AB0612 EFFICACY OF LOW DOSE AND SHORT-TERM IL-2 TREATMENT TO EXPAND ENDOGENOUS REGULATORY T CELLS IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE

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Background: The concept of Mixed Connective Tissue Disease (MCTD) was first proposed by Sharp and his colleagues in 1972.¹ MCTD has overlapping features between at least two autoimmune diseases, such as SLE, SSc, PM/DM and RA. Regulatory T cells (Treg cells) play a critical role in the maintenance of immune tolerance and the regulation of immune responses. Treg cell dysfunction contributes to the initiation of pathogenesis and the maintenance of high disease activity in RA and SLE.² Recently, some studies have indicated that the proportion of Treg cells was different from healthy controls in SSc patients.³ Therefore, MCTD may be associated with Treg cells.

Objectives: To explore the status of CD4+T cells in peripheral blood of patients with MCTD; to explore the effect of low dose interleukin -2 (IL-2) treatment on the balance of Treg cells and Th17 cells in patients with MCTD, and to observe the short-term curative effect.

Methods: CD4+T cells in the peripheral blood of 58 MCTD patients and 33 healthy controls were analyzed by flow cytometry. All of 58 cases were treated with standard therapy, including corticosteroids, NSAIDs, immunosuppressants, or combination therapy. Among them, 26 cases of MCTD without using immunosuppressant (CYC, MTX, LEF, MMF), were as untreated group, another 32 cases were as treated group. Then we compared the difference of CD4+T cells between two groups. In 58 patients with MCTD, a total of 27 patients were treated with low-dose IL-2 (50WU) on the basis of standard treatment for 5 days. The difference of CD4+T cells before and after treatment with IL-2 was compared.

Results: The absolute count of CD4+CD25+FOXP3+Treg cells in peripheral blood of patients with MCTD was significantly lower than those in healthy controls. There was no significant difference in the absolute count of CD4+CD25+FOXP3+Treg cells in the peripheral blood between the treated group and the untreated group. The absolute count of CD4+CD25+FOXP3+Treg cells was significantly higher than those before treatment with IL-2.

Conclusions: The absolute count of CD4+CD25+FOXP3+Treg cells in peripheral blood of patients with MCTD were significantly reduced, which may be the mechanism of immune imbalance in MCTD patients. The decrease of the absolute count of CD4+CD25+FOXP3+Treg cells in peripheral blood of patients with MCTD was not associated with the use of immunosuppressive agents. Low dose and short-term IL-2 treatment may increase the absolute count of CD4+CD25+FOXP3+Treg cells in the peripheral blood in patients with MCTD, so as to restore the immune balance in patients with MCTD.

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AB0613 PULMONARY ARTERY DIAMETER AND PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis may be complicated by pulmonary hypertension.

CT-determined pulmonary artery diameter has been shown to correlate with presence of pulmonary hypertension in idiopathic patients and in interstitial lung disease but not in scleroderma.

Objectives: To determine the utility of CT-determined main pulmonary artery diameter (MPAD) for predicting pulmonary hypertension (PH) in 97 patients with systemic sclerosis who had CT chest within six months of right heart catheterisation.

Methods: Retrospective review of right heart catheter and CT data done within six months in 97 patients. The CT scans were blindly scored by two radiologists.

Results: 97 patients (75 female, 22 male) with systemic sclerosis who underwent CT scan and right heart catheterization were analysed. About 2/3 had the limited subtype (64 limited, 24 diffuse, 6 undefined).

Pulmonary hypertension was present in 55 patients (57%) and interstitial lung disease affecting 20% of the lung or more was present in 42 patients (43%).

Survival was worse in those with pulmonary hypertension. Median survival was 9.3 years in those without pulmonary hypertension (8.1–10.5) and 4.4 years in those with pulmonary hypertension (2.6–6.2). Presence of interstitial lung disease and pulmonary hypertension were independent predictors of survival.

