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AB0108B PREVALENCE AND RISK FACTORS INFLUENCING THE DEVELOPMENT OF ARTERIAL HYPERTENSION IN PATIENTS WITH A GOUT

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Background: Cardiovascular diseases (CVD) is the leading cause of death for gout. Arterial hypertension (AH) is a proven CVD risk factor (CVD-RF).

Objectives: To assess the factors influencing on development of an AH in patients with a gout.

Methods: 286 male patients fulfilling Wallace proposed criteria for gout were included in the study: age 51.2 [42.8;59.4] years (ys), disease duration – 6.2 [3.8;12.1] ys, number of joints involved during disease course – 7 [4;12], subcutaneous tophi – in 35% pts, intraosseous tophi – in 44% pts, nephrolithiasis – in 69% pts, abdominal obesity – in 71%. All pts underwent standard clinical examination, C-reactive protein (CRP), total cholesterol (TC), triglycerides (TG), low and high density lipoproteins (LDL/HDL), serum uric acid, serum creatinine, smoking, family history of AH, body mass index (BMI), diabetes mellitus was performed by standard procedure. We estimated the adjusted odds ratio (OR) and 95% confidence interval (95% CI).

Results: There were two groups of patients with AH diagnosed on clinical data: group 1 (with AH) - 244 (85%) pts, group 2 (without AH) - 42 (15%) pts. The 1st group pts were older (52.3[44.5; 61.1] vs 41.9[38.3; 50.1] ys), had longer duration of gout (6.7[3.9; 13.7] vs 4.5[3; 7.9]), a higher number of joints involved during disease course (8[4; 12] vs 5[3; 9]). The frequency of family history of AH (68.3% vs 48.8%), abdominal obesity (55.3% vs 33.3%), nephrolithiasis (71% vs 54.7%), intraosseous tophi (48% vs 21%) was higher in group 1 as compared with group 2, p<0.05. BMI and CRP level was higher in group 1 compared with group 2: 30.2[27.4; 33.1] vs 27.9[26.3; 30.5] kg/m², and 12.7[5.84; 19.2] vs 7.8[3.7;16.4]mg/l, accordingly, p<0.05. We didn't find differences of lipid profile, serum uric acid, and serum creatinine level in 1 and 2 group. We also didn't find differences the frequency of smoking, diabetes mellitus, subcutaneous tophi in both groups (table 1).

Table 1

Parameters	Group 1	Group 2
Uric acid, mmol/l	494[420; 575.8]	466[397.3; 547]
Creatinine, mmol/l	94[84.7; 108]	93[83.8; 102]
TC, mg/dl	225[190; 266.8]	225[190; 251]
HDL, mg/dl	35.2[28; 44]	38[27.5; 46.8]
LDL, mg/dl	152.8[113.5; 182.4]	132.2[103;175.2]
TG, mg/dl	172.5[120; 262.3]	147[94;240]
Subcutaneous tophi,%	36.5	26
Smoking,%	29.9	28.6
Diabetes mellitus,%	17.6	11.9

Data are present in median values and interquartile range, *p<0.05 (nonparametric paired Mann-Whitney U-test).

Abdominal obesity (OR, 1.247; 95% CI, 1.063-1.462), family history of AH (OR, 2.8; 95% CI, 1.5-5.4), disease duration more 10 ys (OR, 4.5; 95% CI, 1.1-19.4), intraosseous tophi (OR, 3.0; 95% CI, 1.4-6.4), increased the risk for AH in patients with a gout.

Conclusion: Majority (85%) of patients with gout had AH. Abdominal obesity, family history of AH, disease duration more 10 ys, intraosseous tophi were associated with an increased risk of AH in pts with a gout.

