AB0169 SNP (1513A>C AND 489C>T) OF P2X7 RECEPTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH SEROSITIS

Federica Furini[1], Anna Lisa Giuliani[2], Mattia Erminio Parlati[2], Marcello Govoni[1], Francesco DI Virgilio[2], Alessandra Bortoluzzi[1]. *[1]Section of Rheumatology, University of Ferrara and Azienda Ospedaliero-Universitaria Sant'Anna di Ferrara, Departement of Medical Sciences, Cona (FE), Italy; [2]University of Ferrara, Departement of Morphology, Surgery and Experimental Medicine, Ferrara, Italy*

Background: our preliminary data demonstrated that expression and activity of P2X7R was impaired in Systemic Lupus Erythematosus (SLE) and associated with a reduced production of IL-1β[1]. Serositis is a typical manifestation of SLE characterized by a marked inflammation, which has been suggested to be an "inflammasome driven" manifestation.

Objectives: to investigate the role of 1513A>C (rs3751143) and 489C>T (rs208294) Single Nucleotide Polymorphisms (SNPs) which are differently associated with loss or gain of function, respectively, of P2X7R, a potent activator of the NLRP3 inflammasome and IL-1β release, in patients with SLE and with a history of serositis (SLE-S).

Methods: DNA was extracted from whole blood and used for evaluation of 2 P2X7R SNPs (1513A>C and 489C>T). Considering the combined action of these two SNPs, the overall activity of P2X7R was divided, into three groups: GOF (gain of function), normal function (NF), and LOF (loss of function). In addition, peripheral blood mononuclear cells (PBMCs) were isolated from venous blood and employed to evaluate P2X7R and NLRP3 expression by RT-PCR, assess P2X7R activity as Benzoyl ATP (BzATP)-induced intracellular Calcium ([Ca2+]i) increments and evaluate in vitro IL-1β following stimulation with lipopolysaccharide (LPS) and BzATP, either separately or in combination.

Results: 33 SLE patients (pts), 11 with (SLE-S) and 22 without serositis (SLE-NS) were enrolled. Mean age was 40.9±10.9 years and disease duration was 135.3± 108.6 months. No significant difference in disease activity and clinical characteristic was found between the two groups (table 1). Evaluating 1513A>C SNP, 20 pts were positive for A/A and 13 for A/C phenotype respectively, while in case of 489C>T SNP, 7 pts presented C/C, 12 C/T and 14 T/T phenotype with a comparable distribution between SLE-NS and SLE-S (table 1). After combination of different phenotypes, 9 pts presented normal function (NF), 22 gain of function (GOF) and 2 loss of function (LOF) with no significant difference between SLE-S and SLE-NS (table 1). P2X7R activity, (evaluated as IL-1 β production and [Ca2+]i increments,) and expression (evaluated with RT-PCR) were comparable between SLE-S and SLE-NS. No significant difference was found between expression and activity of P2X7R and NLRP3 and the two SNPs evaluated (table 2).

Table 1 Comparison between patients with a positive history of serositis (SLE-S) vs patients without history of se (SLE-NS)

	SLE-NS 22 (66.7%)	SLE-S 11 (33.3 %)	P (SLE-NS vs SLE-S)
Demografic parameters No. female/male	21/1	9/2	ns
Age. mean ± SE years	40.8± 8.4	44.2± 13.1	0.36
Disease duration (months)	134.7 ± 98.3	122.5± 96.2	0.28
Ongoing treatment Hydroxychloroquine (200 mg/day)	18 (81.8%)	8 (72.7%)	0.36
Corticosteroids (2.5 up to 12.5 mg/day)	18 (81.2%)	9 (81.2%)	1
Mayor immunosoppressive treatment (Mycophenolate mofetil, Cyclosporine A, Azathioprine, MTX, PEX, RTX)	10 (45.5%)	4 (36.6%)	0.25
Ongoing dosage of steroids mg mean ± SE	3.7 ± 0.59	5.1 ± 1.6	0.34
Cumulative dosage of steroids gr mean ± SE	19.8± 3.6	19.5 ±6.7	0.95
Current clinimetric parameters SLEDAI-2K. mean ± SE	3.3 ±0.7	3.9±0.8	0.61
SLICC. mean ± SE	0.33 ± 0.7	0.45 ±0.2	0.55
SNP 1513A>C= A/C	9 (40.9%)	4(36.4%)	0.55
SNP 1513A>C =AA	13 (59.9%)	7 (63.6%)	0.54
SNP 489C>T = CC	5 (22.7%)	2 (18.2%)	0.57
SNP 489C>T = CT	7 (31.8%)	5 (45.5%)	0.35
SNP 489C>T = TT	10 (45.5%)	4 (36.4%)	0.45
LOF	7 (31.8%)	4 (36.4%)	0.54
GOF	15 (68.2%)	7(63.4%)	0.55

Conclusion: our data indicate that the 1513A>C and 489C>T SNPs do not seem linked with reduced activity and expression of P2X7R that we previously observed in our cohort of lupus patients. Furthermore, no significant association was found between expression of these SNPs and development of serositis.

