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Editorial

HTLV-1-Assoaciated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP): Neurological Manifestations and Immune Response

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Editorial

Human T-lymphotropic virus type 1 (HTLV-1) infects approximately 15-20 million people worldwide, and it is endemic in several regions of the world. In Brazil the virus has been detected in all regions, with varying prevalence rates and approximately 2.5 million Brazilians are infected. This retrovirus infects T lymphocytes, and this chronic and persistent infection may cause neoplastic and inflammatory diseases [1,2], such as adult T-cell leukemia or lymphoma and HTLV-1-associated myelopathy (HAM), also known as tropical spastic paraparesis (TSP) [3]. However, most of them remain asymptomatic and only $\sim 5\%$ of infected individuals develop disease [3]. Individuals can become infected with HTLV-1 vertically or horizontally. The former occurs via breastfeeding, within the womb, or by perinatal transmission, and the latter occurs through sexual contact, injected drugs and blood transfusions [4].

Some authors believe that the immune response play a great role in pathogenesis of the HAM/TSP. HTLV-1 do not infect only T cells, it is able to infect several distinct cell types such as B cells, dendritic cells, and synovial cells; however, CD4+ T cells is primarily infected and this cell can participate directly in pathogenesis of this disease [4-6]. HAM/TSP patients present a series of immunological dysfunctions, including spontaneous proliferation of HTLV-infected T CD4+ lymphocytes. An increase in the migratory capacity of circulating leukocytes, and increased production of inflammatory cytokines, particularly neurotoxic cytokines such as IFN- γ and TNF- α can affected regions along the spinal cord [7].

There is an imbalance of the immune response. HAM/TSP patients have a predominance of Th1 cytokines (IFN- γ) and a reduction in Th2 cytokines (IL-4 and IL-10), this is likely to cause greater circulation of immune cells between peripheral blood and the central nervous system (CNS), leading to inflammation of the nervous tissue [7], found most frequently in the thoracic spinal cord [8]. The author of the present paper in a study [9] with gene expression with HAM/TSP patients showed higher

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expression of Th1 cytokine (IFN- γ) when compared to Th2 cytokine (IL-4). INF- γ can be an important cytokine that cause neural damage; however, more studies with other technics are necessary to explain this role.

There are various theories trying to explain what happen with HAM/TSP development, but the most widely accepted is that it is a virally induced, cytotoxic, demyelinating inflammatory process of a chronic and progressive nature. The lymphocytes are activated during spastic paraparesis; when they cross the blood-brain barrier, the inflammatory process initiates in the CNS, resulting in lesions [7].

HTLV-1 infection can lead to the development of a wide spectrum of neurological manifestations, termed the HTLV-1 neurological complex and the lower limbs are most affected [4]. The literature show individuals that develop HAM/TSP is characterized by the insidious onset of slowly progressive weakness and spasticity of one or both legs, associated with hyperreflexia, ankle clonus, extensor plantar responses and low-back pain. Other symptoms found in these patients include detrusor instability leading to nocturia, urinary incontinence and minor sensory changes, especially paresthesia and the loss of sense of vibration [2]. The author of the present paper studied the neurological symptoms in HAM/TSP patients [2]. He evaluated the neurological symptoms in HAM/TSP individuals and the results of this study showed great HAM/TSP patients with proximal weakness and spasticity, high fall risk and variety of walking aid [2]. The instruments used were function scales owing to their fast, easy administration. Analyzing neurological symptoms directed toward motor function (muscle strength, muscle tone, balance and walking deficiency) owing to its clinical importance in relation to the progression of the disease. Any motor disability can lead important changes in functional independence and quality of life [2]. The author believes that the physiotherapist is an important member on health team.

Most of the HAM/TSP patients present gait disturbance. This walking difficulty is associated with weakness and spasticity in

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lower limbs that can lead tendency to fall. In a study [10] the walking devices is associated with period of the disease onset. In other words when the patient present sever motor disability requires great walking devices, like wheelchair [10]. The author of the present paper correlate cytokine gene expression and walking aid, trying to associate the role of INF- γ with motor disability. A significant correlation was observed with the gene expression of IFN- γ and the walking aid, i.e., the higher the expression of this cytokine, the greater the degree of walking aid. The higher expression of this cytokine could be involved in aggravation of symptoms in HAM/TSP.

The HTLV-1 infected patients, principally who developed HAM/TSP need physical therapy assistance. Therefore, is very important physiotherapist improve research about neurological symptoms and correlation with immunological disturbance. Clinical studies is necessary and to provide a standard language for the description of health and health related components of wellbeing, the International Classification of Functioning, Disability and Health (ICF) has become an important classification of disability and functioning, allowing an increasingly global view and positive approach to the clinical state of the individual [2]. The author of the present paper studied of the effect of physical therapy on spasticity in HAM/TSP patients using the ICF. The association of ICF and physical therapy on treatment of spasticity reveled a greater functional after the therapy, emphasizing the effectiveness of physical therapy in controlling spasticity and demonstrating the value of the ICF as a tool for the evaluation of spasticity in HAM/TSP patients. Therefore, a study of immune response associate to neurological symptoms is important from the point to clarify the HAM/TSP pathogenesis and using standard language that the world health organization emphasizes.

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