significant association emerged in particular between the presence of NAC and the active videoangiopatia pattern (OR 6.23; 95% CI: 1.058-36.71, p=0.043).

Conclusion: Though current data in the literature on this topic are poor, cardiac autonomic neuropathy is among the clinical manifestations of SSc. In our study population, though the limited sample size, we observed a high percentage of patients with autonomic cardiac neuropathy, which seems much more frequent with the increase in the duration of disease and based on the type of videoangiopatia pattern.

References:

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AB0161

CLONAL HEMATOPOIESIS IS INCREASED AND NOT RELATED TO AGING IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis, microangiopathy and immune dysfunctions including dysregulation of proinflammatory cytokines. Clonal hematopoiesis of indeterminate potential (CHIP) is defined by the acquisition of somatic mutations in hematopoietic stem cells leading to detectable clones in the blood. Recent data have shown a higher risk of cardiovascular disease in patients with CHIP resulting from increased production of proinflammatory cytokines and accelerated atherosclerosis. Eventual links between CHIP and autoimmune diseases are undetermined.

Objectives: The aim of our study was to evaluate the prevalence of CHIP in SSc patients and its association with clinical phenotype.

Methods: Forty-one genes frequently mutated in myeloid malignancies were sequenced in peripheral blood mononuclear cells from 90 SSc patients and from 44 healthy donors.

Results: A total of 15 somatic variants was detected in 13/90 SSc patients (14%) and 4 somatic variants in 4/44 (9%) HD (p=0.58). The prevalence of CHIP was significantly higher in younger SSc patients than in HD: 25% (6/24) vs 4% (1/26) (p=0.045) under 50 years and 17% (7/42) vs 3% (1/38) (p=0.065) under 60 years. The prevalence of CHIP in patients over 70 years was similar in SSc patients and healthy donors.

For SSc patients the most common mutations occurred in DNMT3A (7 variants). Other variants involved ATM, SF3B1, SETBP1, TET2, TP53, NFI or CBL. The distribution of gene mutations was overall comparable in SSc patients and in previously described CHIP series (3).

In most SSc patients, we identified a single CHIP mutation. Several mutations were detected in two SSc patients: SETBP1 and NFI in one and, TET2 and ATM in the other. Clonal mutations included missense (n=10), nonsense (n=3), frameshift (n=1) and a single splice site mutation. In all HD we detected a single CHIP mutation which occurred in DNMT3A, TP53 and CSF3R.

Variant allele frequencies (VAF) of CHIP mutations ranged from 2 to 18.6%.

Conclusion: CHIP mutation was not more exposed than those without CHIP (p=0.75). No patient developed any hematologic malignancy and no cytopenia during the median follow-up of 13 months (0-24 months). One SSc patients with CHIP developed a small lung cancer few months after NGS testing.

Conclusion: Whether CHIP increases the risk to develop SSc or is a consequence of a SSc-derived modified bone marrow environment remains to be explored.

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AB0162

THE SIGNIFICANCE OF M1 AND M2 MONOCYTES IN SYSTEMIC SCLEROSIS

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Background: Recently, the relation between M2 macrophage and fibrosis has been reported in several diseases including systemic sclerosis (SSc). Similar with macrophages, monocytes can be classified into M1 and M2 subset, and the relation of imbalance of these monocytes with disease such as rheumatoid arthritis have been reported 1-6.

Objectives: In this study, we attempted to investigate relationship among M1 or M2 monocytes in SSc.

Methods: This study included 23 SSc patients and 20 healthy donors. Using fluorescence-activated cell sorting, we defined CD14, CD68 and CCR2 positive cells as M1 and CD14 and CD163 positive cells as M2 monocytes. We examined the ability of cytokines/chemokines secretion of CD14 positive cells from SSc by multiplex bead array using MAP human cytokine/chemokine Magnetic Bead Panel which can measure 38 cytokines/chemokines. We next extracted M2 monocytes from CD14-positive cells using FACs, and we used the rest of the CD14 positive cells as M1-dominant monocytes. Then, we evaluated their ability of TGF-β production by multiplex bead array assay.

Results: SSc patients had higher M2/M1 ratio as compared with healthy control (70.3 vs 1.63, P<0.05). And, there was tendency that M2/M1 ratio was higher in SSc patients complicated with interstitial pneumonia. Beads array analysis revealed that CCL4 and MCP-1 production from CD14 positive cells which consists M2>M1 (M2/M1 ratio>1) were higher than that from CD14 positive cells which consists M2<M1. Furthermore, the ability of TGF-β secretion of M2 monocytes was higher than that of M1-dominant monocytes.

Conclusion: Our present study suggested that the imbalance of M1/M2 monocytes might contribute to pathogenesis of SSc.

References:

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AB0163

ANTI-KU ANTIBODIES: MUCH MORE THAN SCLEROMYOSITIS

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Background: Initially, anti-Ku antibodies (Ab) were described in patients with overlap syndrome with systemic sclerosis (SSc) and inflammatory myopathy (scleromyositis), although later they have been linked to a wide variety of systemic autoimmune diseases (SAD) questioning its diagnostic value. Recently, the possible existence of 2 different clinical phenotypes associated with these Ab has been described: one with myositis and high risk of interstitial lung disease (ILD) and another with positive anti-dsDNA Ab and glomerulonephritis.