REFERENCES

[1] *P2X7 receptor in systemic lupus erythematosus (SLE). Exploring a novel pathogenetic pathway in lupus related serositis. F. Furini.* Ann Rheum Dis, *volume 77, supplement Suppl, year 2018, page A871*

Table 2: Activity and expression of P2X7R-NLRP3 inflammasome axis: influence of combinated effect of two SNP

	GOF	LOF	p (GOF vs LOF)
ΔCa^{2+} (Fura2) nM±SE	54.8± 40.0	74.2±14.5	0.42
IL-1β levels in monocytes supernatants pg/ml; mean ±SE			
RPMI	81.3± 29.9	48.2 ± 22.0	0.49
LPS	130.7± 26.9	231.1 ± 70.1	0.71
LPS+BZATP	2159.1± 203.2	2392.7 ± 166.9	0.46
BZATP	110.0 ± 31.6	153.9 ± 55.1	0.46
RT-PCR P2X7R mean (±SE)	1.1± 0.13	0.97±0.1	0.63
RT-PCR NLRP3 mean (±SE)	4.7±0.3	3.7±0.7	0.47

Disclosure of Interests: Federica Furini: None declared, Anna Lisa Giuliani: None declared, Mattia Erminio Parlati: None declared, Marcello Govoni Paid instructor for: Pfizer, Roche, Speakers bureau: Pfizer, Abbvie, MSD, Roche, Eli-Lilly, Celgene, Sanofi, Janssen, Francesco Di Virgilio: None declared, Alessandra Bortoluzzi: None declared

DOI: 10.1136/annrheumdis-2019-eular.5627

AB0170 TUBERCULOSIS IN PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES : THE TUNISIAN EXPERIENCE

Sonia Hammami[1], Hela Sakly[1], Melek Kechida[1], Syrine Daada[1], Rim Klii[1], Hager Ben Brahim[2], Mohamed Chakroun[3]. *[1]University of Monastir, Internal Medicine, Monastir, Tunisia; [2]University of Monastir, Infection diseases, Monastir, Tunisia; [2]University of Monastir, Infection diseases, Monastir, Tunisia*

Background: The incidence of tuberculosis among patients with systemic rheumatic **diseases is much higher than in the general population.** The clinical manifestations of both systemic rheumatic disease activity and tuberculosis, (i.e. fever, weight loss, asthenia) may overlap or lead to confusion. The immunosuppression of systemic diseases makes the management of patients with tuberculosis more complicated.

Objectives: The purpose of our study was to describe the clinical characteristics of patients with systemic rheumatic diseases and tuberculosis.

Methods: A retrospective study, from 1998 to 2018, in the internal medicine service in Fattouma Bourguiba hospital, Tunisia, of 59 patients suffering from connective tissues disease, treated by corticosteroids linked in one or several treatments to immunosuppressants, who subsequently developed tuberculosis.

Results: Fifty nine patients were included (46 women and 13 man) with a mean age of 47years (range from 18-83 years). Systemic illnesses were: systemic lupus erythematous (13.6%, n = 8), Gougerot-Sjögren syndrome (secondary or primary) (18.6%, n = 11), systemic scleroderma (5.1%, n = 3), rheumatoid arthritis (n = 1), Takayasu arteritis (n=1), Horton disease (n=2), periarteritis nodosa (n=1), Wegener's granulomatosis (n= 2) and Behçet's disease (n=1). 45 patients (76.6%) were treated with corticosteroids and/or immunosuppressants in 3 cases (methotrexate in one case, cyclophosphamide in one case and azathioprine in one case) before the tuberculosis was diagnosed. The clinical manifestations most commonly observed were : weight loss in 55.9%, fatigue in 50.8% and fever in 24.7%. The tuberculin skin tets was positive in 45.8%. Quantiferon-TB-Gold was positive in eleven cases. Twelve patients had an abnormal chest X-ray. The location of the tuberculosis was pulmonary (32.3%, n = 19), ganglionic (33.9%, n = 16), urogenital (20.3%, n = 12), lymphatic (n = 5), abdominal (n=4), cerebral (n=2), ocular (n=2), osteoarticular (n= 2) and more than one location in 23.7% of the cases. The diagnosis of tuberculosis was confirmed by bacteriology in 13,6% (n = 8) and in thirteen cases, histologically (22.03%).The systemic rheumatic disease was clinically active at the time of the diagnosis of tuberculosis in 8 patients.The diagnosis of **systemic** rheumatic **diseases** was made before that of tuberculosis in 13 patients and concomitantly in 5. Under tuberculosis treatment by four drugs then by two drugs, the evolution of tuberculosis was favourable in most of our patients. Three of the patients developed an allergy in isoniazid. Nine patients have developped hepatotoxicity with pyrazinamide. Retrobulbar neuritis was observed in 3 cases treated with ethambutol.

Conclusion: This study confirms the often extra-pulmonary character of tuberculosis in patients with systemic disease as well as the difficulty of diagnosis and problems multiplied by this association. The screening strategies for tuberculosis should probably be extended in all patients with systemic rheumatic diseases receiving glucocorticoids and/or immunosuppressive therapy.