BACKGROUND: Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, inflammation, and extensive fibrosis of the skin and organs. Exosomes (EXOs) are cell-derived vesicles 30-150 nm in size that contain microRNAs (miRNAs), microRNAs, and proteins.

OBJECTIVES: Here, we aimed to investigate the roles of EXOs in SSc pathogenesis, especially in angiogenesis.

METHODS: EXOs were respectively isolated from plasma, cultured peripheral blood mononuclear cells (PBMCs), and neutrophil supernatants, and were identified by transmission electron microscopy. The expression of S100A8/A9 was measured by real-time PCR (RT-PCR) and ELISA. Percoll density gradient centrifugation and scratch assays in human dermal microvascular endothelial cells (HDMECs) were used to study the influence of neutrophil EXOs and neutrophil EXOs S100A8/A9. We also performed a genome-wide transcriptome analysis on PBMCs from 19 SSc patients and 18 matched normal controls (NC) using Illumina BeadChip arrays. The ingenuity pathway analysis (IPA) tool and Database for Annotation, Visualization and Integrated Discovery (DAVID) were used for bioinformatics analysis.

RESULTS: Plasma EXOs and neutrophil EXOs from SSc patients suppressed the proliferation and migration of HDMECs. Using a microarray analysis, we found 28% genes upregulated in PBMCs could exist in EXOs, especially in the S100 protein family, including S100A8/A9. High levels of S100A8/A9 were consistently verified in SSc plasma, PBMCs plasma EXOs, PBMC EXOs, and neutrophil EXOs. Particularly, S100A8/A9 expression in neutrophil EXOs was distinctly higher than that in PBMC EXOs in SSc patients. Furthermore, we found that neutrophil EXOs S100A8/A9 inhibit the proliferation and migration of HDMECs, and that they may through Toll-like receptor 4 (TLR4) pathway.

CONCLUSION: S100A8/A9 is one of components of neutrophil EXOs that regulates vascular endothelial cell angiogenesis in SSc patients, most likely by activating the TLR4 signalling pathway.

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AB0213 RELATED FACTORS TO RENAL INVOLVEMENT IN SYSTEMIC SCLEROSIS PERUVIAN PATIENTS

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Background: Systemic sclerosis (SSc) can affect multiple organ systems including the kidney. Renal disease, especially chronic kidney disease (CKD), remains an important cause of morbidity and mortality in SSc. The spectrum of renal complications in SSc include scleroderma renal crisis (SRC), normotensive renal crisis, antineutrophil cytoplasmic antibody-associated glomerulonephritis, penicillamine-associated renal disease, and reduced renal functional reserves. Furthermore, subclinical renal impairment affects approximately 10-55% of SSc patients and might be associated with other vascular manifestations. However, the available evidence on CKD in patients with SSc residing in low-middle income countries (LMIC) is scarce. Because the health system of LMIC, and especially Peru, could have great differences in access to diagnosis and management of SSc, it is important to identify which clinical factors would be associated with CKD in patients with this autoimmune disease.

OBJECTIVES: To identify the associated factors to renal involvement in Peruvian patients with SSc.

METHODS: We analyzed the associated factors to renal involvement in SSc patients at Hospital Nacional Edgardo Rebagliati Martins Lima-Peru, a national reference hospital in Peru. Between June 2001 and December 2018, we included ambulatory patients, older than 18-year-old with SSc that met the ACR-EULAR classification criteria. In patients who accepted to get informed consent, a complete clinical assessment and a sociodemographic survey were done. Additional clinical data were collected from their clinical records. Multiple Poisson regression with robust standard errors was used to identify significant and independently associated factor. Two models were estimated: one based on theoretically selected variables and another parsimonious model based on variables that was selected using a manual backward selection procedure with a predetermined alpha of 0.2. Adjusted prevalence ratio (aPR), 95% confidence interval and p-values were reported.

RESULTS: One hundred and five patients with SSc were included in this study, 15.1% had chronic kidney disease. The average age was 57.8
years; 92% were women, and the average time of illness was 8.2 years. The model based on theory showed that age (aPR = 1.03, 95% CI = 0.99-1.07, p = 0.143) and exposure to Penicillamine (aPR = 0.51, CI 95% = 0.19-1.33, p = 0.170) were marginally associated (p < 0.2) with CKD, while pulmonary hypertension (aPR = 2.76, 95% CI = 1.29-5.89, p = 0.009) and arterial hypertension (aPR = 3.51, 95% CI = 1.06-11.6, p = 0.04) were significantly associated (<0.05) with CKD. The parsimonious model retained pulmonary hypertension (aPR = 3.74, 95% CI = 1.67-8.36, p = 0.001) and arterial hypertension (aPR = 7.45, 95% CI = 3.31-16.7, p < 0.001) as significantly associated factors to CKD.

