report secondary Sjögrens syndrome to be associated with an increased risk of organ damage in SLE.

Funding Source(s): This work was supported by grants from the Swedish Rheumatism Association, the County Council of Östergötland, the Swedish Society of Medicine, the King Gustaf Vs 80 year anniversary foundation and the King Gustaf V and Queen Victorias Freemasons foundation.

265

ASSOCIATION OF PCSK9 SERUM LEVELS WITH LIPID METABOLISM DYSREGULATION, ACTIVITY/DAMAGE SCORES AND SUBCLINICAL ATHEROSCLEROSIS IN SLE PATIENTS

¹Ivan A Ferraz-Amaro*, ¹Hurma Sanchez, ²Juan Carlos Quevedo-Abeledo, ³Iñigo Rúa-Figueroa, ⁴Beatriz Tejera-Segura, ⁵Antonia De Vera-Gonzalez, ⁵Alejandra González-Delgado, ⁵Laura De Armas-Rillo, ⁵Federico Díaz-González. ¹Servicio de Reumatología; ²Hospital Dr. Negrín; ³Department of Rheumatology, Dr Negrín General University Hospital, Las Palmas de Gran Canaria; ⁴Hospital Insular; ⁵Hospital Universitario de Canarias

10.1136/lupus-2019-lsm.265

Background SLE patients are characterized by a lipid metabolism dysregulation. Proprotein convertase subtilisin/kexin type 9 (PCSK9) regulates cholesterol metabolism through low-density-lipoprotein (LDL) receptor degradation. PCSK9 has been linked to cardiovascular risk (CVR) in general population. The purpose of this study is to examine whether PCSK9 levels are related to disease activity, damage and severity scores; abnormalities in the lipid profile; and the subclinical atherosclerosis that occur in SLE patients.

Methods Cross-sectional study that encompasses 195 SLE patients. PCSK9 and lipoproteins serum concentrations were assessed. Activity (SLEDAI), severity (Katz) and damage (SLICC) index scores, and carotid ultrasound sonography were evaluated. A multivariable analysis was performed to evaluate the association of PCSK9 with SLE related dyslipidemia, subclinical atherosclerosis and activity/damage status

Results In the univariate analysis, body mass index, waist circumference, traditional CVR factors and triglycerides were related with PCSK9 serum levels. On the contrary, HDL cholesterol and apolipoprotein A levels showed a negative association. LDL cholesterol exhibited a trend to a negative association (beta coeff. -0.30, 95% CI -0.67-0.07, $p=0.11$). Carotid plaques and cIMT were not associated with PCSK9 levels although a trend was observed. Patients with longer disease duration (beta coeff. 1.25, 95% CI 0.15-2.35, $p=0.026$) and higher C reactive protein levels (beta coeff. 1.42, 95% CI 0.61-2.22, $p=0.00$) disclosed higher PCSK9 levels. Prednisone intake was positively associated with PCSK9 (beta coeff. 35.48, 95% CI 14.29-56.6), $p=0.001$), and patients that were taking any DMARD or hydroxychloroquine disclosed significant lower levels of PCSK9 (beta coeff. -27.91, 95% CI -54.5--1.32, $p=0.040$ and beta coeff. -39.21, 95% CI -62.21--16.21, $p=0.001$ respectively). Higher values of SLICC (beta coeff. 9.66, 95% CI 4.47-14.84, $p=0.000$) and patients that were in the high/very high SLEDAI activity category (beta coeff. 62.98 95% CI 18.10-107.86, $p=0.006$) disclosed significant higher values of PCSK9. When multivariate analysis was performed these positive associations with both SLICC and SLEDAI and the use of prednisone were maintained, as well as negative associations with LDL levels and the use of hydroxychloroquine.

Conclusions PCSK9 serum levels are independently related to SLE activity and damage scores. This would imply that the mechanisms leading to lipid metabolism dysregulation in SLE patients may be mediated or be a consequence of PCSK9.

