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Background: The CD4⁺ T cell subsets plays an important role in its pathogenesis, and its new research are constantly being published, but its specific changes between SSc and MCTD are still unclear.

Objectives: The aim of the present study was to explore the absolute numbers of CD4⁺ T subsets in peripheral blood(PB) of patients with SSc and MCTD using our modified flow cryometric method and investigate the role in the pathogenesis of both.

Methods: The PB samples from 54 patients with SSc, 51 patients with MCTD as well as 30 healthy control subjects were analyzed for lymphocyte subsets using flow cytometry. Of these patients, 19 had pulmonary involvement, including 9 patients with SSc and 10 patients with MCTD. Using directly the percentages from flow cytometry combined with internal standard beads calculated absolute number of peripheral lymphocyte subsets from the subjects in each group.

Results: Although there were some changes among CD4⁺ T cell subsets in PB from these SSc patients and MCTD patients, the major alteration was the reductions of Treg cells. Compared with the normal controls, the absolute number of CD4⁺CD25⁺FOXP3⁺Treg cells were significantly decreased in SSc patients and MCTD patients, and the absolute number of Th1 cells in MCTD patients is also significantly reduced. Notably, the absolute numbers of Th17 and Th2 cells were not different from those of normal controls, but the ratios of Th17/Treg in SSc patients and MCTD patients were significantly higher, causing by insufficient number of Treg cells (Fig 1). In addition, in patients with pulmonary involvement, we found that the absolute number of Treg cells was significantly reduced in patients with MCTD, while the absolute number of Th2 cells and Th17 cells was significantly reduced in patients with SSc(Fig 2).

Fig 1. Comparison of the levels of CD4⁺ T lymphocyte subsets in SSc patients, MCTD patients and healthy controls: (A) The absolute number of peripheral Th1 cells in patients with MCTD was significantly reduced; (B and C) There was no significant difference in the absolute number of Th2 cells in peripheral blood of different subjects; (D and E) The ratio of Th17/Treg cells in PB of patients with SSc and MCTD were significantly higher.*P < 0.05; **P < 0.01; ***P < 0.001.

Conclusion: The number of peripheral Treg cells in patients with SSc and MCTD was significantly reduced, suggesting that that SSc and MCTD progression is associated with the imbalances between pro-inflammation cells to anti-inflammation Treg cells. In addition, we also found that the decrease in peripheral numbers of Treg cells may contribute to the development of MCTD-associated lung disease, whereas in SSc patients who had lung involvement, the reduce in peripheral number of Th17 cells may result in a severe imbalance of Th17/Treg cells, thereby promoting disease progression.

Fig 2. Comparison of the levels of CD4⁺ T lymphocyte subsets in patients who had pulmonary involvement and healthy controls: (A) There was no significant difference in the absolute number of Th1 cells in peripheral blood of different subjects; (B and C) The absolute number of peripheral Th2 cells and Th17 cells in patients with SSc were significantly reduced; (D and E) The ratio of Th17/Treg cells in PB of patients with MCTD were higher.*P < 0.05; **P < 0.01; ***P < 0.001.

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FRI0262 INCREASED PLASMA LEVELS OF HSP90 ARE ASSOCIATED WITH MORE SEVERE LUNG AND SKIN INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Our previous study demonstrated that Hsp90 is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc in a TGF-β dependent manner. We showed that Hsp90 is a new regulator of canonical TGF-β signaling and its inhibition prevents the stimulatory effects of TGF-β on collagen synthesis and dermal fibrosis¹.

Objectives: The aim of this study was to evaluate plasma Hsp90 of SSc patients and characterize its potential association with skin changes and SSc-related features.

Methods: A total of 92 patients (79 females; mean age 52.7; disease duration 6.0 years; diffuse cutaneous (dc)SSc / limited cutaneous (lc)SSc = 38/54) and 92 age- and sex- matched healthy individuals were included. Plasma Hsp90 levels were measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median (IQR).