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Rheumatoid arthritis - etiology, pathogenesis and animal models

AB0109 SYSTEMIC OVEREXPRESSION OF INTERLEUKIN-22 INDUCES EXPRESSION OF THE NEGATIVE IMMUNE-REGULATOR SOCS3 AND POTENTLY REDUCES COLLAGEN-INDUCED ARTHRITIS IN MICE

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Background: High interleukin-22 (IL-22) levels are detected in serum and synovial fluid of rheumatoid arthritis (RA) patients. The increased IL-22 serum levels in RA patients correlated positively with multiple clinical disease parameters like disease activity score (DAS)28 and serum levels of rheumatoid factor. The role of IL-22 in autoimmunity and inflammation appears to be greatly contradictory, being both pro- and anti-inflammatory. Especially the anti-inflammatory properties of IL-22 are not well understood.

Objectives: We aimed to investigate the anti-inflammatory and immune-suppressive effect of IL-22 during experimental arthritis.

Methods: Collagen-induced arthritis was induced in DBA1 mice by immunization and booster with bovine collagen type II (CII). After booster, but before arthritis onset, IL-22 was overexpressed either locally or systemically using an adenoviral construct (AdIL-22) or Luciferase as control (AdLuc). 1x10⁷ plaque-forming units (PFU) of the adenoviruses were injected intra-articularly for local overexpression, or 3x10⁸ PFU was injected intravenously for systemic overexpression in immunized mice, and mice were sacrificed 10 days later. Macroscopic scoring and histological analysis was performed, and mRNA expression and protein production of various pro- and anti-inflammatory mediators was determined in synovial tissue, spleen, and serum.

Results: Local overexpression of IL-22 by injection of AdIL-22 in the knee joint of CII-immunized mice resulted in an unaltered arthritis incidence and severity as compared to the control virus AdLuc. Accordingly, no changes in mRNA expression or protein production were observed in CIA mice locally overexpressing IL-22. In contrast, systemic overexpression of IL-22 potentially reduced disease incidence and severity, which was also confirmed by histological analysis. Systemic levels of IL-1 β , IL-17, GM-CSF and MCP1 were unaltered in mice overexpressing IL-22 systemically. However, these mice showed significantly lower serum levels of IFN γ , TNF α , MIP1 α , and IL-10. Interestingly, the significantly enhanced splenic SOCS3 expression was found to negatively correlate to serum TNF α and MIP1 α levels, which is in line with our hypothesis that that the observed reduction in the cytokine levels is mediated in a SOCS3-dependent manner.

Conclusion: With this study, we revealed clear anti-inflammatory effects of IL-22 overexpression during collagen-induced arthritis, which are completely dependent on the systemic route of administration. Additionally, we were the first to show that this protective effect of IL-22 during experimental arthritis is likely orchestrated via up-regulation of the negative regulator SOCS3.

Disclosure of Interests: None declared

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AB0110 RITUXIMAB INDUCED GRANULOMATOUS HEPATITIS WITH A SARCOIDOSIS LIKE REACTION: A BLINDED TRIAL IN MICE

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Background: Rituximab is useful in patients with rheumatoid arthritis (RA) with persistently active disease despite adequate trials with other disease-modifying antirheumatic drugs (DMARDs).

Objectives: To determine whether the inhibition of the B cell CD20 receptor by rituximab results in acute hepatitis in BALB/c mice.

Methods: Twenty BALB/c mice were studied. Ten mice received subcutaneous (SC) injection of rituximab (0.31 mg per 25g body weight per 0.03 ml normal saline) at 0, 1, 2 and 4 weeks. For the control group, 10 mice received a SC injection of normal saline (NS) (0.03 ml). At the 10th week post injection, the mice were sacrificed, and histopathological studies were conducted.

Results: Of the rituximab-treated group, 1/10 mice died. Liver histology for the rituximab-treated group showed that 7/9 displayed histopathological changes in the lobular cellular infiltrates of eosinophils, lymphocytes and histiocytes, in addition to granuloma formation. In contrast, only minimal inflammation was observed in 3/10 mice in the control group (p=0.051).

Conclusion: To our knowledge this is the first experimental controlled study demonstrating rituximab may play a role in inducing granulomatous hepatitis with a sarcoidosis-like reaction.

