**THU0345**

**EFFECT OF THE LONG-TERM RITUXIMAB TREATMENT ON B-LYMPHOCYTES AND ANTINUCLEAR AUTOANTIBODY LEVEL IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Anti-B-cell therapy is seen as a promising therapeutic option for systemic sclerosis (SSc). The study of antinuclear antibody levels during treatment with rituximab (RTX) in patients (pts) with SSc could have theoretical and practical interest.

**Objectives:** To assess the changes in ANA, anti-topoisomerase-1 (Scl-70) levels and B-lymphocytes (B-lymph) count during RTX therapy during prospective observation.

**Methods:** This prospective study included 88 pts with SSc, 83% of them had interstitial lung disease and 75% had positive Scl-70 autoantibody. The mean age was 47 yrs (17-71), female-73 pts (83%), the diffuse cutaneous subset of SSc was 11,7±4,4 yrs. All patients received prednisolone at a dose of 11,7±4,4 mg, immunosuppressants received 42% of them. Patients were divided into groups depending on the duration of the disease: group 1 (n=33) - up to 3 yrs, group 2 (n=25) - from 3 to 6 yrs, group 3 (n=30) - more than 6 yrs (6-18yrs). The results are presented in the form of mean values, median, upper and lower quartiles.

**Results:** Parallel to clinical improvement in most patients (96%) we found percentile changes in many parameters at the end of the study compared to the baseline. The Rodnan skin score decreased from 11,21±9,33 to 6,19±4,74 (p<0,001). The disease activity index (ESCSG-AI) decreased from 2,91±1,74 to 1,36±1,15 (p<0,001). Forced vital capacity %, predicted, increased from 76,35±19,65 to 84,37±21,04 (p<0,001). Diffusing capacity for carbon monoxide %, predicted, increased from 45,56±17,72 to 47,62±16,96 (p<0,019). The dose of prednisolone decreased from 11,7±4,4 mg to 9,2±3,2 mg (p<0,001). The absolute number of B-lymphocytes (B-lymph) count during RTX therapy during prospective observation, the number of pts with high (1/640-1/1280) ANA titers decreased in all groups. At baseline 63 pts (75%), had positive Scl-70 with equal levels in all groups. At the end of the study level of Scl-70 decreased from 125,02±89,12 to 84,37±21,04 (p<0,001). The pts of the group 1 showed the highest values of B-lymph at baseline and level of B-lymph decreased from 0,326±0,22 to 0,017±0,07 (Δ0,318) at the end of the study. In group 2 depletion was less pronounced (from 0,151±0,16 to 0,019±0,07 (Δ0,131), p<0,001) and the lowest depletion was observed in group 3 (from 0,15±0,16 to 0,01±0,07 (Δ0,143), p<0,001) for all groups. An initially positive ANA was found in 92% of pts (range 1/320-1/1280). During observation, the number of pts with high (1/640-1/1280) ANA titers decreased from 70 to 41 (p<0,001), and the average level of ANA decreased by 30-40% in all groups. At baseline 63 pts (75%), had positive Scl-70 with equal levels in all groups. At the end of the study level of Scl-70 decreased from 125,02±89,12 to 108,6±86,89 units/ml (p<0,007). A negative correlation was found between the duration of the disease and ANA (r = -0,54; p<0,003) and Scl-70 (r = -0,44; p=0,017).

**Conclusion:** In our study a clinical improvement was shown in most pts at the long-term complex therapy, including RTM. We found a significant decrease in the absolute number of B-lymph, as well as decrease of ANA and Scl-70 levels. Initially with pts a short duration of the disease had a higher level of B-lymph and in these pts depletion was more pronounced, compared to those with a longer duration of the disease. However, the level of Scl-70 and ANA decreased both to those who started RTX therapy at an early stage of the disease (<3yrs) and to those who had a long disease duration.

**Disclosure of Interests:** None declared

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**THU0346**

**SARC-F PERFORMANCE FOR SARCOPENIA SCREENING IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Because the method of diagnosing sarcopenia is complex and is considered to be difficult to introduce into routine practice, the European Working Group on Sarcopenia in Older People’s (EWGSOP) recommends use of the SARC-F questionnaire as a way to introduce assessment and treatment of sarcopenia into clinical practice. Only recently, some studies have focused their attention on the presence of sarcopenia in systemic sclerosis (SSc) and there is no data about the performance of SARC-F in this population.

**Objectives:** To test the diagnostic properties of the SARC-F questionnaire for sarcopenia screening in SSc patients.

**Methods:** Cross-sectional study, including 94 SSc patients assessed by clinical evaluation, laboratory and pulmonary function tests. Sarcopenia was evaluated using the EWGSOP2 diagnostic criteria updated in 2019 (EWGSOP2): dual-energy X-ray absorptiometry, handgrip strength, and short physical performance battery (SPPB). Participants also completed the SARC-F questionnaire. The questionnaires’ performances were evaluated through receiver operating characteristic (ROC) curves and standard measures of diagnostic accuracy were computed using the EWGSOP2 criteria as the gold standard for diagnosis of sarcopenia.

