AB0593

PREDICTORS OF FATIGUE AND SEVERE FATIGUE IN A LARGE MULTICENTER INTERNATIONAL COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE FATILUP STUDY

L. Arnaud¹, P.-E. Gavand², Z. Amoura³, G. Blaison⁴, R. Voll⁵, A. Schwartzing⁶, N. Magy Bertrand⁷, F. Maurier⁸, J.-L. Pennaforte⁹, V. Poindron², P. Kieffer¹⁰, B. Bonnote¹¹, H. Lorenz¹², C. Fiehn¹³, J. Sibilia¹, T. Martin², on behalf of LBBR working groupe. ¹Rheumatology, ²Clinical immunology, CHRU Strasbourg, Strasbourg; ³Clinical immunology, APHP, Paris; ⁴Internal medicine, CH Colmar, Colmar, France; ⁵rheumatology, uniklinik, Freiburg; ⁶Internal medicine, Acura Rheumatology Center Rhineland Palatinate, Bad Kreuznach, Germany; ⁷Internal medicine, CHU Besançon, Besançon; ⁸Internal Medicine, CH Metz, Metz; ⁹Internal Medicine, CHU Reims, Reims; ¹⁰Internal Medicine, CH Mulhouse, Mulhouse; ¹¹Internal Medicine, CHU Dijon, Dijon, France; ¹²University of Heidelberg, Heidelberg; ¹³Unit for Rheumatology and Clinical Immunology, Medical Center Baden-Baden, Baden Baden, Germany

Background: Fatigue is an important issue in systemic lupus and has a major impact on quality of life of the patients. Data are controversial about the factors associated with this complex symptom.¹

Objectives: To identify the factors associated with fatigue and severe fatigue in patients with systemic lupus erythematosus (SLE) in a large cohort using a multivariate model to precise the importance of each parameter in this multidimensional symptom.

Methods: We used the LBBR data base, a German French data base of SLE patients. All patients fulfilled the 1997 ACR criteria for SLE. The Fatigue Scale for Motor and Cognitive Functions (FSMC) was used to assess fatigue and severe fatigue. The depression and anxiety were measured with Hospital Anxiety and Depression Scale (HADS). Tests were performed at sampling.

Results: A total of 570 patients were included (89.1% female). The median age was 42 years (QR25–75: 34–52). The median value of the SELENA-SLEDAI was 2 (QR25–75: 0–4) and 136 patients had a SELENA-SLEDAI score >6. Fatigue was reported by 386 patients (67.7%) including severe fatigue by 209 (36.7%). In univariate analysis among the individual components of the SLEDAI arthritis (p=0.003) and oral ulcers (p=0.002) were associated with severe fatigue. In multivariate analysis fatigue was strongly associated with anxiety (OR: 4.49 [95%CI: 2.60–7.77], p<0.0001) and depression (OR: 4.72 [95%CI: 1.39–16.05, p=0.01]. It was also associated with age at sampling (OR: 1.01 [95%CI: 1.00–1.03, p=0.03] per 1 year increase), SLEDAI (OR: 1.05 [95%CI: 1.00–1.12, p=0.043] per 1 SLEDAI point increase) and glucocorticoids treatment (OR: 1.54 [95%CI: 1.00–2.38, p=0.04]). It was not associated with physical activity. Severe fatigue was strongly associated with depression (OR:6.87 [95%CI: 3.12–15.11], p<0.0001) and anxiety (OR: 3.80 [95%CI: 2.46–5.87], p<0.0001) but not with SLEDAI or physical activity.

Conclusions: Fatigue is a common symptom in SLE patients and is strongly associated with anxiety and depression. While remission remains an important therapeutic target, these manifestations should also be taken care of with psychological counselling and pharmacological intervention, when needed.

REFERENCE:

- Cleanthous S, Tyagi M, Isenberg DA, Newman SP. What do we know about self-reported fatigue in systemic lupus erythematosus? *Lupus*. 2012 Apr;21(5):465–76

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2188

AB0594

PREVALENCE OF FRAGILITY FRACTURES IN WOMEN WITH SLE, THEIR CONNEXION WITH THE COURSE OF THE DISEASE AND THE NATURE OF PHARMACOTHERAPY

S. Shevchuk, L. Denyschych, E. Shevchuk. *National Pirogov Memorial Medical University, Vinnytsya, Ukraine*

Background: Patients with rheumatic diseases are known to have the risk of osteoporosis and fragility fractures, which is significantly higher than in the healthy population. Recent studies demonstrate that age, sex, postmenopausal status, inactivity, glucocorticoid use, nutrition etc. play an important role in the reduction of bone mineral density (BMD) in systemic lupus erythematosus (SLE) patients. The role of the disease severity and the activity of the inflammatory process in the reduction BMD and the incidence of fractures in SLE patients is discursive.

