AB0688

NEOPLASTIC RISK IN SYSTEMIC SCLEROSIS: A MONOCENTRIC STUDY

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Background: an increased risk of malignancies (1.5-5 times) was found in Systemic Sclerosis (SSc). Well recognized risk factors are the diffuse form, advanced age and (1), more recently, the positivity for anti-RNA Polymerase III antibodies (aRNAP3) has assumed considerable importance (2).

Objectives: the aim of this study was to evaluate the frequency of neoplasms and precancerous conditions, as well as the main risk factors, in our cohort of patients with SSc.

Methods: we enrolled 312 consecutive patients (288/92% females and 24/8% males, mean age 62.3 years, average disease duration 108 months) afferent at our department from 2000 to 2018, with a diagnosis of SSc confirmed according to the 2013 ACR/EULAR criteria (3). All patients underwent clinical, instrumental and laboratory evaluation. In 93 patients, negative for anti-topoisomerase I antibodies (aSci70) and anti-centromere antibodies (ACA), the presence of aRNAP3 antibodies was evaluated by an ELISA method (QUANTA Lite™ RNA Pol III).

Results: we found a limited form of disease in 229 patients (73.4%) and a diffuse form in 83 (26.6%). Eighty eight (28.2%) patients were positive for aSci70, 112 (35.9%) for ACA and 17 (5.4%) for aRNAP3. In the whole group, 44 (14%) patients had a positive familiar history for neoplasm while 105 (33.65%) had a history of neoplasms and/or precancerous conditions. Among these 105 cases, 44 (41.9%) were malignant, 50 (47.6%) benign and 11 (10.5%) had precancerous conditions. The most frequent neoplasms were breast carcinomas (14 cases/14.9%), thyroid (7 cases/7.4%), lung and kidney (3 cases/3.1%), melanomas (5 cases/5.3%). The most frequent precancerous condition was Barrett's esophagus (7 cases/63.3%). Regarding the antibody profile, 5 (4.8%) patients were positive for anti-RNAP3 and only 2 (1.9%) of these patients presented a malignant neoplasm, breast cancer in both cases. In 30 cases (28.6%) these neoplastic/precancerous conditions had arisen in the close period ($\pm$ 36 months) at the SSc diagnosis and only 3 of them were anti-RNAP3 positive. Among the evaluated risk factors. Only familiarity was significantly associated with the development of neoplasia ($p = 0.003$), confirmed at the multivariate analysis (OR 2.9, IC95% [1.5-5.7]; $p=0.002$).

Conclusion: our study evaluated not only malignant neoplasms, but also benign neoplasms and precancerous conditions and identified familiarity as the only significant risk factor. In our cohort we didn't find any relationship between the presence of anti-RNAP3 antibodies and the development of neoplasms, not even stratifying for the type of neoplasm. However, to better define our data, we should analyze anti-RNAP3 also in the double negative (antiSci70 and ACA) cases, in light of the recent evidence of double antibody positivity, as well as other newly investigated rare autoantibodies, associated with neoplasm in many connective tissue diseases, including SSc.

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EVALUATION OF CARDIOVASCULAR DETERMINANTS OF DISEASE OUTCOME IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by microvascular abnormalities. Cardiopulmonary and vascular manifestations in SSc are the most important survival factors in the disease.

Objectives: Correlations between different cardiovascular parameters (ejection fraction (EF), diastolic dysfunction, wall motion disturbance, estimated systolic pulmonary arterial pressure (sPAP), flow-mediated vasodilatation, arterial stiffness parameters (augmentation index - Alx, pulse wave velocity - PWV) and disease outcome and death were measured.

Methods: Thirty-six SSc patients were involved who underwent detailed arterial stiffness and vasodilatation examinations in 2007. In our work a 10-year period was analysed till 2017 following the progression of organ manifestations and survival.

Results: During the 10-year follow-up, 13 of the 36 patients died. The average survival time was 26.59 (22.36-37.64) years. Significant correlation was found between the initial Alx and PWV with cardiac wall motion disturbance ($p = 0.018$ and $p = 0.016$), Alx with restrictive ventilation dysfunction ($p = 0.029$) and PWV with obstructive ventilation dysfunction ($p = 0.015$). During the 10-year period, the occurrence of diastolic dysfunction was significantly increased ($p = 0.0016$), the incidence of arrhythmia did not change significantly. A significant risk factor for survival has been the decrease in EF ($p = 0.011$), where 1% reduction in EF was associated with 1.9% increase in mortality and 1 mmHg increase in sPAP involved 13% increase in mortality.

