P24 CORRELATION BETWEEN SERUM AUTOANTIBODIES AND CLINICAL MANIFESTATIONS IN JSLE

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Background Systemic Lupus Erythematosus (SLE) has a large clinical spectrum, ranging from mild to severe disease. Some studies have proven correlations between specific autoantibodies and particular clinical manifestations. The aim is to assess if there is any correlation between autoantibodies and clinical manifestations in our sample.
Methods Retrospective longitudinal study of juvenile-onset SLE patients evaluated in Pediatric Rheumatologic unit of a tertiary Hospital. All patients fulfilled both 2012 and 2019 EULAR/ACR classification criteria for SLE. Juvenile-onset was defined as age at diagnosis <18 years. Demographics and clinical characteristics were collected. Statistical analysis was performed with qui-square test by SPSS® software. Results were considered statistically significant if $p<0.05$.
Results 30 jSLE patients were included (90%female) with median (min-max) age of 21 (16–35) years old, with mean (SD) age of diagnosis of 15.8 ± 2.1. Mucocutaneous manifestations occurred in 25, articular involvement in 16, hematologic in 14, renal in 12, pulmonary in 1, pleuropericardial in 2 and another 2 with thrombotic events. All were positive for antinuclear antibodies: 18 with speckled pattern, 11 homogeneous and 1 nucleolar. 11 jSLE were positive for antinucleosomal autoantibodies, 10 anti-SSA antibodies, 8 anti-histone, 7 anti-ribossomal P protein antibody, 4 anti-Sm, 4 anti-RNP, 4 Lupus anticoagulant, 3 had autoantibodies against β2-*glycoprotein* I, 2 anti-cardiolipin and 2 anti-SSB antibodies. The presence of antinucleossomal ($p=0.003$) and anti-SSA ($p=0.04$) antibodies was significantly associated with articular involvement; anti-histone with renal manifestations ($p=0.005$) and lupus anticoagulant in serosal involvement ($p=0.02$).
Conclusions Anti-histone antibodies have been linked to lupus nephritis disease activity. The other associations are not described in the literature. Sample size is a limitation and further studies in our population are required.

P25 DISRUPTED PLACE CELL PROPERTIES IN THE HIPPOCAMPUS REPRESENT THE NEURAL SUBSTRATE FOR COGNITIVE IMPAIRMENT IN NEUROPSYCHIATRIC LUPUS

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Background A poorly understood facet of lupus is its neurological component, known as Neuropsychiatric Systemic Lupus Erythematosus (NPSLE). Patients with NPSLE display severe cognitive impairment, particularly in the spatial domain. We have studied a mouse model of NPSLE in which animals carry a lupus antibody (termed DNRAb) that binds DNA and the GluN2A and GluN2B subunits of the N-methyl-D aspartate receptor (NMDAR).
Methods Female mice (Balb/c, C57) are immunized with either a lupus-inducing antigen (DNRAb+) or a control antigen (DNRAb–). A month later, the blood-brain barrier is abrogated to allow antibody entry to the hippocampus. We investigate spatial cognition with the object-place memory (OPM) task and the neural substrate with tetrode recordings in the CA1 region of the hippocampus. Neural data are analyzed via spike sorting (Spike2) to reveal place cell properties of CA1 neurons, as well as power spectral densities of network oscillations (Matlab, Chronux).
Results A discrimination ratio reveals that DNRAb+ mice examine the moved object significantly less than controls during OPM, indicating impaired spatial memory. The neural data show abnormal place cell properties in DNRAb+ mice, such as expanded place field size, reduced stability, and lower spatial information when compared to DNRAb– mice. Bayesian path reconstruction analysis reveals that DNRAb+ place cells have significantly higher error compared to the DNRAb– group. Moreover, we find significantly altered co-modulation of theta-gamma oscillations when the mice examine the objects during OPM.
Conclusions Our studies reveal that the CA1 ensemble encodes critical aspects of the OPM task through place cell dynamics and theta-gamma coupling. The disruptions of these processes caused by DNRAbs may explain the abnormal spatial encoding that occurs in NPSLE. Our data offer a neural substrate for bioelectronic therapies aimed to alleviate NPSLE-related cognitive impairment.
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P26 SERUM BAFF AND APRIL AS CANDIDATE BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A PROSPECTIVE FOLLOW-UP STUDY

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Background BAFF and APRIL are cytokines involved in B cell development and they take place in SLE pathogenesis. The aim of this study was to investigate the relationship between serum BAFF/APRIL levels with clinical features and disease activity in SLE patients.
Methods We included 79 patients with SLE (SLICC criteria) and 27 healthy controls into the study. Serum BAFF and APRIL levels were assessed by ELISA. In 19 patients with active disease, BAFF/APRIL levels were reassessed at least 6 months later and disease activity was evaluated by SLEDAI. New renal involvement was observed in 16 patients during the study and renal involvement was previously detected in 12 patients.
Results Although both BAFF (median 0.7 vs 0.41 ng/ml) and APRIL (median 2.3 vs 1.05 ng/ml) levels were higher in patients with SLE compared to the control group ($p<0.001$), no correlation was found between BAFF/APRIL levels and SLEDAI scores. When patients were grouped according to disease activity as no activity (SLEDAI = 0), low

disease activity and active disease, there was no difference in BAFF/APRIL levels between groups. Serum BAFF levels were higher in patients with renal disease activity (median 0.94 ng/ml vs 0.61 ng/ml, p=0,01), and there was a positive correlation between APRIL levels and proteinuria (r=0.42, p=0,02). There was no association between BAFF/APRIL levels and anti-dsDNA positivity but a weak inverse correlation was observed between BAFF and C3 levels (r=0.25, P=0.02). No correlation was found between BAFF/APRIL levels and renal SLEDAI scores, histopathologic activity and chronicity index scores. In the active disease group after follow-up, there was no significant changes in BAFF (from 1,63 ng/ml to 1,2 ng/ml) and APRIL levels (from 2,11 ng/ml to 2,31 ng/ml).

