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Pregnancy meets rheumatic patients

OP0310 PREGNANCY OUTCOME IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS, A MULTICENTER COHORT-STUDY

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Background: Systemic lupus erythematosus (SLE) predominantly affects women during their fertile period. During pregnancy SLE patients are prone to pregnancy complications and may experience increased disease activity.
Objectives: To investigate disease activity around/during pregnancy and pregnancy complications in a European cohort according to antiphospholipid antibody (aPL) status. Additionally data on lifetime pregnancy outcomes and comparison of first and consecutive pregnancies were analyzed.
Methods: All ongoing pregnancies of >16 weeks gestation of SLE patients (according to the ACR revised criteria) receiving joint care from rheumatologists and gynecologists in two tertiary centers in the Netherlands between 2000–2015 were included. Disease activity (using SELENA-SLE(P)DAI around and during pregnancy), flare rate according to the SELENA- SLEDAI definitions and pregnancy complications were assessed by medical chart review.
Results: From 96 women (84% Caucasian) 144 pregnancies were included. Before (<6 months), during and after pregnancy (<6 months) the median SELENA-SLE(P)DAI score was 2 and mild/moderate flare rates were 6.3%, 18.8% and 13.9% respectively. Three patients developed a severe flare during pregnancy, 2 patients postpartum; all were aPL negative. Severe maternal complications (preeclampsia, eclampsia or HELLP-syndrome) occurred in 16.2% of aPL negative, 21.4% of aPL positive SLE patients, and in 30.8% of SLE patients with antiphospholipid syndrome (APS) (GEE; no significant differences between groups). HELLP-syndrome occurred in 23.1% of SLE patients with APS and in 3.1% of SLE patients without APS (Chi-Square; p<0.01). The perinatal complications intrauterine fetal death, preterm birth, small-for-gestational age and neonatal lupus occurred in 4.1%, 32.7%, 14.8%, 1.4%, respectively (GEE; no significant differences between groups). Maternal and perinatal complication rates were similar in first (18.5% and 41.4%) and consecutive (17.6% and 35.1%) pregnancies (Chi-Square; p=0.88 and p=0.44). Of all patients, 42.7% developed a complication during all of their pregnancies (obstetrical history included).
Conclusions: This is the first study in patients with SLE demonstrating that incidence rates of pregnancy complications do not decrease in consecutive pregnancies compared to first pregnancies, in contrast to findings in the general population. Except for HELLP-syndrome, pregnancy complications were not significant different between aPL groups. Despite overall low disease activity and the absence of aPL in the majority of patients, almost half of the patients developed a complication during their pregnancies.
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OP0311 HIGH MATERNAL EXPRESSION OF SIGLEC1 ON CD14+ MONOCYTES AS A SURROGATE MARKER OF A TYPE I INTERFERON SIGNATURE IS A RISK FACTOR FOR THE DEVELOPMENT OF AUTOIMMUNE CONGENITAL HEART BLOCK

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Background: Autoimmune congenital heart block (CHB) is a severe manifestation of neonatal lupus syndrome that is associated with placental transcytosis of maternal autoantibodies directed against the ribonucleoproteins Ro/SS-A and, to a lesser extent, La/SS-B.(1) Around 2/3 of affected mothers are diagnosed with either systemic lupus erythematosus (SLE) or primary Sjögren's syndrome (pSS),(2) which are both pathogenically driven by an upregulation of type I interferons (IFN).(3)
Objectives: Although the pleiotropic effects of type I IFN on the immune system are well documented, a potential role of type I IFN in the development of CHB has not yet been investigated. This study therefore aimed to compare maternal levels of type I IFN activation in affected and unaffected mothers, in order to provide first insights into a potential role of type I IFN in CHB development.
Methods: Blood samples, clinical data and serological parameters from 9 women with CHB pregnancies, 15 pregnant women with antibodies against Ro/SS-A but without a CHB complication ("Disease Controls", DC), and another 30 healthy pregnant women without the respective autoantibodies as controls were studied. Plasma levels of IFN-α (ELISA), interferon-gamma induced protein 10 (IP-10) (Bioplex®) and the expression of SIGLEC1 on CD14+ monocytes (flow cytometry) were analysed.
Results: Pregnant females with a CHB complication had a significantly higher expression of SIGLEC1 (p=0.0034) and IFN-α (p=0.014), but not of IP-10 (p=0.14, all MWU), compared to the DC group. Receiver operating curve (ROC) analysis between the CHB group and the DC group showed that a SIGLEC1 median fluorescence intensity (MFI) of >904 could distinguish between the groups with a sensitivity of 100% and a specificity of 64%, and a concentration of IFN-α >0.70 pg/ml with a sensitivity of 67% and a specificity of 86%. Healthy pregnant females without the respective autoantibodies had the lowest levels for all three parameters. In a cohort of 5 females, both the expression of SIGLEC1 and plasma levels of IFN-α were reduced by hydroxychloroquine and oral glucocorticoids.

