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Review Article

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Full Recovery from Chronic Fatigue Caused by Reactivation of the Epstein-Barr Virus Through the Use of Basic Micronutrition and Specific Micronutrition

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ABSTRACT

Background and objective: Chronic fatigue syndrome (CFS) is a disorder whose main symptom is tiredness that fails to improve with rest and worsens with exercise. It is a complex and chronic disorder of unknown etiology with general, physical and neurophysical manifestations.

There are numerous theories regarding its etiology. Prominent among them are problems related to mitochondrial bioenergetic functioning and latent infections with the Epstein-Barr virus (EBV) and cytomegalovirus (CMV). The objective of this case was to address the intense fatigue caused by EBV and CMV.

Method and Results: Man, 43 years of age, suffering from incapacitating CFS since 2016 and with a prior history of immune dysfunction in the form of recurrent tonsillitis and infectious mononucleosis. Viral serology testing detects reactivation of the EBV and elevated CMV and IgG.

A diet free of gluten, dairy products, and saturated fats is prescribed. At the same time escitalopram is discontinued, his lorazepam dose is lowered, and supplementation with micronutrients, probiotics, micotherapy, and micro-immunotherapy is started. In the first and second control visit (3.5 months), different adjustments are made in response to the improvement in the fatigue and clinical symptoms. After three months (third visit), specific micronutrients aimed at stimulating mitochondrial metabolism and increasing NAD+ are given. Three months later, in the last visit, he reports a spectacular change in his energy level compatible with family and work life, restful sleep, and satisfactory physical activity.

Conclusion: The increased NAD+ levels and supplementation with micronutrients that play a part in biochemistry and mitochondrial dynamics were essential factors in recovery from the intense fatigue and improvement of the mitochondrial machinery related to the immune response.

Keywords: Micronutrition, Basic Micronutrients, Specific Micronutrients, Mitochondria, EBV, NAD^+

Introduction

Chronic fatigue syndrome (CFS) is a disorder whose main symptom is tiredness that does not improve with rest and worsens with exercise. It is a complex and chronic disorder of unknown etiology with general, physical, and neurophysical manifestations.

There are numerous theories as to its etiology. Prominent among them are problems related to mitochondrial bioenergetic functioning and latent infections with the Epstein-Barr virus (EBV) and cytomegalovirus (CMV).

Diagnosis

Chronic fatigue due to reactivation of the Epstein-Barr virus.

Therapeutic Intervention

In September 2021 a diet free of gluten, dairy products, and saturated fats is prescribed. At the same time escitalopram is discontinued, his lorazepam dose is lowered, and micronutritional supplementation with water- and fat-soluble vitamin complexes, minerals, coenzyme Q10, lipoic acid, a balanced combination

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of omega-3 and omega-6 fatty acids is started, accompanied by probiotics, mycotherapy and myco-immunotherapy. In the first and second control visit (3.5 months), a series of adjustments are made in response to the improvement in the fatigue and clinical symptoms.

Patient Profile and Medical History

Gender and age	Male, 43 years of age
Diet, lifestyle, and toxicity	Diet rich in carbohydrates, red meat, and sweets, with low consumption of fruits and vegetables. Difficulty digesting gluten and gastrointestinal symptoms if cow's milk is consumed. Was exercising regularly until the first symptoms appeared.
Relevant pathological history	Recurrent tonsillitis since childhood which ceased following a tonsillectomy when the patient was 32 years of age. Rheumatic fever. Infectious mononucleosis at the age of 30. Allergic rhinitis.
Current symptoms and disease status	In 2016, symptoms of fatigue and exhaustion appear which prevent him from leading a normal life. He needs to rest frequently during the day to be able to carry out work and family activities and physical exercise. Unrestful sleep.
Past treatments and results	Acupuncture, lorazepam 1 mg at night and escitalopram 1 mg daily without results.
Relevant clinical findings	Homocysteine 14.05 µmol/L; CMV IgG: 141, AU/ml; EBV VCA IgG: 80; EVB EBNA IgG>5; EBV VCA IgG/EBNA: 16.

