Cysticercosis and the immunossupression: what are the mechanisms involved?

Cisticercose e a imunossupressão: quais os mecanismos envolvidos?

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The human neurocysticercosis (NC) is caused by the presence of the larval form of *Taenia solium* in the central nervous system, after the consumption of water or food contaminated with parasite eggs. The prevalence of NC is related to socioeconomic and cultural factors, representing an important public health problem in countries with deficient sanitary conditions, and in industrialized countries receiving immigrants from epidemic areas. The disease is one of the most severe parasite infections affecting the central nervous system, with complex biological parasite-host interactions due to the occurrence of different parasite antigens in different stages of evolution, and individual genetic variations interfering with the host response, impairing the understanding of the dynamics of parasite survival and host defense mechanisms[1].

The diagnosis of NC is based on clinical, epidemiological, and laboratorial criteria using both imaging and laboratory analyses of cerebrospinal fluid (CSF) samples, including cytomorphological, biochemical, and immunological examinations[2]. The detection of antibodies in serum is another important marker for the NC diagnosis[3].

There are only few studies available regarding aspects of the cellular immune response, most of them showing immunosuppression in humans[4], pigs[5], and in experimental mouse models[6-9]. A study from our group using a lymphoproliferation assay with *T. solium* and *T. crassiceps* antigens as stimuli showed an antigen-specific suppression in NC-patients, suggesting that the antigenic components play a suppressor role in the host immune response[10].

Correa et al.[5] observed a decrease in the CD4/CD8 ratio in these patients, and they have suggested that CD8 cells are involved in immunosuppression. We also identified these cells as predominant in peripheral blood of patients with NC presenting degenerating cysts[11], with higher expression of activation cell marker (CD69) during this inflammatory form[12]. The CSF samples from inflammatory NC-patients also showed a predominance of CD8 cells and a higher expression of HCAM and ICAM adhesion molecules. CD19 and CD56 cells, as well anticysticercus antibodies, were observed in the CSF samples from both inflammatory and non-inflammatory NC-patients, with high CD69 expression[12].

The immunosuppression observed in experimental cysticercosis seems to be related to the cytokine profile[8,13-15]. Our contribution in this field showed that by using *T. solium* antigen as stimuli, there is a predominance of Th1 response in inflammatory NC-patients and a mixed Th1/Th2 pattern in noninflammatory NC-patients[12].

Some experimental cysticercosis studies have attempted to determine the causes of immunosuppression: release of antigenic products[16] that form circulating immunocomplexes[17], suppressing lymphocyte cytokine production or inducing chromosome instability[18]; increase and/or decrease in CD8 cells depending on the evolution phase of the disease[19]; genetic instability and chromosome alterations in circulating lymphocytes induced by infection[20,21]; macrophages with activity involving the programmed death ligand 1 pathway[7]; and Th1 and/or Th2 cytokines[6,8,9,13-15,22,23]. Recently, it was reported the Toll-like receptor 2-dependent pathways as involved in the recognition of *T. crassiceps*, with subsequent activation of the innate response and production of the inflammatory cytokines[24]. However, these studies on the cellular immunological aspects of cysticercosis do not permit a precise conclusion about the alterations in the host immune response, caused by the parasite or its products.

In this Issue of Arquivos de Neuropsiquiatria, Camargo and Bertolucci[25], from Federal University of São Paulo, report a study that investigated the correlation between neuronal death and NC, quantifying the soluble FAS apoptotic factor in CSF from 36 NC-patients by the immunoenzymatic assay. The authors showed higher CSF of soluble FAS protein at NC-patients with active and calcified form. The result represents a contribution to the field here pointed, since the presence of this pro-apoptotic protein could also suggest the involvement of apoptosis in the suppression observed in the NC, indicating that more studies in this area will be helpful to elucidate such field.

Also in this Issue, Matos-Silva et al.[26], from Federal University of Goiás, report the development of an experimental model to NC studies involving two mice lineages by using *T. crassiceps* cysticerci. The authors observed in this original study that C57BL/6 mice showed greater capability on provoking early necrosis in the cysticerci with a chronic inflammation pattern, while BALB/c mice showed necrosis on late stage parasites with an acute inflammation pattern. This experimental model may become a reproducible method for human NC studies, since as pointed by the authors, the *T. crassiceps* cysticerci caused a dynamic inflammatory response from the host and present other advantages such as its rapid development cycle, facilities in maintenance and antigenic similarities to *T. solium* cysticerci.

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