and CRP scores (p=0.005, p=0.003) were significantly lower respectively. No statistical significance was found in terms of NLR and PLR (p>0.05).Significant positive correlation was found in RA patients with high disease activity between ESR, CRP, NLR and PLR. In AS patients with high disease activity significant positive correlation was found between ESR, NLR and PLR. No correlation was found between disease activity indices, NLR and PLR.

Conclusions: With the advantage of cost effectiveness and easy calculation NLR and PLR in RA patients, and NLR in AS patients might be used as indicators of inflammation together with ESR and CRP or instances when they are not applicable.Although NLR and PLR are useful in the discrimination of healthy and diseased subjects, they are not sufficient to determine disease activity because not only laboratory parameters but clinical findings and self assessment of the patient are also included in activity measurement.

References:

[1] Yang HB, Xing M, Ma LN, Feng LX, Yu Z.Prognostic significance of neutrophil-lymphocyte ratio/platelet-lymphocyte ratio in lung cancers:a meta-analysis. Oncotarget. 2016 Nov 22;7(47):76769–76778.

[2] Wiwanitkit V. Neutrophil-to-Lymphocyte Ratio,Platelet-to-Lymphocyte Ratio and Heart Failure.Arq Bras Cardiol. 2016 Mar;106(3):265.

[3] Mercan R, Bitik B, Tufan A, Bozbulut UB, Atas N, Ozturk MA, Haznedaroglu S, Goker B. The Association Between Neutrophil/Lymphocyte Ratio and Disease Activity in Rheumatoid Arthritis and Ankylosing Spondylitis. J Clin Lab Anal. 2016 Sep;30(5):597–601.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4800

AB0035 ANGIOPOIETINS: THE MISSING LINK IN POEMS SYNDROME?

F. Coutant[1], Z. Tatar[2], P. Rouzaire[1], B. Evrard[1], A. Dosgilbert[1], O. Tournilhac[3], G. Le Guenno[4], R. Lemal[3], M. Soubrier[2]. *[1]Laboratoire d'Immunologie; [2]Rhumatologie et Immunologie Clinique, CHU Gabriel Montpied; [3]Hématologie Clinique; [4]Médecine Interne, CHU Estaing, Clermont-Ferrand, France*

Background: POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes) is a rare multiorgan disease related to plasma cell dyscrasia. The pathogenesis of the POEMS syndrome is currently unknown, but microangiopathy involving neoangiogenesis and increased vascular permeability may explain some of the features of the disorder. Although vascular endothelial growth factor (VEGF) is constantly highly abundant in the serum of patients with POEMS syndrome, therapeutic approaches targeting the VEGF have led to conflicting results, suggesting that other mediators sharing functional similarities with the VEGF contribute to the pathogenesis. Angiopoietins are known to be involved in the development, remodeling and stability of blood vessels. It is thus tempting to speculate that altered expression of angiopoietins might contribute to the pathogenesis.

Objectives: The aim of this study was to evaluate the circulating levels of three major angiogenic cytokines in patients before and after treatment: VEGF, angiopoietin-1, which plays an essential role in the stabilization and the maturation of blood vessels, and angiopoietin-2 that facilitates angiogenesis in the presence of VEGF.

Methods: Circulating levels of VEGF, Angiopoietin-1 and angiopoietin-2 were determined by ELISA in the serum of 3 patients with POEMS syndrome, before and after therapy. All patients had polyneuropathy, organomegaly, a monoclonal gammopathy (2 IgAl, 1 IgGk) and osteosclerotic lesions. Two patients had typical skin lesions, oedema and one patient had a Castleman disease.

Results: As expected, the serum of patients before treatment exhibited high levels of VEGF (2901±920 pg/mL). Strikingly, angiopoietin-1 levels were highly abundant before treatment (67286±20395 pg/mL) and successful treatment led to a strong reduction in both VEGF and angiopoietin-1. Angiopoietin-1 levels strongly correlated with levels of VEGF (r=0.83). By contrast, angiopoietin-2 levels did not differ significantly before and after treatment.