Objectives: The aim of the study was to determine the frequency of osteoporosis and fragility fractures in the Ukrainian SLE patients and to establish their connexion with the course of the disease.

Methods: The main study group involved 91 women with a diagnosis of SLE according to the American College of Rheumatology criteria. The disease activity was determined using the SLE Disease Activity Index (SLEDAI), and organ damage was measured using the Systemic Lupus International Collaborating Clinics American College of Rheumatology (SLICC/ACR) Damage Index. In all patients the cumulative dose of glucocorticoids was calculated. Serum CRP and IL-6 levels were determined by immunoassay. BMD at the lumbar spine (L1–L4) and femoral neck were measured using dual-energy X-ray absorptiometry. For premenopausal SLE patients BMD by Z-score <2.0 SD was defined as «below expected range for age». For postmenopausal women osteoporosis was defined by T-scores ≤ -2.5 SD, and osteopenia – between -1.0 and -2.5 SD. To determine fractures female SLE patients were examined with x-ray.

Results: In premenopausal SLE patients the abnormal BMD of the lumbar spine was found in 9.8%, at the level of the femoral neck it was in 11.1%, in postmenopausal SLE patients – 18.4 and 13.6%, respectively. In the control group there was any premenopausal woman with low bone mass at both sites, whereas among postmenopausal individuals, these were 12.5 and 6.2%, respectively. Osteoporotic fractures were detected in 13 (14.2%) SLE patients, of which 30.7% had hip fractures and 69.3% had vertebral fractures. The reduction of bone strength and fractures were associated with a high damage index. In particular, in persons with fractures it equaled to 4.85±0.65 points, and in persons without fractures – 3.09±0.22 points. A similar tendency was detected by the disease activity SLEDAI. Glucocorticoid use also had a negative effect on the bone strength in patients with SLE. Thus, in women with fractures, the cumulative dose of glucocorticoids defined 60.9±6.63 g, and was by 37.1% higher than in patients without fractures.

Conclusions: In patients with SLE the prevalence of low BMD and fragility fractures is high. Progressive loss of the BMD and the occurrence of osteoporotic fractures are closely associated with the severity of organ damage and glucocorticoid use.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3355

AB0595

ANTIPHOSPHOLIPID SYNDROME (HUGHES SYNDROME) IS A DISEASE WITH PROTEAN FACES: MULTIDISCIPLINARY APPROACHES ON SERBIAN COHORT OF APS PATIENTS

L. Stojanovich, A. Djokovic, N. Stanisavljevic, G. Bogdanovic, M. Zdravkovic. *Internal medicine department, University Hospital Center Bezanjska Kosa, Belgrade, Serbia*

Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterised by thrombophilic state and circulating antiphospholipid antibodies (aPL) including anti beta2-GPI.

Objectives: Since then it became one of the most systemic conditions. In the last three and half decades, a variety of clinical manifestations involving almost all organs and tissues (cardiac, pulmonary, neurological, renal, cutaneous, hematologic, gastrointestinal, ocular, skeletal and endocrinology), have been described associated with antiphospholipid antibodies (aPL).

Methods: Our study comprises a total of 608 patients: 420 primary APS (PAPS) patients and 188 SLE patients with secondary APS (SAPS). aPL analysis included detection of aCL, aβ2GPI, and LA.

Results: Thrombosis was diagnosed in 46.5% patients, with higher prevalence in PAPS compared to SAPS patients: 51.2% and 38.3%, respectively, p=0.045. Pseudo-infective endocarditis was observed in 12.8% secondary APS patients and 3.1% in primary APS patients (p=0.004). 30% of the patients with high levels of aCL IgG antibodies had valve thickening and dysfunction, as compared to 4.1% without valve abnormalities (p=0.002). Presence of β2GPI IgG was significantly related to stroke, and overall β2GPI (IgG and IgM) positivity was significantly related to TIA in SAPS patients. Valvular manifestations were significantly related to TIA in both groups of patients and were independent risk factors for TIA in PAPS (OR 3.790 CI 1.597–8.998 p=0.003; table 2). In PAPS, epilepsy correlated with β2GPI-IgM, migraine with aCL-IgM, thrombocytopenia with aCL-IgM, aCL-IgG, anti β2GPI-IgG and LA. Livedo reticularis was more prominent in PAPS with high levels of aCL-IgG. Skin ulcerations were more prevalent in aCL-IgM positive SAPS patients and epilepsy more frequently had high levels of anti β2GPI-IgG in SAPS.

