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Letter to the Editor

IMMUNOLOGICAL RESPONSE IN MULTIPLE SCLEROSIS

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INTRODUCTION

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system (CNS) that results in demyelination. The disease affects millions of individuals worldwide (1), afflicting more women than men (2). MS is characterized by T lymphocytes attacking and destroying myelin, a process that leads to neurological disease. Patients affected by MS present neurological and physical disabilities with motor impairment and difficulty with movement coordination.

Neurodegenerative diseases, including MS, are characterized by inflammation in the CNS, due to the activation of immune cells. In recent scientific literature, many studies have dealt with MS and notable progress has been made in both diagnosis and therapy (3-5). Today, several drugs are available for this chronic progressive disease, although all the currently available therapies are still unsatisfactory. The diagnosis should be made as early as possible, even though it is often difficult in patients who do not present typical symptoms.

MS is an autoimmune disease that creates inflammatory damage, affecting nerve cells in the brain and causing physical and mental disorders. Widespread brain damage occurs with inflammation, demyelization, and damage to neurons both in the CNS and at the medullary level, affecting both the white matter and deep gray matter (6). White matter lesions, which are visible with magnetic resonance imaging, are now treated with better results, however there is still no specific therapy. The disease can affect young individuals, including those under 35 years of age, and occurs with a ratio between females and males of approximately 3 to 1, respectively. Interestingly, over the last century, the incidence of MS in women has risen while there has been no increase in that of men (7). The main symptoms that occur in MS are loss of sensation, weakness, depression, cognitive impairment, diplopia, and others (Table I).

Table I. *Some of the symptoms that occur in multiple sclerosis.*

• weakness	• unstable mood	• incontinence
• fatigue	• ataxia	• dysphagia
• cognitive impairment	• pain	• diarrhea
• depression	• loss of sensation	• muscle spasms
• anxiety	• paraesthesia	• problems with speech or swallowing
• diplopia		

The diagnosis of MS is mainly based on the symptoms and behaviour of the patient. Clinical tests include MRI scans, which can highlight demyelization plaques that appear in the brain and spinal cord. Diagnostic help is also given

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by the examination of the cerebrospinal fluid through a lumbar puncture, which highlights leucocytosis with an increase in antibodies (presence of elevated IgG) that testify to the excessive immune response.

Therapy in this disease is somewhat deficient because there are no specific drugs for treating MS, although treatment with corticosteroids has been seen to delay the worsening of the pathological state and prevent secondary effects (immunosuppression). The individual suffering from MS should undergo both physical and psychological rehabilitation. The disease has been roughly classified into four clinical aspects: a) relapsing and remitting, b) secondary progressive, c) primary progressive, and d) progressive relapsing. These four categories often present overlapping clinical signs that do not precisely define the state and complexity of the disease.

MS is multifactorial and is most likely a combination of immune dysfunction, genetic tendency, and environmental factors. Regarding genetic risks, patients show risk alleles in the genes for the major histocompatibility complex, but also dysfunctions of the receptors of some cytokines such as T cell growth factor (TCGF) (also called IL-2) and IL-7 (8). In addition, it was recently seen that MS is also associated with low levels of vitamin D, some viruses such as the Epstein Barr virus, and cigarette smoking.

The immunological response in multiple sclerosis

Autoimmune diseases affect approximately 5% of the population in industrialized countries (9). These are very complex and poorly understood diseases that involve the immune system and in particular, T cells or B cells. In these cases, the immune system intervenes without any infection or other apparent pathology, causing damage throughout the body. In MS, the immune system attacks the self-components, in particular, myelin which is the protective sheath surrounding nerve fibers.

At the immune level, the disease originates in the thymus, which is unable to eliminate immunoreactive cells that react against the patient's own body. The immune cells involved in this process are T and B lymphocytes, as well as macrophages, which intervene with CD68 in demyelinated areas.

Adaptive immunity is involved in MS, and CD4+ T cells represent a genetic risk factor. Th1-type cells also take part in this pathological disease by mediating inflammation. Th1 cells generate the interferon gamma-producing cytokines TGF-β1, IL-23, IL-6, and IL-21, which differentiate Th17 cells that in turn produce IL-17. The pathogenic effect of these cells is limited by Treg cells, which produce the anti-inflammatory cytokine IL-10, and the dysregulation of these leads to a pathological effect of T cells. CD8+ cells contribute to the MS disease state and are found in high numbers in the white and gray matter of patients, causing damage to the CNS. CD8+ lymphocytes produce pro-inflammatory cytokines such as IL-17.

In MS, innate immunity participates in CNS damage with several cells, including mast cells (MCs) which are present in large numbers in plaques. MCs contribute to the inflammatory state by secreting cytokines and chemokines, as well as histamine, tryptase, and chymase, that promote neuronal degeneration. Innate immune cells such as macrophages are also involved in neurodegeneration and inflammation. The disease is characterized by immune cell-derived inflammation that damages myelin and this causes plaques to become chronic.

The underlying causes of MS are still unknown. It is certain that the disease is characterized by the loss of myelin due to an abnormal immune response. This characterizes it as an immune disease in which self-cells attack myelin as if it were recognized as non-self. Various hypotheses concerning the onset of MS have been studied in recent years. The factors that are most taken into consideration are: climate, genetic predisposition, infectious agents, and ethnicity. MS occurs more often in higher-latitude countries (where vitamin D is lacking), in individuals whose lifestyle includes habits such as the use of alcohol and cigarette smoking, and in subjects of Caucasian origin (10). However, infectious agents such as bacteria and viruses, and genetic predisposition can also be predisposing elements for developing MS. The hereditary factor in MS is also very important and involves the HLA region of chromosome 6, a phenomenon that occurs in many autoimmune diseases. However, all these hypotheses still need to be evaluated and confirmed by scientific research.

CONCLUSIONS

MS is a disabling disease that affects the brain and spinal cord, causing pathological effects throughout the body with degeneration of the CNS. The pathogenesis of the disease involves different immune cells with B lymphocytes and effector CD4 T-cells playing important roles. Additionally, CD8 T cells may also play a distinguishing role in the disease. In fact, these lymphocytes represent the main therapeutic target for MS. T and B cells activated by autoantigens expand and contribute to the inflammatory state, affecting the neuroaxonal degeneration of the CNS. In addition, some cytokines such as IFN-γ and IL-17 appear to be more involved in the pathogenesis of the disease, where they are found in abundant quantities both in the CNS and in the cerebrospinal fluid.

New therapies have helped improve longevity in MS and hindered disease progression, but research needs to continue to provide better diagnostic and therapeutic options for treating patients.

Conflict of interest

The author declares that they have no conflict of interest.

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