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Caspase-1 is active since the early phase of rheumatoid arthritis

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by joint destruction. We have previously reported an increase in interleukin (IL)-1β levels in the serum of very early RA and in the synovial fluid (SF) of RA patients. Therefore, the molecular mechanisms that regulate IL-1β activation, such as caspase-1, might play a relevant role and have potential as therapeutic targets in RA.

Aim

The main goal of this study was to evaluate the state of activation of caspase-1 in early polyarthritis and established RA patients.

Patients and methods

Blood samples were collected from 12 untreated early polyarthritis patients with less than 12 months of disease duration, 12 methotrexate (MTX) treated established RA patients and from 10 healthy controls. Caspase-1 activity was assessed using the Caspase Assay kit.

Results

We found that both early polyarthritis and established RA patients have higher levels of active caspase-1 than healthy controls. Surprisingly, caspase-1 activation levels in patient cells remain unchanged when cells were stimulated with E. coli and ATP for 4h and 24h, whereas in healthy control cells caspase-1 levels are significantly increased after stimulation. We observed no significant differences when comparing early polyarthritis with established RA samples. However, in RA samples from patients with higher disease activity (DAS28>5.2) the active caspase-1 ratio is higher.

Conclusions

Our results suggest that leukocytes in both early polyarthritis and established RA patients have high baseline levels of activated caspase-1, which cannot be significantly increased by bacterial and ATP stimulation. We also show that MTX treatment does not affect caspase-1 activation. Altogether, our data supports the hypothesis that caspase-1 is already activated in the early phase of RA.

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