Conclusion: Based on our findings vascular stiffness parameters can be the predictors not only of the cardiovascular mortality but pulmonary manifestations with restrictive ventilation disturbances also in SSc.

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USE OF MYCOPHENOLATE IN SYSTEMIC SCLEROSIS. CASE SERIES

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Background: At present, there are not specific targets to treat or prevent Systemic Sclerosis (SSc), but there are some to reduce the impact of its associated complications. Although mycophenolate (MP) is not recommended in latest EULAR SSc guidelines to treat cutaneous and pulmonary manifestations, its efficacy is known, based on observational studies and the Scleroderma lung study II.

Objectives: To describe our center's experience in treating SSc patients with MP.

Methods: Descriptive series of SSc patients treated with MP from November 2017 to December 2018. Demographic, clinical, analytical, spirometric, radiological (HR-CT) and modified Rodnan skin score (mRSS) data were collected.

Results: Case 1: woman diagnosed at 42 years old with diffuse SSc, having positive anti-topoisomerase-I antibody (ATA), telangiectasias, pitting scars, scleroderma and Non-specific Interstitial Pneumonia (NSIP) without significant alterations in spirometry. One year after diagnosis, as a result of skin worsening (mRSS 21), we started MP in association with prednisone (mean dose 5 mg. a day). After treatment for 14 months, she showed significant improvement (mRSS 9) without spirometric changes.

Case 2: woman diagnosed at 30 years old with diffuse SSc, having positive ATA, pitting scars, gastroesophageal reflux disease (GERD) and scleroderma. This same year, we started MP due to skin involvement (mRSS 14), improving significantly (mRSS 9) after 14 months of treatment.

Case 3: woman diagnosed at 35 years old with diffuse SSc, having positive anti-RNA polymerase-III (ARA), pitting scars, telangiectasias, calcinosis, myopathy and scleroderma. 40 months after diagnosis, MP and prednisone (mean dose 5mg. a day) were started to treat skin (mRSS 19) and muscle (confirmed by biopsy) involvement. Both showed significant improvement after 8 months of treatment, with mRSS 13, myopathy symptoms resolution and creatine kinase (CK) normalization.

Case 4: a woman diagnosed at 35 years of age with limited SSc, having positive anti-Ro52, telangiectasias, skin involvement (mRSS 14) and NSIP with non-assessable spirometry. Clinical respiratory improvement was shown after just 1 month of treatment, without mRSS changes.

Case 5: woman diagnosed at 54 years old with diffuse SSc, having positive ATA, hands edema, scleroderma (mRSS 11), GERD and NSIP (FVC 56%, FEV1 64%, non-assessable DLCO). After 25 months of disease

progression and skin involvement, we started MP with prednisone (mean dose 8mg. a day), observing no significant changes after treating for 8 months on skin or lung disease, only improving the hands edema.

Case 6: woman diagnosed at 47 years old with diffuse SSc, having telangiectasias, scleroderma, positive ATA and NSIP. At 100 months from diagnosis, after 6 cyclophosphamide cycles followed by azathioprine (both ineffective) due to lung function (FVC 76%, FEV 83%, DLCO 26%) and skin (mRSS 30) worsening, MP and prednisone (mean dose 15mg. a day) were started. Currently, we are still waiting to assess clinical response.

Conclusion: Despite it is not included in EULAR current recommendations for SSc complications, our patients have remarkably improved with MP, especially skin involvement, with a good safety profile. These data reaffirm those obtained in previous studies and encourages us to continue considering its use.

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INCREASED CARDIOVASCULAR RISK IN MIXED CONNECTIVE TISSUE DISEASE: EVALUATION OF MACROVASCULAR INVOLVEMENT AND ITS PREDICTORS BY AORTIC PULSE WAVE VELOCITY

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Background: Macrovascular involvement and cardiovascular (CV) risk have not been sufficiently studied in patients with mixed connective tissue disease (MCTD). In particular, the gold standard assessment method of aortic stiffness carotid-femoral pulse wave velocity (cfPWV) (1) has never been evaluated in patients with this disease.