Table 1. Antibody profiles

	CHB pregnancies (n=9)	Disease controls (n=14)	Healthy controls (n=30)
Anti-Ro (SS-A), n (%)	9 (100%)	14 (100%)	0
– anti-Ro52, n (%)	7 (78%)	12 (86%)	0
– anti-Ro60, n (%)	9 (100%)	8 (57%)	0
Anti-La (SS-B), n (%)	2 (22%)	4 (29%)	0

Conclusions: This is the first study to report increased type I IFN activation in pregnant females with a CHB complication. Also, we show here that IFN-α directed therapy, e.g. with hydroxychloroquine, may be especially beneficial in these females.
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Neuronal and hormonal alterations in arthritis

OP0312 A PROTEOMIC SIGNATURE OF FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

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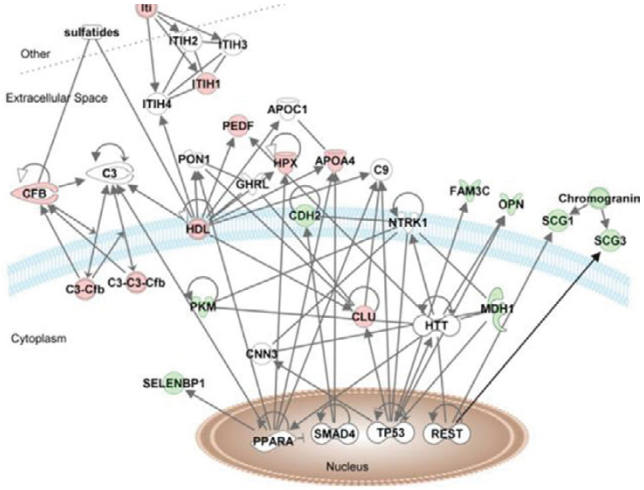
Background: Fatigue is a frequent and often disabling phenomenon in patients with chronic inflammatory and immunological diseases, neurodegenerative diseases, and cancer. The underlying biological mechanisms of fatigue are largely unknown and hypotheses are conflicting. It is important to uncover the pathophysiology and identify signalling pathways that generate and regulate this substantial phenomenon.
Objectives: Based on the hypothesis that fatigue originates from cerebral processes, we investigated whether relevant proteins and/or signaling pathways for fatigue could be revealed in the cerebrospinal fluid (CSF) of patients with primary Sjögren's syndrome.
Methods: Label-free shotgun mass spectrometry was performed to analyze the CSF proteome of 20 patients with primary Sjögren's syndrome. Fatigue was measured with the fatigue Visual Analogue Scale (fVAS).
Results: After depletion of high-abundance proteins, more than 800 proteins were identified and quantitated. Multivariate analyses showed that patients with low and high fatigue could be separated based on their CSF protein profiles, and 15 proteins were selected as top discriminatory proteins. Among these were apolipoprotein A4, hemopexin, pigment epithelium derived factor, secretogranin-1, secretogranin-3, selenium-binding protein 1, and complement factor B.
The figure shows the top network from Ingenuity Pathway Analysis (IPA) with 14 of

the differentially expressed proteins (red = upregulated, green = downregulated) and proteins that are directly associated to them (white molecules).



Conclusions: Most of the discriminatory proteins have important roles in regulation of innate immunity, cellular stress defense, and/or functions in the central nervous system. Some have been associated with severe depression and loss of appetite, which are important features of chronic fatigue. These proteins and their interacting protein networks may therefore have central roles in the generation and regulation of fatigue, and the findings add new, relevant, and important evidence to the concept of fatigue as a biological phenomenon signaled through specific molecular pathways.

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OP0313 P75 LOW AFFINITY RECEPTOR OF NERVE GROWTH FACTOR ON PERIPHERAL LEUKOCYTES AND CD11C-POSITIVE DENDRITIC CELLS ARE UPREGULATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The nervous system regulates rheumatic diseases in neurogenic inflammation (NI). Nerve growth factor (NGF) plays a pivotal role in NI and chronic nociceptive pain of degenerative musculoskeletal diseases [1]. Clinical trials using NGF antagonists have shown impressive analgesic efficacy in these disorders [2]. However, the role of NGF in autoimmune inflammatory diseases is not completely understood although NI perhaps induces and/or mediates disease activity. NGF-receptor expression on peripheral lymphocytes may reflect NI activity.

Objectives: The aim of this study was to identify the expression levels of the NGF receptor with high affinity (TrkA) and low affinity (p75) on leukocyte subsets of SLE patients, as compared to healthy controls (HC).

