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ANALYSIS AND OVERVIEW OF MYALGIC ENCEPHALOMYELITIS: A LITERATURE REVIEW

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Abstract: Myalgic encephalomyelitis (ME) is a complex and debilitating condition characterized by chronic fatigue that does not improve with rest, affecting millions of people around the world. With more recent studies, investigating social and pathophysiological profiles, the association of immunological and inflammatory dysfunction as possible causes for BD can be noted. In addition, projecting specificity at the time of diagnosis, changes were observed in the cytokine profiles and plausible 23 genes, in order to find a biomarker for the purposes of further research, aiding in better technologies for diagnosis, as well as for treatments of BD. **GOAL:** The current article aims to highlight the updated panorama about BD, analyzing new studies that demonstrate advances on the disease, clarifying its possible pathophysiology, clinical presentation, diagnoses and treatments. **METHODS:** This is a literature review on an overview of myalgic encephalomyelitis. Articles from SciElo, PubMed, MEDLINE and Lilacs databases were used. Considering the criterion of year of publication between 2016 and 2021. **FINAL CONSIDERATIONS:** Although described since 1869, there is still little progress in its panorama since its discovery, making more advanced research necessary to find a biological marker for the disease and thus direct the best treatment for the patient.
Keywords: Systemic Stress Intolerance Disease, Myalgic Encephalomyelitis, Chronic Fatigue Syndrome.

INTRODUCTION

In 1869, George Miller Beard presented the concept of neurasthenia, but in 1988, the Centers for Disease Control and Prevention (CDC) determined the term as chronic fatigue syndrome (CFS), then in 1994 it was revised by Fukuda, in which in the same year created the CFS diagnostic criteria (CALDERÓN-ELIZONDO, 2017). Also, it is possible to find other synonyms of CFS such as myalgic encephalomyelitis (ME), immune dysfunction of chronic fatigue and systemic intolerance to exertion. However, for Lapp (2016), using the CFS terminology can bring banalization and stigma, making its diagnosis difficult, so we will use ME.

Chronic, multifactorial, complex and debilitating, it is characterized by severe and disabling fatigue, in which there is no improvement with rest, being accompanied by sleep disorders and cognitive dysfunction (PÉREZ-HERNÁNDEZ, 2021). Since BD is associated with permanent physical and neuropsychological manifestations, and of unknown etiology, its diagnosis is based on the exclusion of other diseases, as there is no laboratory biomarker to prove it (ALMENAR-PÉREZ, 2020).

Such a condition causes damage to daily activities, and it can be inferred that BD reduces the quality of life of patients (DA-SILVA-VIEIRA et al, 2020). In addition, it affects young adults between the ages of 20 and 40, being 2 to 3 times more common in women when compared to men (REGAL; JESÚS, 2016). Its prevalence in women is due to genetic and hormonal factors, which consequently increase the immune response (PÉREZ-HERNÁNDEZ, 2021).

PATHOPHYSIOLOGY

According to Montoya (2017), symptoms similar to viral diseases, suspected the pathophysiology of BD as an inflammatory and/or immunological disorder. Additionally, individuals with ME declared that ME started after a viral condition, instigating the theory in which various neurotropic infectious agents chronically present in the CNS would stimulate a reduced immune response, therefore, causing neuroinflammation (KOMAROFF, 2017). Likewise, viral infection was indicated as a trigger, present in ⅔ of patients with ME,

exemplified in 27% of patients with COVID who developed ME in the study (PÉREZ-HERNÁNDEZ, 2021).

Several studies have shown abnormality in the autonomic nervous system (ANS), in synaptic activity, baroreflex and in the reduction of erythrocyte mass. In the metabolic portion, however, they faced deficits in the pathways that produce energy, that is, the increase in the level of lactate in the cerebrospinal fluid, damages oxidative phosphorylation, causing mitochondrial dysfunction in the central nervous system (CNS), such as infection and hypoperfusion in the brain (KOMAROFF, 2017).

Furthermore, the autoimmune response has a neuroinvasive effect caused by viruses that cause inflammatory and ischemic damage to the central nervous system. It produces chronic inflammation by increasing the signaling of pro-inflammatory cytokines and altering Th1, Th17, T regulatory and natural killer functions (PÉREZ-HERNÁNDEZ, 2021). An association made by genotyping HLA-DQB1*03:03 and HLA-C*07:04, found in most patients with BD, allowed the corroboration of the hypothesis of autoimmunity as the pathophysiology of BD (LANDE, 2020).