An ROC curve shows area under the curve of 0.864. MPAD threshold of 25 mm or greater has a sensitivity of 98% and a specificity of 33% for the presence of pulmonary hypertension; 30 mm has a sensitivity of 73% and a specificity of 81% for the presence of pulmonary hypertension; 32 mm has a sensitivity of 56% and a specificity of 88% for the presence of pulmonary hypertension and 34 mm has a sensitivity of 35% and a specificity of 98% for the presence of pulmonary hypertension.

Survival was worse in those with a MPAD of 30mm or greater, with median survival of 5.5 years (3.8–7.2) compared to survival of 9.3 years (7.9–10.7) in those with MPAD smaller than 30mm. It was not a significant predictor of survival after adjustment for presence of pulmonary hypertension and interstitial lung disease.

Conclusions: The CT determined MPAD correlates strongly with the presence of pulmonary hypertension in patients with systemic sclerosis.

Disclosure of Interest: None declared

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AB0614 ANTISYNTHEASE SYNDROME: AUTOANTIBODIES, CLINICAL PATTERN AND MANAGEMENT OF 17 SPANISH PATIENTS

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Background: Antisynthetase syndrome (ASS) is a heterogeneous rare inflammatory condition characterized by myopathy, interstitial lung disease (ILD), arthritis, mechanic hands and Raynaud phenomenon (RP). The hallmark of ASS is the presence of antibodies against aminoacyl-transfer RNA synthetases (anti-ARS). Eight different anti-ARS have been described: anti-Jo1, anti-PL7, anti-PL12, anti-EJ, anti-OJ, anti-KS, anti-Zo, anti-Tyr/YRS. Despite recent publications, correlation between autoantibodies clinical pattern and management in ASS is not entirely well-known.

Objectives: The aim of this study was to define clinical features, autoantibodies and outcomes of a series of ASS patients.

Methods: We retrospectively analyzed the epidemiology, clinical data, lung function parameters, muscle enzymes, electromyogram (EMG) and autoantibodies pattern and its relationship with clinical manifestations, treatment management and outcomes of 17 patients recruited between 2005 and 2016 from the Autoimmune Diseases Division of a Spanish hospital.

Results: A total of 17 patients were reviewed (15 female). Mean age at diagnosis was 55 years. Median time delay to diagnosis was 5 months. Median follow-up was 65 months. Main clinical symptoms were dyspnea (76.5%), polyarthritides (58.6%), muscle weakness and myalgias (52.9%), RP (41.1%) and mechanic

hands (23.5%). Lung involvement was defined by HRCT compatible with ILD (64.7%) and abnormal functional exploration (47.1%): restrictive pattern (87.5%) and diminished DLCO (61%). Muscle involvement was defined by elevated CK (52.9%) with a median maximum value of 517 IU/L, myopathic pattern on 8 of 13 performed EMG (61.1%) with myositis found in 4 of them (50%), and inflammatory myositis in 5 of 8 performed biopsies (62.5%). Anti-ARS findings were anti-Jo1 (11), PL12 (2), PL7 (1), anti-EJ (2) and one patient with both PL7 and PL12. Anti-Jo1 predominant clinical pattern was ILD (72.7%), followed by myopathy (63.6%) and concomitant myopathy and ILD (45.5%). Anti-PL12 was associated with ILD, RP, and esophageal involvement and no myopathy. Anti-PL7 patient showed mild myopathy and cutaneous association alone. A combination of anti-PL12 and PL7 was described in one patient who developed ILD with severe myopathy. Anti-EJ patients had pulmonary involvement but no evidence of muscle disease. There was no evidence of cancer in any of our patients. Corticosteroids therapy was administered in most of them (88.2%), and corticoid dependence was highlighted, being necessary at times to associate one or more immunosuppressants.

Conclusions: Regardless of ASS being a rare disease, 17 patients were collected. Anti-Jo1 was the most described antibody. It is important to note that one patient was found to be positive for both anti-PL7 and PL12 meanwhile they were described as exclusive, showing overlap of clinical pattern with severe muscle injury. This finding suggests that positive results for more than one ASS antibody infer more severity. In contrast with previous literature, pulmonary was more frequent than muscle involvement. The coexistence of both was observed in a small group (35.3%), mostly in anti-Jo1 patients (45.5%). Therefore, we suggest the need to request ASS antibodies in patients with pulmonary or/and muscle involvement at onset although classic clinical pattern is missing.

