CASE REPORT

Treatment of Epstein-Barr Induced Hepatitis with High Dose Intravenous Vitamin C: A Case Report

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Abstract

Introduction: Vitamin C has been previously studied for use with acute and chronic Epstein-Barr Virus (EBV) and hepatitis C. However, it has never been evaluated for its impact on EBV induced hepatitis. In this case report, we present a patient's history with EBV induced hepatitis treated with high dose vitamin C.

Methods: A 36-year-old female presented to the National University of Natural Medicine Health Center with reactivated EBV-induced viral hepatitis. She reported severe fatigue, brain fog, maintenance and initiation insomnia, periocular hyperpigmentation, blurry vision, and decreased concentration. The patient's diagnosis was confirmed with a diagnostic evaluation of her EBV titers and liver enzymes, all of which were elevated. After assessing for contraindications, the patient was treated with intravenous (IV) vitamin C starting at a 10g dose and increasing weekly for 3 weeks to a dose of 25g.

Results: After 12 weeks of treatment with high dose IV vitamin C, as well as other immune-supportive nutrient therapy, the patient reported a decrease in fatigue severity, brain fog, vision disturbances, exercise limitations, and insomnia severity.

Discussion: We recommend that physicians consider the administration of high-dose IV vitamin C for all concurrent cases of EBV and hepatitis in both acute and chronic conditions. As recognition of reactivated viral infections grows, high-dose IV vitamin C for other latent viral infections such as COVID-19, cytomegalovirus, herpes simplex, varicella zoster, and HIV should be considered.

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Introduction

Epstein-Barr Virus (EBV), a member of the herpes virus family, is a common infection, with 85-95% of the world population presenting seropositive.[1,2] EBV infects the B lymphocytes within the oropharyngeal cavity, which remains largely asymptomatic in the oropharynx and blood indefinitely.[3] Because of its high prevalence, primary infection occurs most commonly in adolescents via contact between shedders and unaffected hosts. Acute EBV infections typically present with severe fatigue, fever, headache, tonsillitis and/or pharyngitis, as well as cervical lymphadenopathy. EBV can have manifestations in almost every organ system including sequalae such as myocarditis, pneumonia, glomerulonephritis, pancreatitis and genital ulceration, and multiple sclerosis.[4,5] In addition, due to their highly dense lymphatic involvement hepato- and splenomegaly are also common end organ manifestations of EBV.[6] More than 90% of EBV cases include asymptomatic hepatic involvement, frequently resulting in mild transient transaminitis. Elevated transaminases are typically self-limiting with most cases resolving within 6 months after the primary infection. In 60% of cases, an absolute lymphocytosis is seen on peripheral smear, and in 50% of patients, atypical mononuclear cells make up at least 10% of the total WBC count, both of these increases are 95% specific for viral hepatitis.[7]

As physicians begin to understand the prevalence of chronic viral illnesses due to infections like long-COVID, chronic, and reactivated EBV is slowly gaining recognition.[8,9] Although 70% of patients recovering from EBV-induced hepatitis by the end of the 3rd week of infection,[7] because EBV remains dormant in circulating B lymphocytes, it can be reactivated in immunocompromising conditions such as severe psychological stressors,[9,10] cancer, autoimmune diseases and autoimmune-like diseases, chronic fatigue, myalgic encephalitis and ICU admission.

Oral and IV Vitamin C have both been studied for their virucidal properties, which occur, presumably, via their

Table 1. Case Timeline

Date	Summaries	Vitamin C Dose	Diagnostic Testing
12/29/21	The patient first diagnosed with EBV Vitamin D3 levels deficient		EBV viral Capsid Ab: 85.7 U/mL EBV Nuclear Ag: 59.00 U/mL EBV Early Ag D Ab: 13 U/mL D,25-OH: 26 ng/mL
3/3/22	Transaminitis first seen on labs EBV titers have increased Lymphocytosis seen on CBC Vitamin D3 levels insufficient		AST: 27 (WNL) ALT: 41 (elevated) EBV Viral Capsid Ab: 213 U/mL EBV Nuclear Ag: 83.3 U/mL EBV Early Ag D: 16.3 U/mL Lymphocytes: 49.5% D,25-OH:36 ng/mL
5/23/22	First IV therapy. Patient reports fatigue is 6/10	10 g	
6/9/22	Returned after 1st treatment, experienced a marked increase in energy with	20 g	
6/13/22	Continued improvement in energy levels after treatments.	25 g	
6/30/22	Energy has increased to a 7/10. She feels as if her fatigue no longer inhibits her from getting through the day. She feels much more interested in daily tasks. Still endorsing initiation insomnia.	25 g	
7/7/22	Reporting fatigue is 3/10, no longer interfering with ADLs She reports improved cognitive function, sharper vision, and an increased ability to perform physically strenuous activities	25 g	
7/14/22	Reports fatigue is 2/10 and further improvements in sleep quality, cognitive function, and vision	25g	
7/28/22	Missed a treatment. She felt a significant dip in energy. Less desire to perform physical tasks and ability to focus, and poorer sleep	25g	
8/11/22	Reports significant improvement in energy and symptoms of fatigue. She no longer endorsed blurry vision, poor sleep quality, or brain fog. She reported feeling back to normal.	25g	

