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Letter to the Editor

CHRONIC FATIGUE SYNDROME IN INFLAMMATORY DISEASES

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INTRODUCTION

Chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME), is a complex and debilitating disorder with an unknown cause that can present with mental disorders, depression, mood swings, and "brain fog". CFS results from complex interactions between molecular and biochemical dysfunctions, immune abnormalities, and chronic inflammation (1). The main symptom of CFS is permanent fatigue, which is combined with skepticism regarding whether it is a real disease (Table I). This doubt often causes significant delays in diagnosing CFS and patients suffering from this disease often complain of low quality of life (2). To diagnosis CFS, the symptoms must have been present for at least six months and the patient must present continuous chronic fatigue that is not relieved by rest.

Table I. *In addition to chronic fatigue, the following symptoms may also be present in chronic fatigue syndrome (CFS).*

Mental fatigue	Depression	Sore throat
Muscle fatigue	Brain fog	Tender lymph nodes in the neck or armpits
Headache	Mood swings	Irritable bowel syndrome
Light sensitivity	Polyarthralgia	Irregular heartbeat
Muscle and joint pain	Sleep disturbances	Chills and night sweats
Difficulty concentrating		

CFS usually causes a significant reduction in work, social, and personal activities. CFS must not originate from a known disease, nor should the state of drowsiness be confused with a lack of motivation or disinterest. Therefore, all secondary medical conditions such as tumors, chronic infections, obesity, chronic flu, dementia, hypothyroidism, pituitary gland malfunction, depression, schizophrenia, fibromyalgia, etc., must be excluded in order to diagnose CFS. Biochemical and molecular studies have provided insight into the various immunological and inflammatory mechanisms at play in CFS and understanding these is crucial for developing effective treatments and improving the quality of life for patients.

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DISCUSSION

Patients with CFS often have abnormalities in mitochondrial function, leading to reduced ATP production and energy deficits (3). Increased levels of reactive oxygen species (ROS) and reduced antioxidant defenses have been observed during oxidative stress, contributing to cellular damage and fatigue (4). Metabolic changes, including disruptions in amino acids, lipids, and energy metabolism, have also been highlighted in CFS (5). The dysfunction of the tricarboxylic acid cycle in glycolysis and fatty acid oxidation suggests that there is a dysmetabolism linked to energy production. It has been reported that in CFS, there is a dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis with alteration of cortisol, which may be linked to the stress response and immune reaction (6). In fact, in CFS, there is chronic activation of the immune system with elevated generation of pro-inflammatory cytokines such as tumor necrosis factor (TNF), interleukin (IL)-1, and IL-6, which can mediate low-grade inflammation (1).

T lymphocytes are also involved in CFS, where they appear to be altered in their activation and proliferation. It is possible that this syndrome is mediated by the altered relationship between TH1 cells and TH2 cells (7). Natural killer (NK) cells may also have a reduced capacity for cytotoxicity. At the level of cell-mediated immunity, there may be a dysfunction in the activation of T lymphocytes and their proliferation. These alterations may change the balance between different T lymphocyte subsets (8). NK cells have reduced activity, with impaired immune surveillance and immune imbalance leads to elevated levels of inflammatory cytokines and chemokines in the blood and cerebrospinal fluid, markers that indicate ongoing inflammation.

At the cerebral level, immune cells can activate microglia that induce neurological symptoms (9). Even in the intestine, there can be significant alterations in the composition of the microbiota, with increased intestinal permeability ("leaky gut") and local systemic inflammation (10).

There are no specific therapies for CFS, and it is therefore necessary to use antioxidant agents and anti-inflammatory drugs. Antioxidants such as coenzyme Q10, N-acetylcysteine, and vitamins C and E are being studied to counteract oxidative stress. Additionally, non-steroidal anti-inflammatory drugs (NSAIDs) and cytokine inhibitors are used to help reduce inflammation.

Research is presently focusing on new therapies aimed at restoring the balance of the immune system, such as low-dose naltrexone or immunoglobulin therapy. In addition, supplements that regulate mitochondrial function and metabolic pathways have also been targeted to restore an efficient immune state.

CONCLUSIONS

CFS is characterized by complex interactions between molecular and biochemical dysfunctions, immune abnormalities, and acute and chronic inflammation. However, the mechanisms regulating this complicated disease are not yet clear, and more in-depth studies are needed to improve therapy and the quality of life of patients.

Conflict of interest

The author declares that they have no conflict of interest.

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