THU0409

MANAGEMENT OF SYSTEMIC SCLEROSIS (SSC) RELATED DIGITAL ULCERS (DU) IN EXPERT TERTIARY CENTRES: RESULTS FROM THE ANALYSIS OF THE MULTICENTRE OBSERVATIONAL REAL-LIFE DESSCIPHER/EUSTAR STUDY

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Background: In SSC, the management of DU is a real clinical challenge. It includes the use of vasoactive and vasodilating drugs, but no comparative studies between agents are available. DeSSCipher was the first European multicentre observational study with the aim to decipher the optimal management of SSC.

Objectives: To assess in expert centres the current therapeutic strategy for the management of SSC related DU.

Methods: Baseline demographic and clinical characteristics of patients enrolled in the DeSSCipher/EUSTAR ulcer study and detailed data regarding DU were analysed.

Results: There were 1823 patients enrolled in this study. 277 (15.2%) presented DU at the enrolment visit, 628 (34.4%) had previous DU and 918 (50.4%) had never experienced DU. Patients with DU (current or previous) were more frequently anti-Scl70 positive, had more frequently the diffuse cutaneous subset (40.8% vs 26.7% ($p<0.000$)), gastro-esophageal symptoms (70% vs 63.4% ($p=0.002$)) and lung fibrosis on lung Rx or HRCT (65.7% vs 54% ($p=0.001$)) compared to patients without DU. There were no significant differences in the prevalence of pulmonary hypertension (7.3% patients with DU vs 5.3% patients without DU, $p=0.87$). Treatment of patients with and without DU is shown in table 1.

Abstract THU0409 – Table 1. Treatment of patients with and without DU

	Patients with DU (current or previous) 905 patients	Patients without DU (never developed) 918 patients
Calcium channel blockers	601 (66.4%)	704 (76.9%)* ($p<0.000$)
Bosentan	199 (22%)	41 (4.5%)* ($p<0.000$)
Sildenafil	120 (13.3%)	57 (6.2%)* ($p<0.000$)
Bosentan+Sildenafil	85 (9.4%)	15 (1.6%)* ($p<0.000$)
Iloprost iv in the last 3 months	306 (33.8%)	74 (8.1%)* ($p<0.000$)
No vasodilating therapy	48 (5.3%)	97 (10.6%)* ($p<0.000$)
Immunosuppressants	482 (53.3%)	560 (61%)

Information on recurrent DU were available for 779 (86.1%) of patients with DU. Treatment of patients with and without recurrent DU is shown in table 2.

Abstract THU0409 – Table 2. Treatment of patients with and without recurrent DU

	Patients with recurrent DU (428)	Patients without recurrent DU (351)
Calcium channel blockers	258 (60.3%)	255 (72.7%)* ($p<0.000$)
Bosentan	105 (24.5%)	70 (19.9%)
Sildenafil	58 (13.6%)	45 (12.8%)
Bosentan+Sildenafil	323 (75.5%)	87 (24.7%)* ($p<0.000$)
Iloprost iv in the last 3 months	212 (49.5%)	77 (22%)* ($p<0.000$)
No vasodilating therapy ^a	27 (6.3%)	14 (3.9%)
Immunosuppressants	222 (51.9%)	226 (64.3%)

Conclusions: 90% of SSC patients were on vasodilating and/or vasoactive treatment regardless of the history/presence of DU. Recurrent DU were treated

aggressively, using in 75% of cases Bosentan and Sildenafil combination therapy. Our data indicate frequent use of Sildenafil and Bosentan for DU management in specialised centres, especially for recurrent DU.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3771

THU0410

SURVIVAL OF PATIENTS WITH MUSCLE BIOPSY PROVEN IDIOPATHIC INFLAMMATORY MYOPATHY BASED ON A STUDY IN A TERTIARY UNIVERSITY CENTRE

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Background: Idiopathic inflammatory myopathies (IIM) are characterised by muscle weakness due to muscle inflammation, various organ involvements and the presence of certain specific autoantibodies.

Objectives: To assess survival and characterise subsets based on muscle biopsy and myositis specific autoantibodies.

Methods: Eighty-two patients with muscle biopsy proven IIM were included in the study. Muscle biopsy was reevaluated and categorized by the same investigator (EP). All cases had myositis specific (MSA) and myositis associated (MAA) antibody tests. The MSAs and MAAs (Jo-1, PL-7, PL-12, Mi-2, SRP, Pm-Scl, Ku, ribosomal, AMA-M2) were tested with Western-blot.

Dermatomyositis/DM/, polymyositis/PM/, juvenile PM/DM, inclusion body myositis/IBM/, overlap myositis/OM/ and immune mediated necrotizing myopathy/IMNM/ were identified based on clinical data, immunoserology and muscle biopsy. Patients were treated with glucocorticoids/cytostatics, interstitial lung disease was treated with pulse cyclophosphamide in 15/43 cases. Survival analysis was performed by Kaplan Meier test.

