SAT0283 ANTIBODIES TO CARBAMYLATED VIMENTIN IN PATIENTS WITH SYSTEMC LUPUS ERYTHEMATOSUS ARE ASSOCIATED WITH RENAL INVOLVENMENT

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Background: Vimentin is a cytoskeleton protein of the intermediate filaments family, expressed by mesenchymal cells including vascular endothelial cells and renal tubular cells. Vimentin has been recently proposed as a target of the in situ immune response in lupus nephritis. Antibodies to vimentin have been described in 10–53% of patients with Systemic Lupus Erythematosus (SLE) and account for a fibrous pattern of cytoplasmic immunofluorescence. Post-translational modifications increase the immunogenicity of vimentin, as demonstrated by the detection of anti-modified vimentin antibodies in patients with rheumatoid arthritis. Carbamylation is a non-enzymatic post-translational modification consisting in the addition of a cyanate group on lysine and arginine residues; since carbamylation is time dependent, structural proteins with a slow turnover are more likely to be carbamylated. The role of carbamylated vimentin as an antigenic target in SLE has not been yet evaluated.
Objectives: Aims of the study were to assess the prevalence of anti-carbamylated vimentin in a cohort of SLE patients and to evaluate the possible associations with clinical and serological feature of the disease.
Methods: Patients with SLE classified according to 1987 ACR criteria were enrolled. Clinical features, autoantibodies profile and disease activity – as measured by SLE Disease Activity Index 2000 (SLEDAI 2K) - were collected. Sera obtained from each patient were tested for anti-carbamylated vimentin by a home-made enzyme-linked immunoassay. Data were expressed as mean±standard deviation or median (interquartile range) when appropriate. To investigate difference in anti-carbamylated vimentin prevalence and anti-carbamylated vimentin serum levels Mann-Whitney and Chi square test were applied. P value <0.05 was considered statistically significant.
Results: We enrolled 109 SLE patients (102F:7M, mean age 39.4±12.6 years, mean disease duration 10.5±9.5 years, mean SLEDAI 2K 5±5.5).
Overall, 30 out of 109 patients (27.5%) were positive for anti-carbamylated vimentin. According to the clinical features, the prevalence of anti-carbamylated vimentin was significantly higher in patients with lupus nephritis (18/44) compared to those without renal involvement (12/66) (41.8% vs 18.2%, p=0.006); moreover, anti-carbamylated vimentin serum levels were significantly higher in patients with lupus nephritis [2561 (1783) OD] compared to those without [1970 (1123) OD; p=0.0178]. We didn't find any difference in prevalence or titre of anti-carbamylated vimentin according to presence/absence of other clinical manifestations (musculoskeletal, muco-cutaneous, hematologic, neuropsychiatric) or serology (low complement, anti-dsDNA). Moreover, we did not find any correlation between anti-carbamylated vimentin serum levels and SLEDAI 2K.
Conclusions: Higher prevalence and serum levels of anti-carbamylated vimentin antibodies in patients with lupus nephritis confirm the role of vimentin as a target of the immune response in patients with glomerulonephritis and suggest their possible role as a biomarker of kidney involvement in SLE patients.
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SAT0284 ASSOCIATION OF PATHOGENIC AND REGULATORY B-CELL SUBSETS WITH CLINICAL AND HISTOLOGICAL FEATURES IN PRIMARY SJÖGREN'S SYNDROME

