AB0601

RAPID AND SUSTAINED EFFICACY OF AN INDUCTION TREATMENT WITH A TRIPLE THERAPY INCLUDING HIGH-DOSE INTRAVENOUS IMMUNOGLOBULINS, METHOTREXATE AND GLUCOCORTICOIDS IN ANTI-3-HYDROXY-3-METHYLGLUTARYL-COENZYME A REDUCTASE MYOPATHY

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Background: Anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) myopathy is a new entity, which has been clearly associated to statin use, even if it can be diagnosed in patients without a history of exposure to statin or even in the childhood (1).

Objectives: The aim of the study is to describe the efficacy of a triple therapy regimen consisting in high-doses of intravenous immunoglobulins (IVIG), methotrexate (MTX), and glucocorticoids (GC) in 16 patients with Anti-HMGCR myopathy enrolled in 6 specialized centres.

Methods: A total of 16 patients with anti-HMGCR myopathy (7 females; 9 males) were collected. Mean ($\pm$ standard deviation) age at the onset of disease was 72.4 ± 10.3 years old. All patients were diagnosed having anti-HMGCR myopathy [anti-HMGCR antibodies were measured by chemiluminescence assay (Bio-Flash, Inova, CA)] (2). Median follow-up was 29.5 months (interquartile range: 15.75-60 months). Anti-HMGCR antibodies were available in the follow-up in 8/16 patients.

Results: Thirteen out of 16 patients (81.3%) had been exposed to statin (1/13 to red rice), 3/16 (18.7%) were not exposed. As induction therapy, 11/16 patients have been treated with triple therapy (high-dose IVIG, MTX and GC), 2/16 with double therapy (high-dose IVIG and GC), 2/16 have been treated with GC alone, the patient exposed to red rice resolved only with red rice suspension. Clinical remission and normalization of CPK values within month +24 were obtained in all the patients. All the patients were in remission at the last follow-up. Gradual improvement started soon from the first month, and among the 13 patients treated with an aggressive immunosuppressive therapy including IVIG (13/13), GC (13/13) and methotrexate (11/13), 9/13 normalized the CPK value within 6 months. Clinical and laboratory response was accompanied by significant decrease or normalization of the anti-HMGCR antibody titer. All the patients were either not taking GC (56.3%), or were taking low doses of GC (43.7%) at the last follow-up. Four patients had stopped GC within 6 months. No serious side effects were recorded. After persistent remission, a maintenance immunosuppressive therapy was then administered. Only 3 relapses in 3 different cases were recorded, all of them during drug-free remission in long-term follow-up. Reinduction was again effective in all.

Conclusion: Anti-HMGCR myopathy is a rare and serious myopathy which usually affects older people during statin treatment. After statin suspension, a rapid and sustained remission can be achieved by induction with a triple aggressive therapy consisting in medium-to high doses of GC, high-dose IVIG, and MTX (3). GC should be tapered as soon as possible. Relapse appears infrequent during maintenance treatment. Monitoring anti-HMGCR antibody titer may be clinically relevant.

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AB0602

SYSTEMIC SCLEROSIS: SUBCLINICAL ATHEROSCLEROSIS AND MORBIMORTALITY.

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Background: Rheumatic diseases are associated with accelerated atherosclerosis, and an increase in cardiovascular morbidity and mortality. This process is mediated by classic cardiovascular risk factors (CVRF), chronic inflammation and atherogenic treatments such as corticosteroids. In Systemic Sclerosis (SSc) cardiovascular complications have increased in recent decades, although the studies on subclinical atherosclerosis (sATS) in SSc show discordant results.

Objectives: To evaluate prospectively the relationship between subclinical atherosclerosis, cardiovascular morbidity and mortality in patients with SSc.

Methods: 120 consecutive patients with SSc who attended their medical regular review during November and December 2011 were included. We evaluated the presence of plaques and measured the right CCA IMT by B doppler US for the detection of sATS (IMT > 0.9mm and/or presence of plaque), review of classic CVRF and estimation of Medsger severity and EUSTAR activity index. Patients have been followed for 8 years, with at least annual consultation. In retrospect, the SCTC damage index, published in 2019, was obtained at the time of inclusion in the study. The clinical characteristics of the patients are collected since 1990 in a Prospective Longitudinal Observational Study (PLOS). Descriptive analysis was performed, using contingency tables for qualitative variables, and comparison of means for quantitative variables. The relationship between clinical characteristics, mortality, cardiovascular events (CVE), activity, severity and damage index, and sATS, was analyzed using binary logistic regression, adjusting for age and sex.

Results: 120 patients with SSc were included (93% female, age 60 ± 12 years). 42 of these patients (35%) had subclinical atherosclerosis. Age was statistically significant higher in patients with sATS compared to those without it (67.9 ± 11.5 vs. 56.1 ± 10.4 years, $p < 0.001$). We found no differences between groups in activity, damage and severity index (Table 1). Patients with sATS had higher levels of ESR and CRP, but the difference was not confirmed after adjusting for age (*). During the 8 years of follow-up, 9 CVE in 7 patients (5.8%): three myocardial infarction, one transient ischemic accident, one angor, one intermittent claudication and three refractory heart failure. The incidence of severe CVE was more than double in patients with sATS (10.25% vs. 3.7%), but the difference was not significant. We found no relationship between the mortality of any cause, or the secondary to CVE, with sATS, in the 32 patients who died during the follow-up, 3 due to CVE (9.4%). The results are similar when we analyze only the presence of plaques.