Conclusions BAFF/APRIL levels were found to be significantly higher in patients with SLE compared to controls, but no association with disease activity was found. BAFF levels are correlated with decreased C3 levels. These results suggest that both cytokines are involved in the pathogenesis of SLE, and that serum BAFF and APRIL levels can be valuable biomarkers in SLE especially in patients with renal activity. Long-term studies on the effect of treatment are needed.

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P27 MYXOVIRUS RESISTANCE PROTEIN A IS A USEFUL ADDITIONAL HISTOLOGICAL MARKER FOR CUTANEOUS LUPUS ERYTHEMATOSUS

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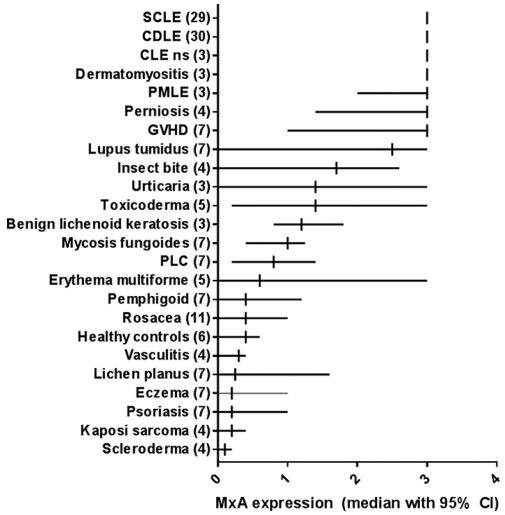
Background Cutaneous Lupus Erythematosus (CLE) is a heterogeneous auto-inflammatory skin disease, that is to a great extent driven by type I and III interferon (IFN). Histology of skin biopsies plays an important role in the diagnostic confirmation of CLE. Unfortunately, no specific histological marker for CLE is available. In this study, we tested the diagnostic potential of immunostaining with Myxovirus resistance protein A (MxA), which is tightly induced by type I and type III IFN, in CLE skin biopsies.

Methods 178 skin biopsy specimens were collected from the local pathology database. Various skin conditions were selected, provided that clinical diagnosis matched with histological diagnosis. Skin sections were incubated with anti-MxA (R&D systems, AF7946). Consecutively, rabbit anti goat-HRP conjugate (Dako, 0449) was added and sections were stained with diaminobenzidine. The expression of MxA was scored semi-quantitatively.

Results MxA staining was strongly positive in 90.3% of lesional CLE skin sections (except lupus tumidus) and had a negative predictive value of 94%. The same MxA expression pattern was found in dermatomyositis, which is also an IFN-driven autoimmune disease. In some conditions, like perniosis and graft versus host disease, high expression could be found, but this was less consistent compared to CLE. Most other inflammatory skin diseases did show no or a low expression of MxA. (See figure 1).



Abbreviations: ns = not specified, SCLE = subacute cutaneous lupus erythematosus, CDLE = chronic discoid lupus erythematosus, PMLE = polymorphic light eruption, GVHD = graft versus host disease, PLC = pityriasis lichenoides chronica.

Abstract P27 Figure 1 MXA expression in all analyzed skin diseases (number of biospsies)

Conclusion MxA is strongly expressed in CLE skin with a high negative predictive value and is thus useful as additional diagnostic histological marker, expectedly resulting in restriction of misdiagnosis and treatment delay.

P28 DECREASED PLATELET SIZE IN SYSTEMIC LUPUS ERYTHEMATOSUS IS ASSOCIATED WITH UP-REGULATION OF TYPE I INTERFERON PROTEINS

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Background Dysregulated apoptosis is of major importance in Systemic Lupus Erythematosus (SLE) pathogenesis, linked to the development of autoantibodies, immune complex formation and type I interferon signaling. Platelets from SLE patients are smaller in size, compared to platelets from healthy individuals, which may suggest an increased rate of apoptosis, a known cause of platelet shrinkage. Our aim with this project was to investigate if decreased platelet size could be explained by increased apoptosis rates.

Methods Platelet activation markers; CD62P, CD41, CD154, CD32, PAC-1 and PAR1 and apoptosis; Annexin V, Caspase 3 activation, mitochondrial content (MitoTracker) and mitochondrial depolarization (JC-1) where analyzed in 23 SLE patients and 10 healthy controls (HC) by flow cytometry. Analysis of the total protein content in platelets from SLE patients of normal (n=5) and decreased (n=5) size were made using mass spectrometry (MS).

Results The level of CD41 (p=0.001) positive platelets and mean expression of CD154 (p=0.004) were higher in SLE patients. A JC-1 ratio (p=0.0001) indicting increased mitochondrial depolarization was significantly associated with