AB0222 ASSOCIATION BETWEEN CENTROMERE AND TOPOISOMERASE SPECIFIC IMMUNE RESPONSES AND THE DEGREE OF MICROANGIOPATHY IN SYSTEMIC SCLEROSIS

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Background: In systemic sclerosis (SSc) more severe microangiopathy has been associated with worse disease outcome. In addition, auto-antibodies are important tools for disease prognostication. To what extent these two biomarkers reflect the same pathophysiological background is not clear. A better understanding of the interaction between the specific auto-immune response and the degree of microangiopathy could not only improve our insight in disease pathophysiology but could also contribute to more reliable disease prognostication. We hypothesized that an ongoing activated immune response, as reflected by higher anticentromere antibody (ACA) or anti-topoisomerase (ATA) specific IgG levels and higher number of ACA or ATA specific isotypes, associates with more severe microvascular damage and with more severe SSc.
Objectives: 1. To evaluate whether ACA and ATA isotype expression associates with the degree of microangiopathy in SSc.
2. To determine the additive value of more activated immune response for prediction of organ involvement.
Methods: ACA and ATA IgG, IgA and IgM levels were measured in serum samples of 129 ACA IgG+ or 102 ATA IgG+ SSc patients, respectively. The degree of microangiopathy was determined based on nailfold videocapillaroscopy (NVC) images, with SSc late pattern reflecting more severe microangiopathy. Associations between ATA and ACA isotype expression and NVC patterns were evaluated. Logistic regression analyses, with NVC pattern, autoantibodies, isotype expression and IgG levels as independent and disease characteristics as dependent variables were performed, adjusted for age, sex and disease duration.
Results: NVC images were available for 164 patients (n=100 ACA, n=64 ATA). Prevalence of SSc early, active and late pattern did not differ between ACA/ATA IgM+ and IgM – patients, nor between ACA/ATA IgA+ and IgA – patients. No associations between isotype expression (Figure 1) or IgG levels and NVC patterns were found. Logistic regression confirmed the association of ATA with pulmonary involvement (multivariable Odds Ratio [OR] 9.0 range 2.3-34.5) and of late SSc pattern with digital ulcers (multivariable OR 12.0 range 3.0-48.0) and pulmonary involvement (multivariable OR 5.0 range 1.5-16.1). Of note, higher topoisomerase and centromere specific IgG levels were independently associated with presence of digital ulcers (OR 3.5 range 1.1-11.0).
Conclusion: We did not observe an association between the quality of the anti-centromere specific or the anti-topoisomerase specific immune response and degree of microangiopathy in SSc patients. This might indicate that specific autoantibodies and stage of microangiopathy reflect different processes in the disease. The association between higher ATA or ACA specific IgG levels with digital ulcers, independent of specific autoantibody and NVC patterns suggests that an ongoing, active immune response is associated with more severe organ involvement.

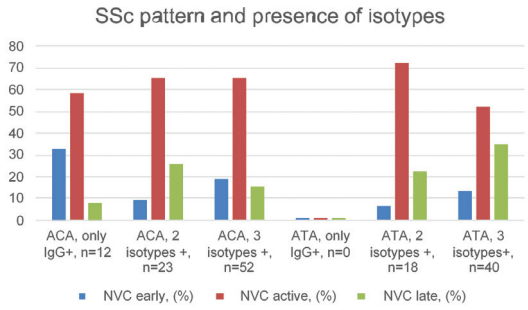

Figure 1. SSc patterns on nailfoldvideocapillaroscopy (NVC) stratified for number of isotypes expressed.

Figure 1

Disclosure of Interests: Nina van Leeuwen: None declared, Jaap Bakker: None declared, Corrie Wortel: None declared, Hans Ulrich Scherer Grant/research support from: Sanofi, BMS, Rene Toes Grant/research support from: Sanofi, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly, Jeska de Vries-Bouwstra: None declared
DOI: 10.1136/annrheumdis-2019-eular.957

AB0223 ASSESSMENT OF DISEASE ACTIVITY IN SYSTEMIC SCLEROSIS: THE COMPARISON BETWEEN REVISED EUSTAR AND ESCSG ACTIVITY INDEXES

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Background: Assessment of disease activity in systemic sclerosis (SSc) is challenging and usually hard to distinguish from damage or chronicity.
Objectives: We aimed to evaluate disease activity by different indexes and compare them in a SSc cohort.
Methods: Disease activity was evaluated by revised EUSTAR (European Scleroderma Trials and Research group) and EScSG (European Scleroderma Study Group) activity indexes in 131 SSc patients fullfiling ACR/EULAR classification criteria (2013). The patients with the scores of EUSTAR activity index ≥2.5 or EScSG activity index ≥3 were accepted as having active disease.