**Results:** Sarcopenia was identified in 15 (15,9%) SSc patients by the EWGSOP2 criteria. Area under the ROC curve of SARC-F scoring for sarcopenia was 0.588 (95% confidence interval [CI] 0.482, 0.688) (figure 1). The results of sensitivity, specificity, positive likelihood ratio (PLR) and negative likelihood ratio (NLR) with the EWGSOP2 criteria as the reference standard were 35.71 (95% CI, 12.76-64.86), 81.01 (95% CI, 70.62-88.97), 1.88 (95% CI, 0.81-4.35) and 0.79 (95% CI, 0.53-1.19), respectively. The optimal cut-off point of SARC-F in our sample was ≥ 4 (Youden index: 0.21), the same cut-off point recommended in the literature. Only 6 (40%) out of the 15 participants with sarcopenia were identified by the SARC-F questionnaire in our population. However, the SARC-F properly identified 4 out of 5 patients who had severe sarcopenia.

**Conclusion:** This is the first study to evaluate the performance of SARC-F questionnaire for sarcopenia screening in patients with SSc. Although it appropriately identifies severe cases of sarcopenia, the SARC-F alone may not be an adequate screening tool in high-risk populations, such as SSc; that may benefit from early intervention and treatment.

**References:**


**Figure 1. Receiver operating characteristic (ROC) curve analyze of SARC-F screening for sarcopenia (n=94). Discrimination was quantified using the area under the curve(AUC). The optimal cut-off point of SARC-F was ≥ 4.**

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**THU0347**

**CLINICAL DESCRIPTION OF A COHORT OF PATIENTS WITH SCLEROTIC-TYPE CHRONIC GRAFT-VERSUS-HOST DISEASE TREATED IN A MULTIDISCIPLINARY PRACTICE**

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Background: Graft versus host disease is the most frequent complication after allogeneic transplantation of hematopoietic progenitors. Its chronic form usually involves a multisystemic syndrome that reflects a complex immune response with varying degrees of inflammation, immune dysregulation and fibrosis, responsible for the characteristic clinical manifestations of the disease. Joint, muscular and fascial involvement represents one of the areas, often unnoticed or poorly evaluated, that negatively impacts the physical function and quality of life of these patients.

Objectives: Describe the presence of musculoskeletal manifestations and their clinical characteristics in patients with chronic GVHD (cGVHD) evaluated in a multidisciplinary consultation

Methods: Descriptive and retrospective observational study to detail the initial presence and during the follow-up of diagnostic and nonspecific musculoskeletal manifestations of cGVHD in a cohort of 103 patients included in the database. The clinical characteristics of 68 patients with a defined diagnosis of sclerotic cGVHD are described. Demographic variables are collected along with clinical conditions about transplant and in a systematic way the assessment according to diagnostic criteria of the American National Institute of Health 2015 highlighting: range of motion scale and photographic range of motion (P-ROM) scale in shoulders, elbows, hands and ankles; and laboratory data: presence of eosinophilia and autoantibodies. Descriptive and frequency statistical analysis was done using Microsoft Office Excel 2007.

Results: Sixty-eight (66%) patients meet diagnostic criteria for sclerotic cGVHD, during follow-up. Forty-five (66.2%) women and 23 (33.8%) men, with a mean age of 54.5 years (range 10-78), Acute myeloid leukemia was the reason for transplant in 20 (29.4%) followed by non-Hodgkin lymphoma in 15 (16.2%). In 40 (58.7%) patients it was performed from a related donor and with reduced intensity conditioning in 43 (63.2%). In one patient the source of hematopoietic progenitors was bone marrow (rest peripheral blood). The average time from transplant to diagnosis was 29.5 months (range 4 -168). Twelve (17.6%) patients presented isolated joint/fascial involvement without objective skin involvement (Table 1).

Table 1. Clinical features of the sclerotic joint/fascial chronic GVHD cohort (N= 68)

