AB0134 BLOOD LYMPHOCYTE SUBSETS ACCORDING TO THE CLINICAL PROFILE IN SJÖGREN'S SYNDROME

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Background: It has been recently described the occurrence of disturbances in lymphocyte subsets in Sjögren's syndrome (SS) which may reflect B cell hyper activation and a T cell adjuvant role.
Objectives: We aim to characterize circulating lymphocyte subsets in SS patients, according to disease activity and antibody profile.
Methods: We have included in this study 53 SS patients (2002 AECG criteria) of which 22 with >10 years since diagnosis and 31 with <2 years since diagnosis, and 22 healthy controls. Lymphocyte subsets, including follicular (Tfh) and regulatory T (Treg) cells, maturation subsets, plasmablasts (PB) and regulatory B (Breg) cells, were characterized by flow cytometry. Statistical analysis was performed with GraphPad. Significance was considered for $p<0.05$.
Results: Compared to controls, SS patients had lower absolute counts of B (p=0.0337) and T cells (p=0.0012), lower CD4 (p=0.0002) and higher CD8 percentages (p=0.0006), resulting in an increased CD4/CD8 ratio (p=0.0006). Additionally, there was decrease in absolute counts of Tregs (p=0.0008) and Th17 cells (p=0.0005) in SS patients. Moreover, there was a decreased absolute counts ($p<0.0001$) of Tfh cells, identified by CXCR5 expression, though higher levels of IL21$^+$CD4 T cells (p=0.0209) and Tfh1 cells (p=0.0092). SS patients also presented higher % of naïve B cells (p=0.0412), lower % and absolute counts of memory (%, p=0.0161; abs p=0.0002) and unswitched memory (%, p=0.0106; abs p=0.0005) B cells and lower absolute counts (p=0.0001) of switched memory B cells, with higher naive/memory B cell ratios, compared to healthy subjects (p=0.0219). Accordingly, using the Bm1–5 classification, we have found decreased Bm1 (%, p=0.0087; Abs, p=0.0007), eBm5 (Abs, p=0.0005) and Bm5 cells (Abs, p=0.0015) in SS patients. Similar Bm2+Bm2'/eBm5+Bm5 ratios were observed in patients and controls. CD24$^+$CD27$^+$ Bregs were also decreased ($p\leq0.0012$) in SS patients.
SS patients had also an increase in IL21$^+$CD4 T cells, particularly in patients with extra-glandular manifestations (EGM) (n=12), who also presented less Tfh17 cells (p=0.0409) comparing to patients without EGM. PB were decreased in patients with EGM only when compared to controls (p=0.0434).
SSA$^+$ patients (n=36) had more frequently EGM than SSA$^-$, higher ESSDAI score, γ-globulin levels and lower salivary flow. Compared to SSA$^-$ and controls, increased IL21$^+$CD4 T cells were detected in SSA$^+$patients ($p\leq0.0284$), who also had higher Tfh1 cells than controls ($p\leq0.0065$). Lower Bm1 cells ($p\leq0.0305$) were observed in SSA$^+$patients compared to SSA$^-$ and controls, with an increase % of Bm3+Bm4 cells (p=0.011) compared to SSA$^-$.
Conclusions: The immune profile of SS patients has distinctive features, with decreased memory B cell subsets, including CD24$^+$CD27$^+$ Bregs. Moreover, an increased capacity of IL21 secretion by T cells, together with a more prominent Tfh1 signature seem to be the hallmark of SS, particularly in patients with EGM and autoantibody production, suggesting an immune environment prone to proinflammatory processes, in severe patients. Comprehending the immune dynamics in SS may be valuable for diagnosis, follow-up and future therapeutic decisions.
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AB0135 PLASMATIC AND URINARY ENDOTHELIAL MICROPARTICLES ARE INCREASED IN PATIENTS WITH LUPUS NEPHRITIS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease presenting with a wide array of clinical manifestations and incompletely understood pathogenesis. SLE is characterized by alterations in both the innate and adaptive immune system ultimately leading to the loss of immunologic tolerance and occurrence of autoantibodies against nuclear material. Lupus nephritis is one of the most severe features of SLE determining an increase in morbidity e mortality rates. Renal biopsy still represent a fundamental diagnostic and prognostic tool for LN. Therefore, non-invasive surrogate biomarkers of active LN are urgently needed. Circulating, heterogeneous subcellular microparticles (MPs) are released from cells and platelets constitutively and upon cellular activation or apoptosis. Such MPs may reflect the state of their parental cells and tissues, and could serve as markers of pathology. Particularly in SLE, MPs are potential biomarkers and triggers of autoimmunity. Recent studies have demonstrated increased levels of plasmatic EMPs in patients with SLE active disease and their reduction after treatment.