Results: Fifty-nine women and 23 men with a mean age of 49.3 ± 14.6 years were included. Mean follow-up of the patients was 7.5 ± 4.5 years. Interstitial lung disease (ILD) (51.2%), arthritis (51.2%), Raynaud's phenomenon (42.7%), skin symptoms (45.1%), dysphagia (24.4%) and significant cardiac involvement (15.9%) were the most prevalent disease manifestations. 15 cases were associated with malignancies.

The distribution of myositis subsets is as follows: 26.8% ($n=22$) PM, 30.5% ($n=25$) DM, 1.2% ($n=1$) juvenile PM/DM, 8.5% ($n=7$) IBM, 22% ($n=18$) OM, and 11% ($n=9$) IMNM.

Malignancy was most frequently associated with IMNM (7 out of 9 patients).

Altogether 18 patients died from which 15 deaths can be connected to myositis related events. Eight patients died of malignancies (4 in the IMNM, 2 in the PM and 2 in the DM group), 5 patients due to cardiac events (heart failure, arrhythmia), 2 due to lung fibrosis and 3 by unknown causes. The worst prognosis with a 10 year survival of 31% was in the IMNM subgroup ($p<0.01$), followed by patients with PM (68%), IBM (84%) OM (85.1%) and DM (85.3%). Mi-2 positive patients had a favourable prognosis with a 10 year survival of 100. Patients with muscle histology corresponding with IMNM had the worst prognosis (10 year survival of 31.1%), followed by PM (76%), DM and IBM (85.7% each). Non specific muscle changes unclassifiable to any of the previous groups were associated with a relatively favourable prognosis (5 year survival of 80%) ($p<0.01$).

Patients with antisynthetase antibody-positivity had worse prognosis compared with patients with other antibodies or no identifiable antibodies (10 year survival of 55%, $n=16$) ($p<0.05$). When comparing patients with MSA or MAA, the worst prognosis was seen in patients with both MSA and MAA positivity (10 year survival of 35.6%, $n=10$).

Conclusions: The worst survivals were seen in the IMNM and PM groups, due to the high frequency of the underlying malignancies and cardiac manifestations. Although ILD was the most frequent involvement, it was not a major determinant of outcome.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2405

THU0411

MYASTHENIA GRAVIS WITHOUT THYMIC PATHOLOGY AND POLYMYOSITIS: A RARE ASSOCIATION

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Background: Myasthenia gravis(MG) is an autoimmune disease frequently associated with antibodies against the acetyl-choline receptor. These antibodies contribute to the characteristic defects in neuromuscular transmission. Inflammatory myopathies, as polymyositis(PM), are immune-mediated neuromuscular

diseases. PM and MG present both with muscle weakness and other similar features; electrophysiological and laboratory features of each of them are distinct. In Literature there are only few reports about PM and MG association

Objectives: To evaluate the prevalence of MG in patients with PM in our case series

Methods: We enrolled patients with PM/DM visited in our Centre in past 10 years; diagnoses of PM/DM were based on Bohan and Peter criteria. The follow-up was conducted until December 2017

Results: We made 17 PM/DM diagnosis:14 F and only 3 M aged 41–85 years (mean 65 y). We found 6 patients (42.8%) with association of PM and MG. They are all F, aged 51–78 years (mean 61 y) who developed inflammatory myositis confirmed by increasing of CK, EMG, autoantibodies pattern positivity and deltoid biopsy. Paraneoplastic, post-infectious or post-vaccinal syndromes was excluded. At the onset all presented progressive proximal muscle weakness and pain and asthenia. After initial treatment with oral corticosteroids (0.5–1 mg/kg/day methylprednisolone) a minimal response was observed only as improvement of asthenia and decreasing of CK levels. After one month of therapy 2 patients developed a bilateral palpebral ptosis, one dysphagia and mild dyspnea, one a severe intestinal pseudo-obstruction, 2 a mild dysarthria, ipovision and a worsening of muscular tone. Pyridostigmine test was positive in all patients; antiAChR antibodies levels were high. We started high doses corticosteroids (methylprednisolone 500–1000 mg/day for 5 days) and pyridostigmine (180–240 mg/day) with smart improvement. After this we introduced an immunosuppressant: azathioprine in 3 patients, mycophenolate mofetil in 4 patients. At the same time, because of the severity of the disease, monthly cycles of high doses IgV (20 g/kg in 5 days) were performed in 5 patients. A stable remission was achieved and maintained in all patients