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Background: Several data pointed out that B-cells play a central role in the development, maintenance and progression of primary Sjögren's syndrome (pSS). B-lymphocyte hyperactivity, salivary gland (SG) infiltration, and the development of B-cell follicles containing germinal center (GC)-like structures, represent hallmarks of the disease. On this basis, B-cell depleting therapy with anti-CD20 monoclonal antibody rituximab (RTX) has been employed in pSS showing promising results. However, currently available data do not allow to draw definitive conclusion on its efficacy.
Objectives: Aim of the study was to assess mature and regulatory B cell subsets in patients with pSS and explore possible associations with clinical and histological features and their possible modulation by RTX treatment.
Methods: We evaluated by flow cytometry peripheral blood (PB) B-cell subsets (mature B cells: Bm1, Bm2, Bm2', Bm3, Bm4, early(e)Bm5, Bm5; IL-10-producing B-cells), in 17 pSS patients and in 10 healthy donors (HD). Nine pSS patients received a course of RTX (1000 mg at days 1 and 15) and PB B-cell subsets were also evaluated after 3 (T3) and 6 (T6) months and compared to baseline values (T0).
Results: We confirmed that the percentage of Bm1, eBm5 and Bm5 was lower and that of Bm2, Bm2' and Bm3+Bm4 was higher in pSS patients compared to HD (all $p<0.05$). When we divided patients according to the ESSDAI score (<5 or ≥ 5) or to SG-GC (presence/absence), we observed for the first time that the percentage of Bm2' cells, also called GC founders, was higher in patients with ESSDAI≥ 5 ($p=0.02$) compared to those with lower ESSDAI score and in pSS patients with GC ($p=0.02$) compared to those without GC. Although we observed a reduction of all B-cells subsets at T3 and T6 after RTX treatment, the proportion of Bm1, Bm3+Bm4, eBm5 and Bm5 persisted lower and the percentage of Bm2 and Bm2' persisted higher in pSS patients ($p<0.05$) compared to HD. No differences regarding IL-10-producing B-cells was obeserved between pSS patients and HD. However, the percentage of IL-10-producing B-cells was higher in patients with ESSDAI≥ 5 compared to patients with ESSDAI<5 ($p=0.02$).
Conclusions: We demonstrated for the first time that a subset of circulating mature B-cells, Bm2', also called GC founders, is strongly associated with higher disease activity and with the presence of SG-GC. Moreover, a higher ESSDAI is associated with higher percentage of circulating IL-10-producing B-cells. Pathogenic B-cell hyperactivity is a hallmark of pSS, however B-cells are also a source of inhibitory cytokines such as IL-10 and TGF-beta and the increase of IL-10 producing B cells that we observed in active pSS patients may suggest an ongoing compensatory mechanism to counteract chronic inflammation. Therefore, the design of novel B cell targeted therapies should ensure that only pathogenic B cells are depleted and regulatory B cell subsets are not hampered while, ideally, potentiated.
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SAT0285 THE PHYSICAL PERFORMANCE OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH LOW DISEASE ACTIVITY: COULD THE CARDIOPULMONARY EXERCISE TESTING REFINE ITS ASSESSMENT?

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Background: Even during remission, the systemic lupus erythematosus (SLE) patients have reduced exercise performance and this contributes to impairment of their quality of life[1]. Several causes as depression and deconditioning, arthritis, anemia, cardiovascular and respiratory involvement are widely accepted; however the weight of each factor is less known in particular individuals.
Objectives: Our study aimed to assess through cardiopulmonary exercise testing (CPX) the exercise performance of a SLE cohort and to establish its main determinants.
Methods: Thirty-one SLE patients with low disease activity underwent a CPX on cycle ergometer; the main metabolic parameters and standard 12-leads ECG were recorded; before exercise testing, a cardiac Doppler ultrasound was performed. The patient's characteristics, cumulative organ damage and laboratory data were retrieved by medical chart review. The control group consisted of 25 age and sex-matched healthy, non-trained individuals.
Results: Within the study group, 28 (90.3%) were female, the mean age was 42.7±10.6 years and disease median duration 7.9 years. The aerobic performance was decreased by 16.2% (17.6 vs 21.36 ml/kg/min, p=0.022); the main disease characteristics which correlated with maximum oxygen uptake (VO2Mx) were anemia (p=0.035), renal involvement (p=0.05) and antiphospholipid syndrome (APS) (p=0.042) but not disease duration, cumulative damage or the immunological tests (hypocomplementemia, anti-Ro, anti-Sm, anti-dsDNA, AAN or APL antibodies).
One quarter of patients did not reach the ventilatory anaerobic threshold (VAT, expressed as a percentage of calculated VO2Mx), mainly due to musculoskeletal pain (5 patients), dyspnea (2 patients with history of pulmonary embolism) and sudden rise in blood pressure (1 patient). Among the rest of them (23 patients, 74%), the VAT was at the lower limit of normal range (41.03% vs 54.0% for controls, p=0.014) corresponding to a "training reserve" of 31%. Of particular importance from this point of view were the criteria for test termination: dyspnea in 4 patients (1 with anemia, 1 with pulmonary fibrosis and 2 by hyperventilation proved by mean VE/VCO2 =41.5), fatigue (9 patients) and arthralgia (7 patients). Notably, among patients with established diagnosis of mild pulmonary fibrosis, COPD, ischemic or valvular heart disease, not dyspnea but arthralgia or fatigue was the reason for test termination, even if the VO2Mx was lower than recorded in the rest of the group (15.8 vs 19.2 ml/kg/min, p=0.037).
Conclusions: The exercise aerobic capacity of SLE patients is diminished and correlates with anemia, renal involvement and with hystory of pulmonary embolism. Surprisingly, even in patients with mild cardiovascular or respiratory involvement, the decreasing of exercise performance is limited mainly from musculoskeletal symptoms and from deconditioning.
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training program on exercise tolerance, aerobic capacity, and quality of life in patients with systemic lupus erythematosus. Arthritis Rheum 2005;53(6):838–44.