Conclusions: Thus, angiopoietin-1 seems to be a crucial proangiogenic cytokine overproduced in patients with POEMS syndrome that might explain some of the features of the pathology. The overproduction of VEGF and angiopoietin-1 is likely to promote manifestations encountered in POEMS syndrome such as organomegaly, osteosclerotic lesions or glomeruloid hemangioma. Restoring the balance between angiopoitein-1, angiopoietin-2 and VEGF could constitute a very promising therapeutic strategy in this disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3697

AB0036 ASSOCIATION BETWEEN SYNOVITIS AND INFLAMMATORY CITOKINES SERUM LEVELS IN A COHORT OF PATIENTS AFFECTED BY PRIMARY KNEE OSTEOARTHRITIS

F. Ceccarelli[1], C. Perricone[1], V.A. Pacucci[2], C. Scirocco[1], C. Alessandri[1], G. Valesini[3], F. Conti[3]. *[1]Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma; [2]Reumatologia, Dipartimento Medicina Interna e Specialità Mediche; [3]Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza, Università di Roma, Roma, Italy*

Background: Osteoarthritis (OA) is characterized by progressive loss of cartilage, deterioration of subchondral bone and mild synovial inflammation. Classified for a long time as a non-inflammatory arthropathy, a growing number of evidences has suggested that OA course could be driven by systemic and localized inflammation. In particular, serum levels of Interleukin (IL)-6 have been associated with higher prevalence of osteophytes in older adults with knee OA. Furthermore, high levels of other inflammatory cytokines have been identified in serum and synovial fluid of OA patients.

Objectives: In the present cross-sectional study, we aimed at analyzing the correlation between articular inflammatory state, reflected by ultrasonographically-detected synovitis, and the serum levels of 27 cytokines, chemokines and growth factors in a cohort of primary knee OA.

Methods: We consecutively enrolled 47 patients (M/F 16/31, mean age ±SD 63.8±7.8 years, mean onset interval ±SD 70.0±78.6 months) affected by knees OA according to clinical and radiographic ACR criteria. Patients were excluded if they had received non-steroidal anti-inflammatory drugs or other analgesics within the 2 days before enrollment. Pain was assessed with a 100-mm visual analogue scale (VAS), and the Lequesne algo-functional index was used to measure the OA severity. BMI was registered. Each patient underwent ultrasonographic (US) assessment of both knees performed by a single operator. According with OMERACT definitions, we assessed the presence of synovial effusion, synovial hypertrophy and power Doppler. These elementary lesions were scored according to a semi-quantitative scale (0 = absent, 1 = mild, 2 = moderate and 3 = severe), the sum of them allows obtaining a total score of the patient's inflammatory state (0–18). Finally, blood samples for laboratory assays were obtained and commercially available multiplex bead based immunoassay kits (Human 27-plex, Bio-Rad laboratories, Hercules, CA) were used to measure concentrations of IL-1β, IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17, FGF-Basic, G-CSF, GM-CSF, interferon-γ, IP-10, MCP-1, MIP-1α, MIP-1β, PDGF, RANTES, TNF, VEGF.

Results: At the study enrollment, OA patients showed a mean±SD US synovitis score of 4.4±2.7, a mean±SD VAS pain rating of 53.3±16.6 mm (range 18–90 mm), a mean±SD Lequesne index of 10.2±4.2 (range 1.5–19), a mean±SD BMI of 26.8±4.2 (range 20–34.7). Positive correlations among US synovitis score and serum levels of IL-6 (r=0.3, p=0.01), IL-2 (r=0.3, p=0.01), IL-5 (r=0.3, p=0.01), IL-7 (r=0.3, p=0.03), MIP-1b (r=0.3, p=0.01), VEGF (r=0.3, p=0.02) were found. Moreover, US synovitis score positively correlated with Lequesne index (r=0.4, p=0.004) and BMI (r=0.4, p=0.04).

Conclusions: The results of the present study confirmed that OA may be associated with systemic inflammatory changes, as demonstrated by the positive correlation between US synovitis and several inflammatory cytokines serum levels.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5289

AB0037 SERUM CYTOKINE SIGNATURE IN MUCOCUTANEOUS AND OCULAR BEHÇET'S DISEASE

G. Lopalco[1], O.M. Lucherini[2], L. Cantarini[2], A. Lopalco[3], V. Venerito[1], M. Fornaro[1], D. Natuzzi[1], M. Galeazzi[2], G. Lapadula[1], F. Iannone[1]. *[1]Department of Emergency and Organ Transplantation, University of Bari, Bari; [2]Research Center of Systemic Autoinflammatory Diseases and Behcet's Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Siena, Italy; [3]Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, United States*

Background: Behçet's disease (BD) is a multi-systemic inflammatory disorder consisting of recurrent oral aphthosis, genital ulcers, and chronic relapsing bilateral uveitis. However, many other organs including the vascular, gastrointestinal, neurological, and musculoskeletal systems can be affected. Pathogenetically, both innate and adaptive immunity have shown to play a pivotal role, and several proinflammatory cytokines derived from Th1 and Th17 lymphocytes seem to be involved in different pathogenic pathways leading to development of the clinical manifestations.

