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Acute Coronary Syndromes

INTERFERON GAMMA INDUCES A GREAT IMBALANCE IN MATRIX METALLOPROTEINASE-9/TISSUE INHIBITOR-1 RATIO IN CIRCULATING MONOCYTES FROM CORONARY PATIENTS

Poster Contributions
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Background: An imbalance in the expression of MMP-9/TIMP-1 in unstimulated circulating CD14+ monocytes was recently demonstrated in patients with different stages of coronary artery disease. In this study, circulating monocytes of patients with chronic stable angina (SA) or acute unstable angina/non ST-segment elevation myocardial infarction (UA/NSTEMI), were stimulated with IFN-γ or IL-4 to investigate the effects on secreted matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1) and on their balance.

Methods: The research and the ethics committees of our institution approved the study. Thirty patients with SA, 29 with UA/NSTEMI and 30 healthy controls were studied. Samples were obtained from peripheral blood. Leucocytes were incubated for 24 hours. Adherent monocytes (1 x 105) were cultured and further stimulated with recombinant IFN-γ (10 ng/mL) or IL-4 (30 ng/mL). Supernatants were harvested after 48 hours. Serum levels of IFN-γ and IL-4 and supernatants concentrations of MMP-9 and TIMP-1 were determined by quantitative sandwich immunoassay technique with commercial kits (R&D Systems). One-way ANOVA nonparametric tests were used (Kruskall Wallis).

Results: Serum concentrations of IFN-γ were significantly higher in UA/STEMI patients than in the other groups; no differences were found in IL-4. Mean MMP-9/TIMP-1 baseline ratios were unbalanced (>1) only in UA/NSTEMI patients (4.4). Upon stimulation with IFN-γ, MMP-9 secretion increased in all groups but TIMP-1 decreased in patients. As a consequence, monocytes of both groups of patients strikingly increased their mean secreted MMP-9/TIMP-1 ratios. That of UA/NSTEMI rose to 59, and the ratio of SA went up to 47, whilst that of controls only increased to 2.8. IL-4 had little effects upon secretion of MMP-9 or TIMP-1.

Conclusions: Our results suggest an altered responsiveness of circulating monocytes from patients with coronary disease that could be a reflection of an intrinsic inflammatory milieu, but that could also -with the appropriate inflammatory conditions- contribute to break a stable condition and possibly to induce a vulnerable state and thus plaque disruption.