Conclusions: In this cross-section analysis of a large cohort of APS patients we analysed that APS patients can be presented with a wide variety of thrombotic

and nonthrombotic manifestations. The key the success is multidisciplinary approach in all time of patient's life. Antiphospholipid syndrome is really a disease with protean faces.

REFERENCES:

- [1] Hughes GR. The antiphospholipid syndrome: ten years on. *Lancet* 1993; 342:341–4.
- [2] Ardalan MR, Vahedi A. Antiphospholipid syndrome: A disease of protean face. *J Nephropathology* 2013; 2(1):81–4.
- [3] Stojanovich L, Markovic O, Marisavljevic D, et al. Influence of antiphospholipid antibody levels and type on thrombotic manifestations: results from the Serbian National cohort study. *Lupus* 2011; 0: 1–8.
- [4] Stojanovich L, Kontic M, Djokovic A, et al. Association between systemic non-criteria APS manifestations and antibody type and level: results from the Serbian national cohort study. *Clin Exp Rheumatol*. 2013; 31(2):234–42.

Acknowledgements: Acknowledgement: Funding: This work was supported by research grant number 175041, and TR 32040 for 2011–2018, issued by the Ministry of Science of the Republic of Serbia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1915

AB0596

THE IMMUNE COMPLEXES OF IGG/IGM BOUND TO B-2-GLYCOPROTEIN I ARE ASSOCIATED WITH LIVEDO RETICULARIS, THROMBOCYTOPENIA AND SICCA IN APS PATIENTS

D. Pérez¹, L. Stojanovich², L. Naranjo¹, N. Stanisavljevic², G. Bogdanovic², M. Serrano¹, A. Serrano¹. ¹Immunology, Hospital Universitario 12 de Octubre, Madrid, Spain; ²Internal medicine, Bezanjska Kosa, University Medical Center, Belgrado, Serbia

Background: Several manifestations strongly associated with APS have been excluded as classification criteria.^{1,2}

Objectives: The aim of this study was to investigate correlation between circulating immune-complexes of IgG or IgM antibodies bound to B2GPI (B2G-CIC and B2M-CIC) and clinical manifestations in Serbian cohort of APS patients.

Methods: A total of 57 patients with APS were evaluated: 35 with PAPS and 22 patients with SAPS. Mean age was 47.6±1.6 years; 36 (63.2%) were women. All patients have met the 2006 revised Sydney criteria for APS. Quantification of B2G-CIC and B2M-CIC levels was performed as previously, for detect B2G-CIC was used anti-human IgG HRP-conjugate and for B2M-CIC human IgM HRP-conjugate, both from INOVA (INOVA Diagnostics Inc., San Diego, CA, USA).

Results: In our cohort Serbian APS patients the prevalence of CIC was 19.29% (11/57); 8 patients with B2M-CIC and the remain 3 patients with B2G-CIC. Livedo reticularis was diagnosed with higher prevalence in patients with CIC compared with patients without CIC; 63.6% and 23.9%, respectively (OR: 5.57, p=0.01). In patients with CIC, thrombocytopenia and leukopenia were more prominent; 54.4% vs 17.4% (OR: 5.70, p=0.01) and 45.5% vs 13.0% (OR: 5.56, p=0.01), respectively. Ophthalmic sicca was more prevalent in patients with CIC; 54.4% vs 8.7% (OR: 12.6, p<0.001). Although complement consumption was more frequent in patients with CIC (figure 1).

Figure 1. Mean levels of C3 (A) and C4 (B) complement in groups. Mean levels of C3 (115.6±9.2 mg/dL and 140.9±4.3 mg/dL, group-1 and group-2 respectively) and mean levels of C4 (140.9±4.3 mg/dL and 30.8±1.6 mg/dL, group-1 and group-2, respectively).

Conclusions: B2G-CIC and B2M-CIC are strongly associated with clinical manifestations related to APS. Widening the APS spectrum is indispensable to better understand this syndrome.

REFERENCES:

- [1] Stojanovich L, Kontic M, Djokovic A, Marisavljevic D, Ilijevski N, Stanisavljevic N, et al. Association between systemic non-criteria APS manifestations and antibody type and level: results from the Serbian national cohort study. *Clin Exp Rheumatol*. 2013 Mar-Apr;31(2):234–42.
- [2] Stojanovich L, Markovic O, Marisavljevic D, Elezovic I, Ilijevski N, Stanisavljevic N. Influence of antiphospholipid antibody levels and type on thrombotic manifestations: results from the Serbian National Cohort Study. *Lupus*. 2012 Mar;21(3):338–45.

