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AB0120

THE EFFECT OF INFLAMMATORY SERA FROM DIFFERENT FORMS OF AXIAL SPONDYLOARTHRITIS ON THE OSTEOCLASTOGENIC POTENTIAL OF MONONUCLEAR PRECURSORS IN BLOOD

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Background: Spondyloarthritis (SpA) is characterized by pathological bone resorption and higher risk of osteoporosis. Inflammation accompanying the disease may activate mononuclear precursors in blood that are able to differentiate into osteoclasts, bone resorbing cells^[1,2], and thus substantially contribute to bone resorption and aggravation of symptoms characteristic for this chronic disease.

Objectives: The aim of this pilot study is i) to figure out whether the inflammatory factors present in blood sera of SpA patients activate the osteoclastogenic potential of peripheral blood monocytes (PBM) derived from healthy subjects; ii) to find out whether this effect differs among sera from three forms of SpA, short-term non-radiographic (nr-axSpA) and radiographic (r-axSpA) SpA, and long-term ankylosing spondyloarthritis (AS), and finally iii) to assess whether the stimulatory effect of serum from SpA patients on osteoclastogenesis of healthy PBM reflects the altered clinical markers of inflammation and bone metabolism.

Methods: To simulate inflammatory condition characteristic for nr-axSpA, r-axSpA or AS, we created pool of 10 AS sera together with age- and sex-matched pools of nr-axSpA, r-axSpA and AxC (sera from healthy subjects). Disease duration of nr-axSpA and r-axSpA was set up to less than 2 years. The ASDAS score of AS form was significantly higher compared to the score of short-term forms of disease ($P < 0.05$). PBM from 6 healthy donors were cultured for 14 days in DMEM supplemented with 25ng/ml macrophage colony-stimulating factor (M-CSF), 0.5ng/ml receptor-activator of nuclear factor kappa B ligand (RANKL) and in parallel with 10% pooled human sera nr-axSpA, r-axSpA, AS and AxC. TRAP positive cells with 3 or more nuclei were recognized as osteoclasts and counted.

Results: Cultivation of PBM in the presence of both, diseased and healthy human sera increases number of osteoclasts in comparison to cultures without human sera. The strongest osteoclastogenic capacity develop PBM affected by pooled AS sera (2.9 times increase in osteoclast number compared to culture without human sera, $P < 0.05$), the lowest osteoclastogenic potential was detected in culture with pooled sera from healthy donors (2.1 times, $P = \text{NS}$). Pooled nr-axSpA, r-axSpA and AS sera do not appear to differ significantly among each other in size of their effect on PBM; nevertheless, trend to lowest numbers of osteoclasts can be seen in culture with r-axSpA sera ($P = \text{NS}$).

Conclusion: Cytokine milieu in human sera seems to have a pro-osteoclastogenic effect regardless of its origin with respect to healthy condition. However, inflammatory factors present in the sera of SpA patients enhance the osteoclastogenic potential of PBM, as documented especially in AS sera presenting with significant, 7fold increased serum CRP levels ($P = 0.003$), and thus may contribute to aggravation of the osteoporotic condition of SpA patients.

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AB0121

ASSESSMENT OF GLOBAL DNA METHYLATION IN PERIPHERAL BLOOD CELL SUBPOPULATIONS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: PRELIMINARY RESULTS

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Background: Axial spondyloarthritis (ax-SpA) corresponds to a group of chronic inflammatory disease mainly affecting the axial skeleton. TNF α and IL-17A have been identified as key inflammatory mediators driving the inflammatory process of ax-SpA. Epigenetics refers to different mechanisms that alter gene expression without involving changes in DNA sequence. The mechanisms of epigenetics include microRNA, histone modifications or DNA methylation. DNA methylation is associated with a repressed chromatin state and inhibition of gene expression. It is recognized that aberrant DNA methylation can result in immune cell autoreactivity.

Objectives: Epigenetics have been rarely evaluated in ax-SpA. We previously reported that patients with ankylosing spondylitis (AS) had an imbalance between HAT and HDAC activities. In this study, we aimed to evaluate the global DNA methylation of patients with ax-SpA.

Methods: Case-control study (NCT03092583). Patients with radiographic (AS) or non radiographic (nr) ax-SpA (ASAS criteria) and healthy controls (HC) were evaluated. All the patients were biologic naïve and under NSAIDs. Disease activity was evaluated by BASDAI and ASDAS. CD4+T cells and CD14+ monocytes were isolated from peripheral blood and then DNA was extracted (E.Z.N.A. Blood DNA kit, Omega Bio-Tek). Global DNA methylation (5-mC) was determined using MethylAmp global DNA methylation quantification kit (Epigentek) using 150ng of total DNA.

Results: 25 patients with AS (18M; mean age $\pm$ SEM: 48.9 $\pm$ 3.5 y; mean disease duration: 14.9 $\pm$ 2.2 y; B27+: 84%), 21 with nr-axSpA (11M; age: 42 $\pm$ 3.3 y; disease duration: 7.9 $\pm$ 2.3 y; B27+: 68%) and 11 HC (7M; age: 48.4 $\pm$ 3.9 y) were evaluated. Patients had active disease (BASDAI and ASDAS in AS and nr-axSpA: 5.1 $\pm$ 0.4 and 5.4 $\pm$ 0.5; 4.7 $\pm$ 0.4 and 5 $\pm$ 0.4, respectively). In CD4+ T lymphocytes, global DNA methylation was lower in the whole group of patients (AS and nr-axSpA) compared to HC (0.91 $\pm$ 0.26 vs 1.08 $\pm$ 0.19 % of 5-mC) (NS). Conversely, DNA methylation was higher in monocytes from patients compared to HC (1.43 $\pm$ 0.16 vs 1.15 $\pm$ 0.5 % of 5-mC) (NS). When analysing the results between ax-SpA subgroups, a hypomethylation was more evident in the CD4+T lymphocytes from patients with nr-axSpA compared to AS and HC, a result that was not observed in the monocyte subpopulation (Figures).

Conclusion: A global DNA hypomethylation is observed in patients with ax-SpA, especially in the nr-axSpA subgroup. These results are more evident in T CD4+ lymphocytes. Additional analysis on a larger series of patients is required to confirm these preliminary results. In addition, we aim to examine the specific DNA methylation status of the TNF promoter gene.

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Figure. global DNA methylation of CD4+ T lymphocytes and monocytes from patients with ankylosing spondylitis (AS), non radiographic axial spondyloarthritis (nr-axSpA) and healthy controls (HC)

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