Viruses & Autoimmune Disease: The Infection Connection

FMTown

Nikolas R. Hedberg, D.C., D.A.B.C.I.

Viruses

- Viruses consist of a nucleic acid (either DNA or RNA) associated with proteins encoded by the nucleic acid. The virus may also have a lipid bilayer membrane (or envelope) but this is acquired from the host cell, usually by budding through a host cell membrane. If a membrane is present, it must contain one or more viral proteins to act as ligands for receptors on the host cell.
- Since many viruses make few or no enzymes, they are dependent on host cell enzymes to produce more virus particles. Thus, virus structure and replication are fundamentally different from those of cellular organisms.
- Viral dependence on the host cell for various aspects of the growth cycle has complicated the development of drugs since most drugs will inhibit cell growth as well as viral multiplication (because the same cell enzymes are used).
- Enveloped viruses do not necessarily have to kill their host cell in order to be released, since they can bud out of the cell - a process that is not necessarily lethal to the cell - hence some budding viruses can set up persistent infections.

Diagnosis

- Any history of autoimmune disease
- Check blood chemistries
- Specific antibodies for each virus
- Chronic fatigue
- Chronic fever of unknown origin
- Swollen lymph nodes
- Symptoms seem to go up and down

Blood Chemistry Patterns

- High WBC during acute phase
- Low WBC during chronic infection
- High lymphocytes and monocytes in chronic infection
- High C-reactive protein, ESR, Fibrinogen
- Check ANA, RF and other autoimmune markers based on clinical findings

Classic Chronic Viral Infection

CBC, Platelet Ct, and Diff

WBC	**3.2**	**Low**	x10E3/uL	4.0 - 10.5
RBC	4.63		x10E6/uL	4.10 - 5.60
Hemoglobin	14.4		g/dL	12.5 - 17.0
Hematocrit	43.5		%	36.0 - 50.0
MCV	94		fL	80 - 98
MCH	31.1		pg	27.0 - 34.0
MCHC	33.1		g/dL	32.0 - 36.0
RDW	13.1		%	11.7 - 15.0
Platelets	240		x10E3/uL	140 - 415
Neutrophils	**34**	**Low**	%	40 - 74
Lymphs	**56**	**High**	%	14 - 46
Monocytes	9		%	4 - 13

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Intracerebral propagation of Alzheimer's disease: Strengthening evidence of a herpes simplex virus etiology.

Ball MJ, Lukiw WJ, Kammerman EM, Hill JM.

Department of Pathology, Oregon Health & Science University, Portland, OR, USA; Department of Neurology, Oregon Health & Sciences University, Portland, OR, USA. Electronic address: ballm@ohsu.edu.

A faulty human protein, abnormally phosphorylated tau, was recently publicized to spread "like a virus" from neuron to neuron inAlzheimer's patients' brains. For several decades, we have been amassing arguments showing that herpes simplex virus type 1 (HSV-1), not p-tau, propagates this interneuronal, transsynaptic pathologic cascade.

METHODS:

We reiterate convincing data from our own (and other) laboratories, reviewing the first anatomic foothold neurofibrillary tangles gain in brainstem and/or entorhinal cortex; the chronic immunosurveillance cellularity of the trigeminal ganglia wherein HSV-1 awakens from latency to reactivate; the inabilities of p-tau protein's physical properties to promote it to jump synapses; the amino acid homology between human p-tau and VP22, a key target for phosphorylation by HSV serine/threonine-protein kinase UL13; and the exosomic secretion of HSV-1-infected cells' L-particles, attesting to the cell-to-cell passage of microRNAs of herpesviruses.

RESULTS:

The now-maturing construct that reactivated HSV-1 best accounts for the intracerebral propagation of AD changes in the human brain should at last seem highly attractive. This hypothesis might even explain statins' apparent mechanism in some studies for lowering AD incidence.

CONCLUSION:

Provided that funding agencies will quickly ignite a new realm of investigation, the rejuvenated enthusiasm for testing this optimistic construct holds incalculable potential for rapid, efficacious clinical application, through already available and relatively safe antiviral therapeutics.

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HEPATITIS C VIRUS INFECTION OF A THYROID CELL LINE: IMPLICATIONS FOR PATHOGENESIS OF HCV ANDTHYROIDITIS.

