AB0555

ANTI-RO POSITIVITY EFFECT ON CLINICAL CHARACTERISTICS AND MORTALITY IN A SINGLE-CENTER COHORT OF ANTISYNTHEASE SYNDROME PATIENTS

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Background: Antisynthetase syndrome (ASSD) is an heterogeneous disease characterized by the occurrence of anti-synthetase antibodies (ARS) and the classic triad of arthritis, myositis and Interstitial Lung Disease (ILD). Pulmonary involvement bears an increased risk of life threatening events, being the main cause of mortality in these patients. No significant differences in mortality have been noticed among the different ARS specificities. However the role of extractable nuclear antigen antibodies on mortality in these patients is still matter of debate.

Objectives: To assess the effect of anti-RO antibodies on clinical characteristics and mortality in a large Italian single-center cohort of ASSD patients.

Methods: Cohort study of outcome, clinical and laboratory characteristics, at baseline and at last follow-up, of 55 ASSD patients progressively enrolled and followed-up at our out-patient clinic. Survival was estimated with Kaplan-Meier function and comparison between frequencies of clinical characteristics was studied with Chi-square test.

Results: We identified 30 anti-Ro+ (M:F=1:4) and 25 anti-Ro- (M:F=1.5:1) ASSD patients. No difference in the age of onset was observed (p value=0.83). Classic triad prevalence and evolution was similar between the two groups with only significant difference of ILD prevalence at last follow up, higher in anti-Ro+ patients group (p value=0.01). Overall mortality was of 13 subjects (23%) during the follow-up period (median 53 months, IQR 16-114). Despite the significantly higher pulmonary involvement in the anti-Ro+ group no difference between mortality in anti-Ro positive and negative groups was observed. Adjusting mortality to include disease-related events only did not provide any additional difference (p value=0.5) (Table 1). Survival curves of the two groups were not different at any time point (Log-rank test, p value 0.98) (Figure 1).

Table 1. Clinical and Demographic Characteristics of the cohort

ASSD	Ro+	Ro-	P value
PZ (M:F)	30 (6:24)	25 (14:10)	/
Age (years) at disease onset (median, IQR)	56 (43-69)	54 (46-68)	0.83
Disease duration (months) (median, IQR)	55 (23-112)	52 (13-130)	0.681
Arthritis at onset (%)	22 (73)	17 (68)	0.664
Arthritis at last follow-up (%)	26 (86)	18 (72)	0.175
Myositis at onset (%)	12(40)	15 (60)	1
Myositis at last follow-up (%)	19 (63)	21 (84)	0.086
ILD at onset (%)	20 (66)	12 (48)	0.162
ILD at last follow-up (%)	30(100)	20 (80)	0.01
Complete form at onset (%)	8 (26)	4 (16)	0.34
Complete form at last follow-up (%)	17 (56)	13 (52)	0.729
Raynaud phenomenon (%)	7 (23)	8 (32)	0.472
Mechanic's hands (%)	12 (40)	12 (48)	0.551
Death (%)	7 (25)	6 (24)	0.953
Disease related death (%)	3 (42)	4 (66)	0.506

Figure 1. Kaplan-meier curve of anti-Ro+ and anti-Ro – ASSD patients.

Conclusion: The clinical spectrum and the time course of ASSD is not significantly affected by the presence of anti-Ro antibodies, although ILD seems to be more associated to anti-Ro antibodies. Despite higher prevalence of ILD in Ro positive group no difference in mortality was observed in respect to anti-Ro negative patients.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5615

AB0556

PRIMARY SYSTEMIC SCLEROSIS HEART INVOLVEMENT (PSSCHI): A SYSTEMATIC LITERATURE REVIEW (SLR), CONSENSUS-BASED DEFINITION AND PRELIMINARY VALIDATION.

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Background: pSScHI may cause tissue, functional and conduction abnormalities with varied clinical manifestations. The absence of a clear definition of pSScHI impairs the significance and ability of focussed research, frequently not allowing the distinction between primary and secondary involvement.

Objectives: We aimed to establish an expert consensus definition for pSScHI, to be used in clinical trials and everyday clinical practice, and to start its validation process.

Methods: A SLR for cardiac manifestations and alterations in SSc was conducted using PubMed, Web of Science and Embase. Articles published from inception to December 31st, 2018 were identified. Inclusion criteria included papers in English on adult SSc patients, with heart involvement as outcome. We excluded non-human studies, secondary heart involvement (eg PAH, drugs, infections), reviews and case reports. PRISMA recommendations were followed where applicable. Extracted data were categorized into relevant domains (signs, symptoms, anatomical site involved, physiological abnormalities, pathological changes, prognostic outcomes), which informed the consensus definition. Sixteen senior experts (7 rheumatologists, 8 cardiologists, 1 pathologist) discussed the data and, using a nominal group technique, added expert opinion, provided statements to consider and ranked them. Consensus was attained for agreement >70%. Sixteen clinical cases were evaluated in two rounds to test for face validity, feasibility, inter- and intra-rater reliability and criterion validity (gold standard set by agreed evaluation between expert rheumatologist, cardiologist and methodologist).