Table 1. Relationship between clinical characteristics and activity, severity and damage index with the presence of accelerated atheromatosis.

	Absent n=78	Present n=42	
Diffuse cutaneous SSc	37.18%	26.12%	NS
mRSS	7.71 ± 6.32	6.38 ± 4.92	NS
High mRSS	9.69 ± 8.33	7.57 ± 4.74	NS
Arthritis	32.05%	28.57%	NS
Lung involvement	33.33%	30.95%	NS
PAH	10.26%	7.14%	NS
Cardiac involvement	15.38%	9.52%	NS
Digital ulcers	35.90%	35.83%	NS
AntiScl70	25.64%	21.43%	NS
ESR	20.12 ± 13.77	26.88 ± 17.25	$p = 0.037^*$
CRP	0.65 ± 0.61	0.89 ± 0.7	$p = 0.041^*$
High activity index	11.54%	19.05%	NS
Damage index	6.67 ± 5.56	5.62 ± 4.9	NS
Σ Medsger index	5.37 ± 3.5	5.05 ± 3.45	NS

Conclusion: In our study subclinical atherosclerosis is not related to higher mortality in patients with SSc, but it does seem to influence the occurrence of cardiovascular events. In addition, our results suggest that SSc does not influence the onset of accelerated atheromatosis.

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AB0603 PDGFA AS A POTENTIAL BLOOD MARKER IN DSSC

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Background: PDGF is a potential important factor in the pathogenesis of scleroderma. PDGF is almost undetectable in healthy skin or lung. Immunohistochemical studies have revealed increased presence of PDGF α and PDGF β receptors in scleroderma skin biopsies.

Objectives: The aim of this study was to determine the mRNA level of *IFN α 1*, *IL-4*, *TGF β 1*, *TGF β 2*, *PDGF α* , *PDGF β* , *TNF α* in whole blood in SSc patients in the aspect of clinical

Methods: A group of 14 patients (50% were women) with systemic sclerosis based on EULAR / ACR 2013 criteria was included in the study. The modified Rodnan Skin Score (mRSS) was evaluated by same assistant at the beginning of the study and six months later. DLCO, HRCT, echocardiography and NFC were measured. Gene expression was determined using validated TaqMan probes in qPCR. Constitutive mRNA level of selected genes was analyzed using Δ Ct method. Comparison between different groups of patients was determined using non-parametric Mann-Whitney U test. Correlation was analyzed using non-parametric Spearman test.

Results: The mean age of the patients was 60 ± 15.66 . 100% of patients had organ involvement as pulmonary fibrosis. 78% - had active changes -features of ground glass. 64% of patients had mild mRSS-1-10 skin involvement, 36% had moderate to severe skin involvement. In SSc patients *TGF β 1* and *IFN α 1* revealed the highest level of expression in comparison to other analyzed genes. Additionally, very high and significant correlation between *TNF α* and *TGF β 1* ($r=0.7$ $p=0.004$) has been noted. High and significant correlation between mRNA *PDGF β* and *TNF α* levels have been observed. We did not reveal significant differences in analyzed genes expression when compare limited and diffuse SSc. Nevertheless, patients with dSSc were characterized by higher level of *IFN α 1* (almost 2 times) and *TGF β 1*. On the border of significance higher *PDGF α* mRNA level was observed in dSSc patients when compared to ISSc. Average *PDGF α* expression is higher in SSc patients with Scl70 positive than in patients without Scl70 ($p=0.04$).

In the aspect of clinical parameters, patients with ESR ≤ 12 mm/h revealed almost 6 times higher level of *IFN α 1* ($p=0.01$) in comparison to the patient with ESR >12 mm/h. Patients with mRSS above 10 points revealed significantly higher of *PDGF α* expression in comparison to patients with mRSS ≤ 10 ($p=0.04$). In these group of patients CRP and ESR were not different significantly.

In the case of patients with active fibrosis (ground glass) in HRCT *IFN α 1* expression was almost 2.5-times higher than in patients with HRCT non-active. Significantly higher *PDGF α* has been revealed in patients with active HRCT when compared with patient with non-active HRCT. Nevertheless these two groups did not differ in ESR or OB parameter.

SSc patients in active phase of NFC revealed almost 3 times higher level of *IFN α 1* expression in comparison with the patient in late phase.

