infection and risk for MS and, in particular, evidences for Epstein-Barr virus (EBV) has been increasing over the last 30 years (Pender, 2009) for some key aspects of EBV infection in the modulation of the human immune system (Lünemann et al., 2007). EBV, a virus that infects more than 90% of the adult population worldwide, is a human Herpes virus with the unique ability to infect, activate and persist in latent form in B lymphocyte for the duration of the infected individual’s lifetime (Pender, 2009). A strong association between EBV viral capsid antigen (VCA) IgG titres and Magnetic Resonance Imaging (MRI) evidence of MS progression has been reported (Zivadinov et al., 2009). Elevated EBV nuclear antigen 1 (EBNA1) IgG, a marker of the latent phase of the virus, has been found in subjects affected by MS and correlated with GD-enhancing lesions on brain MRI and change in Expanded Disability Status Scale score (Farrell et al., 2009).

However, literature lacks of studies that compare the serum and cerebrospinal fluid (CSF) EBV-positivity between MS and other neurological autoimmune or not autoimmune diseases.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired demyelinating disease of the peripheral nervous system and it is believed to be an autoimmune disorder in which myelin is the target of the immune attack. CIDP can be considered the peripheral counterpart of MS, because of similarities between the two diseases in the relapsing or progressive disease course, the presence of focal demyelination and concomitant axonal damage (Toyka and Gold, 2003). A recent paper (Lünemann et al., 2010) showed that this disease was associated with a moderately enhanced IgG reactivity to EBV-encoded antigens expressed during both B cell transformation and productive viral replication. Moreover, cellular EBV copy numbers were 3-fold increased in patients with CIDP. In contrast, humoral immune responses to other Herpes viruses (Cytomegalovirus, Herpes Simplex Virus) as well as virus-specific IgM responses were unchanged (Lünemann et al., 2010).

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder of the aging nervous system with a polygenic, multifactorial aetiology (Eisen, 2009). No significant differences in antibody distribution of Herpes simplex, Cytomegalovirus (CMV), Measles and Mumps viruses, in serum and CSF, were evident in ALS patients compared with MS patients (Provinciali et al., 1988).