immunomodulatory properties.[11–13] In vitro, millimolar levels of vitamin C has been shown to slow viral replication.[14] In immune cells, vitamin C congregates in high concentrations within leukocytes, lymphocytes, and macrophages[15,16] and can improve chemotaxis, enhance neutrophil phagocytic capacity and oxidative killing while supporting the proliferation and function of lymphocytes.[15,17] In an acute infection, circulating vitamin C levels are decreased due to metabolic consumption,[17] and supplementation may reduce disease duration and severity.[12]

Currently, no effective antiviral therapies are available for EBV in immunocompetent patients. Antiviral medications, such as acyclovir, have largely proven ineffective clinically and have only been recognized for their ability to decrease EBV replication in vitro.[18] High-dose IV vitamin C has been successfully studied previously for chronic and acute EBV infections,[22] but it has yet to be studied for EBV hepatitis specifically. To our knowledge, this paper describes the first clinical evidence of efficacious treatment for EBV-induced hepatitis and was accomplished using high-dose intravenous (IV) vitamin C.

Case Presentation

A 36-year-old cis-female was referred to the NUNM clinic for IV therapy in May of 2022. She presented with recurrent elevated levels of EBV as measured by IgG antibodies, elevated alanine amintotransferase (ALT), right upper quadrant pain, and hepatomegaly indicating viral hepatitis. However, she did not have elevated IgM antibodies, indicating this was a reactivated EBV infection. EBV has been shown to recur during episodes of both severe physiologic and psychologic stress demonstrated by increases in EBV titers.[8,9,19]

The patient reported experiencing severe fatigue as her main complaint while endorsing brain fog, maintenance, initiation insomnia, periocular hyperpigmentation, blurry vision, and difficulty concentrating. Upon presenting to the NUNM clinic, she had modified her thrice weekly exercise regimen to once per week to accommodate for her severe fatigue. After receiving her diagnosis, she also experienced a surge in daily stress due to her husband undergoing chemotherapy and becoming the primary caretaker of both him and their two children.

The patient has a family history of carcinoma, hypertension, and mental health diagnoses with a personal health history of vitamin D deficiency and chronic vaginitis. Vitals and injection site assessment were regularly performed at our clinic, but no other physical exams were performed due to the nature of the comprehensive referral from the patient's primary care provider (PCP). Based on her laboratory findings seen in Table 1 -transaminitis and EBV titers as well as absolute lymphocytosis, right upper quadrant pain, and confirmatory symptom picture, she was diagnosed with EBV-induced hepatitis by her PCP.

Upon EBV diagnosis in December 2021, her PCP prescribed a mushroom complex to provide immune support and 1 g of oral vitamin C daily. Before initiating treatment at the NUNM clinic, the patient's G6PD status was evaluated, as a positive result would be contraindicated with a high dose of vitamin C. She did not have a history of alcohol or drug use or travel to areas of infectious disease endemicity within the previous 6 months. As previously described by Wexler and Fuller,[20] prior to initiation of IV therapy, patient contraindications are evaluated, including possible nutrient sensitivities or

allergies and previous responses to injections or needles. An assessment including a thyroid panel, complete blood count, and a comprehensive metabolic panel are also completed before initiating treatment. For this patient, treatments were administered using a 25 g catheter placed in the antecubital fossa, delivered at 100-120 drops per minute based on the patient's tolerance and comfort. Heat was applied superiorly to the insertion site per the patient's request to prevent vasospasm.

