OP0211-PARE **WHO CARES? AN INVESTIGATION OF THE HEALTH AND PERCEIVED SOCIAL CARE NEEDS OF PEOPLE WITH RHEUMATOID ARTHRITIS LIVING IN SCOTLAND**

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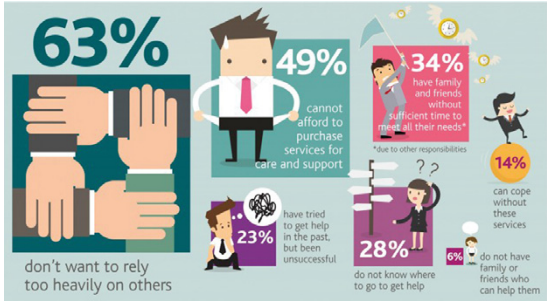
Background: Effective and sufficient levels of care and support for individuals newly diagnosed and those with established Rheumatoid Arthritis (RA) are needed to ensure optimal physical and mental health, as well as health-related quality of life. The aim of this study was to explore the extent of care needs among individuals with RA living in Scotland, UK and the factors that contribute to them, such as co-morbidities, perceived caregiver burden and complex care needs.
Objectives: To establish whether the health and social care needs of people with RA in Scotland were being met, if there was regional variation and what other factors impacted such as wealth and age.
Methods: A cross-sectional study of individuals with RA who responded to an online survey (available 11 Nov 2015 to 22 Jan 2016) who were aged ≥16 years, lived in Scotland and reported they had received a clinical diagnosis of RA. Respondents were allowed to skip questions they wished not to answer; standardised instruments were used (e.g., the Self-administered Comorbidity Questionnaire and the Self-Perceived Burden Scale). Descriptive analyses of quantitative data and thematic analyses of free text responses were conducted.
Results: Overall, 387 individuals participated. The majority were female, of White Scottish or White British background, 45–64 years, and lived in a household with ≥2 people. The majority, 83%, reported well established RA (diagnosis ≥2 years ago) and at least one other comorbidity (78%) – most commonly depression (30%). The average number of medications taken for RA was 3.2 (range 0–7) and 30% reported taking 3 medications in total. Of those receiving care, the majority (97/101) named family or friends/neighbours as caregivers and 76% (80/97) had an elevated level of self-perceived burden on their caregiver. Respondents who reported anxiety or depression had significantly higher average self-perceived burden scores when compared to those without, 33.0 versus 27.3.
89% responded that they did not know what types of circumstances might make them eligible for care and support from their local Council, and only 10% reported receiving information about care and support from their local council. Very few (n=40) had an assessment, with half being deemed eligible for support from their local council.



Conclusions: Survey responses suggest individuals with RA lack fundamental information about qualifying for and accessing formal resources and services provided by their local council. This is especially crucial for two reasons: 1) respondents indicated they do not want to rely heavily on others, like family or friends who are often the primary caregivers; 2) depression and anxiety are highly prevalent in this population. It is important to ensure those with RA do not have unmet needs at any stage, from being newly diagnosed to having established RA, so that they can flourish at home, at work and in their leisure time. Local councils should make access to information about help with formal social care easily accessible and ensure that health professionals know how best to sign-post people.
Acknowledgements: A partnership between the National Rheumatoid Arthritis Society (UK) and the University of Aberdeen
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1858

THURSDAY, 15 JUNE 2017

Macrophage M2 polarization: implications in fibrotizing diseases

OP0212 **ENDOTHELIN-1 INDUCES A PROFIBROTIC PHENOTYPE IN CULTURED HUMAN MICROVASCULAR ENDOTHELIAL AND CIRCULATING MONOCYTE/MACROPHAGE CELLS**