Results: Plasma Hsp90 levels were increased in SSc patients compared to healthy controls [12.5 (9.6–17.9) vs. 9.8 (7.7–12.4) ng/mL, *p*=0.0001]. Hsp90

levels in all patients positively correlated with CRP ($r=0.271$, $p=0.015$). Furthermore, Hsp90 concentrations were negatively associated with functional parameters of ILD: FVC ($r=-0.291$, $p=0.013$), FEV1 ($r=-0.248$, $p=0.036$), DLCO ($r=-0.290$, $p=0.012$) and SpO_2 ($r=-0.317$, $p=0.038$). When adjusted for CRP, these correlations still remained significant in multivariate analysis. Higher Hsp90 concentrations were associated with presence of synovitis [17.6 (15.4 – 24.0) vs. 12.2 (9.3 – 17.3), $p=0.039$]. In addition, only in patients with dcSSc, Hsp90 levels positively correlated with the mRSS ($r=0.437$, $p=0.006$). In a prospective analysis of patients with progressive SSc-ILD treated with 6 ($n=21$ patients) or 12 ($n=14$ patients) monthly i.v. pulses of cyclophosphamide (CPA, 10 mg/kg) we did not observe any significant differences between the baseline sample (month 0) and blood drawn after 1, 6 and 12 months. However, baseline Hsp90 was able to predict long-term response after one year of CPA treatment (DLCO_{m12-m0}; $r=-0.494$, $p=0.037$). Moreover, change in Hsp90 after one month of CPA treatment (Hsp90_{m1-m0}) was able to predict the short-term inflammatory response (CRP_{m3-m0}, $r=-0.495$, $p=0.019$; ESR_{m3-m0}, $r=-0.496$, $p=0.031$). Concentrations of extracellular Hsp90 were not significantly affected by other main clinical parameters of SSc.

Conclusion: We demonstrated higher plasma levels of Hsp90 in SSc patients compared to healthy controls. Concentrations of extracellular Hsp90 increase with higher inflammatory activity, with deteriorated lung functions in ILD and also with the extent and severity of the skin involvement in patients with diffuse cutaneous SSc. These data further highlight the role of Hsp90 as a significant regulator of fibroblast activation and tissue fibrosis in SSc. In addition, Hsp90 could become a predictor of treatment response.

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FRI0263

QUANTITATIVE MUSCLE ULTRASOUND IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES-A PRELIMINARY STUDY

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Background: Muscle involvement is the most frequent clinical feature in patients with idiopathic inflammatory myopathies (IIM). In addition to muscular enzymes, muscular magnetic resonance has been investigated for the assessment of disease activity, but it is limited by high costs and it is not readily available. Muscle ultrasound (MUS) has been recently proposed as a valuable tool for the diagnosis and activity assessment of muscle involvement in IIM patients.

Objectives: To define the role of MUS in the diagnosis and assessment of disease activity in IIM through quantitative analysis of MUS

Methods: This was a prospective study conducted from February 2019 to November 2019. 41 patients with IIM: 17 men and 24 women, median age 61.4 years, of which 20 were polymyositis (PM), 16 dermatomyositis (DM) and 5 inclusion body myositis (IBM) were included. 30 healthy subjects (HS), comparable in age and gender to patients, were recruited as controls. In every patient and control MUS of upper and lower extremities was performed (in total 10 muscles per side) and digital images were saved. Quantitative muscle echo intensity (QME) was calculated using an image processing program (ImageJ) to obtain the mean value of greyscales (mGS) for each muscle. For patients with IIM creatine phosphokinase

(CPK) levels were recorded, duration of disease (in months) was calculated and clinical evaluation tools for the assessment of disease activity were performed, such as manual muscle testing (MMT8), patient and physician visual analogue scales (pVAS, phVAS), health assessment questionnaire (HAQ) and myositis disease activity assessment tool (MDAAT).