Blackard J, Kong L, Huber A, Tomer Y.

Source

University of Cincinnati College of Medicine, Division of Digestive Diseases, ML 0595, 231 Albert Sabin Way, Cincinnati, Ohio, United States, 45267, 513-558-4389, 513-558-1744, jason.blackard@uc.edu.

Abstract

Background: Autoimmune and non-autoimmune thyroiditis frequently occur in persons with HCV infection. Treatment with interferon alpha (IFNα) is also associated with significant risk for the development of thyroiditis. To explore HCV-thyroid interactions at a cellular level, we evaluated whether a human thyroid cell line (ML1) could be infected productively with HCV in vitro. Methods and Results: ML1 cells showed robust surface expression of the major HCV receptor CD81. Using a highly sensitive, strand-specific RT-PCR assay, positive-sense and negative-sense HCV RNA were detected in ML1 cell lysates at days 3, 7, and 14 post-infection with HCV. HCV core protein was expressed at high levels in ML1 supernatants at days 1, 3, 5, 7, and 14 post-infection. The non-structural protein NS5A was also detected in ML1 cell lysates by Western Blot. HCV entry into ML1 cells was shown to be dependent on the HCV entry factors CD81 and Claudin-1 (CLA1), while IFNα inhibited HCV replication in ML1 cells in a dose-dependent manner. Supernatants from HCV-infected ML1 cells were able to productively infect fresh ML1 cells, suggesting that infectious virions could be transferred from infected to naïve thyroid cells in vivo. Additionally, HCV infection of ML1 cells led to increased expression of the pro-inflammatory cytokine IL-8. Conclusions: For the first time, we have demonstrated that HCV can infect human thyroid cells in vitro. These findings strongly suggest that HCV infection of thyrocytes may play a role in the association between chronic HCV infection and thyroid autoimmunity. Furthermore, the thyroid may serve as an extrahepatic reservoir for HCV viral replication, thus contributing to the persistence of viral infection and to the development of thyroid autoimmunity.

Risk factors associated with elevated blood cytomegalovirus pp65 antigen levels in patients with autoimmunediseases.

Fujimoto D, Matsushima A, Nagao M, Takakura S, Ichiyama S.

Source

Department of Infection Control and Prevention, Kyoto University Hospital, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto, Kyoto, 606-8507, Japan.

Abstract

To further assess the relationship between elevated levels of cytomegalovirus (CMV) pp65 antigen in blood, as indicative of viral load, during treatment-free follow-up and CMV diseases in patients with autoimmune diseases and to identify any risk factors associated with elevated viral loads.

METHODS:

This was a retrospective review of the electronic medical charts of 148 patients with autoimmune diseases who tested positive for CMV pp65 antigen in the blood.

RESULTS:

A total of 106 patients were analyzed. During follow-up, elevated viral loads were detected in 35 patients who were not on antiviral therapy, of whom five developed CMV diseases. Elevated viral load was significantly associated with CMV diseases [5/35 vs. 0/71 (no elevated viral load); P = 0.001). Multivariate analysis revealed that lymphopenia [lymphocyte numbers <700/mm(3), odds ratio (OR) 34.44, 95 % confidence interval (CI), 7.82-151.66; P < 0.001], systemic lupus erythematosus (SLE) (OR 6.71, 95 % CI, 1.23-36.49; P = 0.028), and polymyositis/dermatomyositis (PM/DM) (OR 10.62, 95 % CI 1.41-79.77; P = 0.022) were significantly associated with elevated viral load.

CONCLUSIONS:

Elevated viral load was significantly associated with CMV diseases. Patients with SLE or PM/DM and lymphopenia would therefore benefit from a detailed viral load follow-up and careful physical examination.

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Role of early viral infections in development of multiple sclerosis.

Djelilovic-Vranic J, Alajbegovic A. Neurology Clinic, Clinical Center of University of Sarajevo, Sarajevo, Bosnia and Herzegovina.

Multiple sclerosis is a chronic inflammatory, autoimmune, demyelinating, disease but also degeneration of axons, with mainly progressive course, causing greater or lesser degree of disability. In addition to genetic predisposition the environmental factors, with particular importance of early viral infection, have an essential role in the development of MS. These are called long-acting viruses that remain hidden in the body for years by encouraging latent immunological changes in the body, eventually resulting in autoimmune demyelination and the appearance of disease symptoms, which confirms the high titer of antibodies to certain viruses in patients with the MS. To first of all herpes simplex virus, Epstein Barr virus, cytomegalovirus and rubella virus.

