Methods: Eight SSc pregnant patients were compared with 16 patients with other rheumatic diseases (ORD) and 16 healthy controls (HC), matched for gestational age. Clinical data were collected. Placentas biopsies were obtained for histopathological analysis and immunohistochemistry for CD3, CD20, CD11c, CD68 and ACKR2. Frozen placenta samples from 4 SSc, 8 ORD and 8 HC were analysed by qPCR for ACKR2 gene expression and proteins were extracted for multiplex assay for cytokines, chemokines and growth factors involved in angiogenesis and inflammation. Statistical analysis was performed with parametric or non-parametric tests depending on samples distribution.

Results: The number of placental CD3 (p<0.05), CD68 (p<0.001) and CD11c+ (p<0.001) cells was significantly higher considering the group of patients affected by rheumatic diseases (SSc+ORD) compared to HC. The SSc group alone did not show significance due to the lower sample size. No differences were observed between HC groups in terms of vascular alterations or fibrosis. The percentage of stained area for ACKR2 and the ACKR2 transcripts levels were comparable between groups. Hepatocyte growth factor (HGF), involved in angiogenesis, was significantly increased in the group of rheumatic diseases patients (SSc+ORD) compared to HC (p<0.05), while the chemokine CCL5 was significantly higher in SSc patients compared to patients affected by ORD (p<0.05) and to HC (p<0.01). CCL5 levels directly correlated with the number of all inflammatory cells considered and higher levels were associated to histological villitis (p<0.01).

Conclusion: The higher number of placental inflammatory cells and the alterations in the levels of HGF and especially CCL5 could play a role in the pathogenesis of the obstetrical complications in SSc. ACKR2 does not seem involved in the pathogenesis of obstetrical complications of SSc.

References:

Disclosure of Interests: None declared

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SAT0282 ASSOCIATION BETWEEN A VARIANT OF THE SRP55 SPlicing FACTOR GENE AND SYSTEMIC SCLEROSIS IN AN ITALIAN POPULATION

E. Romano1, M. Manelli2, J. Kosaka-Wegiel2, B. S. Fioretto3, I. Rosa, E. Stich1, S. G. Suiduci4, S. Bellando-Randone5, L. Ibba-Mannescchi1, M. Matsucri-Cerinic1, 1University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy; 2Jagiellonian University Medical College, Department of Medicine, Cracow, Poland

Background: In systemic sclerosis (SSc), alternative splicing of the last exon (exon 8) of vascular endothelial growth factor (VEGF)-A pre-mRNA is a key element in the switch from proangiogenic to antiangiogenic VEGF-A isoforms. The mRNA-binding protein serine/arginine protein 55 (SRP55, also known as SFRS6) is a key regulatory splicing factor that promotes distal splice-site selection in the exon 8 region of VEGF-A pre-mRNA and subsequent upregulation of the exon 8b-containing VEGFb antiangiogenic isoform. Overexpression of both VEGFb and SRP55 has been implicated in SSc-related angiogenesis impairment and peripheral vascular damage. Moreover, differential splicing of the VEGF-A gene has been shown to be critical for development of pulmonary fibrosis. Of note, previous studies reported the lack of sequence variations in the VEGF-A alternatively spliced region, while a single nucleotide polymorphism (SNP) in the SRP55 gene (rs2235611) has been associated with susceptibility to disturbed ocular angiogenesis in proliferative diabetic retinopathy.

Objectives: This case-control pilot study examined the possible implication of SRP55 rs2235611 SNP in the genetic predisposition to SSc susceptibility and clinical phenotype.

Methods: A total population of 872 white Italian individuals (414 SSc patients, 458 controls) was studied. All patients were classified as limited and diffuse cutaneous SSc (lcSSc and dcSSc, respectively) and were clinically evaluated for the presence of autoantibodies (antitrombomere, anti-Sc70 antibodies), pulmonary fibrosis and digital ulcers. The SRP55 rs2235611 SNP was genotyped by TaqMan Real-Time PCR.

Results: SRP55 rs2235611 genotype distribution and allele frequency were similar in SSc and healthy controls, though a trend toward significance was observed for genotype distribution (p=0.07). The SRP55 rs2235611 AA genotype significantly influenced the predisposition to SSc (OR 2.55, 95% CI 1.11 to 5.57.

Disclosure of Interests: None declared

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SAT0283 BIOSAMPLES FROM AT RISK SSc PATIENTS SHOW CLASSIC PATHOLOGICAL SIGNS OF SCLERODERMA: OPPORTUNITY FOR DIAGNOSIS OF PRE-CLINICAL SSc


1University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine and Biomedical Research Centre, Leeds, United Kingdom; 2San Carlo Hospital of Potenza, Rheumatology Institute of Lucania (IReL) and Rheumatology Department of Lucania, Lucania, Italy; 3The University of Manchester, Division of Musculoskeletal & Dermatological Sciences (L5) Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom; 4University College London, Experimental Rheumatology, UCL Division of Medicine, London, United Kingdom; 5Chapel Allerton Hospital, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom

Background: The VEDOSS study has recently indicated that more than 80% of patients affected by Raynaud’s phenomenon (RP) with specific SSc auto-antibodies and capillaroscopy changes satisfied ACR/EULAR 2013 criteria within 5 years. These data suggest that there is a window of opportunity for early detection of SSc in these patients.

Objectives: Here we aimed to determine whether sera, skin biopsies and skin fibroblasts cultured from these patients showed any biomarker signature of SSc.