Objectives: Aims of the present study were to examine cfPWV in MCTD and to evaluate its associations with MCTD associated parameters and traditional CV risk factors.

Methods: cfPWV measurements were performed in 43 MCTD patients and 107 healthy controls. The difference between cfPWV in the two groups was statistically examined and subsequently controlled for the effect of possible confounding factors. Association of cfPWV with MCTD associated organ involvement, routine laboratory parameters and immunoserological markers was also evaluated. Finally, relationship of cfPWV with medications and traditional CV risk factors was examined.

Results: Adjusted statistical analyses for confounding factors showed significantly higher cfPWV values in MCTD patients in comparison to controls ($p_{adj}<0.001$). cfPWV correlated in both the patients and the control group significantly with age ($\rho=0.69$, $p<0.001$ and $\rho=0.67$, $p<0.001$ respectively), diastolic arterial pressure ($p_{adj}=0.024$ and $p_{adj}=0.032$ respectively) and mean arterial pressure ($\rho=0.44$, $p=0.004$ and $\rho=0.49$, $p<0.001$ respectively). Moreover, cfPWV correlated in the control group with systolic arterial pressure ($p_{adj}<0.001$) (Fig. 1). Higher cfPWV values could be documented in the subset of MCTD patients without lung involvement ($p=0.049$).

Conclusion: To our knowledge, this is the first study to show that patients with MCTD have significantly higher aortic stiffness and thus CV risk in comparison to controls. Except the disease itself, age and blood pressure were the main predictors of cfPWV.

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Figure 1 (a, b, c, d). Correlations of cfPWV (m/s) with age (years) and MAP (mm Hg) in the control and the MCTD group (all; * $p < 0.05$).

cfPWV carotid femoral pulse wave velocity, MAP mean arterial pressure, MCTD mixed connective tissue disease

AB0692

ASSESSING RECOVERY TIME AFTER COLD CHALLENGE AND THUMB INVOLVEMENT CAN HELP TO RULE OUT SYSTEMIC SCLEROSIS IN PATIENTS PRESENTING WITH RAYNAUD'S PHENOMENON

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Background: Distinguishing primary Raynaud's phenomenon (PRP) from Raynaud's phenomenon secondary to systemic sclerosis (SSc) is crucial in the early detection of SSc. Recently we reported that patients with more severe vasculopathy suffer from a prolonged ischemia time during Raynaud's attack. [1] Additionally, it appears that the thumb is more frequently involved in SSc, where it seems to be spared in PRP. [2] These two characteristics are easily recognized by patients and physicians, and can help rising awareness for SSc.

Objectives: The aim was to study if the recovery of a Raynaud's attack and involvement of the thumb are differentiators for SSc in patients with Raynaud's phenomenon (RP).

Methods: A stepwise cooling and recovery procedure was performed, provoking an RP attack, in patients with PRP and SSc. One hand was submerged up till the radiocarpal joint in water. The water temperature was lowered in steps of 3 degrees Celsius every four minutes, from 33 until at least 9 degrees Celsius. Afterwards ten minutes of recovery in room air of 23 degrees Celsius was observed. During the procedure perfusion of the fingertips was assessed by photo-electric plethysmography.

Results: In total 18 patients with SSc and 68 patients with PRP underwent the procedure. Seventeen (94%) SSc patients had no restoration of perfusion after ten minutes in one or more fingers, compared to 28 (41%) PRP patients (figure 1), with a negative predictive value of 98%. During cooling, 17 (94%) SSc patients developed abnormal perfusion in the thumb compared to 48 (71%) PRP patients ($p=0.036$), with a negative predictive value of 95%. There was no difference in involvement of the other fingers during cooling (all $p>0.05$). Positive predictive values were low.

Conclusion: In patients with RP, when there is restoration of perfusion in all fingers after ten minutes or when the thumb is spared, the presence of an underlying SSc is very unlikely. Although this objective measurement needs to be verified with patient's reports, these results suggest that these simple signs can help physicians to assess if the patient needs to be referred for additional tests.