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

nr-AxSpA was made based upon the presence inflammatory low-back pain, human leukocyte antigen B27 positivity, and presence of sacroiliitis only in MRI. SLE was diagnosed with butterfly-shaped rash on her cheeks, inflammatory arthritis, photosensitivity, erythema involving dorsal inter-joint area of hand fingers, alopecia together with antinuclear antibody (ANA) and anti-dsDNA positivity, low serum complement levels, leucopenia and thrombocytopenia. Additional presence of sicca symptoms, low Schirmer I test, anti SSA/Ro and anti-SSB/La positivity, supported by positive labial salivary gland biopsy led to the diagnosis of SjS.

Results Furthermore, this patient also had miscarriage at 16th week and cerebral vascular disease at 33 years. Besides, IgG and IgM anticardiolipin antibodies were found to be positive twice. Therefore, she was also diagnosed as secondary APS. She fulfilled the relevant criteria for AxSpA, SLE, SjS and APS.

Conclusions To our knowledge, this is the first case report showing the association of these four diseases, with different genetic, etiopathogenetic and clinical systemic inflammatory diseases.

Funding Source(s): No

270

THE DISCORDANCE BETWEEN PATIENT AND PHYSICIAN PERCEPTION OF THE DISEASE: THE PARADIGM OF SLE

¹Elena Elefante*, ²Chiara Tani, ³Francesco Ferro, ²Chiara Stagnaro, ³Alice Parma, ²Linda Carli, ²Viola Signorini, ⁴Marta Mosca. ¹University of Siena, Siena, Italy; ²Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; ³University of Pisa; ⁴Director Rheumatology Unit, Associate Professor in Rheumatology, University of Pisa

10.1136/lupus-2019-lsm.270

Background Background: a discordance exists between patient and physician perspective in the evaluation of SLE and it may negatively impact on patient care. Our purpose was to compare patient and physician evaluation of the disease in a monocentric cohort of SLE patients, analyzing factors that influence patient perception.

Methods Methods: this is a cross-sectional study that enrolls adult patients with a diagnosis of SLE (ACR 1997 criteria). For each patient, demographics, comorbidities, treatment history, clinical and laboratory data were collected. Disease activity was evaluated with the SELENA-SLEDAI score and organ damage with the SLICC/DI. At enrollment each patient completed the following PROs: SF-36, FACIT-F, LIT, SLAQ and BILD. The Spearman test has been used for linear correlation between continuous data.

Results Results: we included 223 adult SLE patients (97,24% Caucasian, 91,93% female, mean age 44,9413,17 years, median disease duration 13 years). Median SLEDAI at enrollment was 2 (IQR 0–4); 18,22% of patients had SLEDAI >4; 49,33% had SLICC/DI>0. 11,8% of the cohort had a concomitant fibromyalgia. At enrollment, the most frequent active disease manifestations were articular (36/223) and hematological (33/223), while only 15 patients had active renal involvement.

The median score of the SLAQ questionnaire was 11 (IQR 6–16). No correlation was found between patients self-evaluation of the disease and the physicians assessment: SLAQ and SLEDAI scores were not significantly correlated.

Abstract 270 Table 1 Correlation between SLAQ and PROs

	SLAQ
PF	$r = -0,56$ $p < 0,001$
RP	$r = -0,58$ $p < 0,001$
BP	$r = -0,67$ $p < 0,001$
GH	$r = -0,50$ $p < 0,001$
VT	$r = -0,65$ $p < 0,001$
SF	$r = -0,64$ $p < 0,001$
RE	$r = -0,55$ $p < 0,001$
MH	$r = -0,57$ $p < 0,001$
LIT	$r = 0,74$ $p < 0,001$
FACIT	$r = -0,72$ $p < 0,001$

Among active disease manifestations, only arthritis ($p=0,03$) and skin involvement ($p=0,04$) resulted significantly associated with higher SLAQ scores. Moreover, the SLAQ score resulted significantly influenced by fibromyalgia ($p<0,001$): patients with fibromyalgia seems to overestimate SLE disease activity. Finally, while SLEDAI didnt show any correlation with PROs on HRQoL, higher SLAQ scores were strongly associated with a worst patient perception of QoL, fatigue and SLE impact, as expressed by SF-36, FACIT-F and LIT (table 1).

Conclusions Conclusion: differently from the physicians assessment, SLE patients evaluation of their disease is influenced by milder manifestations but with a heavy impact on daily functioning, like arthritis and fibromyalgia. Patients self-evaluation has a strong impact on their perception of health status and disease burden. The integration of patient-driven data to the traditional clinical evaluation may improve the management of SLE patients.