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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