of Treg compared with the pre-depletion group. Furthermore, the post-depletion group also exhibited lower fibrogenic cytokine-producing T cell frequencies, suggesting that the change in T cell cytokine production could not account for the more strongly reduced fibrosis observed in the pre-depletion group. Therefore, we examined other immune cell response to B cell depletion. Recent studies have revealed that macrophages are divided into two subtypes: M1 and M2 and that M2 macrophages show fibrogenic effects in SSc. This study showed that macrophages cultured with B cells from BLM-induced SSc mice exhibited enhanced M2 differentiation compared with control B cells. Remarkably, frequencies of M2 macrophages with fibrogenic capacity significantly decreased in the pre-depletion group compared with the post-depletion group, which could account for the more strongly inhibited tissue fibrosis in the pre-depletion group.

Conclusions: Our results indicate that therapeutic effects of B cell depletion on tissue fibrosis exert through regulating macrophage differentiation rather than T cell cytokine production in SSc, first demonstrating that interaction between B cells and macrophages in development of fibrosis in SSc.

Disclosure of Interest: None declared


FR0413

ARYL HYDROCARBON RECEPTOR EXPRESSION IS ASSOCIATED WITH LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is characterised by autoantibody production, microvascular injury and systemic excessive fibrosis. Genetic and environmental factors are thought to be important for the trigger of development of the disease, however, direct connexion between these factors and pathogenesis of SSc is not yet elucidated. Recent reports showed that environmental toxic pollutants, such as dioxins, play a significant role in the disturbance of immune system and the trigger of autoimmunity through binding aryl hydrocarbon receptor (AhR). However, little is known about the association between AhR and pathogenesis of SSc yet.

Objectives: To elucidate the association between AhR and the clinical characteristics of SSc.

Methods: Twenty-one patients with SSc who fulfilled 2013 ACR/EULAR classification criteria and 10 healthy controls (HC) were analysed. Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized whole blood by using gradient centrifugation and total RNA was prepared from PBMCs. Expression of Ahr mRNA was detected by quantitative polymerase chain reaction and standardised by mRNA level of 18S ribosomal RNA in each sample. Level of Ahr mRNA in the cells was compared between SSc and HC and also between SSc patients with and without various clinical features.

Results: The proportion of diffuse cutaneous subset (dcSSc) was 33%. Mean disease duration was 9±9 years. The positive proportion of anticientromere antibodies, anti-topoisomerase I antibodies, anti-U1 ribonucleoprotein antibody, anti-RNA polymerase III antibody and antinuclear antibody positive without SSc-specific antibodies among 21 patients were 33.3%, 33.3%, 4.8%, 9.5% and 9.5%, respectively. Antinuclear antibody was negative in 2 (9.5%) patients. AhR mRNA expression level was tended to be higher in SSc compared to HC (1.7±1.1 versus 1.2±0.6, p=0.1). Notably, the expression level of Ahr mRNA in dc SSc was tended to be higher than that of limited cutaneous SSc (p=0.15), whereas no significant difference was detected between with or without SSC related autoantibodies, vasculopathy such as pulmonary arterial hypertension or digital tip ulcer. Importantly, the expression level of Ah mRNA was significantly higher in patients with interstitial lung disease (ILD) (n=14) than those without (n=7) (2.0±1.1 versus 1.0±0.4, p=0.05). Furthermore, AhR mRNA expression level was significantly and negatively correlated with DLCO% predicted (r=−0.57, p=0.05).

Conclusions: Expression level of AhR mRNA was higher in patients with SSC, especially in SSc patients with ILD. In addition, AhR expression level was correlated with a parameter of pulmonary function test, DLCO% predicted. These results collectively suggest that AhR possibly plays an important role in the disease process of ILD in SSc.

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FR0414

EVALUATION OF A NOVEL MULTI-ANALYTE ASSAY FOR THE DETECTION OF AUTOANTIBODIES IN THE DIAGNOSIS OF SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease characterised by vascular changes and progressive fibrosis of skin and various internal organs. In SSc a variety of autoantibodies have been detected which are useful for the diagnosis and management of the disease. Some of these autoantibodies are well-established tools strongly associated with SSc (e.g. anti-centromere, anti-topoisomerase I, anti-RNA polymerase III). Other autoantibodies are less frequent and/or less specific for SSc but may be useful to better assess disease subsets and prognosis.

Objectives: Our goal was to assess the frequency of SSc-related autoantibodies detected using a novel technology as well to study the associations between these antibodies and clinical features in an Italian SSc cross sectional cohort.

Methods: Serum samples from 218 consecutive patients with SSc collected at three Italian sites were tested for a variety of autoantibodies (see table 1) using a novel fully automated system utilising bead-based immunoassays (research use only, Inova Diagnostics, San Diego, CA). The Italian cohort included: women 200 (92%), limited cutaneous SSc (lc-SSc) 166 (76%), patients with history of digital ulcers 91 (42%), calcification 46 (21%), lung fibrosis 84 (39%), heart involvement 38 (17.4%), pulmonary arterial hypertension 20 (9%), and esophageal involvement 138 (63.3%).

Results: The prevalence of antibodies is summarised in the table 1 below. Of note, anti-B1C2, anti-CEP-B, and anti-nucleosome antibodies were significantly associated with lc-SSc subtype (p<0.0237, p<0.0001, p=0.0096, respectively), while anti-Ro60, anti-SSB, anti-Scl-70, and anti-DSF70 antibodies were significantly associated with the diffuse cutaneous SSc (dc-SSc) subtype (p=0.0102, p<0.0001, p=0.0032, respectively). When analysing all antibodies with multivariable analysis, SSc patients showed significant clustering based on antibody profile and clinical phenotype.

Disclosures and Interest: None declared