Objectives: The aim of this study was to investigate plasmatic and urinary levels of endothelial microparticles in a cohort of SLE patients with and without renal involvement compared to healthy controls.
Methods: Consecutive SLE patients and sex- and age-matched HC were included in the study. MPs were isolated from plasma and urine and characterized by flow cytometry using AnxV (a probe that binds to the exposed phosphatidilserine - PS) and antibodies against surface markers endothelial cells (CD31+CD41-). Mann-Whitney and Spearman correlation tests were used. A p value <0.05 was considered statistically significant.
Results: Sixty SLE patients (55F:5M, age 41,7±9.6 Y disease duration 149±112 months) and 29 healthy controls were studied. Twenty-eight patients had renal involvement.The total number of plasmatic MPs was lower in SLE patients than HC (p=0.001). In contrast there was no significant difference in levels of EMPs between the two groups. When the patients were divided according to renal involvement, the patients with active lupus nephritis (A-LN) showed lower plasmatic level of EMPs in comparison to inactive LN (I-LN) (p=0.01), while the patients with I-LN had higher levels of EMPs than HC (p=0.002). There was no significant difference of total urinary level of MPs between SLE patients and HC. Urinary levels of EMPs were higher in SLE and in lupus nephritis patients than HC.
Conclusions: The results of the present study show increased urinary and plasmatic levels of EMPs in patients with lupus nephritis in remission. Circulating EMPs have been considered as a potential biomarker of endothelial activation and damage in several autoimmune disorders, and higher EMP levels have been detected in patients with vasculitis and associated with disease activation. According to our results, plasmatic EMPs levels are higher in inactive LN patients than in healthy donors. These results may suggest a potential role of EMP as a biomarker of lupus nephritis
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AB0136 MICROPARTICLES FROM SLE PATIENTS ARE A SOURCE OF INTERFERON-ALPHA

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Background: Systemic lupus erythematosus (SLE) is the prototype of systemic autoimmune disorders. In the late 1970s, increased serum levels of interferon (IFN) were shown for the first time to be significantly associated with SLE and to correlate with disease activity. IFNα is a pleiotropic cytokine that can affect multiple cell types involved in lupus.Plasmacytoid dendritic cells have a special role in the production of IFN and are the main sources of serum interferon. IFN has the potential to dramatically influence the development, progression, and pathogenesis of SLE as it can influence the function and activation state of most major immune cell subsets and function as a bridge between innate and adaptive immunity.Lupus-prone mouse models, indicates that the type I interferon system may play a pivotal role in the pathogenesis of several lupus and associated clinical features, such as nephritis, neuropsychiatric and cutaneous lupus.Circulating microparticles (MPs) are ubiquitous in the blood of healthy individuals, These MPs play an active role in coagulation and intercellular communication and assist in activation or suppression of the immune system, depending on their parental cell origin. Changes in the concentration and/or composition of circulating microparticles have been described in various autoimmune diseases, including rheumatoid arthritis (RA) systemic sclerosis (SSc) and systemic lupus erythematosus (SLE). For SLE, the reported microparticle-related changes remain somewhat inconclusive.
Objectives: To better understand the role of MPs in SLE patients, we analyzed the presence of interferon alpha on MPs surface.
Methods: MPs were isolated from citrate-treated plasma; blood cells were removed by two steps of centrifugation process (2500g for 15min at 20 C two time). The resulting platelet-poor-plasma (PPP), was analyzed by flow cytometry with specific antibody against IFN alpha
Results: 20 consecutive SLE patients (10 with active lupus nephritis) and 10 sex- and age-matched healthy control subjects were included in the study. We found that MPs from SLE patients carry on their surface IFN alpha.Moreover, the percentage IFNalpha + MPs was higher in SLE patients and in lupus nephritis patients than in HC, but there was not significant difference between patients with and without renal involvement.
Conclusions: The results of the present study show for the first time the presence of IFN alpha on MPs surface.We may assume that INF+ MPs derive from dendritic cells. In lupus nephritis patients the increased recruitment of dendritic cells was at tubular interstitial level, with subsequent IFN alpha production. Interestingly, MPs (containing RNA and DNA) could stimulate type I IFN production in plasmacytoid dendritic cells and MPs releasing.
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AB0137 ALTERATIONS IN MICRORNA EXPRESSION PROFILES IN PRIMARY SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: MicroRNAs (miRNAs) are single-stranded, endogenous non-