Objectives: To analyze the clinical relevance and the main diagnosis of a series of patients with positive anti-Ku Ab.

Methods: Descriptive observational study of patients with anti-Ku Ab in two third level hospitals between 2011 and 2019. Their determination was made at the criteria of the requesting physician.

Results: Twenty-three patients (20 women) with a median age of 59 ± 14 years (range, 24-83) and a follow up time (median) of 37 months (1-208) were identified. The main clinical and analytical characteristics, as well as the final clinical
diagnosis of these patients are shown in Table 1. In the cluster analysis we could not identify clinical phenotypes, perhaps because of the small sample size. Only 50% of patients with myositis developed ILD. Regarding the final diagnosis, only 1 patient (2%) was diagnosed of scleromyositis. Besides detecting them in patients with SSc (39%) and idiopathic inflammatory myopathy (9%), anti-Ku Ab were detected in other SAD, the most frequent were systemic lupus erythematosus, rheumatoid arthritis (RA) and overlap syndrome of SSc + RA.

Table 1. Main clinical-analytical manifestations and final diagnosis of patients with anti-Ku Ab.

<table>
<thead>
<tr>
<th>FINAL CLINICAL DIAGNOSIS</th>
<th>Systemic sclerosis (SSc) 6</th>
<th>6 (Pre-scleroderma); 3, limited SSc: 3.</th>
<th>Systemic lupus erythematosus: 2</th>
<th>Rheumatoid arthritis: 2</th>
<th>Overlap syndrome RA + limited SSc: 2</th>
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<tbody>
<tr>
<td>PRIMARY BINARY CINHOS</td>
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Background:
Systemic sclerosis (SSc) is an autoimmune disease characterized by vascular damage and fibroblast activation. Primary SSc pathogenetic mechanisms, especially vascular disease and fibroblast activation, is widely considered. Overall increase of oxidative stress in patients with higher disease activity, as well as depletion of antioxidant capacity can be also linked with disturbance of purine metabolism through XO and XDH modulation. Pathogenetic influence of this imbalance can also be mediated through initial phase of neutrophil extracellular traps (NETs) formation, an eventual source of nucleoprotein containing autoepitopes.

Disclosure of Interests: None declared

Conclusion: Anti-Ku Ab are related to a great variety of SAD, without being a specific marker of any of them, nor being associated with any specific clinical manifestations. We couldn't confirm the existence of clinical phenotypes associated with the presence of these antibodies.

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ACTIVITIES OF THE OXIDATIVE-RELATED ENZYMES IN SYSTEMIC SCLEROSIS

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Background: The oxidative-related enzymes are involved in the pathogenesis of various stages of systemic sclerosis (SSc). SSc is a chronic autoimmune disorder that is intimately associated with vascular damage and therefore with chronic perfusion/reperfusion and oxidative organ injury. Mesenchymal cell activation in SSc is now also considered to be mediated primarily through oxidative burst. Regulation of oxidative stress by specific enzymes including several purine metabolism enzymes is likely to play an important role in SSc progression.

Methods: The study was performed according to bioethical standards. 51 patients with SSc and 30 healthy controls were included in the study. The diagnosis was verified according to ACR/EULAR 2013 criteria. We assessed SSc activity in compliance with the original activity scale that is commonly used in Russia [Guseva N.G., 1993] and by the 2001 European Scleroderma Study Group Activity Index. XO (EC 1.17.3.2), XDH (EC 1.17.1.4), and SOD (EC 1.15.1.1) plasma activities were measured using spectrophotometric techniques as previously described [Dubinina E.E., 1986; Karpova O.V., 2006]. Results are expressed as means±SD. The Mann-Whitney U test and Spearman's correlation coefficient were used for statistical analysis.

Results: Mean age of patients was 42.8±1.3 years, mean SSc duration was 7.9±0.7 years. Mean enzymatic activities in normal controls were 3.4±0.56 nmol/ml/min (for XO), 5.19±0.71 nmol/ml/min (for XDH), and 5.4±0.1±0.03 units (for SOD). The respective enzymatic activities in SSc group were 3.9±1.62 nmol/ml/min, 7.10±0.71 nmol/ml/min, and 7.10±2.19 units. All these mean activities were significantly higher in patients with SSc compared to healthy individuals (p<0.001). XO and XDH activities positively correlated with SSc activity (r=0.499, p<0.001, and r=0.741, p<0.001, respectively). The opposite but weaker trend was observed for SOD activity and SSc disease activity (r=0.190, p=0.188).

Conclusion: SSc is characterized by an increase in the intensity of oxidative and antioxidant processes, more pronounced in high disease activity. A close relationship between function of prooxidant/antioxidant enzymes and some of the key SSc pathogenetic mechanisms, especially vascular disease and fibroblast activation, is widely considered. Overall increase of oxidative stress in patients with higher disease activity, as well as depletion of antioxidant capacity can be also linked with disturbance of purine metabolism through XO and XDH modulation. Pathogenetic influence of this imbalance can also be mediated through initial phase of neutrophil extracellular traps (NETs) formation, an eventual source of nucleoprotein containing autoepitopes.

Disclosure of Interests: None declared

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