Funding Source(s): This work was supported by a grant to I.F.-A. from the Spanish Ministry of Health, Subdirección General de Evaluación y Fomento de la Investigación, Plan Estatal de Investigación Científica y Técnica y de Innovación 2013-2016 and by Fondo Europeo de Desarrollo Regional - FEDER - (Fondo de Investigaciones Sanitarias, FIS PI14/00394, PI17/00083)

266

ANTI-OVARIAN ANTIBODIES ARE NOT FOUND MORE COMMONLY AMONG SLE WOMEN WITH PRE-MATURE MENOPAUSE

¹Martha Tsalliki, ²Kristi A Koelsch, ³Eliza Chakravarty, ⁴Hal Scofield*. ¹University of Oklahoma Health Sciences Center; ²Oklahoma Medical Research Foundation; ³University of Oklahoma Health Sciences Center; ⁴Oklahoma Medical Research Foundation; ⁵University of Oklahoma; ⁶Oklahoma Medical Research Foundation; ⁷University of Oklahoma; ⁸Oklahoma City US Department of Veterans Affairs Medical Center

10.1136/lupus-2019-lsm.266

Background Systemic lupus erythematosus (SLE) is commonly treated with broad immunosuppression, including cyclophosphamide. Use of this agent can result in ovarian toxicity leading to premature menopause. Ovarian failure is associated with concomitant hypothyroidism. We hypothesized that hypothyroidism might be a marker for ovarian autoimmunity because organ-specific autoimmune diseases tend to occur together. We undertook this study to determine whether anti-ovarian antibodies are associated with premature ovarian failure among SLE women who received cyclophosphamide.

Methods All SLE women with a history of cyclophosphamide therapy were identified in the Lupus Registry and Repository (LFRR). All subjects were shown to meet the revised ACR classification criteria. Premature menopause was defined as spontaneous lack of menstrual periods prior to age 45. Anti-ovarian antibodies were measured by ELISA (Anti-Ovarian Ab ELISA, IBL, Minneapolis, catalog # IB9184). Data were analyzed by Students T test and chi square testing. The protocol received ethical approval from the University of Oklahoma Health Sciences Center and Oklahoma Medical Research Foundation IRBs.

Results Among ~3000 SLE women enrolled in the LFRR who had received cyclophosphamide, we found 169 with menopause before age 45 along with 73 who underwent menopause after age 45 and 16 patients over age 45 who were still having menstrual periods at the time of evaluation. Thus, there were a total of 89 SLE women who did not have premature menopause. Mean anti-ovarian antibodies in the 169 with premature ovarian failure was 16.2 units (SD=20.3), while the mean among those without premature menopause was 17.4 units (SD=21.7). These values were not statistically different between the groups. 11 of 169 (6.5%) prematurely menopausal SLE women had a positive result and 8 of 89 (8.9%) without premature menopausal were positive (2=0.53, $p=0.46$, OR=1.02 (95% CI 0.95-1.1).

Conclusions Anti-ovarian antibodies were present at low levels (~10% positivity) among women with SLE. However, the presence of these antibodies was not related to premature ovarian failure after cyclophosphamide.

Funding Source(s): NIH grants AR053483, AI082714, GM104938. VA grant BX0011451

267

RELATIVE EXPRESSION STRENGTH OF HLA-DRB1 IN HETEROZYGOTES IS ASSOCIATED WITH RHEUMATIC DISEASES

¹Sehwan Chun, ²So-Young Bang*, ²Hye-Soon Lee, ²Sang-Cheol Bae, ³Kwangwoo Kim. ¹Kyung Hee University; ²Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; ³Department of Biology, Kyung Hee University, Republic of Korea

10.1136/lupus-2019-lsm.267

Background HLA-DRB1 is characterized by highly complex genetic variants associated with susceptibility to and autoantibodies of rheumatic autoimmune diseases including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), highlighting the primary associations of multiple amino acid changes on the epitope-binding groove of HLA-DR molecules. However, in contrast to the missense variants in HLA-DRB1, an effect of expressional changes in HLA-DRB1 has been poorly understood.

Methods Both three-field HLA-DRB1 alleles (# of alleles>10) and RNA-Seq data in 48 Koreans and 357 Europeans were simultaneously analyzed to determine the most likely HLA-DRB1 genotypes in each individual and to measure allele-specific expression levels. The relative expression strength of each HLA-DRB1 allele compared to all the other alleles was calculated and tested for contribution to phenotypes associated with amino-acid changes in HLA-DRB1.

Results Strong cis-eQTL signals of HLA-DRB1 were detected around HLA-DRB1, causing highly imbalanced allelic expressions in HLA-DRB1 heterozygotes. The reported associations of HLA-DRB1 with the level of anti-cyclic citrullinated peptide (anti-CCP) autoantibodies in RA or the susceptibility to SLE were re-assessed in Korean RA (n>1,000) and SLE-control (n>5,000) genetic data, taking the relative allelic expression strength into account, and were additionally explained by the skewed allelic expressions of HLA-DRB1 in heterozygotes.