Table 1

	ATA Late NVC n=18	ATA Other NVC n=46	ACA Late NVC n=15	ACA Other NVC n=85
Female, n(%)	13 (72)	34 (74)	14 (93)	75 (88)
Age, mean (SD)	60 (14)	50 (15)	64 (11)	57 (13)
Since non RP, median(IQR)	6 (0-12)	2 (1-4)	15 (8-26)	4 (1-10)
DcSSc, n(%)	6 (33)	14 (30)	0 (0)	0 (0)
Digital Ulcers, n(%)	4 (22)	6 (13)	10 (67)	16 (19)
Pulmonary involvement, n(%)	5 (28)	3 (7)	2 (13)	5 (6)
Cardiac involvement, n(%)	4 (22)	7 (15)	4 (27)	8 (9)
PAH, n(%)	5 (28)	3 (7)	2 (13)	5 (6)
IgA positivity, n(%)	18 (100)	46 (100)	10 (67)	61 (72)
IgA level [aU/mL], median (IQR)	1810 (890-6868)	2782 (1148-9399)	102 (23-178)	67 (34-141)
IgM positivity, n(%)	14 (78)	30 (65)	12 (80)	65 (77)
IgM level [aU/mL], median (IQR)	1514 (492-7719)	693 (325-1818)	50 (23-1210)	110 (14-571)
IgG level [aU/mL], median (IQR)	394 (164-641)	498 (167-869)	630 (181-1094)	375 (169-1027)

Results: Demographics, disease characteristics and nailfold video-capillaroscopic (NVC) pattern details were summarised in table-1. The scores of EUSTAR and EScSG activity indexes were correlated well (r=0.576, p=0.000) and the agreement between two scores for activity was moderate (cohen kappa:0.407). The percentages of SSc patients described as having active disease or not according to two activity indexes were summarised in table-2. Of the patients, 9.9% had active and 70.9% had inactive disease according to both indexes in this SSc cohort. Twenty - one (for EUSTAR) and 4 patients (for EScSG) were described as active according to one index and not to the other. Revised EUSTAR activity index was found to have 76.5% sensitivity and 81.6% specificity when the activity was defined by EScSG activity index.

Table 1.

Table-1: Demographics, Characteristics and NVC pattern in SSc patients

		All SSc pts n=131
Age (years) ±SD		50,3±12,4
Gender F/M		122/10
Duration of Raynaud's (years) ±SD		9,6±8,9
Duration of non-Raynaud's (years) ±SD		6,2±6,5
Cutaneous involvement	diffuse	33 (24.4%)
	limited	93 (71%)
	sclerodermic	6 (4.6%)
ANA		120 (91.6%)
	anti-Scl70	38 (29%)
	anti-centromer	33(25.2%)
Clinical findings	Digital ulcer	60 (45%)
	Flex contr	18 (13.7%)
	Low DLCO	59 (45%)
	Lung disease	51 (38.9%)
	pulmHT	19 (14.5%)
NVC	Normal	7 (5.3%)
	Early	29 (22.1%)
	Active	23 (17.6%)
	Late	69 (52.7%)
	Cap number/mm	5,9±2,1
Mod Rodnan Skin Score		7,3±6,5
Disease Severity Score (Medsger)		5,3±3,6
ESR (mm/h)		30,2±18,3
CRP (mg/dl)		6,2±10,5
Treatment	Immunosuppressivas	68 (51.9%)
	Anti-vasculopathic	34 (26%)

Table 2.