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AB0111 THE ROLE OF KLOTRO IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic and disabling disease affecting 0.5–1% of the general population. It is characterized by the presence of autoantibodies including rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA). Klotho is a membrane-bound protein predominantly expressed in the kidney, parathyroid gland and choroid plexus that displays enzymatic and co-receptor functions, being involved in the prevention of aging, in the calcium-phosphate balance and in the reparative and fibrotic processes. Klotho seems to play an essential role in the maintenance of vessel tone control, in tissue regeneration and reparation and in the electrolytic balance.

Objectives: We aimed to compare serum Klotho levels between RA patients and healthy controls and the possible association between soluble Klotho with different characteristic of the disease.

Methods: This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed at the Vega-Baja Hospital (Orihuela, Spain) and 65 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. ACPAs were detected using a second-generation ELISA (ACPAs) kit (ORGENTEC Diagnostika GmbH, Mainz, Germany) while IgM RF was determined as part of routine analysis by turbidimetric assay (Siemens Healthcare Diagnostic Inc. NY, USA) according to the manufacturers' instructions. Serum Klotho was analyzed using ELISA.

Results: The mean serum total ACPAs and RF were 571.22±1040.89 U/ml and 173.73±751.8 U/ml, respectively. Serum Klotho concentrations were significantly higher in the RA patients than those in the control group: [4.68 (1.4–7.8) vs. 3.5 (0.6–6.1), ng/mL; $P < 0.0001$]. They were positively associated with the presence of ACPA and RF ($p < 0.05$). Klotho serum levels were higher in RA patients treated with biologic agents than in those undergoing conventional therapy ($p = 0.008$).

Conclusion: The increased serum Klotho levels in RA patients, especially in those undergoing biologic therapy, may indicate a potential implication in the pathogenesis of the disease.

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AB0112 EVALUATION OF A NEW MULTIPLEX TECHNOLOGY ASSAY FOR ANTI-CITRULLINATED PEPTIDE ANTIBODIES DETERMINATION

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Background: Anti-citrullinated peptides antibodies (ACPA) are highly specific RA markers. In 2010, experts included them in the ACR/EULAR criteria for disease diagnosis, usually, measured by ELISA. However, a new assay has been developed, recently: Multiplex technology, which allows searching IgG ACPA directed against four citrullinated peptides: Human (HCP1 and 2) and Viral (VCP1 and 2).

Objectives: First, assess ACPA diagnostic performances using Multiplex technology and then compare them to those obtained with the reference technique (ELISA).

Methods: We studied sera of 273 RA patients versus 165 controls (64 healthy controls and 101 patients with other pathologies). We realized ACPA dosage by Multiplex technology and compared them with ELISA assay results. In the end, we looked for a correlation between ACPA production and shared epitope expression in RA patients.

Results: The overall agreement calculated between the two methods was about 91.3%. As to the comparison of diagnostic values of Multiplex technology vs. ELISA, it revealed a sensitivity of 80.2% vs. 82.4% and a specificity of 95.8% vs. 95.5%. Then, for a better evaluation, we plotted ROC curves for ACPA detected by Multiplex technology and ELISA ones. Therefore, we obtained the following areas under the curve (AUC) (p value < 0.0001): Anti-: HCP1 (0.775), HCP2 (0.798), VCP1 (0.715) and VCP2 (0.837) and ACPA ELISA (0.867). Finally, our results reveal higher serum levels of ACPA detected by Multiplex technology, in case of SE expression [SE (+) vs. SE (-)] (p value < 0.0001).

Conclusion: Diagnostic performance of ACPA detection methods is comparable with relatively good agreement. Our study demonstrated an association between elevated serum levels of anti-HCP and anti-VCP and SE expression, in RA patients.

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AB0113 ARTHRITIS IS ASSOCIATED WITH CEREBROVASCULAR ENDOTHELIAL DYSFUNCTION: MECHANISTIC INSIGHTS IN THE RAT ADJUVANT-INDUCED ARTHRITIS MODEL

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Background: Stroke is the second cause of premature mortality and sudden death in rheumatoid arthritis (RA) after myocardial infarction¹. The mechanisms involved in the high risk of stroke are currently unknown, but data from the general population argue for a contribution of cerebrovascular dysfunction.