Although CD24<sup>hi</sup>CD27<sup>-</sup> B-cells frequencies and absolute counts did not differ between patients with active (n=27) or inactive disease (n=30), (16.9% vs 17.0%, p=0.946; 25 vs 31 cells/µL, p=0.179), patients with higher disease activity (ESSDAI<sub>5</sub>) (n=9) presented lower absolute counts of CD24<sup>hi</sup>CD27<sup>-</sup> B-cells (18 vs 31 cells/µL, p=0.096) and lower CD4<sup>+</sup>CD38<sup>-</sup> B-cells (4 vs 10 cells/µL, p=0.075), and higher Th1/Breg CD4<sup>+</sup>CD27<sup>-</sup> B-cell ratios (16.2 vs 9.2, p=0.064).

Considering all patients, a negative correlation was found between the ESSDAI score and the absolute numbers of either CD24<sup>hi</sup>CD27<sup>-</sup> B-cells (ρ = -0.727, p=0.037) and Tregs (ρ = -0.311; p=0.019).

Correlations with ESSDAI were stronger when looking at patients with ESSDAI≥5: for the percentages of CD24<sup>hi</sup>CD27<sup>-</sup> B-cells, r=0.705; p=0.023; for CD24<sup>+</sup>CD27<sup>-</sup> B-cells absolute counts, r=-0.644; p=0.045; and for the absolute counts of Tregs, r=-0.862; p=0.001.

Using ROC curves to discriminate pSS from HC, better AUCs were obtained for CD24<sup>hi</sup>CD27<sup>-</sup> B-cells cutoff (cut-off 34 cells/µL, AUC=0.81), Tregs/CD24<sup>hi</sup>CD27<sup>-</sup> Breg ratio (cut-off 1.98, AUC=0.74) and Th1/CD24<sup>hi</sup>CD27<sup>-</sup> Breg ratio (cut-off 12.23, AUC=0.70), corresponding to a specificity for pSS of 0.83, 0.75 and 0.70, respectively, and sensitivity of 0.75, 0.72 and 0.67, respectively.

In pSS, lower CD24<sup>hi</sup>CD27<sup>-</sup> B-cell counts, as well as higher Tregs/CD24<sup>hi</sup>CD27<sup>-</sup> Breg and Th1/CD24<sup>hi</sup>CD27<sup>-</sup> Breg ratios, were associated to a higher frequency of autoantibodies and higher gammaglobulin.

Conclusion: Our findings demonstrated a significant decrease in the Breg-enriched CD24<sup>hi</sup>CD27<sup>-</sup> B-cell subset in pSS, which presented a negative correlation with the disease activity. We have demonstrated significant differences in the CD24<sup>hi</sup>CD27<sup>-</sup> B-cell subset and respective ratios, presenting a good discriminatory capacity compared to HC. Therefore, this subset may have diagnostic utility in pSS, as it may support the presence of immune dysregulation in suspected cases that do not fulfill the pSS classification criteria. Further studies with increased number of samples and a prospective design are needed to explore this hypothesis.

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AB0162 IMPLEMENTATION OF HYDROXYCHLOROQUINE AT THE PRE-CONCEPTIONAL STAGE IN THE TREATMENT OF ANTIPHOSPHOLIPID SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The problem of correcting the antiphospholipid syndrome (APS) at the planning stage of pregnancy of patients with systemic lupus erythematosus (SLE) is an important task of rheumatology.

Objectives: To study the effect of hydroxychloroquine (HC) on the level of anti-phospholipid antibodies titer in women with SLE of low degree of activity at the planning stage of pregnancy.

Methods: The study included 7 women aged from 18 to 44 years with a definite laboratory tests, the level of antibodies to cardiolipin (lgM/IgG), 2-glycoprotein I (lgM/IgG), β2-glycoprotein I (lgM/IgG) was determined in 95% confidence interval (95% CI). Comparison of dependent samples was performed using non-parametric methods (Wilcoxon Signed Ranks Test). The statistical significance of the hypotheses was accepted at a level of p < 0.05.

Results: The initial SLEDAI2K index constituted 4.0±1.0 points. The median of the level of antibodies to cardiolipin is defined as 69.2% (95% CI 57.4-80.0) U/mL, to β2GPI - 69.24% (95% CI 49.7-87.5) U/mL. After 3 and 6 months from the start of HC administration, the SLEDAI2K index did not statistically significantly decrease (p = 0.09). 3 months later, a statistically significant decrease in the level of antibodies to cardiolipin (lgM/G) by 30.4% was determined relative to the initial one [Me 21.43% (95% CI 20.2-46.1), p = 0.001]. The second aim was to compare molecular profiles of the immunoregulatory mediators between pSS patients and healthy controls. The second aim was to identify key predictors of fatigue in pSS.

Methods: Serum levels of the three molecules were measured in 124 patients with pSS and 28 healthy non-fatigued controls selected from the United Kingdom Primary Sjögren’s Syndrome Registry using various assays. IL-10 concentrations were measured using a cytometric bead array-based immunoassay, melanotonin levels were determined using ELISA and TGF-β concentrations were quantified using a bioassay in which HKC-8 cells were stably transfected with a TGF-β inducible CAGA-luciferase reporter construct. Patient fatigue levels were evaluated with a validated self-complete questionnaire and the scores were compared with the immunoregulatory molecules levels using analysis of variance. Significance in immunoregulatory mediators between the patients and controls was determined using the Wilcoxon test. Ordinal logistic regression analysis was performed in a smaller subset of patients (N = 75) to identify the key predictors of fatigue in pSS.

Results: IL-10 was significantly higher in the sera of patients with pSS compared to the healthy controls (p=0.0001). Melatonin showed a positive correlation with fatigue levels within the patient cohort (p=0.1664) whereas IL-10 and TGF-β were inversely related to fatigue severity (p=0.1265 and p=0.0843 respectively). The regression model used the three investigated immunoregulatory molecules, disease specific, haematological and clinical parameters as well as patient reported depression, anxiety and pain as predictors. The model was able to predict fatigue levels to a 67% accuracy.

Conclusion: The study suggests that melatonin may play a role in regulating the immune response in pSS and may affect fatigue levels in patients. Dryness, anxiety, pain and melanotonin appear to be the most powerful predictors of fatigue in pSS. Further research into the effects of these immunoregulatory molecules is necessary to gain a better understanding of the pathophysiology of fatigue in pSS.

REFERENCES

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