under OA conditions and is able to reduce the severity of cartilage destruction during OA.
Disclosure of Interest: None declared
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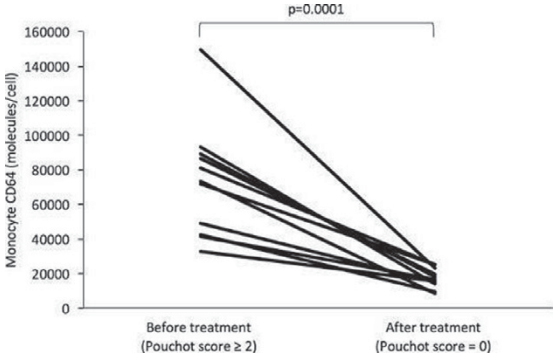
AB0032 UPREGULATION OF CD64 EXPRESSION ON MONOCYTES IN PATIENTS WITH ACTIVE ADULT-ONSET STILL'S DISEASE: A POSSIBLE BIOMARKER FOR ASSESSING DISEASE ACTIVITY

E. Oguro[1], T. Shimizu[1], A. Kikuchi-Taura[2], S. Tsuji[1], Y. Okita[1], M. Shigesaka[1], H. Matsuoka[1], T. Nii[1], S. Teshigawara[1], E. Kudo-Tanaka[1], Y. Harada[1], M. Matsushita[1], S. Ohshima[2], Y. Saeki[2]. *[1]Department of Rheumatology and Allergology; [2]Department of Clinical Research, NHO Osaka Minami Medical Center, Osaka, Japan*

Background: Adult-onset Still's disease (AOSD) is a systemic inflammatory disease of unknown etiology. Overproduction of multiple inflammatory cytokines and subsequent hyperactivation of monocytes/macrophages are prominent characteristics of AOSD. However, there are no convenient and precise methods for evaluating monocyte/macrophage activation in AOSD. We previously reported that monocyte CD64 (mCD64) expression could be quantitatively measured by flow cytometry and its expression was tightly correlated with the activity of systemic lupus erythematosus.
Objectives: We examined the association between mCD64 expression and AOSD disease activity.
Methods: This was a prospective, single-center, observational study conducted between January 2013 and December 2016. Eleven active AOSD patients who fulfilled the Yamaguchi's criteria for AOSD and had the modified Pouchot score of $\geq$2 were enrolled. The mCD64 expression levels were quantitatively measured by flow cytometry and individually assessed both before (Pouchot score $\geq$2) and after treatment (score 0). Other disease-related laboratory data, such as C-reactive protein, ferritin, and white blood cell count, were simultaneously measured. As a control, 16 active systemic lupus erythematosus (SLE) patients (SLE disease activity index $\geq$6), 22 active rheumatoid arthritis (RA) patients (disease activity score with 28-joint counts $>$3.2), and 20 healthy controls (HC) (female, 55%; mean age, 38.7±9.1 years) were enrolled. Statistical analysis was performed by the Mann-Whitney and Wilcoxon-paired tests.
Results: The median mCD64 expression levels were 73,339 [interquartile range (IQR), 45,861–88,181] and 16,443 (IQR, 45,891–88,181) molecules/cell before and after treatment, respectively. Thus, mCD64 expression levels were significantly decreased during the inactive phase compared with those in the active phase in AOSD (p=0.0001). The mCD64 expression levels were significantly higher in patients with active AOSD than in those with active SLE [34,648 (IQR, 44,204–24,657) molecules/cell, p=0.001], active RA [25,167 (IQR, 35,778–22,301) molecules/cell, p$<$0.0001], and in HC [14,174 (IQR, 13,413–17,774) molecules/cell, p$<$0.0001].



Conclusions: These results suggest that mCD64 expression levels are highly upregulated in AOSD and tightly correlated with disease activity. The mCD64 expression level may be a useful biomarker for assessing the disease activity of AOSD.
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AB0033 THE IDENTIFICATION OF IL-17A+, IL-17RA+ AND IL-17RC+ LYMPHOID AND MYELOID CELLS IN BLOOD OF TREATMENT NAÏVE EARLY AND IN SYNOVIAL FLUID OF ESTABLISHED PSORIATIC ARTHRITIS PATIENTS

X. Xu[1], N. Davelaar[1], A.-M. Otten-Mus[1], P.S. Asmawidjaja[1], H. den Braanker[1], H. Alves[1], J.P. van Hamburg[1], C. Gaillez[2], J.M. Hazes[3], R. Bisoendial[4], M. Vis[3], F. Kolbinger[5], E. Lubberts[1]. *[1]Rheumatology and Immunology, Erasmus Mc, University Medical Center, Rotterdam, Netherlands; [2]Novartis Pharma AG, Basel, Switzerland; [3]Rheumatology, Erasmus Mc, University Medical Center; [4]Rheumatology, Maasstad Hospital, Rotterdam, Netherlands; [5]Novartis, Basel, Switzerland*

