" Initial thymus characterization during the evolution of experimental encephalomyelitis"

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Abstract

The experimental autoimmune encephalomyelitis (EAE) is a model of a T CD4+ lymphocyte-mediated autoimmunity disease¹. T cells goes through the process of maturation, differentiation and selection inside thymus, which besides other processes, should inhibit the release of autoaggressive cells. Thymus is a primary organ responsible for T cell development; and despite this unique function it is a target organ in many different diseases. In this project, we aim to characterize thymus alterations during the clinical course of EAE. Previously, we demonstrated that thymus from EAE mice, after 15 days post immunization, presented reduction in thymus relative weight, loss of cortical-medullary delimitation and loss of double positive thymocytes. Here in, we demonstrate that thymus atrophy is directly related to the clinical score of the disease and that the loss of cortical-medullary is followed by alterations in the expression pattern of molecules involved on neural transmission during the evolution of EAE. Our results add new information about thymus atrophy that might contribute to a better understanding of development of autoreactive cells in EAE as well as to further knowledge about the thymic interaction at different pathological processes.

Key words:

immune system, thymocytes, EAE.

Introduction

The experimental autoimmune encephalomyelitis (EAE) is a model of autoimmune disease mediated by T CD4+ cells¹. The full development of T cells depends on the continuous migration of hematopoietic precursors by the thymic microenvironment which is composed of lymphoid and non lymphoid components². The intrathymic migration is essential for T cells to find the signals required for survival, proliferation, differentiation and generation of repertorie diversity. Thymus and the immune system as a whole is under a tight control of the central nervous system. Whereas T lymphocytes have their origin in the thymus and as this organ is essential for the correct development of T cells and selection of auto-reactive T lymphocytes, thymus analysis during EAE is important for a better understanding of the dysregulation of T lymphocytes found in autoimmune diseases. Our preliminary data demonstrated that during the development of EAE thymus has its relative size lowered and there is a loss of cortical-medullary boundary, which suggest major changes in the thymic microenvironment and a consequent alteration in T lymphocytes pattern in the periphery of the immune system, during the stage of exacerbation of disease. In this study, we evaluate the expression of molecules involved on neuronal transmission in front of thymic atrophy during the evolution of EAE.

Results and Discussion

Immunized animals showed a decreased thymic index (thymus weight (g) / body weight (g) x100) when compared to control animals during the clinical course of the EAE. Here in, we demonstrate that there is a direct relation between the thymic atrophy and the clinical score of EAE.

The reduction in the relative weight suggested changes in thymic microenvironment⁴ and, in fact, an abnormal expression of cytokeratin specific for cortical

and medullary epithelium were found. The thymic cortical area of animals at the peak of EAE presented a reduction in comparisson with control animals thymus of the same age. Also, we found a diffusion pattern in the medullary área.

It's important to note that both atrophy, and the histological changes had followed the evolution of the disease.

The analysis of neuronal molecules (hidroxilase tyrosine, adrenergic receptors) by immunostaining revealed changes in the pattern of expression in thymus from EAE mice when compared to control samples.

Conclusions

The data confirm our hypothesis that thymus is also a target organ in EAE disease, with an importatn commitment of molecules involved on neuronal transmission and fault in the correct T lymphocyte development.

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⁴ Savino 2006