Methods: The number of TrkA- and p75-positive cells was quantified in 13 SLE patients (diagnosed according to the 1997 ACR revised criteria). CD4, CD8, CD11b, CD11c, CD14, CD16, CD19, CD56 and CD66b antibodies, and isotype controls were used. Cells were quantified by multicolour flow cytometry and compared to gender and age-matched HC (n=13) using the Mann-Whitney-U-Test. Values <0.05 were considered statistically significant. Patients were further subgrouped for high or low disease activity as determined by SLEDAI, ANA, anti-dsDNA, CRP, complement C3/C4 and ESR, and compared to HC using the Kruskal-Wallis test and Mann-Whitney-U-test. NGF serum concentrations were determined by ELISA.

Results: In SLE, *TrkA* expression on peripheral leukocytes (%±SD) was not different from HC and was highest on CD14+ cells (15.5±20.6). In contrast, *p75* was significantly increased on CD16+ (2.4±3.0 vs. 0.9±0.6, p=0.044) and CD56+ leukocytes (1.5±1.7 vs. 0.4±0.3, p=0.022) in SLE vs. HC. Further subgroup analyses showed that *TrkA* (0.6±0.3 vs. 1.8±1.3, p=0.035) and *p75* (0.4±0.3 vs. 2.3±1.8, p=0.014) were decreased on CD56+ cells in patients with high SLEDAI vs. patients with low SLEDAI scores. Similarly, a reduction of *p75* on CD19+ B cells was associated with high SLEDAI (0.8±0.7 vs. 10.8±16.5, p=0.018) whereas *p75* expression was significantly higher on CD56+ cells in SLE with low SLEDAI as compared to HC (2.3±1.8 vs. 0.2±0.2, p=0.007). CD11c+ dendritic cells (DC) did not show differential expression for TrkA or p75, however, they were increased in SLE as compared to HC (5.4±2.5 vs. 2.5±0.6, p=0.0001). Interestingly, DC were also significantly elevated in SLE with high SLEDAI, anti-dsDNA, ANA and ESR. NGF serum concentrations did not differ between SLE and HC.

Conclusions: Our data for the first time demonstrate differential NGF receptor expression on an extensive panel of peripheral blood leukocytes in SLE and HC. p75 appears to be the major differentially regulated receptor for NGF. The decrease of TrkA and p75 on CD56+ and p75 on CD19+ cells in patients with high SLEDAI activity is unclear and may reflect a negative feedback mechanism. The increased CD11c+ DC might indicate additional inflammatory activation in SLE. Further studies are needed to analyse these findings.

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Fighting osteoporosis fragilities

OP0314-HPR A HOME-BASED FALL PREVENTION PROGRAMME REDUCES FEAR OF FALLING IN SENIORS

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Background: Every year, over 80,000 elderly persons in Switzerland have accidents caused by tripping and falling, and half of these falls happen at home or in the direct vicinity (1). Falls, due to its often severe medical consequences and persistent mobility impairments, together with the demographic development, are one of the most important musculo-sceletal problems and public health issue. Falls are often due to a combination of internal risk factors (such as vertigo, osteoporosis, cognitive impairments, decreased ability for dual tasking) and external risk factors (such as medication and environmental risk factors) (2). The Swiss League Against Rheumatism (SLAR) has developed a multidimensional home-based fall prevention programme, which is supported by health insurances. Trained physiotherapists (PTs) and occupational therapists (OTs) visit the seniors at home in order to perform a detailed assessment of the senior's individual risk of falling. Subsequently the PT or OT eliminates identified environmental risk factors and provide tailored exercises. After 4 weeks, a telephone call was made by the PT/OT to discuss unclear instructions and after 16 weeks, follow up data were collected by telephone.

Objectives: The objective was to evaluate the effects of the fall prevention programme.

Methods: A retrospective analysis was carried out on the data of 671 participants in 2015. Available data were participant's characteristics, fall risk factors, determined by the Timed "Up&Go" with additional motor and cognitive task) (4). Fall Efficacy Scale (5), the recommendations made by the PTs/OTs and satisfaction of the seniors.

Results: The participants were mainly female (62.6%) and had a mean age of 81.7 years (SD=5.5, range 66.1–100 years). Several risk factors were present: 64.1% fell at least once in the last year and 45% were not able to perform a dual task (TUG + additional cognitive task).

Main recommendations made by PTs/OTs were "fixing down of carpets" (56.6%) and instruction of an exercise programme (strength, balance and multi-task capability) (82.6%). After four months, fear of falling had decreased (change in FES-I: -1.24 points 95% CI: (-1.44, -1.04), p-value<0.001). 92% of the participants self-reported to follow the recommendations and 98.4% were satisfied with the programme and would recommend it to others.

Conclusions: The low-threshold, multidimensional home-based fall prevention developed by the SLAR was feasible and effective. Participants implemented the recommendations and the fear of falling' decreased. Reduced fear of falling is considered a strong predictor of falling, however a prospective study is needed to determine if the reduced fear of falling leads to a decreased number of falls.

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