<table>
<thead>
<tr>
<th>Unspecific musculoskeletal symptoms:</th>
<th>46 (67.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Artronymatia</td>
<td>39 (57.3%)</td>
</tr>
<tr>
<td>- Edema</td>
<td>13 (19%)</td>
</tr>
<tr>
<td>- Stiffness</td>
<td>4 (5.8%)</td>
</tr>
<tr>
<td>Fascitis/contractures</td>
<td>28 (41.2%)</td>
</tr>
<tr>
<td>Restricted ROM1</td>
<td>23 (33.8%)</td>
</tr>
<tr>
<td>- Mild/Moderate/Severe</td>
<td>34 (50.2%)</td>
</tr>
<tr>
<td>Impaired mobility</td>
<td>26 (38.2%)</td>
</tr>
<tr>
<td>- Shoulders</td>
<td>23 (33.8%)</td>
</tr>
<tr>
<td>- Elbows</td>
<td>21 (30.8%)</td>
</tr>
<tr>
<td>- Wrist/fingers</td>
<td>29 (42.6%)</td>
</tr>
<tr>
<td>- Ankles</td>
<td>21 (30.8%)</td>
</tr>
<tr>
<td>Sclerodermatous involvement</td>
<td></td>
</tr>
<tr>
<td>- Superficial/deep</td>
<td>6 (8.8%)</td>
</tr>
<tr>
<td>- Mixed (sclerodermaform + lichenoid)</td>
<td>7 (10.3%)</td>
</tr>
<tr>
<td>- Overlapping skin sclerosis</td>
<td>20 (29.4%)</td>
</tr>
<tr>
<td>NIH Global Score</td>
<td>25 (36.7%)</td>
</tr>
<tr>
<td>- Mild/Moderate/Severe</td>
<td>13 (19.2%)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>21 (30.8%)</td>
</tr>
<tr>
<td>Autoantibodies</td>
<td>14 (20.6%)</td>
</tr>
</tbody>
</table>

1ROM (range of motion) 2NIH: National Institute of Health

Conclusion: Joint involvement secondary to sclerosis is very common in our cohort, mainly of the dorsal wrist flexion with deleterious repercussion on physical function. It needs to be recognized and evaluated early with validated scales. The search for new biomarkers associated with fibrosis, the use of advanced imaging techniques and the multidisciplinary approach can help improve the prognosis of patients with cGVHD.

References:

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THU0348

ALTERED IMMUNE RECOGNITION OF SPECIFIC GUT BACTERIA BY IMMUNOGLOBULINS IN EARLY SYSTEMIC SCLEROSIS

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Background: Gastrointestinal tract (GIT) involvement is highly prevalent in systemic sclerosis (SSc) and associates with GIT symptoms that are present early and progress over time. Changes in gut microbiota are often reported in inflammatory disease settings but whether GIT symptoms associate with altered immune recognition of specific gut bacteria in early SSc is unknown.

Objectives: Here, we profiled Ig coating patterns of gut bacteria in early disease from two well-characterized SSc cohorts to determine if the pattern and extent of bacterial immunoglobulin (Ig) coating differs in early SSc.

Methods: We collected fecal material from early SSc patients (<36 months from time of diagnosis) at Oslo and Lund University Hospitals and from healthy age and gender matched controls (HC). To assess whether adaptive immunity was triggered against gut microbiota in early disease, we sorted and sequenced IgA, IgM and IgG coated bacteria from fecal samples by flow cytometry and performed 16s rRNA sequencing to compare the relative Ig coating of early SSc patients to HC. Data was resolved to the family level, rarefied to 5101 reads and converted to relative abundance. Taxonomic profiles, relative abundance, IgA, IgM and IgG coating patterns and extent of Ig coating were assessed. Unadjusted p-values <0.05 were defined as significant.

Results: We included 50 SSc patients (26 from Oslo, 24 from Lund) with early SSc and 9 gender and age matched HC. Mean age of SSc patients at time of inclusion was 53 years, mean time since diagnosis was 13 months; 82% were female, 61% had limited cutaneous SSc and 43% were anti-centromere antibody positive. In all, 82% were treatment naïve while 18% had received either cyclophosphamide or mycophenolate mofetil immunosuppressants. We found increased relative abundance of IgA coated Desulfovibrioaceae in both SSc cohorts compared to HC and increased IgM and IgG coating of Veillonellaceae and Streptococcaceae (Figure 1). All of these bacteria have previously been associated with other autoimmune diseases or pro-inflammatory status; Desulfovibrioaceae to immune activation in the gut, and Veillonellaceae and Streptococcaceae to other chronic inflammatory and fibrotic conditions. While abundance of IgA coated Desulfovibrioaceae was higher in cyclophosphamide or mycophenolate mofetil-treated SSc patients than untreated patients, Veillonellaceae and Streptococcaceae were not affected by treatment. A lower abundance of IgA and IgM coated Akkermansiaceae; and IgM and IgG coated Bifidobacteriaceae was detected in treated compared to treatment naïve early SSc patients (Figure 2).

Figure 1: Phylogenetic tree of gut bacteria based on the 16S rRNA gene sequence showing relative abundance of IgA, IgM and IgG coated gut bacteria on the Lund (SK) and Oslo (SK) early SSc cohorts compared to healthy controls (HC) with high abundant gut bacteria in orange and low abundant gut bacteria in green

Figure 2: Phylogenetic tree of gut bacteria based on the 16S rRNA gene sequence showing relative abundance of IgA, IgM and IgG coated gut bacteria on the Lund (SK) and Oslo (SK) early SSc patients with early disease with high abundant gut bacteria in orange and low abundant gut bacteria in green

Conclusion: We find the pattern and extent of Ig coating to inflammatory-associate gut bacteria differs between treatment-naïve, early SSc patients treated with cyclophosphamide or mycophenolate mofetil and HC which suggests...