Therapeutic Intervention

In addition to high dose IV vitamin C, other immune-supportive nutrients included in a typical Myer's cocktail (see Table 2), were added to the weekly treatments.[21] The patient began treatment with a 10 g dose of vitamin C, increasing weekly until a dose of 25 g per treatment was reached in week 3 (outlined in Table 1). Due to bowel intolerance, high dose vitamin C is generally delivered via IV, a route of administration that also limits nutrient loss that would otherwise occur during intestinal absorption. The Myer's cocktail was chosen to aid immune support, reduce fatigue, and eliminate toxins. The formula was modified throughout her treatment due to product availability and balancing of osmolarity. This included slight fluctuations in the volume of the carrier fluid, calcium gluconate, magnesium sulfate, and selenium. Each treatment began with an assessment of contraindications included in the acronym ATHUMB[20] including manual blood pressure readings pre- and post-treatment.

Follow-up and Patient Perspective

Throughout her treatment at NUNM she reported less fatigue and increased energy, improved vision, improved sleep quality, and improved cognitive function or "brain fog". The patient did not experience any adverse effects or unanticipated events during or after treatment. Throughout and after the cessation of treatment, she reported only positive responses. She experienced the aforementioned (Table 1) increase in fatigue after missing one week of treatment, which indicated to her that the therapy was effective and may continue to confer benefit. She was impressed with the ability of IV nutrient therapy to improve how she felt physically and mentally. After treatments she described feeling much more capable of taking on her husband's role within the family while he underwent chemotherapy.

Due to care team dynamics, and our role as adjunctive providers for intravenous therapy, follow up with this patient was sporadic, but at 3 months out, she has reported that her symptoms have resolved completely, and she denies a relapse since finishing her course of treatment. Future clinical research should attempt to closely monitor patient EBV titers throughout treatment to evaluate the impact of IV therapy on laboratory markers of disease progression and relapse.

Table 2. Myer's Cocktail Formulation

Nutrients	Volume (mL)	Concentration (mg/mL)
Sterile Water	250	0
Pyridoxine	2	100
Dexpanthenol	2	250
B-Complex[a]	3	100
Hydroxy/Methylcobalamin	2/1	1000 mcg
Magnesium Sulfate	4	500
Calcium Gluconate	1	1%
Sodium Selenate	1	200 mcg
Sodium Bicarbonate	3	8.4% solution

[a]B Complex: Thiamine HCl 100 mg/mL, Riboflavin-5-Phosphate 2 mg/mL, Pyridoxine HCl 2 mg/mL, Dexpanthenol 2 mg/mL, Niacinimide 100 mg/mL

Discussion

This patient presented with a rarer manifestation of a very common infection. Due to the systemic clinical presentation of this patient's symptoms, we approached the development of her treatment plan through the lens of whole person health.[23] The nutrients selected were to support the patient's physical condition and the life stress she was experiencing during treatment. By focusing our attention on the patient as a whole, we saw rapid improvements in clinical outcomes.

Previously, oral vitamin C supplementation at 1g per day has been studied for hepatitis. It has been found to decrease liver enzymes including ALT, AST, ALP, albumin, total direct and indirect bilirubin, and improve clinical outcomes.[24] In a 2014 study of 178 patients with elevated EBV IgG and 40 patients with elevated EBV IgM antibodies who were treated with IV vitamin C, dosages ranging from 7.5 g to 50 g. Most of these patients had previously been diagnosed with chronic fatigue syndrome, and only a small percentage of these patients had EBV as the etiological cause of their fatigue. The authors found that a high dose of vitamin C reduced viral antibody loads and disease duration and demonstrated an inverse correlation between plasma levels of vitamins C and D to EBV antibody levels.[22] Our patient also presented with increased EBV antibodies and hypovitaminosis D consistent with this described trend.

Based on our findings, we recommend that physicians consider the administration of high-dose vitamin C for all concurrent cases of EBV and hepatitis in both acute and chronic circumstances. As recognition of reactivated viral infections grows within the public and medical community due to the rise in prevalence of long-COVID, high dose intravenous vitamin C for other latent viral infections such as COVID-19, cytomegalovirus, herpes simplex, varicella zoster, and possibly even HIV should be considered.

Conflict of Interest

The authors do not have any conflicts of interest.

Informed Consent

Through participation in healthcare services at NUNM, a teaching clinic, this patient has provided informed consent for use of their anonymized medical history in research.

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