Goal of this study is to analyze the incidence of early infection with rubella virus, herpes simplex, cytomegalovirus and Epstein-Barr, in MS patients using titers of IgG and IgM antibodies.

The study included patients treated at the Neurology Clinic in Sarajevo, with a diagnosis of multiple sclerosis (newly discovered) in the period January 2009-December 2011. To all patients beside history and neurological examination and tests to confirm the MS (brain MRI, evoked potentials and CSF examination) made serological tests for viruses, HSV, Rubella virus, cytomegalovirus and Ebstain-Barr'svirus, with reference to the previous parameters (old) and new viral infection.

RESULTS:

In this period there were 118 newly diagnosed multiple sclerosis from which 69.5% (82) female and 30.5% (36) male patients aged 23-56 years. IgG antibodies to herpes simplex virus was positive in 93.2% (110 patients) (72 F and 38 M and IgM only in 0.84% (1 patient). Ig G in Cytomegalovirus was positive in 86.44% (102 subjects, 71 females and 31 males), while IgM was negative in whole sample. IgG Rubella virus was positive in 61.01% (72 patients, 52 F and 20 M) and IgM was negative in all, while IgG in Ebstain-Barr's virus was positive in 83% (98 patients).

CONCLUSION:

Early infection by herpes simplex virus, cytomegalovirus, Epstein-Barr and Rubella is present in patients with multiple sclerosis in a significant number so the conclusions is the fact that in the development of multiple sclerosis an important role early exposure to these viruses. Key words: early viral infection, multiple sclerosis.

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CD8+ T-Cell Deficiency, Epstein-Barr Virus Infection, Vitamin D Deficiency, and Steps to Autoimmunity: A Unifying Hypothesis.

Pender MP.

Source

School of Medicine, The University of Queensland, Brisbane, QLD 4072, Australia.

Abstract

CD8+ T-cell deficiency is a feature of many chronic autoimmune diseases, including multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, systemic sclerosis, dermatomyositis, primary biliary cirrhosis, primary sclerosing cholangitis, ulcerative colitis, Crohn's disease, psoriasis, vitiligo, bullous pemphigoid, alopecia areata, idiopathic dilated cardiomyopathy, type 1 diabetes mellitus, Graves' disease, Hashimoto's thyroiditis, myasthenia gravis, IgA nephropathy, membranous nephropathy, and pernicious anaemia. It also occurs in healthy blood relatives of patients with autoimmune diseases, suggesting it is genetically determined. Here it is proposed that this CD8+ T-cell deficiency underlies the development of chronic autoimmune diseases by impairing CD8+ T-cell control of Epstein-Barr virus (EBV) infection, with the result that EBV-infected autoreactive B cells accumulate in the target organ where they produce pathogenic autoantibodies and provide costimulatory survival signals to autoreactive T cells which would otherwise die in the target organ by activation-induced apoptosis. Autoimmunity is postulated to evolve in the following steps, (1) CD8+ T-cell deficiency, (2) primary EBV infection, (3) decreased CD8+ T-cell control of EBV, (4) increased EBV load and increased anti-EBV antibodies, (5) EBV infection in the target organ, (6) clonal expansion of EBV-infected autoreactive B cells in the target organ, (7) infiltration of autoreactive T cells into the target organ, and (8) development of ectopic lymphoid follicles in the target organ. It is also proposed that deprivation of sunlight and vitamin D at higher latitudes facilitates the development of autoimmune diseases by aggravating the CD8+ T-cell deficiency and thereby further impairing control of EBV. The hypothesis makes predictions which can be tested, including the prevention and successful treatment of chronic autoimmune diseases by controlling EBV infection.

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Autoimmune disease: A role for new anti-viral therapies?

Dreyfus DH.