Conclusions This study identified the allele-specific expression of HLA-DRB1 that contributed to disease risk and autoantibody production in rheumatic autoimmune diseases.

Funding Source(s): This study was supported by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Science, ICT & Future Planning (2017R1E1A1A01076388) and Korea Healthcare Technology R and D Project funded by the Ministry for Health and Welfare (HI15C3182) in Republic of Korea.

268

PD-L1 EXPRESSING MYELOID-DERIVED SUPPRESSOR CELLS (MDSCs) HAVE POTENT IMMUNOREGULATORY ACTIVITY AND CONTROL LUPUS-LIKE AUTOIMMUNITY

¹Min-Jung Park*, ¹Jin-Ah Baek, ¹Se-Young Kim, ²Sung-Hwan Park, ²Mi-La Cho, ²Seung-Ki Kwok. ¹The Catholic University of Korea; ²The Catholic University

10.1136/lupus-2019-lsm.268

Background Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of myeloid cells that modulate pathogenic response in the autoimmune microenvironment. However, the precise roles of MDSCs in systemic lupus erythematosus (SLE), the prototype autoimmune disease, are not

completely understood. Indeed, their immunosuppressive functions in lupus model remain controversial with heterogeneity among MDSCs and differential effects among subpopulations receiving much attention. Programmed death-ligand 1 (PD-L1) is an inhibitory ligand that binds to PD-1 to suppress T cell activation. Multiple studies have explored the potential role of PD-L1 as a mediator of MDSC effects in various cancers. However, the role PD-L1 expression in MDSCs on autoimmune disease is still largely unknown.

Methods In the present study, we investigate the role of PD-L1 expressing MDSC in the MRL/MpJ-Fas^{lpr} (MRL-lpr) mouse model.

Results Here we show that the PD-L1 expressing MDSCs express higher amount of immunosuppressive mediators including arginase-1, iNOS and IL-10 than PD-L1 negative MDSCs and exhibit more potent immunoregulatory activity *in vitro*. We have also identified that *in vivo* treatment with PD-L1 expressing +MDSC reduced serum autoantibody titres, proteinuria level and mitigated the development of kidney damage. Infusion of PD-L1 expressing MDSCs significantly reduce the double negative T cell population and Tfh cell population in spleens of MRL-lpr mice. Moreover, treatment of PD-L1 expressing MDSCs resulted in an expansion of the regulatory B cell population.

Conclusions Our results indicate PD-L1 expression is critical in MDSCs to maintain MDSC immune regulatory function. Taken together, our results suggest that PD-L1 expressing MDSCs may be a potential cell therapeutics for the treatment of autoimmune diseases like SLE.

Funding Source(s): None

269

COEXISTENCE OF AXIAL SPONDYLOARTHRITIS, SYSTEMIC LUPUS ERYTHEMATOSUS, SJÖGREN'S SYNDROME AND SECONDARY ANTIPHOSPHOLIPID SYNDROME: CASE REPORT TARHAN F*, KESER G, ÇELİK Ö*, KLNÇ RM*, AKAR S

¹Emne Egen Tarhan*, ²Gokhan Keser, ¹Ozgur Ilhan Celik, ¹Raba Mhrban Kilic, ³Servet Akar. ¹Mugla Stk Kocman University; ²Ege University; ³Katip Celebi University

10.1136/lupus-2019-lsm.269

Background Axial spondyloarthritis (AxSpA) is a chronic inflammatory disease of the axial skeleton which manifests as inflammatory back pain and progressive stiffness of the spine. Patients with axial disease and other features of SpA but no unequivocal sacroiliitis in conventional X-ray now termed as non-radiographic axial spondyloarthritis (nr-AxSpA). Those patients can be diagnosed on the basis of the presence of active inflammation in magnetic resonance imaging (MRI) or human leukocyte antigen B27 (HLA-B27). Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown etiology that may affect the skin, joints, kidneys, lungs, nervous system, serous membranes, and/or other organs of the body. Sjögren's syndrome (SS) is the second most common autoimmune rheumatic condition characterized by lymphocytic infiltrate of the exocrine glands, resulting in dysfunction and destruction of them. Antiphospholipid syndrome (APS) is the association of thrombosis and/or pregnancy morbidity with antiphospholipid antibodies (aPL) (lupus anticoagulant [LA], anticardiolipin antibodies (aCL), and/or anti-2-glycoprotein-I antibodies (a2 GPI).

Methods Case Presentation

We report a 55-year-old female patient having the association of nr-AxSpA, SLE, secondary APS, and SjS. Diagnosis of