Table-2: The percentage of the patients as having active or inactive disease according to indexes

		EUSTAR activity index	
		active	inactive
EScSG activity index	active	13(9.9%)	4(3%)
	inactive	21(16%)	93(70.9%)

Conclusion: This SSc cohort predominantly had limited cutanous disease, digital vasculopathy and late scleroderma pattern. Defining active disease was differed in 19% of the patients according to EUSTAR and EScSG activity indexes, former described higher frequency for activity. This difference might be related to validation procedures of these indexes in patients with different predominant stages of SSc disease, content of the index and the features of the cohort.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.6167

AB0224 SYSTEMIC SCLEROSIS SINE SCLERODERMA: CHALLENGES WITH VERIFICATION IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Background: Recognizing systemic sclerosis (SSc) in patients without cutaneous involvement is a real challenge due to inapparent clinical picture. 1980 ACR classification criteria for SSc fail to verify the diagnosis in the majority of cases. Therefore, the diagnosis is usually established years and decades after SSc onset at the stage of full-blown visceral disease. Introduction of 2013 ACR/EULAR classification criteria into clinical practice allow early diagnosis of SSc even in cases without skin involvement thanks to the fact, that list of considered criteria includes telangiectasia, pulmonary arterial hypertension (PAH), abnormal nailfold capillaries and SSc-related autoantibodies.

Objectives: To identify specific features in the clinical course of SSc sine scleroderma (ssSSc) in patients with PAH.

Methods: 11 patients with verified SSc diagnosis according to 2013 criteria were included; participants did not have any SSc-specific signs of skin involvement, such as puffy fingers, fingers' skin thickening/induration or skin atrophy. PAH was diagnosed in 11 patients during of right heart catheterization.

Results: Isolated Raynaud's phenomenon (RP) was along-standing diagnosis (more than 5 years) in all patients, except for one whoman, in whom the disease manifested with signs of Sjogren's syndrome (SjS) (parotitis). Benign, chronic, and gradually progressing during a long time disease was documented in all patients. In 7 patients out of 11 SSc diagnosis was initially suspected by cardiologists, and later confirmed by detection of antinuclear autoantibodies. The following signs were documented in SSc patients as initial manifesting non-Raynaud symptoms: esophageal dysmotility – in 3 patients, digital ulcers – in 2, telangiectasia – in 2 patients, and dyspnea (PAH symptom) – in 1 patient. None of the patients ever experienced skin thickening typical for SSc. RP was present in all 100%, but digital ischemic alterations – digital tip ulcers, pitting scars were found only in 3 patients. SSc diagnosis was verified based on abnormal nailfold capillaries (in 100% cases), and based on identification of SSc-specific antibodies (anticentromere antibodies – ACA) – in 7 patients. Anti-Ro-antibodies were found in 4 patients, anti-RNP-70 – in 3. SjS was established in 3 out of 4 anti-Ro-antibodies – positive patients and ruled out in one. Myositis was documented in past-medical history in one patient with anti-RNP-70-antibodies positivity. It should be noted, that 3 ACA-negative patients had, nevertheless, a "threshold" score value (9 scores) for SSc diagnosis, exhibiting many clinical features in favor of SSc diagnosis beyond any doubt. Esophageal dysmotility and associated symptoms were found in 10 out of 11 SSc patients. One patient had an SSc–rheumatoid arthritis overlap syndrome (erosive arthritis, joint deformities, positive ACA, rheumatoid factor, anti-CCP).

Conclusion: Introduction of 2013 ACR-EULAR classification criteria for SSc into clinical practice was highly relevant for identification of SSc cases without cutaneous involvement, providing therefore a timely diagnosis in this group of patients, and allowing to prognosticate the clinical course of PAH. 2013 ACR-EULAR classification criteria for SSc is an algorithm for SSc verification in patents with PAH, especially in the absence of typical for SSc cutaneous disease. The earlier PAH-SSc is diagnosed and PAH-specific therapy is initiated, the longer will be patient' lifespan.

Disclosure of Interests: Natalia Yudkina: None declared, Alexander Volkov : None declared, Ekaterina Nikolaeva: None declared, Ildar Kurmukov: None declared, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc.

DOI: 10.1136/annrheumdis-2019-eular.7207

AB0225 CLINICALSUBTYPE OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS

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Background: Despite the similar pathogenesis and clinical picture, pulmonary arterial hypertension in systemic sclerosis (PAH-SSc) in comparison with idiopathic pulmonary arterial hypertension (IPAH) is characterized by a more severe course, an unsatisfactory response to PAH-specific therapy, a poor survival and a