THE PRESENCE OF AUTOANTIBODIES TO MULTIPLE KILLER CELL IMMUNOGLOBULIN-LIKE RECEPTORS IS ASSOCIATED WITH NEPHRITIS IN SLE PATIENTS

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Purpose Natural killer cell cytotoxicity is regulated by inhibitory receptors recognizing HLA. These include the CD94/NKG2A and the killer cell immunoglobulin-like receptors (KIR). Previously we described functional autoantibodies to CD94/NKG2A, in patients with systemic lupus erythematosus (SLE). Here we investigated whether patients with SLE, primary Sjögren’s syndrome (pSS) or systemic sclerosis (SSc) have autoantibodies to KIR-receptors and whether presence of such autoantibodies correlates to clinical manifestations.

Method HEK293-transfectants expressing KIR2DL1, KIR2DL2, KIR2DL3, KIR3DL1, KIR3DL2, KIR2DL4, KIR2DS2 or KIR2DS4 were incubated with serum from 191 SLE, 121 pSS, 48 SSc patients and 100 healthy donors. Binding of human IgG to each transfectant was determined using flow-cytometry and the median fluorescence intensity (MFI) was divided by the MFI of untransfected cells. The cut-off for autoantibody-positivity was set at the mean +4 standard deviations of healthy donors. Clinical data were tested for association to the presence of anti-KIR autoantibodies using Fischer’s exact test.

Results Autoantibodies to KIR-receptors were identified in 23.0% of SLE, 10.7% of pSS and 12.5% of SSc patients compared to 4.0% of healthy individuals. Anti-KIR antibodies to all eight receptors studied were detected in SLE and pSS sera, whereas SSc sera reacted with four of the receptors. The highest titers of anti-KIR antibodies were found in SLE sera. All KIR-positive healthy donor sera and the majority of KIR-positive pSS (76.9%) and SSc (50.0%) sera reacted with 1 KIR-receptor. In contrast, 36.3% and 22.6% of the anti-KIR-positive SLE sera reacted with 2–3 and >3 KIR-receptors, respectively. Autoantibodies to >3 KIRs were associated with an increased risk for lupus nephritis (80.0% vs 27.2%, p=0.001), an increased number of ACR criteria fulfilled (7 vs 6, p=0.02), presence of anti-Sm (50.0% vs 13.6%, p=0.01) and anti-RNP (70.0% vs 23.1%, p=0.003) antibodies compared to patients without anti-KIR antibodies. Age at disease onset (21 vs 30, p=0.74), SLICC damage index (1.5 vs 1.0, p=0.31) or presence of anti-dsDNA (70.0% vs 60.5%) were not significantly different.

Conclusion Autoantibodies to KIR-receptors are found in patients with SLE, pSS and SSc. Given the association with lupus nephritis such autoantibodies may have a clinical importance.

PS1:17 LUPUS NEPHRITIS: SEVERELY REDUCED URINARY DNASE I LEVELS REFLECT LOSS OF RENAL DNASE I, DISEASE PROGRESSION AND MAY REDUCE THE NEED FOR RENAL BIOPSIES

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Loss of renal DNase I leads to progression of lupus nephritis. Therefore, we determined if loss of renal DNase I reflects a concurrent loss of urinary DNase I, and whether absence of urinary DNase I predicts disease progression, which thus may reduce the need for renal biopsies. Here, mouse renal DNase I mRNA was determined by qPCR, whereas mouse and human DNase I protein and DNase I endonuclease activity levels were determined by Western blots, and gel and radial zymography assays, respectively, during different stages of the murine and human forms of the disease. Cellular localization of DNase I was analysed by immunohistochemistry, immunofluorescence, confocal microscopy and immune electron microscopy. We further compared DNase I levels in human native and transplanted kidneys to determine if the disease depended on autologous renal genes, or whether the nephritis process proceeded also in transplanted kidneys. We also analysed if DNase I levels in urine samples reflected expression levels in the kidneys, and if the mouse data were translatable to humans.

The data indicates that silencing of the renal DNase I gene expression level relates to serious progression of lupus nephritis in murine, human native, and transplanted kidneys. Notably, silencing of renal DNase I correlates with loss of DNase I protein and endonuclease activity in the urine samples. Thus, urinary DNase I levels reflects the renal DNase I expression and activity levels, and may therefore be used as a marker of lupus nephritis disease progression and reduce the need for renal biopsies.

PS1:18 ECHOCARDIOGRAPHY FOR THE ASSESSMENT OF CARDIOVASCULAR BURDEN IN LUPUS: A SINGLE CENTRE COHORT STUDY

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Despite major achievements in understanding the pathobiology and management of Systemic Lupus Erythematosus (SLE), cardiovascular burden remains a complex challenge in routine practice. Echocardiography emerges as a valuable non-invasive technique widely recommended for the screening, evaluation and monitoring of cardiac involvement in different SLE settings.

Objectives to evaluate the prevalence and nature of the clinical and subclinical cardiac involvement in SLE, and to identify potential relation with several disease-related parameters.

Design and methods Retrospective observational study in 120 consecutive SLE (fulfilling either 1987 ACR or new 2012 SLICC/ACR criteria), mean age 36.9±15.2 years and mean disease duration 9.2±8.5 years, attending the outpatient rheumatology department at least once. Demographic, clinical, immunologic profile, disease activity (SLEDAI), organ damage (SLICC/ACR) data were collected.

Patients were assessed according to a standardised protocol focused on clinical, immunologic profile, disease activity (SLE- DAI), severity and organ damage (SLICC/ACR); cardiac involvement (valve damage, systolic and diastolic dysfunction, pericardial...