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SAT0348

CLINICAL SPECTRUM TIME COURSE OF ANTISYNTHEASE SYNDROME PATIENTS POSITIVE FOR ANTICENTROMERE ANTIBODIES

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Background: ASSD is characterized by antisynthetase antibodies (ARS) and the triad arthritis/myositis/Interstitial Lung Disease (ILD). ASSD and systemic sclerosis (SSc) may share features, like Raynaud's phenomenon (RP), capillaroscopic alterations, and also some SSc specific autoantibodies.

Objectives: To evaluate the characteristics of ASSD + for anticentromere antibodies (ACA).

Methods: Retrospective analysis of clinical and laboratory characteristics of ACA + ASSD. Patients were identified in an established international cohort, randomly matched 1:1 for sex, age, disease duration and ARS positivity with a group of ACA - ASSD.

Results: 18 ACA + ASSD (15 females, 83%, 15 anti-Jo1, 2 anti-PL7, 1 anti-PL12 ARS) patients were identified. In comparison to ACA - group, no differences were observed in disease clinical presentation and evolution. Though, 9 ACA + patients (50%) satisfied the ACR/EULAR 2013 classification criteria for SSc and only 1 in ACA - group (p=0.007) (Table 1).

An incomplete ASSD (lack of at least one triad finding) was observed in 15 patients in both ACA + and - group (p=1). Among these patients, 13 ACA + and 11 ACA - developed de-novo triad finding during disease course (p=0.651). In ACA + group, a de-novo arthritis was observed in 4 patients (vs 1, p=0.565), a de-novo myositis in 8 (vs 5, p=1), and a de-novo ILD in 7 (vs 10, p=1). The prevalence of complete forms was similar between ACA + and - group at both disease onset (3 vs 3, 17%, p=1) and last follow-up, (10 vs 11, 56% vs 61%, p=1). Of note, only 1 patient (6%) for each group died (p=1).

Conclusion: The clinical spectrum time course of ACA+ and - ASSD is similar, even when ACA + patients could be classified as SSc. By considering the high prevalence of arthritis and myositis we observed, we suggest that ACA+ patients with arthritis and myositis, should be tested for ARS antibodies even when an ASSD is not clearly suspected.

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Table 1. Patients characteristics. IQR, interquartile range; ILD, interstitial Lung Disease; SSc, systemic sclerosis

	ACA+ (18)	ACA - (18)	p
Age (years) at disease onset (median, IQR)	47 (37-63)	47 (39-63)	0.834
Disease duration (months) (median, IQR)	81 (62-169)	77 (58-165)	0.486
anti Ro52 antibody (%)	12 (67)	11 (61)	1
Arthritis onset	10 (56)	13 (72)	0.489
Arthritis last follow-up (%)	14 (78)	14 (78%)	1
Myositis onset (%)	7 (39)	11 (61)	0.318
Myositis last follow-up (%)	15 (83)	16 (89)	1
ILD onset (%)	9 (50)	6 (33)	0.5
ILD last follow-up (%)	16 (89)	16 (89)	1
Complete form onset (%)	3 (17)	3 (17)	1
Complete form last follow-up (%)	10 (56)	11 (61)	1
Raynaud phenomenon (%)	13 (72)	9 (50)	0.305
Mechanic's hands (%)	6 (33)	7 (38)	1
Teleangiectasias (%)	2 (11)	0 (0)	0.486
Cutaneous sclerosis (%)	5	1	0.177
Acral ulcers (%)	1 (6)	0 (0)	1
Scleroderma pattern at NVC	8 (44)	7 (39)	1
Pulmonary arterial hypertension (%)	3 (17)	2 (11)	1
2013 ACR/EULAR SSc classification criteria	9 (50)	1 (6)	0.007

Disclosure of Interests: Giovanni Zanframundo: None declared, Gianluca Sambataro: None declared, Veronica Codullo: None declared, Alessandro Biglia: None declared, Emanuele Bozzalla Cassione: None declared, Elena Bravi: None declared, Florenzo Iannone Consultant of: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD, Speakers bureau: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD, Marco Fornaro: None declared, Konstantinos Triantafyllidis: None declared, Alberto Pesci: None declared, Paola Tomietto: None declared, Øyvind Molberg: None declared, Salvatore Scarpato: None declared, Reinhard Voll: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Actelion, Lilly, Boehringer Ingelheim, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Carlomaurizio Montecucco: None declared, Lorenzo Cavagna: None declared

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SATURDAY, 06 JUNE 2020

Spondyloarthritis - etiology, pathogenesis and animal models

SAT0349

CTLA4-IG DECREASES TH17 CELL LEVELS BUT MAINTAINS ILC3S WITH AN INCREASE IN THE ILC3/ ILC1 RATIO IN THE GUT OF SKG MICE AS A MODEL OF SPONDYLOARTHRITIS.

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Background: SKG mice have been known for their autoreactive Th17 cells resulting from the insufficient thymic negative selection due to a Zap70 mutation^{1,2}. Under specific pathogen-free conditions, they acquire features of spondyloarthritis (SpA) by intraperitoneal injection of curdlan, a (1,3)-β-glucan³. Several reports have shown that Th17 cells also increase in human SpA⁴. However, CTLA4-Ig, which ameliorates rheumatoid arthritis by suppressing pathogenic cells such as effector T cells, was unable to show adequate efficacy as much as expected in SpA patients⁵. Around the same time, innate lymphocytes began to be focused on, in the pathogenesis of SpA, including innate lymphoid cells (ILCs), which abundantly reside in the gut⁶.

Objectives: This study aimed to clarify the effects of CTLA4-Ig on the pathogenesis of SpA by using curdlan-treated SKG mice, focusing on type 3 immunity such as Th17 cells and ILC3s.

Methods: Two- to three-month-old female SKG mice were injected intraperitoneally with 3mg of curdlan or PBS at the beginning and with 500 μg of CTLA4-Ig or PBS every other week (n=5 per group). The body weight and arthritis score were measured weekly for a month. Then, the changes in the proportion of T cells and ILCs in the spleen and Peyer's patches (PPs) were analysed by flow cytometry (FCM). BALB/c mice, without treatment, were also examined by FCM as a control cohort. In addition, a next-generation analysis of their feces was performed on 16S ribosomal coding genes before curdlan and CTLA4-Ig treatment.

Results: SKG mice contained not only more Th17 cells but also more ILC1s and ILC3s than BALB/c mice, in their guts (the PPs). The feces of SKG mice intrinsically showed a decrease in the number of bacterial species, suggesting a dysbiosis. Then, in curdlan-treated SKG mice, CTLA4-Ig administration decreased the proportion of both Th17 cells and ILC3s in the spleen, but did not decrease the proportion of ILC3s in the PPs. Moreover, the ILC3/ILC1 ratio in the PPs was from low to high in the order of SKG mice without treatment, SKG mice injected with curdlan, and SKG mice injected with both curdlan and CTLA4-Ig. The phenotype corresponding to SpA features, in curdlan-treated SKG mice, continued after repeated CTLA4-Ig administration.

Conclusion: Curdlan provoked SpA features in SKG mice with an intrinsic dysbiosis. Additional CTLA4-Ig injection decreased the proportion of Th17 cells but maintained that of ILC3s with increased ILC3/ILC1 ratio in the gut. This result supports the hypothesis that in the SpA pathophysiology, a weakened acquired immunity in the gut might lead to ILC3 activation, via dysbiosis, and its continuous disease progression, suggesting that ILC3s are a promising therapeutic target in SpA.

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