Conclusions: This is one of the largest case series of patients with PM/DM-MG overlap. Our findings suggest that this association is not so rare and that patients affected by PM presenting palpebral ptosis, diplopia, gastrointestinal or oral symptoms, bulbar symptoms, weakness, asthenia, should be evaluated to exclude a concomitant MG, despite the absence of thymic pathology. A patient with PM-MG overlap should allow us for proper management of both conditions. This may include a more adequate therapy providing simultaneous association between immunosuppressant, pyridostigmine and, if necessary, a short time of high doses IgV therapy

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3555

THU0412

ABSOLUTE REDUCTION OF PERIPHERAL CD4 + REGULATORY T CELL SUBSET OF PATIENTS WITH SYSTEMIC SCLEROSIS AND ITS RESTORATION BY SHORT-TERM AND LOW DOSE IL-2 TREATMENT

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Background: Systemic sclerosis (SSc) is a chronic inflammatory disease with complex pathogenesis. The role of regulatory T cells (Tregs) in the development of SSc has started being studied during the last decade with new aspects being disclosed continuously. Although there is a general agreement in the medical literature regarding the decreased functional capacity of circulating Tregs in SSc, the alteration of absolute number of Treg cells as well as other CD4 + T lymphocyte subsets in SSc is still unclear.

Objectives: The aim of the present study was to explore the absolute number status of CD4 + T subsets in peripheral blood of patients with SSc using our modified flow cytometric method and investigate whether the imbalance of Th17 and Treg cells can be corrected by supplementing low dose interleukin -2 (IL-2).

Methods: The peripheral CD4 + T subsets from 54 patients with SSc and 30 healthy control subjects were analysed. The patients were divided into the untreated group (n=29) and treated group (n=25). The patients were also divided into group A (n=28) who only used low-dose glucocorticoids (GCS), and group B (n=26) who also used immunosuppressant cyclophosphamide (CYC), methotrexate (MTX), leflunomide (LEF) or mycophenolate mofetil (MMF). In addition, 21 patients from 54 patients, given a small dose of IL-2 (50WU) treatment for a 5 day

course, divided into pre-treatment group and post-treatment group. Directly using the results from flow cytometry combined with internal standard beads, absolute number of peripheral CD4 + T subsets from the subjects in each group were calculated.

Results: Although there were some changes among CD4 + T cell subsets in peripheral blood from these SSc patients, the major alteration was the reductions of Treg cell absolute number. Compared with the normal controls, the number of CD4 + CD25 + FOXP3 + Treg cells were significantly decreased in all patients (p=0.001), in untreated group (p=0.029), in treated group (p=0.029), in group A (p=0.006) and in group B (p=0.004). The ratio of Th17/Treg in total patients (p=0.008) and group B (p=0.001) were significantly higher than that in normal control group, and the group B was significantly higher than the group A (p=0.032). Moreover, the number of Th17 cells in group B was significantly higher than that in group A (p=0.023). After IL-2 treatment, the absolute number of CD4 + CD25 + FOXP3 + Treg cells (p<0.001) were significantly increased, while the number of Th1, Th2 and Th17 cells were slightly higher than those before treatment with IL-2 (p>0.05). Since Th17 cells increases significantly lower than Treg cells, so their ratio decreases significantly (p=0.001) to get re-balance.

Abstract THU0412 – Figure 1. Comparison of the levels of CD4+ T lymphocyte subgroups among different groups. (A and D) The percentage of Th2 cells were significantly increased in untreated group and Group A compared with healthy controls. (B and E) The number of CD4+CD25+FOXP3+ Treg cells decreased in patients with SSc, whether or not they use immunosuppressive agents. (C and F) The ratio of Th17/Treg cells was found to be significantly increased in Group A, as well as between Group B and Group A. *P<0.05; **P<0.01; ***P<0.001.

Abstract THU0412 – Figure 2. Comparison of the levels of CD4+ T lymphocyte subgroups among different groups as well as before and after IL-2 treatments. (A) The percentage of Th2 cell were significantly increased before and after IL-2 treatment compared with healthy controls, and the percentage of Treg cells significantly increased after IL-2 treatment. (B) The number of CD4+CD25+FOXP3+ Treg cells decreased in patients before IL-2 treatment, but increased significantly after IL-2 treatment (p<0.05); while Th1, Th2 and Th17 cells after IL-2 treatment were slightly higher than those before treatment (p>0.05). (C) The ratio of Th17/Treg cells were found to be significantly increased after IL-2 treatment. *P<0.05, **P<0.01, ***P<0.001.

Conclusions: The absolute number of peripheral CD4 + CD25 + FOXP3 + Treg cells decreased in untreated patients, indicating that this reduction arising from the disease itself. Our findings suggest that SSc progression is associated with the absolute decrease of peripheral Treg cells. Although there was no statistically