Furthermore, laboratory studies have indicated the hypothalamic-pituitary-adrenal (HPA) axis as one of the main favors for BD. That is, physical or mental stress activates the HPA, causing an increase in cortisol production, influencing the immune system. However, in patients with ME, this cortisol production rate is reduced, causing immune activation and decreasing the response to inflammatory processes (CALDERÓN-ELIZONDO, 2017).

CLINICAL PRESENTATION

It understands the etiopathogenesis as multifactorial, of intense, persistent, oscillating and inexplicable fatigue, which worsens after physical or cognitive activity that does not recover in a period of idleness and lasting more than 6 months (GIMENO-PI et al, 2016). As well as, allowing different intensities of the disease, designating it in a heterogeneous syndrome, interfering with the quality of life of patients (MONEGHETTI, 2018).

Its symptoms vary with sudden or gradual onset, and may present significant functional impairment, generalized muscle pain and joint pain, hypersensitivity to noise, light or specific foods, changes in physical fitness, observed in low muscular resistance and reduced cardiopulmonary capacity, with high effort during physical exercise and low fatigue tolerance (YU, 2021).

Stressors such as emotional exhaustion, depersonalization, tiredness, irritability, anguish and dissatisfaction at work are important to assess the burden on workers exposed to these situations, and studies have observed the relationship between burnout and BD, with a response to the environment in which they are exposed. the individual works (CANTOS-ALCÍVAR, 2019).

DIAGNOSIS

To determine a diagnosis for the patient, in 1994 Fukuda defined an evaluation for BD, in which the major or main criteria must be present, which have two factors, they are: the first is persistent chronic fatigue lasting more than 6 months since the onset, with no improvement with rest and reduction of daily activities. The second is the exclusion of chronic fatigue related to other diseases. Then the minor criteria that have 8 criteria, 4 or more being necessary, lasting at least 6 months after the onset of fatigue: cognitive deficit, odynophagia, myalgia, painful axillary or cervical lymphadenopathy, headache of different pattern, polyarthralgia without signs

of edema or erythema, non-restorative sleep and post-exertion malaise for more than 24 hours (CALDERÓN-ELIZONDO, 2017).

Studies have shown that stressful events in an individual's life such as bullying, partner abuse, eating disorders, pregnancy, traffic accidents, economic problems and changes in sleep habits are related to the triggering of BD, being 2 or 3 times more frequent in people who were subjected to these factors in childhood. Using these results in primary care consultations, it can reduce diagnosis time, contributing to an early diagnosis (GIMENO-PI et al, 2016).

LABORATORY EXAMS

In a longitudinal study, they demonstrated the relationship between the severity of EM and the pro-inflammatory cytokine leptin, whose function is to regulate the recruitment of neutrophils to the brain, that is, both leptin and resistin have the ability to cross the blood-brain barrier, thus causing a neuroinflammation, an irregularity present in patients with ME (MONTOYA, 2017).

Likewise, they showed an increase in the TGF-β protein, an anti-inflammatory cytokine, which, according to the variation in the immunological environment, its function can change. That is, the increase in TGF-β levels promotes the stimulation of inflammation and a fibrotic environment resistant to certain types of treatment (MONTOYA, 2017).

It was also pointed out an increase in the numbers of circulating cytotoxic CD8 and cells carrying activation antigens and a decrease in resistin, a pro-inflammatory cytokine in moderate to severe disease, but an increase in resistin levels in milder cases (MONTOYA, 2017).). The reduction of creatine phosphokinase (CK) was observed in more severe cases, with 96% sensitivity, however, a rate lower than 50% for specificity. Being able to compose a laboratory marker for more critical cases (ALMENAR-PÉREZ, 2020).

Because it is a difficult disease to diagnose, discouraging both the patient and the doctor in the process, an exam is necessary to speed up the confirmation of the BD. Therefore, recent research is based on microRNA expression to discover possible biomarkers, in which 23 genes for ME have already been found, which can be used as biomarkers and possible targets for better treatment (METSELAAR, 2021).

TREATMENT

As it does not have a specific treatment, it varies according to the intensity of symptoms and associated diseases, therefore, it consists of relieving symptoms and treating psychological sequelae that incapacitate in the long term, and aims to improve the quality of life of patients. It has two categories: pharmacological and non-pharmacological. The non-pharmacological ones are: application of cold or heat, physical therapy, acupuncture, relaxation and neurofeedback techniques. And the pharmacological ones are: low dosage of naltrexone, whose mechanism consists of disinhibiting the TRPM3 ion channel and stimulating natural killer cells. Which has shown promising results in the relief of pain and neuroinflammation, since it is a μ-opioid receptor antagonist. Furthermore, in severe cases, they use cyclophosphamide, metformin, supplementation with KPAX002 (PÉREZ-HERNÁNDEZ, 2021).

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