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Background: The alteration of microvascular endothelial cell (EC) functions and the presence of macrophages in the immune inflammatory infiltrate, followed by the transition of these cell types into a profibrotic phenotype, represent early and crucial pathological features of the fibrotic process in systemic sclerosis (SSc) (1). The alternatively activated macrophage subset M2a was found in several diseases characterized by extensive fibrosis (1). M2a macrophages express specific phenotype markers, CD206 (mannose receptor), CD204 and CD163 (scavenger receptors) as well as profibrotic molecules, primarily transforming growth factor-β1 (TGFβ1) (1). Endothelin-1 (ET1) and/or TGFβ1 are known to induce the transition of fibroblasts into profibrotic myofibroblasts, which are key mediators of fibrosis in SSc.
Objectives: To investigate the effects of ET1 in inducing a profibrotic phenotype in cultured human microvascular ECs (HMVECs) and macrophages.
Methods: HMVECs, at 3rd culture passage, were grown in endothelial cell medium (EGM2MV) and treated for 6 days with ET1 (100nM) or treated for 1 hr with ET1 receptor antagonist ($ET_{A/B}$RA, bosentan 10μM) before stimulation with ET1.
Human monocytes were isolated from peripheral blood mononuclear cells of healthy subjects using a monocyte isolation kit. The cells were maintained in RPMI growth medium for 24 hrs and then treated for 6 days with ET1 or treated for 1 hr with bosentan before stimulation with ET1.
Cultured HMVECs and monocytes maintained in EGM2MV and RPMI growth medium, respectively, were used as untreated cells. Gene and protein expression of profibrotic myofibroblast markers –α-smooth muscle actin (α-SMA), fibroblast specific protein-1 (S100A4), type 1 collagen (COL1) and fibronectin (FN) – were evaluated by quantitative real time polymerase chain reaction (qRT-PCR), Western blotting (WB) and immunocytochemistry (ICC) in cultured HMVECs. Gene and protein expression of M2a phenotype markers (CD206, CD204, CD163) and TGFβ1 were investigated by qRT-PCR and WB in cultured human macrophages. Statistical analysis was carried out by Mann-Whitney non-parametric test.
Results: In cultured HMVECs, ET1 induced the significant upregulation of the gene expression of α-SMA, S100A4 (myofibroblast markers), COL1 and FN, compared to untreated cells ($p<0.001$;$p<0.001$;$p<0.05$;$p<0.01$). $ET_{A/B}$RA significantly contrasted the ET1 mediated transition of HMVECs into a profibrotic phenotype ($p<0.05$ for α-SMA, COL1 and FN; $p<0.01$ for S100A4 vs. ET1-treated cells).
In cultured human macrophages, ET1 induced the significant overexpression of M2a markers ($p<0.05$ for CD204 and CD163;$p<0.01$ for CD206) and TGFβ1 ($p<0.01$) compared to untreated cells. $ET_{A/B}$RA significantly contrasted the ET1-mediated transition of cultured macrophages into profibrotic M2a ($p<0.05$ vs. ET1-treated cells, for all investigated proteins). Data were confirmed by WB and ICC on both cultured cell types.
Conclusions: ET1 seems to be involved in the early phases of the fibrotic process by inducing the transition of both cultured HMVECs and macrophages into a profibrotic phenotype, myofibroblast and M2a respectively (observed in SSc), a process which is apparently contrasted by $ET_{A/B}$RA treatment.
References:
[1] Wynn TA et al. Immunity. 2016;44:450–62.
Disclosure of Interest: S. Soldano: None declared, P. Montagna: None declared, R. Brizzolara: None declared, A. Trombetta: None declared, A. Sulli: None declared, C. Pizzorni: None declared, M. Ghio: None declared, S. Paolino: None declared, V. Smith: None declared, M. Cutolo Grant/research support from: Actelion
DOI: 10.1136/annrheumdis-2017-eular.4317

OP0213 **MACROPHAGES FROM A SCLERODERMA SUBGROUP WITH HIGHER SKIN SCORES EXPRESS ACTIVATION MARKERS AND INDUCE FIBROBLASTS IN CO-CULTURE**

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Background: Scleroderma (SSc) is characterized by pathological fibrosis. The mechanisms by which fibrosis occurs in SSc are not fully understood.
Alternatively activated M2-like macrophages are associated with fibrosis and have been found to have an important role in pathological fibrosis in humans. Therefore, there is interest in elucidating their role in SSc. M2 macrophages express mannose receptor CD206 and are known to secrete a number of soluble factors to establish a pro-fibrotic milieu when present in damaged tissues.
Furthermore, we have shown adenosine tri-phosphate (ATP) concentration is increased in the skin of patients with SSc. Within the extra-cellular environment, ATP is a Damage-Associated Molecular Pattern (DAMP), binding the P2X class of purinergic receptors. Such mechanisms may contribute to SSc pathology.
Objectives: In this study, we explore the relationship of macrophage CD206 and $P2X_7$ expression to Rodnan Skin Score. The role of these cells in establishing fibrosis was also examined *in vitro*.
Methods: 17 SSc patients and 9 controls were consented and their skin score recorded. Macrophages were derived from peripheral blood mononuclear cells (PBMCs) and identified through CD14 expression by FACS. CD206 and $P2X_7$