Results: Patients had higher values of mGS across all muscles examined than controls ($p<0.001$). Among patients QME showed a negative correlation with MMT8 ($p<0.001$, $-0.641<r<-0.412$), but no correlation with CPK levels or duration of disease. A positive correlation was found between QME and HAQ ($p<0.05$; $0.320<r<0.599$), pVAS ($0.003<p<0.046$; $0.314<r<0.455$) and phVAS ($0.029<p<0.002$; $0.341<r<0.471$). No significant correlation was found between QME and MDAAT and no statistically significant differences of muscle echo intensity were observed between patients with IBM, DM and PM.

Conclusion: Quantitative analysis of MUS showed to be useful to differentiate IIM patients from healthy subjects, therefore it could be a helpful technique to screen patients with muscular symptoms in which perform additional investigations. In our study, the data collected did not allow to assess the disease activity of IIM patients and did not allow to distinguish between the 3 different subgroups of IIM patients, but further studies may help in the identification of different muscular patterns to guide the clinical suspect and the possible role of MUS in the follow-up of the patients.

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FRI0264

EFFECTIVENESS, SAFETY AND PATTERNS OF USE OF RITUXIMAB IN SCLERODERMA, IN CLINICAL PRACTICE: 9 YEARS' EXPERIENCE IN A TERTIARY HOSPITAL

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Background: Systemic sclerosis (SSc) is a clinically complex and heterogeneous disease. Interstitial lung involvement (ILD) is the main cause of mortality, but progression of skin fibrosis has also been associated with pulmonary dysfunction and mortality. Recently, Rituximab (RTX) has been postulated as a promising therapeutic alternative to cyclophosphamide (CF) or mycophenolate (MFM), but long-term experience is scarce.

Objectives: Describe the effectiveness, safety and long-term use of RTX, in a series of cases with SSc.

Methods: Retrospective observational study of patients with SSc (EULAR/ACR 2013 criteria) treated with RTX in a university hospital from 2010 to 2019. Sociodemographic data related to SSc and treatments were collected. The effectiveness of RTX was evaluated at 6-12 months and at the end of follow-up, by means of these main outcomes: Rodnan's modified cutaneous index (mRSS) for skin fibrosis; CK levels for myopathy, variation >10% in forced vital capacity (FVC) and >15% in lung diffusion capacity of carbon monoxide (DLCO) for ILD. Adverse events (AE) were recorded. Statistical analysis performed with Stata v.14 and statistical significance set for $p\leq 0.05$.

Results: 14 women with SSc (mean age 47 ± 13 years, mean evolution 6.2 ± 4.5 years) were treated with RTX for ILD ($n=9$), skin involvement ($n=11$) and/or inflammatory myopathy ($n=3$). The mean $\pm$ SD of follow-up was 3.36 ± 2.17 years. SSc type: diffuse cutaneous 75.71%, limited cutaneous 21.44%, overlap 35.71% and sine scleroderma 7.14%. Type of antibodies: 50% anti-Scl-70, 14.3% anti-centromere, 21.4% anti-RNA polymerase III and 7.14% anti-Ku. ILD was classified as NINE in 8 patients and NIU in 1. The first cycle of RTX included 2 infusions of 1g and was initiated a mean of 3.36 ± 2.17 years after diagnosis. The retreatments were initially fixed every 6 months and later on demand in 4 patients, and in the rest on demand from the beginning, according to duration of clinical response. A mean of 3.9 ± 2.5 cycles/patient (range: 1-11) were administered. 30% of patients had previously received CF and 21.5% MFM. RTX was administered in association with other DMARDs (MTX 64.29%, hydroxy-chloroquine [HCQ] 35.71%, MFM 57.14%, others 14.28%), CF (14.29%), intravenous immunoglobulins (7.14%) and prednisone (78.57%). In the final visit, the percentage use of DMARDs (50% MTX, 50% MFM and 28.57% HCQ) and prednisone (62.5% patients, 30% doses) was reduced. mRSS improved significantly. Muscle weakness disappeared in 3/3 with normal CK levels in 2/3