Source

Pediatrics, Yale University School of Medicine, New Haven, CT, United States. dhdreyfus@pol.net

Abstract

Many chronic human diseases may have an underlying autoimmune mechanism. In this review, the author presents a case of autoimmune CIU (chronic idiopathic urticaria) in stable remission after therapy with a retroviral integrase inhibitor, raltegravir (Isentress). Previous reports located using the search terms "autoimmunity" and "anti-viral" and related topics in the pubmed data-base are reviewed suggesting that novel anti-viral agents such as retroviral integrase inhibitors, gene silencing therapies and eventually vaccines may provide new options for anti-viral therapy of autoimmunediseases. Cited epidemiologic and experimental evidence suggests that increased replication of epigenomic viral pathogens such as Epstein-Barr Virus (EBV) in chronic human autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus Erythematosus (SLE), and multiple sclerosis (MS) may activate endogenous human retroviruses (HERV) as a pathologic mechanism. Memory B cells are the reservoir of infection of EBV and also express endogenous retroviruses, thus depletion of memory b-lymphocytes by monoclonal antibodies (Rituximab) may have therapeutic anti-viral effects in addition to effects on B-lymphocyte presentation of both EBV and HERV superantigens. Other novel anti-viral therapies of chronicautoimmune diseases, such as retroviral integrase inhibitors, could be effective, although not without risk.

Lupus & Hashimoto's

- 39, female
- Fatigue/malaise, muscle pain, swollen cervical lymph nodes, insomnia, weight gain, joint pain, kidney pain, bloating, anxiety, depression, mood swings.
- Rosacea
- ANA positive
- Blood in urine
- Regular herpes outbreaks

Lupus & Hashimoto's

EBV-VCA IgG / IgM by ELISA 229 Verified 5/25/2012 Serum - 2	5/23/2012	IgM Neg (Index=0.19)	IgG Pos (Index=4.95)	* IgM Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 > * IgG Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 >
EBV-EBNA-1 IgG / IgM by ELISA 230 Verified 5/25/2012 Serum - 2	5/23/2012	IgM Neg (Index=0.64)	IgG Pos (Index=7.31)	* IgM Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 > * IgG Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 >
EBV-EA-D IgG / IgM by ELISA 231 Verified 5/25/2012 Serum - 2	5/23/2012		IgM Pos (Index=1.43) IgG Pos (Index=2.64)	* IgM Index range: Neg: < 0.89, Equivocal: 0.90-1.09, Pos: 1.10 > * IgG Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 >
Cytomegalovirus (CMV) IgG / IgM by ELISA 233 Verified 5/25/2012 Serum - 2	5/23/2012	IgM Neg (Index=0.23) IgG Neg (Index=0.11)		* IgM Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 > * IgG Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 >
Chlamydia pneumoniae IgG / IgM by ELISA * 327 Verified 5/25/2012 Serum - 2	5/23/2012	IgM Neg (Index=0.16) IgG Neg (Index=0.47)		* IgM Index range: Neg: < 0.89, Equivocal: 0.90-1.10, Pos: 1.11> * IgG Index range: Neg: < 0.89, Equivocal: 0.90-1.10, Pos: 1.11>
Mycoplasma pneumoniae IgG / IgM by ELISA 340 Verified 5/25/2012 Serum - 2	5/23/2012		IgM Pos (Index=1.17) IgG Pos (Index=5.18)	* IgM Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 > * IgG Index range: Neg: < 0.90, Equivocal: 0.91-1.09, Pos: 1.10 >
Helicobacter pylori (IgG / IgA) by Western blot * 353 Verified 5/25/2012 Serum - 2	5/23/2012	IgAAlt Neg IgGAlt Neg		IgA: No bands present IgG: No bands present . See attached report.

Lupus & Hashimoto's

- Larrea tridentata
- Olive Leaf Extract
- Lysine
- Monolaurin protocol
- Vitamin C
- Zinc
- Usnea lichen (mycoplasma)
- Whey protein
- N-Acetyl Cysteine

Nutrition

- An alkaline-forming diet is high in Lysine which is anti-viral.
- Sugar devastates the immune system for approximately 6 hours after consumption.
- Coconut, garlic and onion have anti-viral properties.
- Foods high in arginine may feed viruses.
- Ensure adequate protein intake for immune system health ie. Whey protein to boost glutathione

Conclusion

- More and more research is emerging on the connection between viruses and autoimmune diseases as well as disorders related to neurodegeneration such as Alzheimer's disease.
- Identify the virus through blood testing
- Look for chronic fevers and abnormal CBC's
- Treatment can take a few days to months
- Results can come very quickly when the virus is addressed
- www.infectionconnection.net