co-expression was quantified. CD206 immunofluorescence of skin biopsies was also performed.
Macrophages were co-cultured with $8x10^4$ and $2x10^4$ fibroblasts in a collagen matrix and within a monolayer respectively.
Collagen gel contraction was quantified as a measure of fibrotic activity. CTGF and Collagen mRNA expression from gel matrices and cellular monolayers was quantified by qPCR.
Results: CD206 and $P2X_7$ expression is higher on SSc PBMC-derived macrophages (mean fluorescence 776.1 SD=409.1, 724.4 SD=455.3) compared to healthy controls (mean fluorescence 632.2 SD=73.7, 472.9 SD=25.4). There is significant correlation of CD206 expression to $P2X_7$ expression ($p<0.001$, r2=0.76) and CD206 expression is significantly correlated to Rodnan skin score ($p<0.05$, r2=0.26). $P2X_7$ expression is positively correlated to skin score. Double positive P2X7 and CD206 cells were seen in a subgroup with higher skin scores. Healthy fibroblasts co-cultured with scleroderma macrophages showed increased collagen mRNA by qPCR compared to co-culture with healthy macrophages ($p<0.01$). CTGF mRNA was positively correlated with macrophage P2X7 (r2=0.23) and CD206 (r2=0.81) expression. Preliminary work suggests contraction of collagen discs in fibroblast and macrophage co-culture is increased with SSc macrophages compared to healthy controls.
Conclusions: Data indicates a correlation between disease severity and CD206 expression by macrophages. Upregulation of CTGF and collagen expression in fibroblasts co-cultured with macrophages expressing high CD206 suggests a role for these cells in pathogenic fibrosis. The co-expression of high levels of $P2X_7$ with CD206 also indicates a possible role for the purinergic pathway in SSc fibrosis.
Future work will examine the mechanism of macrophage-fibroblast cross-talk and investigate the effect of inhibitors of CD206.
Acknowledgements: Rosetrees Trust
Arthritis Research UK
Scleroderma and Raynaud's UK
Royal Free Charity
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2743

FRIDAY, 16 JUNE 2017

Mucosal B cells: gatekeepers of immune function

OP0214 ACTIVATION STATUS OF MUCOSAL-ASSOCIATED INVARIANT T CELLS REFLECTS PATHOLOGY OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Mucosal-associated invariant T (MAIT) cells are innate-like lymphocytes that express a semi-invariant TCRα chain (Vα7.2-Jα33 in humans). MAIT cells are restricted by the MHC-related molecule-1 (MR1) and uniquely recognize vitamin B metabolites presented by MR1. Like other innate-like lymphocytes, MAIT cells are also activated by cytokines in the absence of exogenous antigens. Human MAIT cells are abundant and constitute approximately 5% of peripheral blood T cells, suggesting possible roles of MAIT cells in various types of immune responses.
Objectives: We aimed to investigate whether MAIT cells are involved in systemic lupus erythematous (SLE).
Methods: Peripheral blood was collected from SLE patients and healthy volunteers. Informed consent was obtained from all individuals according to institutional ethical guidelines. Disease activity was measured based on the SLE disease activity index (SLEDAI) and a SLEDAI score $\geq$5 was defined as active disease. Peripheral blood mononuclear cells (PBMC) were stained with anti-human monoclonal antibodies against CD3, γδTCR, Vα7.2TCR, CD161, CD95 (Fas) and CD69, and then analyzed by FACS. $CD19^+$B cells or $CD14^+$monocytes were isolated from PBMC of healthy controls (HC) or SLE patients by using magnetic cell sorting. MAIT cells from healthy controls were co-cultured with B cells or monocytes in the presence of MR1 ligand (MR1L), and the expression of CD69 on MAIT cells was evaluated by FACS. Cytokine levels in plasma samples and culture supernatants were measured by ELISA and Bioplex assay. PBMC were cultured in the presence of various cytokines, and CD69 expression on MAIT cells was analyzed by FACS.
Results: The frequency of MAIT cells was markedly reduced in SLE. Reduced numbers of MAIT cells were not attributable to the downregulation of surface markers, but were partially due to the enhanced cell death of MAIT cells, possibly by activation-induced cell death. The CD69 expression levels on MAIT cells in SLE correlated with disease activity. Monocytes from patients with SLE exhibited increased ability to induce MAIT cell activation, and the profound MAIT cell activating capacity of lupus monocytes was associated with enhanced IL-12 production in the culture supernatants. The plasma concentration of IL-6, IL-18 and IFNα positively correlated with the expression levels of CD69 on MAIT cells in SLE. MAIT cells were activated by cytokines including IFNα, IL-15, and IL-12 plus IL-18 in the absence of exogenous antigens.
Conclusions: These results suggest that MAIT cells reflect the pathological condition of SLE and their activated status correlates with disease activity.