Conclusion: Hypertension, a classic cardiovascular risk factor, and pulmo-

ary hypertension were important factors associated with CKD. The appropriate management of these factors must be taken into account to prevent CKD. Prospective cohort studies should evaluate the influence of these factors in reducing the incidence of CKD.

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AB0214 MUSCLE INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: The prevalence of myopathy in systemic sclerosis (SSc) or scleroderma patients varies from 5% to 81% depending on the diagnostic criteria used to define the muscle involvement. The histopathological characteristics found in these patients and their correlation with the clinical features and autoantibody profile has not been fully characterized.

Objectives: To characterize the muscle involvement and histopathology findings in patients with SSc.

Methods: This retrospective cross-sectional study included all patients from Sclerodema Cohort of Vall d’Hebron General and Hospital Clinic de Barcelona with muscle biopsies available for review performed at the Muscle Research Unit of Hospital Clinica de Barcelona from May 2004 to November 2018. Muscle biopsies were performed, for weakness or raised CK. Histological sections were independently evaluated by two myopathologists expert looking for inflammation in the endomysium, perimysium and perivascular areas. The presence of necrosis, regeneration, fibrosis, neurogenic atrophy, and fiber type grouping as well as perifascicular atrophy were also recorded. Based on the autoantibody profiles and clustered findings in patients with SSc.

Results: Subjects included were 33 (78.6%) of them were women. Considering the immunological profile 12 had ScI70, 12 PM/Scl, 11 ANA pattern without specificity for anti-Scl70 or antcentromere. Most of patients (90.5%) were Caucasians, 2 (4.8%) were Hispanic, and 2 of other ethnic background. The mean age at the onset of SSc was 42.1 (SD 2.5) years and at the muscular symptoms 50.7 (SD 2.1) years, respectively. Twenty-two (52.4%) patients presented with high CK level (mean 1316 ± 353 U/L; normal value ≤ 200 U/L) whereas 38 (90.5%) exhibited high aldolase level (mean 253 ± 18 U/L; normal value < 6 U/L). Of note, 17 (40.5%) presented moderate to severe inflammatory features in the muscle biopsy. In near half of the muscle biopsies (45.2%) inflammatory infiltrate was present. Compared to other patients, those positive for PM/Scl had more perivascular (75%), endothymial (50%) and perimidal inflammation (75%) and perifascicular atrophy (42%) (all p<0.05), while a reduced prevalence of inflammatory infiltrates was noted in the ScI70 group (17%) (p<0.05).

Conclusion: In our cohort of SSc patients with muscle involvement, two main histopathological patterns were found, fibrosis and inflammation. Almost half patients presented with elevated aldolase with normal CK lev-

els. The muscle disease heterogeneity suggests that a variety of patho-

logic mechanisms play a role in the scleroderma associated myopathy but those patients with histopathological inflammatory features deserve to be treated with immunosuppressive therapy.

REFERENCES:


AB0215 A LATE ONSET OF SYSTEMIC SCLEROSIS IS ASSOCIATED WITH A MORE RAPIDLY PROGRESSING CLINICAL PHENOTYPE IN LCSSC PATIENTS

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Background: SSc is a heterogeneous multisystem connective tissue disease. The majority of patients (pts) develop initial clinical symptoms between the ages of 30–50 years (yrs). It is not yet known whether the age of onset has an influence on the development of a distinct clinical phenotype.

Objectives: Investigating the relationship between age at disease onset and the development of clinical characteristics using data of the German Network for Systemic Scleroderma.

Methods: We evaluated 2928 patient data, subdivided them into 3 age groups at disease onset (<40 years, 40-60 years, and >60 years) and correlated the age at disease onset with specific clinical characteristics.

Results: Overall, 24% of pts developed first non-RP symptoms at the age of <40yrs, 53% between the age of 40-60yrs, and 23% were older than 60yrs. In particular, SSc pts with disease onset >60yrs developed significantly (p <0.001) more the lcSSc subtype (64%) as well as ACA antibodies (42%) with a significantly lower mRSS. They, however, also suffered more often from pulmonary hypertension (PH) and developed less often digital ulcers. Especially lcSSc pts were associated with a more rapidly progressing clinical phenotype, i.e., 25% of the elderly lcSSc pts developed PH after five years. In contrast, less than 5% diagnosed with lcSSc at the age of <40yrs suffered from PH after five yrs (p<0.001).

Conclusion: In this registry, approximately one quarter of pts developed SSc at an age above 60yrs, predominantly having a lcSSc subtype. Although these pts have been diagnosed with the mild form of SSc, pts with a lcSSc subtype at a higher age (>60yrs) had more frequent a PH and showed a more rapid disease progression than the youngest pts. These findings may have an important influence on recommendations on