FRI0330

MALIGNANCIES IN SYSTEMIC SCLEROSIS PATIENTS WITH ANTI-PM/SCL ANTIBODIES: AN EUSTAR CASE-CONTROL STUDY

Maria Grazia Lazzaroni¹, Stefania Zingarelli¹, Jeska de Vries-Bouwstra², Eric Hachulla³, Elisabetta Zanatta⁴, Simone Barsotti⁵, Marie-Elise Truchetet⁶, Giacomo De Luca⁷, Vanessa Smith⁸, Ellen De Langhe⁹, Roger Hesselstrand¹⁰, Francesca Ingegnoli⁷, Cristian Caimmi¹¹, Silvia Bellando Randone¹², Enrico Colombo¹³, Angela Ceribelli¹⁴, Franco Franceschini¹, Yannick Allanore¹⁵, Paolo Airo¹, ¹-, Brescia, Italy; ²-, Leiden, Netherlands; ³-, Lille, France; ⁴-, Padova, Italy; ⁵-, Pisa, Italy; ⁶-, Bordeaux, France; ⁷-, Milano, Italy; ⁸-, Ghent, Belgium; ⁹-, Leuven, Belgium; ¹⁰-, Lund, Sweden; ¹¹-, Verona, Italy; ¹²-, Firenze, Italy; ¹³-, Sassari, Italy; ¹⁴-, Rozzano, Italy; ¹⁵-, Paris, France

Background: The main clinical associations of anti-PM/Scl in Systemic Sclerosis (SSc) include calcinosis, joint and muscle involvement, interstitial lung disease (ILD), and, possibly, scleroderma renal crisis (1,2). A possible association of anti-PM/Scl with cancer was reported in single-centre SSc series (2,3), but was never analysed in large multicentre studies. Moreover, the characteristics of malignancies, in particular their temporal association with the onset of SSc, were not explored.

Objectives: To evaluate the association of anti-PM/Scl with malignancies in a large, international, multicentre cohort.

Methods: 16 EUSTAR centres provided data on anti-PM/Scl+ SSc patients in their cohorts (cases), and on anti-PM/Scl-negative controls, matched for sex, age at onset (± 5 years), cutaneous subset, and disease duration (± 24 months). Only SSc patients with age >16 years at disease onset were included in this analysis. Anti-RNA Polymerase3+ patients were not included in controls, given the known association with synchronous cancer. Malignancies diagnosed between 2 years before and after the onset of SSc were defined as "synchronous to the onset of SSc".

Results: 123 anti-PM/Scl+ SSc patients and 160 matched anti-PM/Scl-controls (28% anti-Topoisomerase I, 40% anti-centromere, 32% others) were compared (Table 1): anti-PM/Scl+ patients had a higher prevalence of myositis ($p<0.0001$) and ILD ($p<0.0001$), and a lower prevalence of oesophageal symptoms ($p<0.0001$). The frequency of malignancies was not significantly different between the 2 groups (14/120 (12%) vs. 9/155 (6%), $p=0.12$). Only 7 malignancies synchronous to SSc onset were identified: 4 among anti-PM/Scl+ cases and 3 among controls (3 breast cancers; 3 other solid tumours; 1 multiple myeloma). Mean age at SSc onset was significantly higher in patients with synchronous malignancies compared to those without (64.9 ± 7.2 vs. 48.4 ± 14.5 years; $p=0.003$), irrespective of the anti-PM/Scl status.

	anti-PM/Scl +	anti-PM/Scl-	p-value
Age at disease onset (years) (mean (SD)) (n available)	47.9 (15.4) (123)	49.5 (14.3) (160)	0.36
Disease duration (months) (mean (SD)) (n available)	124.9 (87.2) (123)	111.3 (77.1) (160)	0.17
Male sex	21/123 (17.1)	19/160 (11.9)	0.23
Limited cutaneous subset	92/123 (74.8)	119/160 (74.4)	1.00
Smoke (current/previous)	32/121 (26.4)	60/157 (38.2)	0.04
Caucasian ethnicity	110/114 (96.5)	133/143 (93.0)	0.27
Raynaud's phenomenon	115/118 (97.5)	158/159 (99.4)	0.32
Esophageal symptoms	69/123 (56.1)	121/160 (75.6)	<0.0001
Scleroderma renal crisis	5/123 (4.1)	3/153 (2.0)	0.25
Active digital ulcers	13/123 (10.6)	22/160 (13.8)	0.47
Joint synovitis	23/123 (18.7)	36/158 (22.8)	0.46
Arrhythmia requiring specific therapy	7/122 (5.7)	22/159 (13.8)	0.03
Lung fibrosis on HRCT	78/119 (65.5)	53/152 (34.9)	<0.0001
PAH confirmed on RHC	4/123 (3.3)	12/158 (7.6)	0.19
Clinical signs of myositis	45/123 (36.6)	17/160 (10.6)	<0.0001
Calcinosis	42/123 (34.1)	34/157 (21.7)	0.02
Death (any cause)	8/123 (6.5)	7/160 (4.4)	0.44
GAVE	3/123 (2.4)	0/160 (0)	0.08
Malignancies (ever)	14/120* (11.7)	9/155* (5.8)	0.12
Malignancies synchronous (≥ 2 years)	4/120* (3.3)	3/155* (1.9)	0.70

Table 1. Univariate analysis comparing anti-PM/Scl+ (cases) and anti-PM/Scl- (controls) SSc patients. *patients with <2 years follow-up were excluded. Results are presented as number/number available data (%) unless stated otherwise. P-Value after Bonferroni correction was obtained for a p value <0.0025

Conclusion: in this EUSTAR multicentre case control-study, the association of anti-PM/Scl with malignancies in SSc patients could not be confirmed. Patients with older age at SSc onset seems to be at higher risk for synchronous malignancies, regardless the autoantibody status.

