AB0084

INCREASED LEVEL OF NEUROPILIN-1 IN CD4+ T CELL AND ITS CORRELATION WITH DISEASE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS

Y. J. Choi¹, E. K. Lee¹, M. S. Lee², C. H. Lee², C. H. Chung², W. H. Yoo¹.
¹Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Internal Medicine, Jeonju, Korea, Rep. of (South Korea); ²Wonkwang University Hospital, Internal Medicine, Iksan, Korea, Rep. of (South Korea)

Background: Semaphorin has been found as a neuronal guidance molecule, but has recently been called "immune semaphorin," as their critical role in immune cell activation, differentiation and migration has been revealed. In particular, class 4 semaphorin has been shown to contribute to lymphocyte activation and immune homeostasis.

Objectives: This study was aimed to investigate the expression of neuropilin-1 (NRP-1), the receptor of class 4 semaphorin, in the murine mouse model of systemic lupus erythematosus (SLE) and the patients with SLE and the correlation between the expression of NRP-1 and disease activity of SLE.

Methods: The expression of NRP-1 was measured in T cells in spleen and renal tissue in control mouse and TLR-7 agonist-induced lupus mouse by flow cytometry, PCR, and immunofluorescence (IF). CD4+ T cells from human peripheral blood were isolated to investigate the expression of NRP-1 in healthy control and the patients with SLE (n=40).

Results: The frequency of NRP-1 positivity in CD4+ T cells in spleen was significantly higher in lupus mouse group (median [interquartile range]: 15.34 [14.84] %) compared to vehicle mouse group (4.0 [2.77]%). The quantitative analysis of fluorescence intensity in kidney stained for NRP-1 revealed the increased level in lupus group compared to vehicle group. The CD4+ T cells from peripheral blood mononuclear cells in the patients with lupus also showed significantly higher frequency of NRP-1 positive CD4+ T cells than those from healthy controls. Comparing the correlation of the expression of NRP-1 and disease activity with SLEDAI, C3, C4, and anti-DNA antibodies, the significant correlation between NRP-1 and disease activity markers were confirmed.

Conclusion: Our results demonstrate that higher expression of NRP-1 in CD4+ T cells and its significant correlation with disease activity of SLE. These results indicate that pathologic contribution of NRP-1 in the pathogenesis of SLE and potential of targeting NRP-1 for the treatment of SLE.

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AB0085

ANTI-MULLERIAN HORMONE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Z. Alekberova¹, R. Goloeva¹, M. Cherkasova¹, A. Lila¹. ¹VA Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases, Moscow, Russian Federation

Background: Anti-Mullerian hormone (AMH) is one of the key parameters for assessing reproductive function and ovarian reserve. The level of AMH correlates with the residual follicular pool in women of reproductive age.

Objectives: To assess AMH levels in SLE female patients of child-bearing potential, and analyze the relationship between AMH levels and disease severity, as well as relationship between serum AMH levels and different therapeutic regimens.
Methods: The study group included 12 women with SLE aged 20-40 years, and the control group - 15 age-matching healthy women. SLE diagnosis was established based on the EULAR/ACR classification criteria, 2019. The SLEDAI 2K was used to evaluate disease activity, and the SLICC index - to evaluate damage. AMH levels was measured using ELISA. AMH reference values ranged within 1.0-10.6 ng/ml. Values <1.0 were interpreted as a decreased ovarian reserve.

Results: SLE patients' mean age was 33.5 [29;38] years, and control group subjects' - 32.0 [26;35] years. Mean disease duration was 11.5 [2.8;18] years. Acute, subacute and chronic SLE was established in 33%, 17%, and 50%, respectively. Disease activity according to SLEDAI 2K was low in 25%, moderate - in 33%, and high - in 42% of pts. The SLICC damage baseline evaluation: no damage - 17%, low - 50%, medium - 16.5%, high-16.5%.