Conclusion: The mRNA level of *PDGF α* may be a potential blood marker to predict worse prognosis in scleroderma

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AB0604 EVALUATION OF PATIENTS WITH ANTISYNTHEASE SYNDROME AND INTERSTITIAL LUNG DISEASE BASED ON THE RADIOLOGICAL PATTERN

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Background: Antisynthetase syndrome is an autoimmune rheumatologic disease characterized by the presence of specific antibodies that are known as antisynthetase antibodies and with a varied clinic, including arthritis, myositis or

interstitial lung disease (ILD), among others. ILD is the manifestation that associates the highest morbi / mortality and can occur with different characteristic radiological patterns: usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), organized pneumonia (OP)

Objectives: Describe the clinical, serological and prognostic characteristics of patients with antisynthetase syndrome with interstitial pulmonary involvement (ILD) based on their radiological pattern.

Methods: Retrospective descriptive study of patients with a clinical diagnosis of antisynthetase syndrome in which they show positive for some antisynthetase antibody and with clinical follow-up of at least 6 months in a reference center consultation between the period from January 2008 to September 2019. In those patients who presented interstitial lung involvement clinical, analytical and prognostic variables were evaluated (including spirometry) based on the radiological pattern presented by high-resolution computed tomography (HRCT) of the chest

Results: 32 patients (24 women and 8 men) were included in the study. 7 cases (21.9%) did not present pulmonary involvement, while the remaining 25 cases (78.1%) presented with interstitial lung involvement. Of the patients diagnosed with ILD, 4 cases (12.5%) had an interstitial pattern UIP, 17 cases (53.1%) had an interstitial pattern of NSIP and another 4 (12.5%) interstitial pattern of OP. From an analytical point of view, the most frequent antisynthetase antibody in our sample was antiJo1 with 29 cases (96.9%) and less frequently the antiPL12 antibody with 2 cases and antiPL7 with 1 case. The specific characteristics depending on the type of EPID pattern are summarized in Table 1.

Table 1.

CHARACTERISTICS	ILD PATTERN		
	Pattern UIP N=4	Pattern NSIP N=17	Pattern OP N=4
Gender (Female) n (%)	4 (100)	11 (64.7)	3 (75.0)
Age at diagnosis	47.5 $\pm$ 12.9	52.9 $\pm$ 10.5	42.0 $\pm$ 12.9
Myositis, n (%)	2 (50.0)	13 (76.5)	4 (100)
Arthritis, n (%)	3 (75.0)	15 (88.2)	3 (75.0)
Fever, n (%)	1 (25.0)	9 (52.9)	2 (50.0)
Mechanic's hands, n (%)	2 (50.0)	7 (41.2)	2 (50.0)
Raynaud's phenomenon, n (%)	1 (25.0)	8 (47.1)	1 (25.0)
Skin involvement, n (%)	2 (50.0)	10 (58.8)	4 (100)
Treatment, n (%)			
Glucocorticoids	4 (100)	16 (94.1)	4 (100)
Immunosuppressants	4 (100)	16 (94.1)	4 (100)
Biological therapy	1 (25.0)	8 (47.1)	2 (50.0)
Drug's number (mean, SD)	3 $\pm$ 0.8	5 $\pm$ 2.9	4.7 $\pm$ 1.8
Antisynthetase antibodies, n (%)			
Anti Jo1	3 (75.0)	15 (88.2)	4 (100)
PL7	0 (0)	1 (5.9)	0 (0)
PL12	1 (25.0)	1 (5.9)	0 (0)
Ro52	3 (75.0)	14 (82.4)	2 (50.0)
RF positive	1 (25.0)	4 (23.5)	1 (25.0)
CK increase	2 (50.0)	11 (64.7)	4 (100)
Aldolase increase	2 (50.0)	12 (70.6)	4 (100)
Functional respiratory tests: mean (CI95%)			
Variation DLCOc (%)	-4.4 (-12.5, 3.7)	-2.5 (-6.1, 1.0)	7.4 (-10.6, 25.3)
Variation FVC (%)	-1.1 (-12.8, 9.1)	6.0 (3.2, 8.8)	7.5 (-9.5, 24.6)
Variation FEV1 (%)	0 (0-2.25)	5.0 (1.9, 8.3)	7.35 (-18.0, 32.7)
Variation FEV1/FVC (%)	0.5 (-7.1, 8.2)	-1.3 (-2.22, -0.37)	-0.4 (-12.88, 11.98)

Conclusion: ILD is a frequent and serious manifestation that can occur in patients with antisynthetase syndrome, which may have different radiological patterns. In our series, the most observed radiological pattern has been the NSIP pattern with 68%. The pattern most associated with the Ro 52 antibody was the UIP pattern and the NSIP pattern. As for the group that required the largest numbers of drugs (including biological therapy) it was the NSIP pattern. When evaluating changes in respiratory function tests, the pattern that shows a tendency to improve over time is organized pneumonia with improvement of the DLCO, FVC, FEV1, FEV1 / FVC, while the UIP pattern showed a worsening of the DLCO and the FVC.

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AB0605 CLINICAL PROFILE AND CHEST HIGH-RESOLUTION COMPUTED TOMOGRAPHY (HRCT) FINDINGS IN PATIENTS WITH CONNECTIVE TISSUE DISEASES AND INTERSTITIAL LUNG DISEASE: EXPERIENCE OF A SINGLE REFERENCE RHEUMATOLOGY CENTER

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