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AB0615 PERSISTENCE OF HUMAN PAPILLOMAVIRUS IN THE CERVIX OF WOMEN WITH SYSTEMIC SCLEROSIS

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Background: Persistent infection by high-risk oncogenic Human Papillomavirus (HPV) is the main cause of the development of dysplastic or malignant lesions of the cervix. Furthermore, a few life habits, such as smoking, sexual habits and hormonal contraception, are known risk factors for cervical HPV infection. In addition, increased frequency of persistent HPV infection or high-grade intra-epithelial lesions rates was anecdotally described in patients affected by immune-mediated diseases, such as systemic lupus erythematosus, rheumatoid arthritis and systemic sclerosis (SSc), in comparison with the general population.

Objectives: To determine the prevalence of persistent HPV infection in an SSc patients series and its possible correlation with the disease clinical features.

Methods: The study retrospectively evaluated 52 consecutive female SSc patients (age 56.7±11.2SD years, disease duration 12.1±7.4SD years), classified according to the ACR/EULAR 2013 criteria, referring to our university-based Rheumatology Unit. Detection of HPV DNA and viral genotyping in cervical swabs were carried out. Moreover, abnormal Papanicolau test smears were classified using the Bethesda system.

Results: Fourteen (26.9%) patients presented a cervical swab positive for HPV infection, including 12 infected by high risk or probable-high risk HPV types. Six (11.5%) patients presented multiple infection (≥2 HPV types), including one case with high-grade intra-epithelial lesion.

Only tabagism was significantly correlated to HPV infection; namely, smoking habit was observed in 41.6% of SSc patients with and in 21.7% of those without HPV infection, respectively; $p=0.006$; moreover immunosuppressive therapies, namely mofetil mycophenolate, cyclophosphamide or rituximab, tended to be associated with HPV infection (presence/absence 21.4 vs 21.7%; $p=0.055$).

More interestingly, among SSc patients over 50, HPV infection was found in 9/38 (23.7%) individuals, a frequency markedly higher than that expected in age-matched general population from the same geographical area (5%).

Conclusions: Persistent HPV infection was observed in over a quarter of SSc patients, notably in women over 50. The HPV positivity was not related to SSc clinical features, while a significant association with tabagism and immunosuppressive therapies was evidenced. Considering the possible clinico-prognostic implication on the overall disease outcome, routinely gynaecological screening of SSc female patients is highly recommendable.

Disclosure of Interest: None declared

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AB0616 COST ANALYSIS RELATED TO SUBCUTANEOUS IMMUNOGLOBULINS IN PATIENTS WITH INFLAMMATORY MYOPATHIES AND IMMUNE-MEDIATED CHRONIC NEUROPATHIES. RESULTS OF AN OPEN LABEL STUDY

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Background: Intravenous Immunoglobulins (IVIg) represent a relevant treatment

option in various immune-mediated disorders such as idiopathic inflammatory muscle diseases (IIMD), immune-mediated chronic neuropathies (IMCN), hematologic autoimmune diseases, Still disease, Felty syndrome, systemic lupus erythematosus, vasculitis, some organ-specific autoimmune disease, and atopic diseases. The IVIg treatment is expensive and need of hospital-based assistance for administration; the recent availability of home-therapy with subcutaneous immunoglobulins (SCIg) may significantly reduce costs and improve the patient's quality of life.

Objectives: The primary objective was to perform an analysis of costs of SCIg administration in patients affected by IIMD or IMCN compared to that of previous IVIg treatments.

Methods: We prospectively evaluated 6 consecutive patients (3 males and 3 females, mean age 65.3 years, range 63 - 77), 2 affected by IIMD in the context of polymyositis and 4 by IMCN, 3 in the context of vasculitis and 1 in the context of undifferentiated connective tissue disease. All patients were previously treated with IVIg at the dosage of 2g/Kg monthly, (mean monthly dosage 143 g, range 98 - 160, average patient weight 71.5 kg, range 49 - 80), with good clinical and humoral response. After a mean therapy duration of 49.8 months (range 12 - 125) all patients were shifted to SCIg at the dosage of 10 g twice a week (80 g monthly). Each patient was followed-up by humoral and clinical evaluation, including Medical Research Council (MRC) score to quantify muscle strength and INCAT Sensory Score to evaluate sensory symptoms. The costs of the two therapeutic strategies were also compared, excluding indirect costs (absences from work and productivity losses, transport and parking, health care sector costs).