REFERENCES:

- [1] Lazzaroni MG, et al. Ann Rheum Dis 2018; 77:(Suppl 2), 421-422.
- [2] Bruni C, et al. Rheumatology (Oxford). 2017;56:317-8.
- [3] Bernal-Bello D, et al. Autoimmun Rev 2017;16:461-8.

Acknowledgement: Authors would like to thank GILS (Gruppo Italiano Lotta Sclerodermia) for the grant to support this project

Disclosure of Interests: Maria Grazia Lazzaroni: None declared, Stefania Zingarelli: None declared, Jeska de Vries-Bouwstra: None declared, Eric Hachulla Consultant for: Received consulting fees or other remuneration from Actelion, GSK, Pfizer, and Bayer, Elisabetta Zanatta: None declared, Simone Barsotti: None declared, Marie-Elise Truchetet: None declared, Giacomo De Luca Speakers bureau: Pfeizer, Sobi, Vanessa Smith: None declared, Ellen De Langhe: None declared, Roger Hesselstrand: None declared, Francesca Ingegnoli: None declared, Cristian Caimmi: None declared, Silvia Bellando Randone: None declared, Enrico Colombo: None declared, Angela Ceribelli: None declared, Franco Franceschini: None declared, Yannick Allanore Grant/research support from: Inventiva, F Hoffmann La-Roche, Sanofi, BMS, Pfizer, Consultant for: Actelion, Bayer, BMS, Boehringer, Roche, Sanofi, Paolo Airo: None declared

DOI: 10.1136/annrheumdis-2019-eular.5569

FRI0331

HISTORY OF SILICA DUST EXPOSURES AND ASSOCIATION WITH CHEST HRCT AND CLINICAL CHARACTERISTICS IN SYSTEMIC SCLEROSIS

Alice Ballerie¹, Catherine Cavalin², Mathieu Lederlin³, Amélie Nicolas⁴, Ronan Garlandezec⁵, Stéphane Jouneau⁵, Claire Cazalets⁶, Nicolas Belhomme⁷, Paul-Andre Rosental⁸, Patrick Jégo⁵, ¹LESCOAT Alain⁵, SILICOSIS project, ERC Advanced Grant. ¹Univ Rennes, CHU Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) – UMR_S 1085, Rennes, France; ²Centre d'études européennes de Sciences Po, 79363, Paris, France; ³CHU Rennes, Univ Rennes, Radiology, Rennes, France; ⁴CHU Rennes, Univ Rennes, Radiology, Rennes, France; ⁵Univ Rennes, CHU Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) – UMR_S 1085, Rennes, France; ⁶CHU Rennes, Univ Rennes, Internal medicine and clinical immunology, Rennes, France; ⁷CHU Rennes, Univ Rennes, Internal medicine and clinical immunology, Rennes, France; ⁸SILICOSIS project, ERC Advanced Grant, Centre for European Studies, Sciences Po and National Institute for Demographic Studies (INED), Paris, France

Background: The association of a history of silica exposure with precise chest high-resolution computed tomography (HRCT) features are still to be determined in SSc patients fulfilling the 2013 EULAR/ACR classification criteria. A recent study highlighted that mediastinal lymph nodes were associated with worse prognosis in all-cause interstitial lung diseases (ILD) (1). Nonetheless, the links between mediastinal lymphadenopathies (LA) and silica exposure in SSc patients have never been studied to date.

Objectives: The aim of this study was to assess the association of exposures to inorganic particles on the whole life course, with the HRCT characteristics in an unselected population of SSc patients.

Methods: A specific questionnaire based on a multidisciplinary approach (social sciences, epidemiology, occupational health and medicine) was used to assess occupational and non-occupational exposures to inorganic particles, with a specific interest on silica exposures in 100 SSc patients fulfilling the 2013 EULAR/ACR classification criteria. Clinical characteristics and chest HRCT at diagnosis were evaluated to assess the association of dust exposure with disease characteristics. The most recent chest HRCT was also evaluated and compared to HRCT at diagnosis to assess pulmonary evolution. All HRCT were evaluated by 3 experts, blinded for the results from dust exposure questionnaire.

Results: Men had significantly higher global and occupational dust-exposure scores than women. Sixty-five percent of men with SSc ($n=17$) had an occupational exposure to silica. Thirty-five percent of patients had thoracic LA and 12% an association of mediastinal and hilar LA. Male gender, history of tobacco use, dcSSc, positivity for ATA, thoracic LA and pneumoconiosis were significantly associated with occupational exposure to silica ($p<0.05$ for all). The presence of mediastinal and hilar LA was also associated with occupational exposure to silica ($p=0.0001$, $OR=13.45$, $95\%CI=3.46-52.27$). After stratification on gender, higher occupational dust-exposure score in men remained associated with mediastinal and hilar LA ($p=0.046$, $OR=6.5$, $95\%CI=1.09-38.63$). Mediastinal and hilar LA were also significantly associated with a more severe evolution of pulmonary involvement in SSc when considering extensive ILD at diagnosis, the use of immunosuppressive drugs, a fibrotic evolution with change of SSc-ILD pattern in the course of the disease, and an increase of pathological parenchyma extent above 10% since diagnosis.

Conclusion: By using a dedicated highly detailed questionnaire, this study underscores the high prevalence of silica exposure in SSc patients, especially in men. Mediastinal and hilar LA, considered as a bad prognostic factor in ILD, were frequent and associated with silica exposure.