Objectives: The primary aim of our study was to compare a core set of proinflammatory cytokines between patients with BD and healthy control (HC). The secondary aim was to evaluate potential correlations between these putative circulating biomarkers, the status of disease activity, and the specific organ involvement at the time of sample collection.

Methods: Fifty-four serum samples were collected from 46 BD patients (17 males, 29 females, mean age 45,5±11,3 years), and 19 HC (10 males, 9 females, mean age 43±8.3 years). Twenty-five serum cytokines (APRIL/TNFS13, BAFF/TNFSF13B, sCD30/TNFRSF8, sCD163, Chitinase3-like1, gp130/sIL-6Rb, IFNb, sIL-6Ra, IL-10, IL-11, IL-19, IL-20, IL-26, IL-27 (p28), IL-28A/IFN-lambda2, IL-29/IFN-lambda1, IL-32, IL-34, IL-35, LIGHT/TNFSF-14, Pentraxin-3, sTNF-R1, sTNF-R2, TSLP and TWEAK/TNFSF-12) were simultaneously quantified using a Bio-Rad cytokine bead arrays.

Results: Serum levels of Chitinase3-like1, gp130/sIL-6Rb, IL-11, IL-26, sTNF-R1, sTNF-R2 were significantly higher in BD patients than in HC. Specifically, serum concentration of sTNF-R1 (p<0.01) and sTNF-R2 (p<0.01) resulted higher in both active- and inactive-BD than HC, whilst Chi-tinase3-like1 (p<0.05) and gp130/sIL-6Rb (p<0.01) serum levels were significantly higher in in-active-BD, and IL-26 (p<0.01) in active-BD than HC. No differences were observed between inactive- and active- BD group. In addition, comparing cytokines levels in patients affected by mucocutenous manifestations with (MO-BD) or without (M-BD) ocular

involvement we observed that gp130/sIL-6Rb, sIL-6Ra, IL-35, and TSLP serum levels were significant enhanced in MO-BD compared to M-BD subgroup.

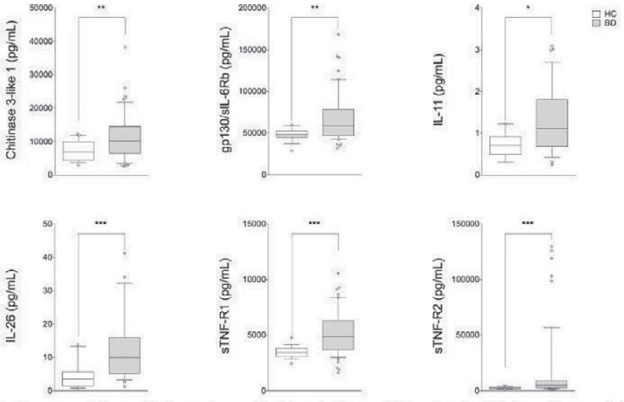


Fig.1. Serum cytokine profile in patients with Behçet's disease. BD patients (n=54) showed up-regulation of serum levels of Chitinase3-like1, gp130/sIL-6Rb, IL-11, IL-26, sTNF-R1 and sTNF-R2 compared with HC (n=19). Mann-Whitney U-test as well as Student's t-test were carried out to check for statistical significance between groups when required (***p<0.001, **p<0.01, *p<0.05). The central line represents the distribution median, boxes span 25th to 75th percentiles, and error bars extend from 10th to 90th percentiles. Dots (°) are outlier values, higher than the 90th percentile. Abbreviations: HC, healthy controls; BD, Behçet's disease.