After three months (third visit), in February 2022, specific micronutrients like NAD+ precursors (tryptophan, nicotinamide, and nicotinic acid), amino acids (glycine and creatine), vitamin factors (taurine and coenzyme Q10), and other coenzymes and coenzymatic precursors and metal factors aimed at stimulating mitochondrial metabolism and increasing NAD+ are given.

Three months later, in May 2022, in the last visit, he reports a spectacular change in his energy level compatible with family and work life, restful sleep, and satisfactory physical activity (Figure 1).

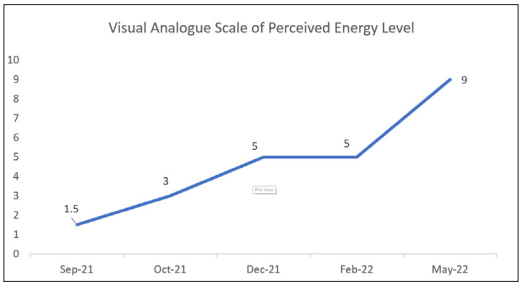

Figure 1: Graph of evolution of the Visual Analogue Scale of Perceived Energy Level

Discussion

Immune response depends directly on mitochondrial function. Many pathogens have developed strategies for altering mitochondrial dynamics and functionality to their benefit (Figure 2).

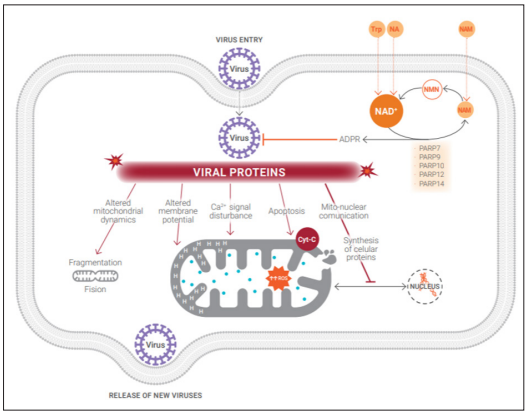

Figure 2: Strategies developed by viruses for altering mitochondrial functionality, and how increased NAD+ can help reduce mitochondrial dysfunction caused by a long-term infection. Trp: L-tryptophan; NA: nicotinic acid; NAM: nicotinamide; NMN: nicotinamide mononucleotide; PARP: poly (ADP-ribose) polymerase; ADPR: adenosine diphosphate ribose; Cyt-C: cytochrome c; ROS: reactive oxygen species.

EBV infection induces a period of very rapid cell division that requires an abundant supply of metabolytes that the infected cells are incapable of obtaining. As a result, they cease proliferation and take on a senescent phenotype. These are cells with reduced levels of mitochondrial respiration, of expression of the genes involved in the Krebs cycle, and of oxidative phosphorylation. The EBV reprograms monocytes, starting a feedback loop which, through inhibition of autophagy, reduces reactive oxygen species (ROS) and mitochondrial biogenesis transcription factors, alters mitochondrial dynamics and DNA replication, and up-regulates glucolysis. In this way, the virus is able to complete its lytic cycle and prevent monocyte differentiation to the dendritic cell.

Cells infected with the EBV have been proven to have high EO levels, as well as high values for the NADP+:NADPH and oxidized glutathione:reduced glutathione (GSSG:GSH) ratios. Thus, studies have confirmed that the use of molecules with antioxidant activity, such as N-acetylcysteine (NAC) and GSH, demonstrably inhibit EBV reactivation. Combined supplementation with NAC and glycine is the most effective option for increasing GSH levels.

Lastly, the patient's improved sleep quality plays an important role in his clinical progress. The relationship between sleep disturbance and reactivation of the Epstein-Barr virus, systemic inflammation, and NAD+ depletion is crucial for understanding how regulation of the sleep and wake system is optimal with repair of mitochondrial function.

Conclusion

Recovery of the micronutritional levels that intervene in mitochondrial biochemistry has been parallel to recovery of vitality in the patient in this case. Changes in the mitochondrial

machinery condition the immune response, as they can regulate the activation, differentiation, and survival of immune cells. Thus, in immune dysfunctions such as long-duration viral reactivations, mitochondria should be considered the therapeutic target, and recovery of basic and specific micronutrients is essential for favorable clinical progress.

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