Results: 2593 publications were identified and screened, 251 full texts were evaluated, 172 met eligibility criteria. Data from the 7 domains were extracted and used to develop the World Scleroderma Foundation – Heart Failure Association (WSF-HFA) consensus-derived definition of pSScHI, as follows:

“pSScHI comprises cardiac abnormalities that are predominantly attributable to SSc rather than other causes and/or complications”. pSScHI may be sub-clinical and must be confirmed through diagnostic investigation. The pathogenesis of pSScHI comprises one or more of inflammation, fibrosis and vasculopathy. *Non SSc-specific cardiac conditions (e.g. Ischaemic heart disease, arterial hypertension, drug toxicity, other cardiomyopathy, primary valvular disease) and/or SSc non cardiac conditions (e.g. PAH, Renal involvement, ILD).”

Face validity was determined by a 100% agreement on credibility; application was feasible, with a median 60 (5-600) seconds taken per case; inter rater agreement was moderate [mKappa (95%CI) 0.56 (0.46-1.00) and 0.55 (0.44-1.00) for the two rounds] and intra rater agreement was good [mKappa (95%CI) 0.77 (0.47-1.00)]. Content validity was reached based on the wide variety of patients in the SLR, criterion validity was reached with 78 (73-84) % correctness.

Conclusion: Using a SLR and modified nominal technique, we have developed a preliminary pSScHI consensus-based definition and started a validation process for it to be used in clinical research and clinical practice.

Acknowledgments: Aleksandra Djokovic, Giacomo De Luca, Raluca B. Dumitru, Alessandro Gollo, Marija Polovina, Yossra Atef Suliman, Kostantinos Bratis, Alexia Steelandt, Ivan Milinkovic, Anna Baritussio, Ghadeer Hasan, Anastasia Xintarakou, Yohei Isomura, George Markousis-Mavrogenis, Silvia Bellando-Randone, Lorenzo Tofani, Sophie Mavrogeni, Luna Gargani, Alida L.P. Caforio, Carsten Tschoepe, Arsen Ristic, Karin Klingel, Sven Plein, Elijah Behr, Yannick Allanore, Masataka Kuwana, Christopher Denton, Daniel E. Furst, Dinesh Khanna, Thomas Krieg, Renzo Marcolongo.

Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Eli Lilly, Maya H Buch Grant/research support from: Pfizer, Roche, and UCB, Consultant of: Pfizer; AbbVie; Eli Lilly; Gilead Sciences, Inc.; Merck-Serono; Sandoz; and Sanofi, Petar Seferovic: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Actelion, Lilly, Boehringer Ingelheim

DOI: 10.1136/annrheumdis-2020-eular.1964

AB0557

CO-EXISTENCE OF SYSTEMIC SCLEROSIS HALLMARK AUTOANTIBODIES ASSOCIATES WITH DISTINCT CLINICAL PHENOTYPE

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Background: Systemic sclerosis (SSc) is typically manifests with distinct SSc-specific antibodies (SSc-Abs): anti-topoisomerase I (ATA), anti-centromere (ACA), anti-RNA polymerase III (ARA), anti-U3RNP (u3RNP), anti-U1RNP (U1RNP), anti-PmScl (PmScl), anti-Ku (Ku) and anti-Th/T0 (Th/T0), each being characterised by different clinical features and prognosis. The presence of >1 SSc-Abs is rare with minimum data about these patients' clinical phenotype.

Objectives: To describe and compare the clinical features of SSc patients with >1 SSc-Abs

Methods: The autoantibody profiles of 2799 SSc patients from February 2001 to June 2017 were retrospectively reviewed. Patients with >1 SSc-Abs were identified. Clinical features were collected and compared to historical cohorts of SSc patients with single SSc-Ab positivity. Patients were excluded if treated prior to their immunology test with rituximab, iv immunoglobulins or stem cell transplantation. Statistical analysis was performed using Fisher exact test.

Results: 72 patients (2.6%) with >1 SSc-Ab were identified. Full clinical data were available for 63 patients. 60 patients (2.1%) had double Ab positivity and 3 patients had triple Ab positivity (0.1%). 13 Ab combinations were present. U1RNP and ATA was the most frequent combination (35%), patients were significantly younger (51.38 years) than both U1RNP (58.64 years, $p=0.050$) and ATA (62.03 years, $p=0.002$) patients and more commonly of diffuse subset (dcSSc) ($p=0.001$ and $p=0.041$ respectively). Compared to ATA patients overlap features were more frequent (43% vs 15%, $p=0.004$) including inflammatory arthritis ($p=0.025$) and myositis ($p=0.013$) (Table 1). U1RNP and ACA had a significantly higher prevalence of pulmonary arterial hypertension compared to U1RNP (young) and ACA ($p=0.022$) patients, and compared to ACA patients they were younger (57.88 vs 68.75, $p=0.015$) with a higher incidence of myositis ($p=0.001$). U1RNP and ARA patients were more frequently dcSSc subtype compared to U1RNP patients (75% vs 21%, $p=0.040$). U1RNP and PmScl patients had a higher prevalence of myositis compared to U1RNP patients ($p=0.006$). ATA and ACA patients behaved similarly to ATA patients with a significantly higher prevalence of lung fibrosis ($p=0.006$) and myositis ($p=0.041$) compared to ACA. ACA and PmScl (7%) had higher prevalence of myositis compared to ACA patients ($p=0.04$).

