AB0051

SERUM AMYLOID A AND PENTAXIN 3: IMMUNE RESPONSE AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease that involves several molecular patterns with a wide spectrum of clinical manifestations and symptoms. Inflammation and related pathway play a role in SLE pathogenesis. The pentaxin superfamily including long and short pentraxin (C, Reactive Protein CRP, Serum amyloid A (SAA), Pentraxin 3 (PTX3)) are key components of innate immune system and induce a variety of inflammation associated pathway. However literature provides several evidences that CRP serum levels not correlated with clinical and immunological manifestations. This situation affected clinical practice and the patient follow up. PTX3 have been identified as a component of inflammatory status in several autoimmune conditions. SAA is an acute phase protein secreted in large quantity during inflammation.

Objectives: We want to evaluated SAA, PTX3 and CRP concentrations, their correlation between SLE Disease Activity Index (SLEDAI), that including complement fractions C3, C4.

Methods: We enrolled fifty patients that fulfilled the SLE American College of Rheumatology criteria and fifty healthy subjects. The SLE disease activity was classified with the SLEDAI (0 to 12). Patients were divided into two groups according to SLEDAI score: inactive group (Group 1, 25 patients, 50%: SLEDAI < 4) and active group (Group 2, 25 patients, 50%: SLEDAI 5 to 12). PTX3 concentration was measured by a sandwich ELISA kit (Hycult) with 2.8ng/mL cut-off point. SAA concentration was detected by nephelometry performed on a BN ProSpec System (Siemens, Germany), with assay kit based on polyclonal antibodies (Siemens Healthcare Diagnostics Products, Germany). High sensitive CRP concentrations were determined using the c8000 platform (Abbott Laboratories Chicago, Illinois).

Results: Plasma PTX3 and serum SAA levels was significantly higher in SLE patients than in the healthy subjects (PTX3115 ± 7.3ng/mL vs 2.3 ± 1.1; p < 0.001; SAA: 87 ±77 mg/L vs 2.6±2.5; p < 0.001). These differences were not evident in CRP levels (8.5 ± 7.8 mg/L vs 6.2 ± 2.5). Considering two groups, there were statistical differences in PTX3 level (Group 2: 14.9 ± 12 ng/mL vs Group 1: 2.16 ±0.5 ng/mL, p<0.05) and SAA concentration (Group 2: 214 ± 89 ng/mL vs Group 1: 3.6 ±1.7 mg/mL, p<0.05) but not in CRP concentration (Group 2: 11.5 ± 8.4 mg/L vs Group 1: 9.5 ±3.5). There was a significantly negative correlation between C3, C4 fractions, PTX3 and SAA levels (respectively r=-0.74, p<0.05, and r=-0.79, p<0.05). No statistical correlation were appeared between C3, C4 fractions and CRP serum levels (r=-0.12, p=0.82, and r=-0.18, p=0.21). We noted a positive significant correlation between SLEDAI, PTX3 and SAA concentration (r=0.79, p<0.05, 0.83, p<0.05, respectively) an increase in PTX3 and SAA levels followed the lupus flare and symptoms. No significant correlation appeared between SLEDAI and CRP (r=0.15, p=0.089).

Conclusion: PTX3 and SAA concentration was significantly higher in SLE patients than the healthy control subjects and their levels reflected disease activity. We showed a direct correlation between PTX3 and SAA. In SLE patients PTX3 and SAA concentrations were correlated with SLEDAI. We suggest an integrate viewpoint in witch SAA and PTX3 may play a role as a biomarker of disease activity, with synergic work during SLE events. Evidences suggested that PTX3 and SAA could trigger the same molecular pathway, by TLR4, via NF-kB.

Disclosure of Interests: None declared

AB0053

BERGENIN, ACTING AS AN AGONIST OF SIRT1, REDUCE SERUM URATE IN MICE THROUGH THE UPREGULATION OF ABCG2

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Background: About 20% of individuals in the USA have asymptomatic hyperuricemia[1]. However, Urate-lowering therapy in asymptomatic hyperuricemia condition is still controversial considering the benefit and side effects[2,3]. Therefore, safe and effective anti-hyperuricemia therapies are necessarily.

Objectives: Bergenin, the major bioactive ingredient isolated from Saxifraga stolonifera, could activate SIRT1 in this study, we identify the effect of bergenin on hyperuricemia, and explored the related mechanisms.

Methods: Significant hyperuricemia was established in C57BL/6N mice treated with oxonate and yeast polysaccharide. Bergemin was administered to the mice at the same time. The serum uric acid and creatinine levels, clearance of uric acid and creatinine, the intestinal uric acid and creatinine, the intestinal uric acid excretion, and renal pathological lesions were determined were used to evaluate the anti-hyperuricemic effects. The location and expression levels of ABCG2 in the kidney and intestine were analyzed. HK-2 and Caco-2 cell lines were exposed to soluble uric acid with or without the treatment of Bergenin. Then the expression of ABCG2 and underlying mechanisms were explored.

