AB0101

ASSOCIATION OF FETUIN-A SERUM LEVEL AND GLUCOCORTICOID INTAKE IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Papichev¹, B. Zavadovsky¹, A. Yury¹, S. L.¹, P. J.¹. ¹Federal State Budgetary Institution "Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovskiy", Treatment and Prevention of Joint Disease Laboratory, Volgograd, Russian Federation

Background: Fetuin-A (FA) is a pluripotential glycoprotein, which plays an important role in bone turnover [1], inflammation, metabolic diseases [2] and etc. Several studies demonstrated association between FA serum level and rheumatoid arthritis (RA) severity and disease activity [3], however, there was made a suggestion that observed associations were due to glucocorticoids intake [4].

Objectives: To study the association of serum FA levels, glucocorticoids intake and RA activity.

Methods: 81 patients with RA verified by ACR/EULAR 2010 criteria were enrolled in our study. 43 patients were under glucocorticoid therapy with mean cumulative dose 7899±9029,4 mg (hereinafter M±SD) and 38 patients were not. DAS28 index was calculated to determine RA activity. FA serum concentrations were measured by ELISA. Correlations between serum FA levels and RA activity were assessed in each group. Statistic analysis was performed using software package "Statistica 10.0".

Results: The mean level of serum FA was 760,72±112,56 µg/ml. There was a negative correlation between FA serum level and DAS28 index ($r=-0,433$; $p<0,0001$) when calculated among all patients. We observed positive correlation between FA serum level and cumulative dosage of glucocorticoids ($r=0,297$; $p=0,008$). At the same time FA serum level and DAS28 index were correlated negatively in patients who were under glucocorticoid therapy ($r=-0,419$; $p<0,0001$) and were not ($r=-0,559$; $p=0,001$).

Conclusion: Serum FA level correlates with RA disease activity and glucocorticoids intake. However, the association between FA serum level and RA disease activity was independent of glucocorticoids intake in our study.

References:

- [1] Akhverdyan Y., Zavadovsky B., Polyakova J., et al. Level of biochemical markers of bone metabolism in patients with osteoporosis in the presence on rheumatoid arthritis. Osteoporosis international 2019; 30(Suppl. 2): S:303.
- [2] Bilgir O, Kebapcilar L, Bilgir F, et al; Decreased serum fetuin-A levels are associated with coronary artery diseases. Intern Med 2010; 49(13): 1281-5.
- [3] Polyakova Y., Papichev E., Kvilidze T., et al. Tissue cytokines and their role in the pathogenesis of rheumatic diseases. Osteoporosis international 2019; 30 (Suppl. 2): S:387.
- [4] Tekeoglu I, Harman H, Sag S, et al. Levels of serum pantraxin 3, IL-6, fetuin A and insulin in patients with rheumatoid arthritis. Cytokine 2016; 83: 171-75.

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AB0102

SPECIALIZED PRO-RESOLVING MEDIATOR RECEPTORS AS INFLAMMATORY RESOLUTION BIOMARKERS IN RHEUMATOID ARTHRITIS

S. Perniola^{1,2}, S. Alivernini^{2,3}, B. Tolusso², M. R. Gigante², M. Gessi⁴, C. Di Mario³, L. Petricca², A. Capacci², A. L. Fedele², G. Ferraccioli³, E. Gremese^{2,3} on behalf of SYNGem (Synovial Tissue Biopsy Unit) - Fondazione Policlinico Universitario A. Gemelli - IRCCS. ¹University of Verona, Department of Medicine, Verona, Italy; ²Fondazione Policlinico Universitario A. Gemelli - IRCCS, Division of Rheumatology, Rome, Italy; ³Università Cattolica del Sacro Cuore, Institute of Rheumatology, Rome, Italy; ⁴Fondazione Policlinico Universitario A. Gemelli - IRCCS, Division of Pathology, Rome, Italy

Background: The regulation of inflammation is a dynamic process involving several molecules as lipid mediators. The Specialized Pro-resolving Mediators (SPMs), such as Resolvin (RvD and RvE), Protectins, Maresins and Lipoxin A4 (LXA4), are bioactive metabolites of omega-3 and omega-6 fatty acids which drive inflammatory resolution phase and promote tissue repair. ERV, ALX/FPR2 and BLT1 are SPM receptors. Although in Rheumatoid Arthritis (RA) lipid mediators role within pathophysiology is under definition, studies on SPMs receptors role are still lacking in this disease.

Objectives: Purpose of this study is to define ERV, ALX/FPR2 and BLT1 expression in blood derived leukocytes and synovial cells and to correlate it to disease activity to define SPM receptors ad inflammatory resolution biomarkers in RA patients.