Table 1. Frequency of clinical features in some of the double antibody group combinations, compared to our cohort of patients with only one of the SSc specific antibody. Significant p values (<0.05) highlighted in bold. ILD (interstitial lung disease), PAH (pulmonary arterial hypertension), SRC (scleroderma renal crisis).

Double antibody group	Comparator group	Clinical features											
		Arthritis		ILD		PAH		SRC		Cardiac		Myositis	
		n	p	n	p	n	p	n	p	n	p	n	p
U1RNP and ATA	U1RNP	6 (29%)		15 (68%)		1 (9%)		1 (1%)		0		4 (19%)	
	ATA	14 (18%)	1	38 (50%)	0.136	12 (16%)	0.287	1 (1%)	1	2 (3%)	1	12 (16%)	0.744
U1RNP and ACA	U1RNP	2 (10%)		2 (10%)		4 (20%)		0		0		1 (10%)	
	ACA	14 (18%)	1	38 (50%)	0.267	12 (16%)	0.039	1 (1%)	1	2 (3%)	1	12 (16%)	0.148
U1RNP and ARA	U1RNP	23 (30%)	0.087	43 (11%)	0.233	56 (15%)	0.022	6 (2%)	1	10 (3%)	1	3 (1%)	0.001
	ARA	0		2 (50%)		0		1 (25%)		1 (25%)		0	
U1RNP and PmScl	U1RNP	14 (18%)	0.311	38 (50%)	1	12 (16%)	1	1 (1%)	0.098	2 (3%)	0.144	12 (16%)	1
	PmScl	4 (13%)	1	64 (45%)	1	15 (10%)	1	34 (24%)	1	4 (13%)	0.131	5 (13%)	
ATA and ACA	ATA	1 (13%)		2 (26%)		12 (16%)	1	1 (1%)		2 (3%)		3 (100%)	
	ACA	14 (18%)	1	38 (50%)	1	12 (16%)	1	1 (1%)	1	2 (3%)	1	12 (16%)	0.006
ACA and PmScl	ACA	7 (13%)	1	27 (50%)	1	3 (6%)	1	3 (6%)	1	1 (2%)	1	21 (39%)	0.009
	PmScl	0		1 (25%)		0		0		0		1 (25%)	
ACA and U1RNP	ACA	28 (10%)	1	213 (79%)	1	12 (4%)	1	17 (6%)	1	20 (7%)	1	10 (4%)	0.533
	U1RNP	23 (30%)	1	43 (11%)	0.006	56 (15%)	1	6 (2%)	1	10 (3%)	1	3 (1%)	0.041
ACA and U3RNP	ACA	1 (25%)		1 (25%)		0		0		0		1 (25%)	
	U3RNP	23 (30%)	0.227	43 (11%)	0.385	56 (15%)	1	6 (2%)	1	10 (3%)	1	3 (1%)	
ACA and U5RNP	ACA	7 (13%)	0.457	22 (50%)	0.612	3 (6%)	1	3 (6%)	1	1 (2%)	1	21 (39%)	1
	U5RNP	0		1 (50%)		0		0		0		1 (50%)	
ACA and U7RNP	ACA	23 (30%)	1	43 (11%)	0.216	56 (15%)	1	6 (2%)	1	10 (3%)	1	3 (1%)	1
	U7RNP	3 (6%)	1	12 (24%)	0.456	13 (26%)	1	5 (10%)	1	6 (12%)	1	9 (18%)	1

Conclusion: Coexistence of hallmark autoantibodies is exceedingly rare in SSc patients. When combined, both SSc-Abs have the potential to synergistically interact and modify the clinical phenotype.

Disclosure of Interests: Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Kristina Clark: None declared, Lauren Host: None declared, Alper Sari: None declared, Svetlana Nihtyanova: None declared, Christopher Denton Grant/research support from: GlaxoSmithKline, CSL Behring, and Inventiva, Consultant of: Medscape, Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Corbus Pharmaceuticals, Acceleron, Curzion and Bayer, Voon Ong: None declared

DOI: 10.1136/annrheumdis-2020-eular.3500

AB0558

RISK FACTORS FOR THE DEVELOPMENT OF BREAST CANCER IN SYSTEMIC SCLEROSIS

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