Results: The administration of bergenin decreased serum uric acid in hyperuricemic mice by the promotion of uric acid excretion both in kidney and intestine. Bergenin reuced the downregulation of ABCG2 in the kidney and hyperuricemic mice and upregulated the expression of ABCG2 in the jejunum and ileum. In
Conclusion: These findings suggest bergenin increases uric acid excretion both in the kidney and intestines, which may be related to the upregulation of ABCG2 via SIRT1-PPARγ pathway.

References:

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4163

AB0054  SYNOVIAL CD163+ MACROPHAGES ARE ASSOCIATED WITH RADIOGRAPHIC JOINT DESTRUCTION IN RHEUMATOID ARTHRITIS

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Background: CD163, a hemoglobin scavenger receptor, has been identified as a marker of M2 macrophages, it can promote the release of IL-10 and carbon oxide. Researches on inflammatory diseases and tumors have suggested that CD163 plays anti-inflammatory effect and promotes tumor growth and metastasis. Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by chronic synovitis with inflammatory cells infiltration including considerable macrophages. However, little is known about the role of CD163+ macrophages in RA synovium.

Objectives: To investigate the expression and clinical significance of synovial CD163+ macrophages in RA.

Methods: Seventy-five RA patients were recruited and clinical data including disease activity, HAQ and Sharp/van der Heijde-modified Sharp score of bilateral hands and wrists were collected. Synovial tissues were obtained by needle biopsies or arthroscopy of knee joints. Eighteen osteoarthritis (OA) and seventeen orthopedic arthropathies (orth.A) patients were included as controls. All synovium were stained with H&E and immunohis- tochemically for CD163, CD3, CD20, CD38, CD68, and CD15. Histologic changes of synovitis in H&E stained sections were graded with Krenn's synovitis score.

Results:
1. Positive CD163 expression were found in both lining synoviocytes and sublining inflammatory cells. Both densities of lining and sublining CD163+ macrophages in RA synovium were significantly higher than that in OA or Orth.A synovium (140.47±66.93 vs. 178.5±77 vs. 19.765±28 and 417.92±249.62 vs. 27.58±14.19 vs. 29.87±9.33, all P<0.001, Figure 1).
2. According to Krenn's synovitis score, there were 68% RA patients showing high synovitis score (score≥4). Both lining and sublining synovial CD163+ macrophages were significantly higher than those showing low synovitis (lining: 158.40±62.91 vs. 122.06±66.74, sublining: 462.96±62.91 vs. 371.65±271.54, both P<0.05). Meanwhile, the densities of lining and sublining CD163+ macrophages were both positively correlated with Krenn's synovitis score (r=0.238 and 0.343, both P<0.05).
3. For clinical relationship in RA, the density of sublining CD163+ macrophages was positively correlated with total Sharp score (mTSS) (r=0.399, P<0.001), joint space narrowing subscore (r=0.248, P=0.032) and joint erosion subscore (r=0.457, P<0.001). While the density of lining CD163+ macrophages was positively correlated with mTSS (r=0.319, P=0.005) and joint erosion subscore (r=0.358, P=0.002). Meanwhile, the densities of sublining and lining CD163+ macrophages were also positively correlated with mTSS (r=0.253 and 0.242, both P<0.05), of which the correlation was weaker than that of CD163+ macrophages (Figure 2). There were no significant correlation between the density of CD163+ macrophages and disease activity or HAQ (all P>0.05).

Conclusion: Synovial CD163+ macrophages are associated with radiographic joint destruction, which imply that CD163+ macrophages may play role in the pathogenesis of joint destruction in RA.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1141

AB0055  SOLUBLE TREM-1 LEVELS IN FAMILIAL MEDITERRANEAN FEVER RELATED AA-AMYLOIDOSIS

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Background: Triggering Receptor Expressed on Myeloid cells-1 (TREM-1) is a monocYTE and neutrophil receptor functioning in innate immunity. TREM-1 produces proinflammatory cytokines and serves for neutrophil degranulation. TREM-1 activity is well known in the pathogenesis of sepsis; hence it can be also present in autoinflammatory diseases such as the most common monogenic one, Familial Mediterranean Fever (FMF).

Objectives: The objective of this study is to measure soluble TREM-1 (sTREM-1) activity in severe FMF cases complicated with systemic AA-Amyloidosis. TREM-1 activity is well known in the pathogenesis of sepsis; hence it can be also present in autoinflammatory diseases such as the most common monogenic one, Familial Mediterranean Fever (FMF).

Methods: The cohort of the study includes regularly followed FMF related AA-amyloidosis patients in a tertiary center outpatient rheumatology clinic. Soluble TREM-1 levels were measured using enzyme-linked immunosorbent assay (ELISA). In addition, demographic data, renal function tests, acute phase reac- tants, and medical prescription history was also noted and analyzed. None of the FMF diagnosed patients had an attack during the collection of the blood samples.

Results: The patients were categorized into 4 groups: FMF related AA-Amyloidosis patients (A+ FMF+), FMF unrelated AA-Amyloidosis (FMF- A+),