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SAT0286 INCIDENCE AND MORTALITY OF PRIMARY SJÖGREN'S SYNDROME: TIME TRENDS OVER A 40-YEAR PERIOD IN A POPULATION-BASED COHORT IN THE UNITED STATES

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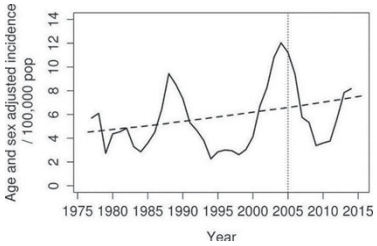
Background:
Few studies have reported the incidence of primary Sjögren's syndrome (pSS) in well-defined populations worldwide, and none of them covered a period of time long-enough to analyze potential time trends in incidence rates. Whether pSS is associated with a higher mortality rate compared to the general population is also unclear from previously published studies.
Objectives: To estimate the incidence and mortality rates of pSS among residents of Olmsted County, Minnesota, and their evolution over time.
Methods: All medical records of patients with a diagnosis or suspicion of SS in Olmsted County, MN, from January 1, 2006 to December 31, 2015 were reviewed to identify incident cases of pSS (defined according to physician diagnosis). All patients with doubtful cases and all patients with an associated systemic autoimmune disease were excluded. These cases were combined with a previous 1976–2005 incident cohort from the same population (reference). Incidence rates were age and sex adjusted to the US white 2010 population. Survival rates were compared with the expected rates in the general population of Minnesota.
Results: With 61 incident cases of pSS diagnosed in Olmsted County in 2006–2015, the total cohort included 172 patients with incident pSS in 1976–2015. Of the 172 patients, 151 (88%) were women and 161 (94%) were white, with a mean (SD) age at diagnosis of 58.3 (16.7) years. The average age- and sex- adjusted annual incidence for 2006–2015 was 5.9 per 100,000 population (95% CI 4.4–7.4), and overall incidence for the entire period was 5.8 (95% CI: 4.9–6.6) per 100,000. Incidence was 2 to 7 times higher in females compared to males in the different age classes (5.9 times higher on average), and increased progressively with age, culminating at 19.6 per 100,000 in females aged 65–74 years, with a slight decline thereafter to 15.9 per 100,000 among females aged 75 years and older. The incidence increased with calendar time over the 40-year period (p=0.005, figure). There was no apparent seasonality in the incidence of pSS, with similar number of cases diagnosed during all four seasons. There was no difference in mortality in the pSS cohort compared to expected (standardized mortality ratio 1.15, 95% CI 0.86–1.50).



