

Doktorsavhandling vid Karolinska Institutet

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Sarcoidosis: Inflammatory mechanisms and markers of activity

Fredagen den 15 november 2002

ISBN: 91-7349-355-4

Diss: 02:647

Abstract:

Sarcoidosis is a disease characterized by an accumulation of CD4+ T-lymphocytes in affected organs. Previous findings of an association between the HLA-allele DR17 and an accumulation in bronchoalveolar lavage fluid (BALF) of CD4+ T-lymphocytes expressing the T-cell receptor (TCR) V gene segment AV2S3, is in line with an aetiological hypothesis claiming that sarcoidosis is elicited by a specific antigen(s) in genetically predisposed individuals.

In the present study immunological features of sarcoidosis were investigated in HLADR17 positive patients with active and clinically resolved disease. Besides, the influence of a polymorphism in the angiotensin-converting enzyme (ACE) gene as well as apoptotic functions in lymphocytes from sarcoidosis patients were investigated.

The study revealed differences between DR17 positive and DR17 negative sarcoidosis patients in inflammatory parameters in BALF and serum. No associations were detected between the ACE gene polymorphism and either susceptibility to sarcoidosis, outcome of the disease or HLA-DR alleles of prognostic interest. A resistance to apoptosis, paralleled by an increased caspase-3 activity, was detected in BALF lymphocytes from sarcoidosis patients but not from healthy controls. The consequences of this finding remain elusive. Clinical resolution of sarcoidosis in BLA-DR17 positive patients was associated with normalization in AV2S3+ CD4+ T-lymphocytes in BALF and a decrease in markers of disease activity in BALF and serum. In DR17 positive patients a difference was found between patients with active and clinically resolved sarcoidosis regarding expression of activation markers, including markers delineating T regulatory cells, by CD4+ T-lymphocytes from BALF and peripheral blood.

In conclusion, immunological differences were found between patients positive and negative for DR17 and between DR17 positive patients with active and resolved disease. The normalization in AV2S3+ lymphocytes strengthens their involvement in the pathogenesis of sarcoidosis.

Nyckelord: Sarcoidosis, HLA class II, T-lymphocytes, CD4-CD8 ratio, T cell receptor, angiotensin-converting enzyme, apoptosis