Mean AMH level was 3.5 ng/ml in SLE pts, and 3.1 ng/ml - in the control group, showing no statistical difference. A decrease in ovarian reserve (AMH less than 1.0 ng/ml) was significantly more common in SLE pts - 42% vs 13% in the control group. No correlation was found between AMH levels and the SLICC damage index, AMH and SLEDAI 2K, as well as AMH and SLE duration or clinical course. Detailed analysis showed that all pts with reduced ovarian function had CP included into their therapeutic regimens; the only exclusion within this subgroup - i.e., normal AMH level-6 ng/ml and preserved ovarian function - was documented in a patient who received a cumulative CP dose of 5.6 g. In all other patients a cumulative CP dose was higher, i.e.: 7.2 g, 7.8 g, 10.6 g, and 18.4 g - 1 patient per each dose value. Three pts with low AMH levels within 0.1 -0.3 ng/ml were 39 years old, while AMH reference values in 33-39y age group are 0.77-5.24 ng/ml. Analysis of gynecological history indicate that episodes of menstrual disorders were significantly more often reported in SLE pts (50% vs 20% in controls, $p=0.001$), similarly, gynecological diseases were also documented in 50% of SLE pts (chronic salpingo-oophoritis, colpitis, endometriosis and uterine endometrioma, subserous uterine myoma, cervical dysplasia, cervical erosion), meanwhile low AMH was found only in 4 SLE pts; there was only 1 subject with gynecological condition - teratoma of the ovaries - in the control group (favorable outcome - surgical removal, preserved fertility and two births after surgery).

Conclusion: Ovarian reserve was significantly more often reduced in women with SLE compared to healthy controls. CP therapy negatively affects ovarian function, and most likely in a dose-dependent manner. In this study, 4 out of 5 patients with reduced ovarian function had gynecological diseases additionally compromising the ovarian reserve. Further studies are needed to clarify potential contribution of both - autoimmune inflammation and SLE therapy - into development of gynecological diseases and loss of fertility.

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AB0086

PREGNANCY OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Z. Alekberova¹, R. Goloeva¹, T. Popkova¹, V A Nasonova Research Institute of Rheumatology, systemic rheumatic disease, Moscow, Russian Federation

Background: There's no doubt that SLE has negative effect not only on the course of pregnancy, but also on maternal and fetal outcomes.

Objectives: To clarify pregnancy outcomes in patients with SLE by means of retrospective analysis.

Methods: The study group included 12 women with SLE aged 20-40 years, and the control group - 15 age-matching healthy women. SLE diagnosis was established based on the EULAR/ACR classification criteria, 2019. The SLEDAI 2K was used to evaluate disease activity, and the SLICC index - to evaluate damage. Completed by all women issue-specific questionnaire covered clinical symptoms of SLE and details of obstetric history (characteristics of menstrual and reproductive function, presence of genital and extragenital pathology, previous pregnancies outcomes; previous intrauterine interventions, a history of coagulopathy).

Results: SLE patients' mean age was 33.5 [29;38] years, and control group subjects' - 32.0 [26;35] years. Mean disease duration was 11.5 [2.8;18] years. Acute, subacute and chronic SLE was established in 33%, 17%, and 50%, respectively. Disease activity according to SLEDAI 2K was low in 25%, moderate - in 33%, and high - in 42% of pts. The SLICC damage baseline evaluation: no damage - 17%, low - 50%, medium - 16.5%, high-16.5%. Past pregnancies were documented in 7 out of 12 SLE patients and 6 healthy subjects from the control group. Spontaneous vaginal delivery of a full-term baby was documented in both groups. Unfavorable pregnancy outcomes were significantly more frequent in SLE pts (31% vs 13% in the control group, $p=0.001$). Two SLE pts after cyclophosphane therapy (10.6 and 18.4 g cumulative dose) and low AMH levels (< 1 ng/ml) failed to become pregnant, although never used contraception.

Table 1. Pregnancy outcomes

Pregnancy, n	SLE, n=16	Control, n=15	p
Birth	9 (56.3%)	13 (87%)	0,00
Abortion	2 (12.5%)	0	0,00
Unfavorable pregnancy outcome	5 (31.2%)	2 (13%)	0,00
Missed miscarriage	4 (25%)	0	0,00
Spontaneous abortion	1 (6%)	2 (13%)	ns

Analysis of gynecological history indicate that episodes of menstrual disorders were significantly more often reported in SLE pts (50% vs 20% in controls, $p=0.001$), similarly, gynecological diseases were also documented in 50% of SLE pts (chronic salpyngo-oophoritis, colpitis, endometriosis and uterine endometrioma, subserous uterine myoma, cervical dysplasia, cervical erosion), meanwhile low AMH was found only in 4 SLE pts; there was only 1 subject with gynecological condition – teratoma of the ovaries – in the control group (favorable outcome – surgical removal, preserved fertility and two births after surgery). **Conclusion:** The incidence of unfavorable pregnancy outcomes is significantly higher in patients with SLE compared to the control group of healthy women.