Conclusions: Our findings showed a signature of IL-6, TNF-α as well as of Th17 response in BD patients due to increased levels of gp130/sIL-6Rb, sTNF-R1, sTNF-R2, IL-26 respectively. This evidence could contribute to improve the knowledge regarding the role of these citokines in the induction of specific BD clinical features

References:

[1] Lopalco G, Lucherini OM, Vitale A, Talarico R, Lopalco A, Galeazzi M, et al. Putative Role of Serum Amyloid-A and Proinflammatory Cytokines as Biomarkers for Behcet's Disease. Medicine (Baltimore) (2015) 94(42):e1858.
[2] Lucherini OM, Lopalco G, Cantarini L, Vitale A, Rotondo C, Lopalco A, et al. Correlation between serum amyloid-A and serum levels of proinflammatory cytokines in patients with Behçet's disease. Pediatric Rheumatology Online Journal (2015) 13(Suppl 1):P6.
[3] Turan B, Pfister K, Diener PA, Hell M, Möller B, Boyvat A, et al. Soluble tumour necrosis factor receptors sTNFR1 and sTNFR2 are produced at sites of inflammation and are markers of arthritis activity in Behçet's disease. Scand J Rheumatol (2008) 37(2):135–41.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1935

AB0038 INCREASED INTERFERON-ALPHA PRODUCTION BY PLASMACYTOID DENDRITIC CELLS STIMULATED WITH A TLR-7 AGONIST IN SYSTEMIC LUPUS ERYTHEMATOSUS

G. Murayama [1,2], N. Furusawa [2], A. Chiba [2], K. Yamaji [1], N. Tamura [1], S. Miyake [2].
[1] Department of Internal Medicine and Rheumatology; [2] Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan

Background: Type I interferon (IFN) appears to contribute to the development of systemic lupus erythematosus (SLE). IFN-α production is known to be increased in peripheral blood mononuclear cells (PBMCs) from SLE patients. Although plasmacytoid dendritic cells (pDCs) is a major source of IFN-α, previous reports showed that IFN-α production by pDCs stimulated with a TLR-9 agonist was decreased in SLE compared to healthy controls (HC).
Objectives: We set out to investigate an other endosomal TLR-signaling pathway in SLE by using TLR-7 agonist stimulation.
Methods: Blood samples were obtained from 55 HC and 73 SLE patients, diagnosed according to the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus (2012). PBMC from SLE patients and HC were stimulated with a TLR-9 agonist, CpG-A oligodeoxynucleotides (CpG-A ODN)-2216, and a TLR-7 agonist, imiquimod. The proportion of pDCs producing IFN-α was investigated by intracellular cytokine staining and flowcytometory. PBMC were pretreated with IFN-α for 24 hours, and then IFN-α production by pDCs was assessed after imiquimod stimulation.
Results: As previously reported, the level of IFN-α production by pDCs stimulated with CpG-A ODN was reduced in SLE compared with HC. However, the proportion of IFN-α producing pDCs stimulated with imiquimod was significantly increased in SLE patients. The percentage of IFN-α producing pDCs stimulated with imiquimod was positively correlated with SLE disease activity index (SLEDAI) score, and that of pDCs stimulated with CpG-A ODN was negatively correlated with SLEDAI. The expression of TLR-7 on pDCs, but not TLR-9, was upregulated in SLE patients compared with HC. Furthermore, pretreatment with IFN-α increased IFN-α production by pDCs upon imiquimod stimulation.
Conclusions: IFN-α production by pDCs form SLE patients was increased when stimulated with a TLR-7 agonist, and this was accompanied with upregulated TLR-7 expression in these cells. In murine lupus-models, TLR7-deletion has been shown to reduce autoimmune disease. The enhanced TLR-7 signaling pathway in pDC may play an important role in lupus pathology.

References:

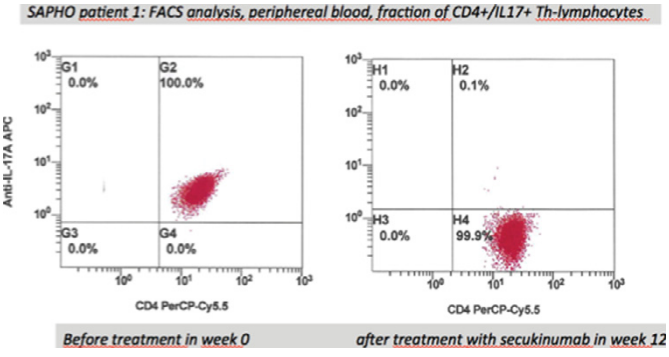
[1] Christensen SR, et al. Toll-like receptor 7 and TLR9 dictate autoantibody specificity and have opposing inflammatory and regulatory roles in a murine model of lupus. Immunity. 2006; 25: 417–28.
[2] Sacre K, et al. Hydroxychloroquine is associated with impaired interferon-alpha and tumor necrosis factor-alpha production by plasmacytoid dendritic cells in systemic lupus erythematosus. Arthritis Res Ther. 2012;R155.
[3] Fukui R, et al. Unc93B1 restricts systemic lethal inflammation by orchestrating Toll-like receptor 7 and 9 trafficking. Immunity 2011; 35: 69–81.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3074