Methods: A cohort of 52 RA patients was enrolled in the study of which 40 with active disease (DAS28= 5,35 (5,18-6,40)) and 12 in sustained remission status (DAS28= 2,1 (1,83-2,42)). Each enrolled patient underwent peripheral blood (PB) drawing and 46 of them underwent US-guided synovial tissue (ST) biopsy. FACS gating strategy was used for PB and ST processing to evaluate percentage of positive cells and the mean fluorescence intensity (MFI) of ERV⁺, ALX/

FPR2⁺ and BLT1⁺ in CD45⁺CD3⁺, CD45⁺CD19⁺ for PB and ST, CD45⁺CD14⁺ and neutrophils for PB only and CD45⁺CD90⁺, CD45⁺CD64⁺CD11b⁺ macrophages (distinct in CD206⁺ and CD206⁻ subpopulations) for ST only. Each included ST was stained with haematoxylin/eosin and categorized by a pathologist, blinded to clinical characteristics, using the Krenn Score (KS) to assess ST inflammation degree. As control group, 11 undifferentiated peripheral inflammatory arthritis (UPIA) patients were enrolled in the study.

Results: Considering the whole RA cohort, DAS28 inversely correlated with BLT1⁺ positive cells on ST-derived CD45⁺ ($r=-0,48$; $p=0,048$), CD3⁺ ($r=-0,56$; $p=0,019$) and CD19⁺ ($r=-0,49$; $p=0,042$) cells, in contrast with CD90⁺ ($r=0,50$; $p=0,041$) cells. Similarly, both DAS28 and KS inversely correlated with ALX/FPR2⁺ positive cells in ST-derived CD45⁺ ($r=-0,42$, $p=0,050$ and $r=-0,41$, $p=0,046$ respectively) cells. Evaluating the MFI levels of the SPM receptors along all RA stages (naïve-to-treatment, resistant-to-treatment, sustained remission) compared with UPIA control group, interestingly ST-derived CD45⁺ cells of remission RA were depleted of ERV1 compared to naïve-to-treatment RA ($p=0,04$), despite comparable ST inflammation. Furthermore, highest ERV1 expression was found in ST-derived CD45⁺CD3⁺ and CD45⁺CD19⁺ cells in naïve-to-treatment RA compared with UPIA patients ($p=0,045$ and $p=0,012$ respectively). Moreover, the lowest BLT1 level was found in remission RA CD3⁺ cells compared with UPIA and naïve-to-treatment RA patients ($p=0,008$ and $p=0,023$ respectively).

Conclusion: SPM receptors expression seem to be tightly related to disease activity in the synovial tissue, suggesting an important involvement in the inflammatory process in RA patient.

References:

- [1] Serhan CN. Nature. 2014.
- [2] Alivernini S, et al. Arthritis Res Ther 2016
- [3] Krenn V et al. Histopathology. 2006.

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AB0103

THE AMBIGUOUS ROLE OF TISSUE CYTOKINES IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

O. Korolik¹, B. Zavadovsky^{1,2}, E. Papichev², Y. Polyakova², S. L.², A. Yury².

¹Volgograd State Medical University, Volgograd, Russian Federation; ²Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovskiy», Volgograd, Russian Federation

Background: Cytokines stimulate the inflammatory response in the synovial membrane with rheumatoid arthritis (RA), initiate apoptosis of chondrocytes, activation of osteoclasts. The progression of comorbid diseases is also associated with the influence of cytokines. At the same time, anti-inflammatory cytokines are produced in various tissues. Their role in the pathogenesis of RA and its complications is ambiguous.

Adiponectin (A) and Fetuin A (FA) are classified as negative acute phase proteins. Their concentration decreases with an increase in the level of pro-inflammatory cytokines: TNF- α , IL-1 and IL-6. Molecules A and FA, regardless of various factors and from each other, have similar effects in relation to pro-inflammatory cytokines, lipid and carbohydrate metabolism.

Visfatin (V) and Nesfatin-1 (N-1) are pro-inflammatory adipokines. B is produced by cells of the mononuclear phagocytic system and connective tissue. N-1 - is produced by the cells of the intermediate and medulla oblongata and by the cells of the gastric mucosa.

Objectives: to study the correlation of B, H-1, A and FA with the severity of inflammation in RA

Methods: 60 patients with RA and 30 healthy individuals were examined. The level of cytokines was determined by an indirect enzyme-linked immunosorbent assay using commercial test systems (Bio Vendor, cat No. RD195023100, Bio Vendor Human Fetuin-A, RaiBiotech, cat No. EIA-VIS-1, RaiBiotech, cat No. EIA-NESF). All patients underwent a full examination. Diagnosed with 2010 EULAR / ACR recommendations.

Results: A decreased level of A (less than 0.8 µg/ml) was detected in 15 patients (25%), F-A (less than 653.55 µg/ml) in 16 (27%), a high level of V (more than 39 ng/ml) - in 55 (91%), N-1 (more than 37.95 ng/ml) - in 36 (60%), which is significantly more often than in healthy individuals. No significant difference in the levels of determined adipokines was found depending on the gender and body weight of patients with RA. The level of cytokines in RA is associated with high activity according to DAS 28, positivity by Anti-CCP, extraarticular manifestations of RA. The greatest correlation with extraarticular manifestations is with