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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2805

OP0215 ROLE OF INHIBITORY IGG FC RECEPTOR IIB ON B CELLS AND MONOCYTES IN YAA-RELATED MURINE LUPUS

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Background: FcγRIIB-deficient C57BL/6 (B6) mice spontaneously develop severe lupus nephritis in combination with *Yaa* locus (TLR7-duplication).
Objectives: The aim of this study is to clarify the cell type-specific roles of FcγRIIB for the pathogenesis of *Yaa*-related lupus.
Methods: We established B cell-specific ($CD19^{Cre}$.*Yaa*), myeloid-derived cell-specific ($C/EBP\alpha^{Cre}$.*Yaa*), and dendritic cell (DC)-specific ($CD11c^{Cre}$.*Yaa*) FcγRIIB-deficient mice on B6.*Yaa* background, and compared the disease features of these mice with full FcγRIIB-deficient B6.$Fc\gamma RIIB^{-/-}$.*Yaa* mice.
Results: $CD19^{Cre}$.*Yaa* mice developed milder lupus nephritis compared to B6.$Fc\gamma RIIb^{-/-}$.*Yaa* mice, indicating that FcγRIIB deficiency on only B cells is not sufficient for the development of severe disease. Surprisingly, $C/EBP\alpha^{Cre}$.*Yaa* mice developed similar mild disease as $CD19^{Cre}$.*Yaa* mice whereas $CD11c^{Cre}$.*Yaa* stayed disease free. These observations indicate that, in B6. $Fc\gamma RIIB^{-/-}$.*Yaa* mice, FcγRIIB deficiency on both B cells and myeloid cells, but not on DCs, contribute to the development of severe lupus with high autoantibody titers. Flow cytometric analysis showed that the frequency of peripheral $Gr\text{-}1^-$, but not $Gr\text{-}1^+$, monocytes was increased and correlated positively with the frequency of splenic PNA^+ activated B cells in B6.$Fc\gamma RIIB^{-/-}$.*Yaa* and C/EBPa^{Cre}.*Yaa*, but not $CD19^{Cre}$.*Yaa*, mice. This suggests a link between FcγRIIB deficiency on monocytes, the high frequency of $Gr\text{-}1^-$ monocytes and B cell activation. Transcriptome analysis of $Gr\text{-}1^+$ and $Gr\text{-}1^-$ monocytes revealed that B cell-stimulating factor-3 (BSF-3), IL-10, and IL-1β were all up-regulated in $Gr\text{-}1^-$ monocytes.
Conclusions: FcγRIIB on B cells and monocytes controls B cell activation and autoimmune responses via different but synergistic pathways in *Yaa*-related lupus nephritis.
References:
[1] Boross P, et al. J. Immunol. 187:1304–1313, 2011.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1315

FRIDAY, 16 JUNE 2017

PsA: the options grow!

OP0216 EFFICACY AND SAFETY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, OR ADALIMUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CSDMARDS): A RANDOMISED, PLACEBO-CONTROLLED, PHASE 3 TRIAL

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Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of psoriatic arthritis (PsA).
Objectives: To assess the efficacy and safety of tofacitinib vs placebo (PBO) in patients (pts) with active PsA.
Methods: Eligible pts in this randomised, PBO- and active-controlled, 12-month Phase 3 trial had $\geq$6-months' PsA diagnosis, fulfilled CASPAR criteria, had active arthritis ($\geq$3 tender/painful and $\geq$3 swollen joints) and active plaque psoriasis at screening, inadequate response to $\geq$1 csDMARD, and were tumour necrosis factor-inhibitor (TNFi)-naïve. 422 pts were randomised 2:2:2:1:1 to tofacitinib 5 or 10 mg twice daily (BID), adalimumab 40 mg subcutaneous injection every 2 weeks, or PBO (advancing to tofacitinib 5 or 10 mg BID at Month [M]3).