Background: Systemic Sclerosis (SSc) is one of the rheumatic diseases burdened with obstetrical complications. An Italian multicenter study showed that women with SSc have a higher-than-normal risk of intrauterine growth restriction, preterm delivery, very-low birth weight babies and pregnancy should be discouraged in patients with severe organ damage. However, with a multidisciplinary management, patients with SSc can have successful outcomes. Little is known about the pathogenesis of obstetrical complications, as studies on placenta are case reports or description of a few cases.

Objectives: The aim of this study was to analyze the placental alterations with a focus on the role of inflammation in the pathogenesis of obstetrical complications in SSc, including the study of the atypical chemokine receptor 2 (ACKR2), involved in immune modulation and known to be highly expressed in circulating leucocytes in SSc patients.

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 analyzed 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 biopsies 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 obstetrical complications of SSc.

References:

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