Results: In 5/6 patients, we observed the maintenance of clinical and humoral status after a mean follow-up of 21 months (range 4 - 51), in particular we observed a stability in MRC score in patients presenting loss of strenght and INCAT score in patients presenting sensory symptoms. Furthermore, the treatment with SCIg was well-accepted and preferred to IVIg by all patients. In one patient SCIg were discontinued after 2 weeks, because of the appearance of a haemorrhagic lesions nearby the injection site (in the same patient IVIg have been stopped because of a hypertensive crisis during the infusion). Direct cost associated to IVIg amount to 252€ for 5 g of immunoglobulins (7,056€ monthly, considering a protocol of 2 g/kg/monthly and a patient-weight of 70kg), while direct costs associated to SCIg (20g weekly) amount to 6,400€/monthly, with a saving of 656€/monthly and 7,872€/yearly. In our case-series the annual saving was 9,686.40€/patient (from 86,486.40€ to 76,800€, for IVIg and SCIg, respectively).

Conclusions: Our experience suggests that the shift to SCIg from IVIg in patients affected by IIMD and IMCN is feasible, cost-effective, safe and well-accepted by patients. Further studies are needed to evaluate the effectiveness of SCIg in first-line therapy of these diseases.

Disclosure of Interest: None declared

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AB0617 CLINICAL CHARACTERISTICS OF DIABETES MELLITUS PATIENTS WITH AND WITHOUT SCLERODEMA BUSCHKE SKIN DISORDER

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Background: Scleredema adutorum of Buschke is a rare disorder characterized by non-pitting hardening of the skin around the neck, shoulders, occasionally the face and the trunk. The most frequent form of scleredema is associated with diabetes mellitus (DM). The histopathologic features of scleredema are characterized by thickened collagen bundles within the reticular dermis that are separated by mucopolysaccharides (mainly mucin) containing fenestrations.

Objectives: To compare clinical data of patients with Buschke-scleredema-DM to diabetic patients without skin involvement patients (Control-DM) with a focus on the late vascular and neurological complications.

Methods: Clinical data of 105 diabetic patients were investigated based on their medical histories and physical examinations. All subjects met the following inclusion criteria: each of their disease duration time of DM had to be more than three years. Twenty-eight patients with Scleredema-DM were collected (three of type 1 and 25 of type 2 diabetes, 19 female, nine male; their mean age (±SD) was 63.0±9.3 and mean DM-duration time was 17.9±9.6 years). Seventy-seven consecutive, age and DM-duration matched patients without skin involvement were investigated as controls (nine patients with type 1 and 68 with type 2 M, 50 female, 27 male, their mean age was 63.3±11.9 and mean DM-duration time was 17.4±10.7 years). For statistical analysis Pearson's Chi-squared, Fisher and Mann-Whitney U tests were used.

Results: In the medical history of the Scleredema-DM group stroke occurred more frequently (8 of 28 cases, 28.6%) compared to the Control-DM group (5/77, 6.5%, $p<0.01$). There were no significant differences in the occurrence of myocardial infarction (5/28, 17.9% vs. 10/77 cases, 13.0%), nephropathy (5/28, 17.9% vs. 10/77 cases, 13.0%), retinopathy (13/28 cases 46.4% vs. 28/77, 36.3%) and of peripheral neuropathy (21/28 patients, 75.0% vs. 49/77, 63.6%) respectively. Higher level of cholesterol and triglycerides was present in the Scleredema-DM group compared to the Control-DM cases (mean cholesterol was: 5.7±1.5 mmol/l vs. 4.6±1.2 mmol/l, $p<0.01$; triglyceride: 2.3±1.1 mmol/l vs. 1.84±1.6 mmol/l