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AB0087

AUTOANTIBODIES DIRECTED AGAINST HOMOCYSTEINYLATED ALPHA 1 ANTITRYPSIN AS A POTENTIAL NEW BIOMARKER FOR ARTHRITIS IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS

F. Natalucci^{1,1}, F. Ceccarelli¹, T. Colasanti¹, G. Olivieri¹, A. I. Cella¹, C. Barbatì¹, M. Speziali¹, F. Ucci¹, C. Pirone¹, C. Ciancarella¹, F. R. Spinelli¹, C. Alessandri¹, F. Conti¹. ¹Policlinico Umberto I, Sapienza University of Rome, Department of Clinical, Internal Medicine, Anesthesiology and Cardiovascular Sciences, Rome, Italy

Background: Joint involvement represents one of the most frequent features in patients affected by Systemic Lupus Erythematosus (SLE). This manifestation is characterized by a great heterogeneity in phenotype and severity: the application of more sensitive imaging techniques identified an erosive damage in about 25% of patients (1). This damage has been associated with autoantibodies, such as anti-citrullinated (ACPA) and anti-carbamylated proteins (anti-CarP), previously identified in patients Rheumatoid Arthritis (RA) patients. Recently, homocysteinylated alpha 1 antitrypsin (Hcy-A1AT) has been identified as a new antigenic target of autoantibodies in seronegative RA patients: in detail, anti-homocysteinylated alpha 1 antitrypsin (anti-HATA) antibodies have been identified in 75.7% of patients (2).

Objectives: In the present study, we aimed at determining the prevalence of anti-HATA in a cohort of SLE patients.

Methods: We evaluated patients affected by SLE according to the 1997 ACR criteria. Demographic, clinical, and laboratory data were collected in a standardized computerized electronically filled form. Each subject underwent peripheral blood sample collection. Hcy-A1AT was obtained by in vitro modification of native A1AT and used as antigens by ELISA to test the presence of anti-HATA in sera obtained from enrolled subjects. Finally, we investigated the presence of ACPA and Rheumatoid Factor (RF) commercial ELISA kits and of anti-CarP (home-made ELISA) by a home-made ELISA in SLE patients' sera. As control, we enrolled 40 patients affected by Osteoarthritis (OA) and 41 healthy subjects (HS).

Results: The present analysis included 88 SLE patients (M/F 6/82 median age 47 years (IQR 17), median disease duration 156 months (IQR 180). Joint involvement was observed in 75 SLE patients (85.2%); in detail, 65 patients referred arthritis and the remaining 10 inflammatory arthralgias. We identified the presence of anti-HATA IgG in 38 SLE patients (43.2%). This prevalence was significantly higher in comparison with OA and HS subjects [15.0% ($p<0.001$) and 0% ($p<0.0001$), respectively; Figure 1A]. Focusing on the SLE cohort, no differences were observed between patients with and without joint involvement in anti-HATA IgG prevalence (41.3% versus 34.7%, respectively; $p=0.34$). However considering SLE patients according to the presence of arthralgia and arthritis, the prevalence of anti-HATA was significantly higher in patients with arthritis in comparison with those patients with arthralgias (46.1% versus 11.1%, $p=0.02$; figure 1B). Finally, no significant association between anti-HATA and the other tested autoantibodies (RF, ACPA, anti-CarP) was found.

Conclusion: We evaluated the prevalence of anti-HATA in a cohort of SLE patients. The prevalence of these autoantibodies was significantly higher in SLE patients than in OA patients and in HS. The association with arthritis suggests a possible role for anti-HATA as biomarkers of SLE-related joint involvement.