Background: Interleukin (IL)-17A is a pro-inflammatory cytokine and is involved in the pathogenesis of psoriatic arthritis (PsA) (1,2). Various cells can produce IL-17A. However, it is not clear which cell types in PsA patients are responsible for the production of IL-17A. In addition, the expression of IL-17RA and IL-17RC on different cell types is not well defined.
Objectives: To identify IL-17A, IL-17RA and IL-17RC positive cells in blood of first diagnosed PsA patients with arthritis and in synovial fluid of established PsA patients with active disease.
Methods: Fresh blood was taken from first diagnosed DMARD and steroid naïve PsA patients (n=10), having arthritis in 1 or more joints (PsA blood). The diagnosis was made by a rheumatologist according to the CASPAR-criteria. In addition, fresh synovial fluid was obtained from established PsA patients (PsA SF) with active disease (n=10) and treated with either methotrexate (n=3) or adalumimab (n=3) or NSAIDs (n=4). Multicolor flow cytometric analysis was performed on PsA blood and PsA SF. For the detection of IL-17A, IL-17RA or IL-17RC the following antibodies were used: IL-17A-PE (eBioscience), IL-17RA or isotype control IgG1k (both Biolegend), IL-17RC or isotype control IgG2b (both R&D systems). The following markers were used to discriminate between different cell populations: T cell subsets (CD3, CD4, CD8, CD45RO, CCR6, TCR$\gamma\delta$), B cells (CD19), NK cells (CD15-CD16+), neutrophils (CD15+CD16+), monocytes (CD33+CD14+CD16+/-), mast cells (CD117+FcER1a+) and eosinophils (CD15+FcER1a+).
Results: Different lymphoid and myeloid cell types were IL-17A positive in PsA blood of first diagnosed PsA patients such as CD3+, TCR$\gamma\delta$+, CD4+, CD8+ lymphoid cells, CD14+ monocytes and eosinophils. In PsA SF of established PsA patients TCR$\gamma\delta$+ T cells, neutrophils, NK cells and eosinophils were IL-17A positive.
In both groups, no difference in expression of IL-17RA and IL-17RC was found on CD4+, CD8+, CD4+CD45RO+CCR6+/-, TCR$\gamma\delta$+ and CD19+ lymphoid cells compared to their isotype control. In contrast, the expression of IL-17RA and IL-17RC was increased compared to their isotype control on neutrophils and monocytes in PsA blood and on neutrophils, monocytes, mast cells and eosinophils in PsA SF.
Conclusions: These preliminary data show that not only lymphoid cells but also specific myeloid cell types may be sources of IL-17A in PsA. Furthermore, not lymphoid cells but IL-17RA/IL-17RC positive myeloid cells such as monocytes, neutrophils, mast cells and eosinophils may be potential target cells for IL-17A.
Together, these data suggest a more broad, but specific IL-17A-IL-17RA/RC signaling network between different cell types important in the IL-17A-driven pathogenesis of PsA.
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AB0034 PARAMETERS OF TOTAL BLOOD COUNT; MIGHT THEY BE INDICATORS OF INFLAMMATION IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS?

O.G. Illeez, F. Unlu Ozkan, I. Aktas. *PMR, University of Saglık Bilimleri, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey*

Background: Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are launched as recent markers of inflammation in chronic inflammation principally in cancer and cardiovascular diseases (1–2).
Objectives: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are chronic inflammatory disorders marked by variable periods of remissions and relapses.Inflammation is most likely the underlying cause in disability, increased comorbidity therefore need to be closely monitored and kept under control (3).For this reason cost effective, accessible and reliable parameters are needed in daily practice. Our aim is to analyze the relation between inflammation and NLR and PLR which are easily calculated from whole blood count parameters.
Methods: Medical records of 425 subjects were analyzed retrospectively.Mean age of the subjects was 44,64±14,07 years (17–89 years),52.9% was female (n=225) and 47.1% was male (n=200).105 of them had RA, 216 of them had AS and 104 were healthy controls.2010 ACR/EULAR classification criteria and modified New York criteria were used for the diagnosis of RA and AS.Erythrocyte sedimentation rate (ESR), C reactive protein (CRP) and whole blood count were recorded with simultaneous DAS28 scores of patients with RA and BASDAI scores of patients with AS.
Results: Hemoglobin levels of RA patients were significantly (p$<$0.05) lower then the levels of control group (p=0.001).ESR, CRP, NLR and PLR were significantly higher then the control group respectively (p=0.001, p=0.001, p=0.001, p=0.040).In AS group hemoglobin, ESR, CRP and NLR values were significantly higher then the control group respectively (p=0.001, p=0.006, p=0.001, p=0.001). No difference was detected between AS and control groups in terms of PLR (p$>$0.05).When patients with high disease activity and patients in remission were compared for both RA and AS groups ESR (p=0.001, p=0.001)

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.

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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

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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

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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