Acknowledgements: This work was supported by research grant number 175041, and TR 32040 for 2011–2018, issued by the Ministry of Science of the Republic of Serbia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2479

AB0597

CHANGES IN THE THYROID HORMONES IN PATIENTS WITH SJOGREN'S SYNDROME IN DOMINICAN REPUBLIC

M. Marte-Robles, R. Jimenez-Candelaria, I. Mercedes-Núñez, E. Tejada-Reyes, R. Muñoz-Louis, V. Rosario, R. Peña-Blanco, T. Valdez-Lorie, R. Alba-Férez. *Rheumatology, Hospital Docente Padre Billini, Santo Domingo, Dominican Republic*

Background: Sjogren's syndrome (SS) is an autoimmune chronic where there is a B-cell activation and lymphocytic infiltration of exocrine glands, this can be primary or secondary and characterised by xerostomia, xerophthalmia and extraglandular manifestations¹. Thyroid involvement is frequent in patients with SS sharing histological and antigenic characteristics². 10–24% of patients with SS have thyroid involvement, the most common are Hashimoto's thyroiditis or Grave's disease are the most frequent autoimmune syndromes. Some reports indicated that Hashimoto's Thyroiditis and Grave's disease has an incidence of 4.2% and 3.4% in the patients with SS respectively. A study showed that in patients with SS 45% had changes in the values of thyroid hormones and 24% autoimmune thyroiditis.³⁻⁵

Objectives: Determine the changes in the thyroid hormones in patients with Sjogren's syndrome.

Methods: A cross-sectional study. The information was collected from the digital records of Hospital Docente Padre Billini Rheumatology department during the period October 2017-January 2018. Inclusion criteria: age ≥18 years old, patients with Sjogren's syndrome according to ACR/EULAR 2016 criteria. Excluded patients who did not thyroid test during the study and patients who have a thyroid disorder under treatment. The data was analysed using SPSS V23 Windows 10.

Results: 79 cases were reviewed, of which 51 met the inclusion criteria. 98% were women, average age of 45 years, 9.8% had hypothyroidism and 3.9% hyperthyroidism by laboratory tests. 82.3% were euthyroid. 82.3% had anti Ro and anti La, 96% Schirmer test + and 37.2% positive biopsy report for SS.

Conclusions: In our study, we found that 9.8% of patients with Sjogren's syndrome could be associated with subclinical hypothyroidism and 3.9% with hyperthyroidism what can mask the clinical manifestations at the time of diagnosis. The screening in high-risk patients such as patients with autoimmune disorders remains important.

REFERENCES:

- [1] Shiboski CH, Shiboski SC, Seror R, et al. 2016 American College of Rheumatology/European League against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: a consensus and data-driven methodology involving three international Patient cohorts. *Arthritis Rheumatol* 2017; 69:35–45.
- [2] José Rosa Gómez, José Miguel Senabre Gallego, et al. Management of extra glandular manifestations of Sjogren's syndrome. *Clinical Rheumatology*. 2010; 6 (s2): 6–11
- [3] Barragán-Garfias JA, et al. Enfermedades tiroideas autoinmunes y del tejido conectivo. *Rev. Med Inst Mex Seguro Soc*. 2013; 51(2):e1–5
- [4] Tsuboi H, Asashima H, Takai C, et al. Primary and secondary surveys on Epidemiology of Sjögren's syndrome in Japan. *Mod Rheumatol* 2014; 24:464–70
- [5] Sumie Moriyama, Reo Yoshikawa, et al. Clinical, Endocrinological and Immunological Characteristics of Japanese Patients with Autoimmune Polyglandular Syndrome Type 3a. *J Endocrinol Metab*. 2016; 6(2):46–51

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5514

AB0598

SIGNIFICANCE OF NON CRITERIA ANTI-PHOSPHOLIPID ANTIBODIES IN THE PATIENTS WITH SYSTÉMIE LUPUS ERYTHEMATOSUS ASSOCIATED WITH ANTIPHOSPHOLIPID SYNDROME

M. Dryglewska¹, A. Majdan², M. Majdan¹. ¹Department of Rheumatology and Connective Tissue Diseases; ²Chair of Oncology, Medical University, Lublin, Poland

Background: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease in which the uncontrolled activation of the immune system leads to overproduction of autoantibodies (Ab) with different mechanisms of action. Coexistence of anti-phospholipid antibodies (aPL) significantly increases the risk of thromboembolic complications and worsens the clinical course and prognosis of SLE.

Objectives: The aim of study was to determine the relationship between the presence of non-criteria aPLs in SLE patients with criteria and non-criteria clinical symptoms of APS.