Conclusions: The average annual incidence of pSS in this population based-cohort was 5.8/100,000, with a progressive increase over the 40 years of the study. Overall survival of pSS patients was not different from the general population.
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SAT0287 TH1, TH2 AND TH17 LYMPHOID SUBPOPULATIONS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: Primary antiphospholipid antibody syndrome (PAPS) is characterized by thrombosis at different levels and maternal fetal complications in the presence of antiphospholipid antibodies (aPL). Lymphoid subpopulations and cellular immune responses have not been fully studied.
Objectives: To analyze the lymphoid subpopulations, Th1, Th2 and Th17 immune response in patients with PAPS and long term evolution.
Methods: Patients with PAPS,>18 years of age, of both sexes and a group of healthy blood donors matched for age and sex were included. All patients were receiving oral anticoagulants (Coumadin type). No patient had a recent episode of thrombosis or other manifestation of APS at the time of the study. Peripheral blood was obtained and lymphoid subpopulations were determined by flow cytometry in order to identified with specific immunological markers for Treg cells: CD4+/CD25+/FoxP3+ and CD8+/CD25+/FoxP3+. The dendritic cells analyzed were: Type 1: Lin1- HLA-DR+/CD11c+; Type 2: Lin-HLA-DR+/CD123+; B lymphocytes with antiCD19-APC; Monocytes with anti-CD14-PE; NK: CD3-/CD16+56+ and NKT: CD3+/CD16+56+ lymphocytes. Th1 cells were identified by IFN-g$^+$ positivity; Th2: positivity for IL-4+; Th17: positivity for IL-17+. Parametric statistics and Mann-Whitney U-test were used.
Results:

	PAPS (cells/μL)	Healthy controls (cells/μL)	p
Total leukocytes	5655	7000	<0.05*
Lymphocites	1800	2085	NS
Total CD3	1033	1338	NS
Total CD4	701	775	NS
Total CD8	258	441	<0.05*
Monocytes	213	219	NS
B lymphocites	41	86	NS
NK	118	177	NS
NKT	33	45	NS
iNKT	9	20	<0.005**
Tγδ Lymphocites	34	45	NS
LTreg 4 Lymphocites	23	13	NS
Treg 8 Lymphocytes	26	13	NS
DC1	2	4	<0.005**
DC2	1	5	<0.0005***

A total of 39 patients with PAPS were included, age: 51.9±12.8, evolution time: 12.8±8.9 years and 35 healthy controls. In patients with PAPS there was a decrease in the total CD8 count ($p<0.05$) in iNKT ($p<0.005$), DC1 ($p<0.005$) and DC2 ($p<0.0005$) cells compared to the control group (Table 1).We found significant decrease in Th1, Th2 and Th17 cytokines basal and after activation compared to healthy controls.
Conclusions: This study shows profound alterations in innate and adaptive immunity in patients with long-term PAPS, characterized by a decrease in certain lymphocyte subpopulations, with consequent functional alteration. These abnormalities can become new therapeutic targets in order to restore immune imbalance. Our findings may explain in part, the development of thrombosis and other complications, despite treatment with oral anticoagulants in PAPS patients with long term disease evolution.
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SAT0288 QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERIYTHEMATOSUS

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Background: The Quality of life (QoL) in patients with SLE is deeply affected by multiple factors including psychological and physical factors, the functional status and the general perception over health.
Objectives: Evaluation of Quality of life and the perceptions over the disease in patients with SLE.functional status and the general perception over health.
Methods: This is a 10 month prospective, cross-sectional study performed on 52 patients hospitalized diagnosed with SLE according to SLICC 2012 criteria. There were evaluated demographic data, organs manifestations, disease activity scores (SLEDAI, SLICC) and treatment. To evaluate the QoL several questionnaires were performed: Health Assessment Questionnaire (HAQ), EuroQol five dimensions questionnaire (EQ5d), Illness Perception Questionnaire and SF-36.
Results: All patients were women with the mean age 49 years with a mean durations of illness 136 month (14). The mean SLEDAI – 5,52 (5,37) and SLICC – 2,25 (1,71).
The mean HAQ value was 0,83 (0,81). The HAQ score doesn't correlate with SLICC (p=0,461) and with SLEDAI (p=0,172), but it was correlated with the neuropsychiatric manifestations. So the psychiatric affectation influences performing the usually daily activities (p=0,005).
When assessing Illness Perception Questionnaire, patients considered their life seriously affected by pain, mean value 6,3 (2,6), 72% consider the illness will be