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SAT0632

NEUTROPHIL ACTIVATION IDENTIFIES PATIENTS WITH ACTIVE POLYARTICULAR GOUT – A NOVEL BIOMARKER?

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Background: Neutrophils are key immune cells participating in host defense through several mechanisms, including the formation of neutrophil extracellular traps (NETs). Although beneficial from a host-pathogen perspective, excessive neutrophil activation has been linked to inflammation and autoimmunity, including systemic lupus erythematosus (SLE) and gout.(1) In gout models, uric acid crystals induce NETosis. Though NETs are known to induce marked inflammation through TLR9- and cGAS-dependent pathways, as well as partake in induction of tissue damage and thrombotic events, the role of NETs in human gout has not been carefully investigated.

Objectives: Our objective is to investigate evidence of systemic neutrophil activation, and the clinical utility of neutrophil-derived biomarkers in gout. We hypothesize that uric acid crystals will activate neutrophils to undergo NET formation, with these processes contributing to immune cell activation, and local joint destruction.

Methods: Plasma samples from 75 gout patients participating in the ‘Reade gout cohort Amsterdam’ were compared with 30 healthy controls (HC). Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using a MPO-DNA ELISA, as well as with fluorometry.(2) Levels of calprotectin (S100A8/A9) were analyzed by ELISA, Mitochondrial (mt) COXII, as well as genomic (n, RPLP0) DNA levels were analyzed by qPCR. All of the analyzed markers were compared between gout patients and healthy individuals, and related to markers of inflammation and disease activity.

Results: Levels of NETs, as well as other neutrophil biomarkers, were significantly increased in gout patients as compared to healthy subjects (p<0.01, Figure 1A). In contrast to SLE, gout patients did not have elevated levels of circulating mtDNA (p=0.96), but only nDNA (p<0.006). No associations were found between markers of cell death (cDNA and NETs) and disease activity. Peroxidase activity correlated with disease activity (RAPID score: r=0.43, p=0.01, RAPID function: r=0.54, p<0.001) and inflammation markers (CRP: r=0.40, p=0.001, and ESR: r=0.43, p<0.001). Involvement of ankle and wrist resulted in significant higher peroxidase levels compared to mono-articular disease (p=0.01, and p=0.03, respectively), suggesting peroxidase activity being a marker of polyarticular gout (Figure 1B). Calprotectin (S100A8/A9) correlated with the inflammation markers CRP and ESR (r=0.30, p<0.001, and r=0.30, p=0.001, respectively) and morning stiffness, especially in patients with chronic polyarticular gout (r=0.61, p=0.001).

Conclusion: To our knowledge, this is the first report demonstrating presence of NETs in the peripheral blood of gout patients. Although markedly elevated, levels of NETs did not associate with markers of disease activity or inflammation, possibly due to the lack of inflammatory mitochondrial DNA within the NETs. Even so, our data demonstrate an important role of neutrophils in gout pathogenesis, with neutrophil activation markers associating with characteristics of active, and more pronounced polyarticular disease.

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SA0633

PREGNANCY SUCCESS RATE AND RESPONSE TO HEPARINS AND OR ASPIRIN DIFFERS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS ACCORDING TO THE GAPSS SCORE

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Background: Current standard of care (SoC) in pregnancy for patients with Systemic lupus erythematosus (SLE) and/or aPL positivity includes treatment with low dose aspirin (75–100mg/day) and low molecular heparin or unfractionated heparin. However, up to 30% of women continue to have pregnancy complications despite SoC. Therefore, identifying patients that are at greater risk to develop pregnancy complications despite the SoC and might benefit from additional therapeutic approaches, is still an unmet clinical need.

Recently, our group conceived and validated the global antiphospholipid syndrome score (GAPPS) [1], as a risk score for predicting aPL-related clinical manifestations (thrombotic and/or pregnancy morbidity).

Objectives: We aimed to investigate response to SoC in women with SLE and/or aPL positivity when stratifying their risk according to GAPPS Score.

Methods: 143 women ever pregnant treated with SoC therapy with SLE and/or aPL positivity were included. Data on cardiovascular risk factors and aPL positivity were retrospectively collected. The individual GAPPS was calculated for each patient by calculating the sum of each risk factor score, as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for antiphospholipid IgG/IgM, 4 for anti-β2glycoprotein I IgG/IgM, 4 for anti-phosphatidylserine/prothrombin antibodies IgG/IgM and 4 for lupus anticoagulant. The patients GAPPS was then grouped according to the patients GAPPS into low risk (<6), medium risk (6–11) and high risk (>12).

Results: The analysis included 143 patients (mean age 30.8 ±6.4) with SLE (122; 85.3%) and/or aPL positivity, for a total of 352 pregnancies.

GAPPS <6 (n=72) GAPPS 6-12 (n=66) GAPPS ≥13 (n=5)

Demographics

Age, mean (±S.D.) 30.7 (±5.9) 30.6 (±6.2) 34 (±11.1)

Diagnosis

SAT0633
The main objective of this analysis was to investigate the impact of AD on the association between structural features of OA and patient-reported pain.

Methods: Baseline data from two phase 3 trials investigating oral salmon calcitonin in OA, NCT00486434 and NCT00704847 (total N=2206), was analyzed in a post-hoc cross-sectional analysis. Patients with self-reported current or previous depression, anxiety or post-traumatic stress syndrome (PTSD) were selected and compared to a control group, matched by sex, age, BMI and JSW. Spearman’s correlation coefficient between JSW and WOMAC pain was calculated for both groups. Multiple regression analyses of both groups with WOMAC pain as the outcome variable, and age, sex, body mass index (BMI) and baseline JSW or KL-grade as explanatory variables were performed.

Results: In the AD group, 149 patients had AD in medical history of which 123 reported the condition as ongoing at baseline. The study groups of AD and matched controls (MC) were comparable in terms of age, sex, BMI, JSW, KL-grade and WOMAC pain. Associations between pain and JSW in the AD group, no significant correlation between JSW and WOMAC Pain score was found, while BMI was found to be weakly associated with WOMAC pain (R= 0.19, p=0.02) in the multiple regression analysis. In the MC group, a statistically significant (p<0.004), correlation (R= -0.24) was found between JSW and pain indicating that lower JSW was associated with higher pain, with JSW accounting for approximately 6% of the total natural variation behind reported pain. In addition, a positive significant association between male sex and WOMAC pain (R=0.18, p=0.04) was found. The univariate linear relationship between JSW and pain is illustrated in Figure 1, and multivariate analyses are shown in Table 1.

Associations between pain and KL-Grade In the model evaluating associations between KL-grade and symptoms, there was no correlation between KL-grade and symptoms in the AD group. Similar to the findings relating to JSW, in the MC group, a weak (R=0.16, borderline