AB0039 REDUCTION OF TH17+ LYMPHOCYTES IN PART OF SAPHO PATIENTS ON TREATMENT WITH SECUKINUMAB

G. Assmann [1], A. Tajali [2], S. Bamberger [1], M. Pfreundschuh [1], C. Schormann [1], F. Neumann [1]. *[1] Rheumatology and Oncology, University Medical School of Saarland, Homburg; [2] Rheumatology, Püttlingen Hospital, Püttlingen, Germany*

Background: The SAPHO syndrome has to be considered as a rare subtype of the disease entity of the seronegative spondylarthritis. The characteristic defining symptoms are synovitis, acne, palmoplantar pustulosis (PPP), and hyperostosis with osteitis. In general, most of SAPHO patients complete the diagnostic criteria for spondylarthritis and/or psoriatic arthritis. The etiology of SAPHO syndrome remains unclear so far, autoimmune dysregulations potentially triggered by bacterial infection with propionibacterium acnes has been discussed. Firinu D et. al (Ref.) has previously published data of higher Th17+ lymphocytes in the peripheral blood in SAPHO patients compared with psoriatic arthritis patients or healthy controls. Activation of the TH17 pathway leads to pro-inflammatory effects mediated by interleukin 17 with stimulation of osteoblast, macrophages, and fibroblasts with the consequences of secretion f pro-inflammatory cytokines such as interleukin 6 and 1, TNF alpha, and MMPs. The interleukin 17 blocking agent secukinumab has been introduced in the armentarium of antirheumatic drugs against seronegative spondylarthritis including psoriatic arthritis.
Objectives: To evaluate the count of Th17+ lymphocytes in patients with SAPHO syndrome and psoriatic arthritis before and under treatment with secukinumab.
Methods: Peripheral blood was derived from 4 patients with SAPHO syndrome and 4 patients with psoriatic arthritis, respectively before and under 12 week treatment with secukinumab 300mg (dosage: 4 times weekly, then monthly). All patients had received at least one conventional DMARDs and one TNF blocking agent in their medical history. All patients showed active disease with elevated scores of DAS28 and/or HAQ, for SAPHO patients the activity scores of osteitis (from 0 to 6) and PPP (0–6) were estimated by physician. The blood specimen were separated in EDTA containing tubes to separate lymphocytes, which were measured using FACS analysis to evaluate the fraction of Th 17+/CD4+ lymphocytes. The Ethics Committee of Saarland has proven the study, all patients gave their consent to take part in the study.
Results: The Th17+lymphocytes were not detectable in 4 patients with psoriatic arthritis and 2 of 4 SAPHO patients before and under 12 week treatment with secukinumab. In 2 of 4 SAPHO patients the fractions of Th17+ lymphocytes were prominent prior to secukinumab application; after treatment duration of 12 weeks one of both developed a depletion of Th17+ cells (figure), the other SAPHO patient a Th17+ cell reduction. Only the two SAPHO patients with diminishing Th17+ lymphocytes have developed treatment response evaluated by reduction of HAQ score (from 1.75 to 1.25), osteitis score (4.5 to 3.0), and PPP score (5.0 to 4.0). Three of 4 psoriatic arthritis patients showed reduced diseases activity under treatment with secukinumab (DAS28 score from 4.22 to 3.45, HAQ 2.25 to 1.5).



Conclusions: The measurement of Th17+lymphocytes in the peripheral blood of SAPHO patients could be suggested for further evaluation as possible predictor of treatment response by secukinumab.

References:

[1] Firinu D, Barca MP, Lorrai MM, Perra S, Cabras S, Muggianu E, Di Martino ML,