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AB0088

QUALITY OF LIFE IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES DIFFERS ACCORDING TO ANTIPHOSPHOLIPID SYNDROME DAMAGE INDEX (DIAPS)

S. G. Fodda^{1,2}, M. Radin^{1,2}, A. Barinotti^{1,2}, I. Cecchi^{1,2}, E. Rubini^{1,2}, S. Sciascia^{1,2}, D. Roccatello^{1,2}. ¹Turin, Università di Torino, Turin, Italy; ²Turin, Center of Research of Immunopathology and Rare Diseases - Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, Turin, Italy

Background: Antiphospholipid syndrome (APS) is a rare autoimmune disorder that mainly affects young individuals. Due to the potentially devastating effects of some of its clinical manifestations, such as ischemic stroke and thrombotic microangiopathy, APS can have a deep negative impact on the quality of life (QoL) of the affected patients due to damage accrual (2).

To capture the full consequences of the disease, including both thrombotic and extra-criteria APS specific features, the antiphospholipid syndrome (APS) damage index (DIAPS), a 37-item score, was conceived.

Objectives: The aim of this study was to validate the DIAPS in a cohort of antiphospholipid antibodies (aPL) positive subjects, comparing it to the risk stratification score for the development of clinical manifestations of APS (Global APS Score -GAPSS) and QoL questionnaires filled out by APS patients.

Methods: This retrospective study included a total of 84 consecutive persistent aPL positive patients who attended the San Giovanni Bosco Hospital (Turin, Italy). Patients were then divided based on their diagnosis in 3 groups: primary APS (PAPS), secondary APS (SAPS) and aPL positive patients without clinical manifestations of APS, according to Miyakis criteria (1). Demographic, clinical and laboratory characteristics, were retrieved from electronic medical records and are summarized in Table 1. DIAPS was calculated as previously reported by adding together all points corresponding to the clinical manifestations of the patients (3).

Results: A total of consecutive 84 patients were enrolled in the study: 39 primary APS patients (PAPS), 28 secondary APS patients (SAPS) and 17 aPL positive patients without APS-related clinical manifestations. APS patients had significantly higher levels of DIAPS when compared to aPL asymptomatic patients (mean DIAPS 2.6 ± 1.8 vs. 1.5 ± 1.9 , respectively; $p<0.05$). Moreover, SAPS patients had significantly higher levels of DIAPS when compared to PAPS patients (mean DIAPS 3.1 ± 1.9 vs. 2.2 ± 1.7 , respectively; $p<0.05$). When comparing GAPSS and DIAPS levels in all the patients, we found a significantly positive correlation between these two scores (mean GAPSS 11.9 ± 5.2 and mean DIAPS 2.4 ± 1.9 ; Pearson 0.241; $p<0.05$). Finally, when applying the SF-12 score to our cohort, the mean physical component score and mental component score were lower than the average population (39.3 ± 11.3 and 42.3 ± 8 , respectively) and we observed a negative correlation trend between DIAPS and both PCS and MCS (Pearson -0.133 and -0.183).

Table 1. Clinical and laboratory characteristics of the patients

	PAPS (n=39)	SAPS (n=28)	aPL asymptomatic (n=17)
Anagraphic			
Mean age (S.D.) at data collection	50.6±13.7	47.4±12.1	48.6±11.3
Sex (females), n	29 (74.4%)	29 (74.4%)	29 (74.4%)
Secondary diagnosis, n	N/A	SLE 24 (85.7%) SSJ 1 (3.6%) UCTD 1 (3.6%) MCTD 2 (7.1%)	SLE 8 (45.1%)
Clinical manifestations of APS			
Thrombosis, n	30 (76.9%)	26 (92.9%)	N/A
Arterial thrombosis, n	20 (51.3%)	14 (50%)	N/A
Venous thrombosis, n	17 (43.6%)	15 (53.6%)	N/A
Pregnancy morbidity, n	11 (28.2%)	4 (14.3%)	N/A
aPL profile at diagnosis			
LA, n	31 (79.5%)	23 (82.1%)	12 (70.6%)
aCL (IgG/M), n	22 (56.4%)	18 (64.3%)	10 (58.9%)
Anti-β2GPI (IgG/M), n	18 (46.2%)	16 (57.1%)	3 (17.6%)
aPS/PT (IgG/M), n	23 (59%)	21 (75%)	8 (47.1%)